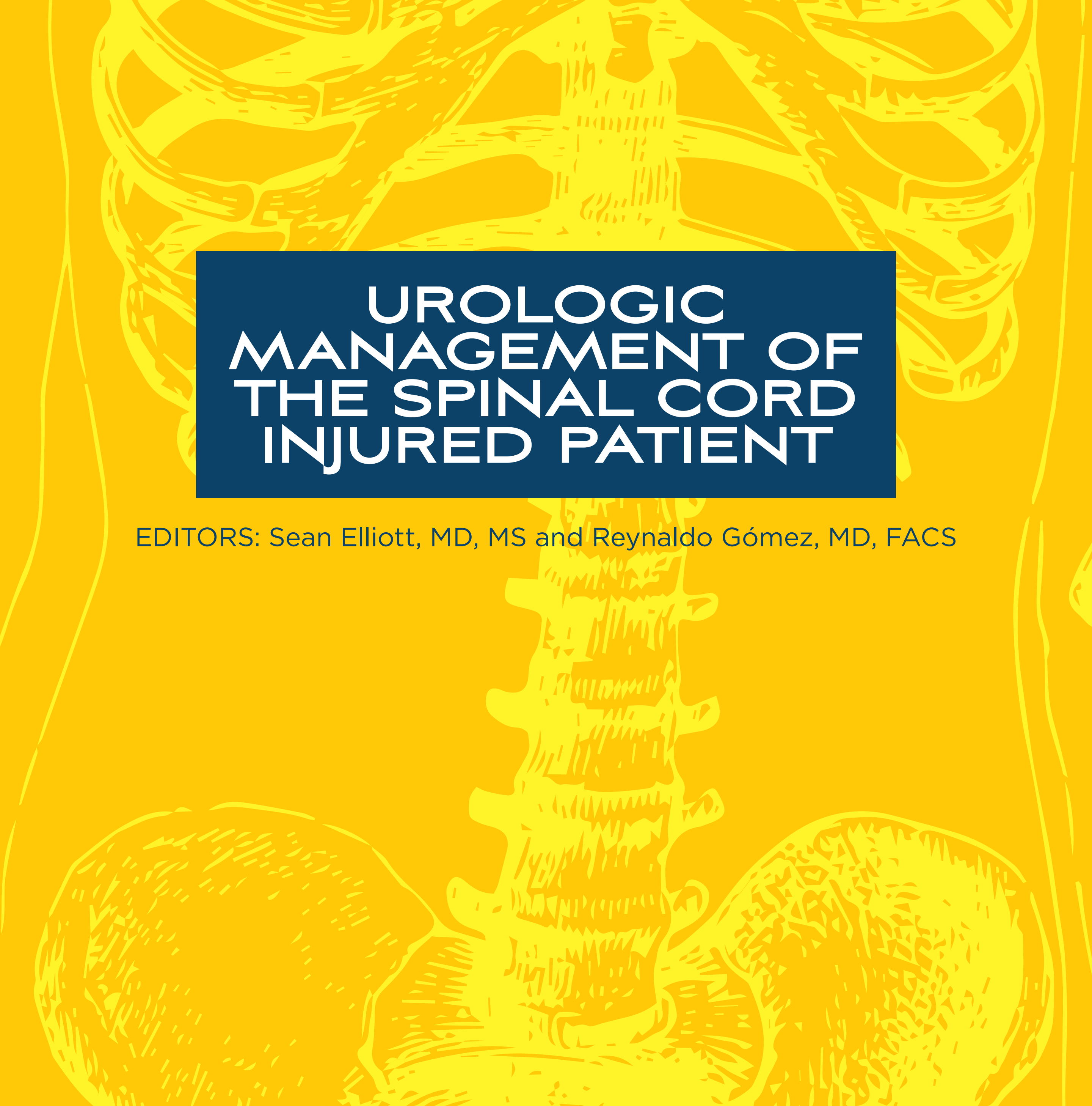

UROLOGIC MANAGEMENT OF THE SPINAL CORD INJURED PATIENT

EDITORS: Sean Elliott, MD, MS and Reynaldo Gómez, MD, FACS

A Joint SIU-ICUD International Consultation

Buenos Aires, Argentina, October 22, 2016

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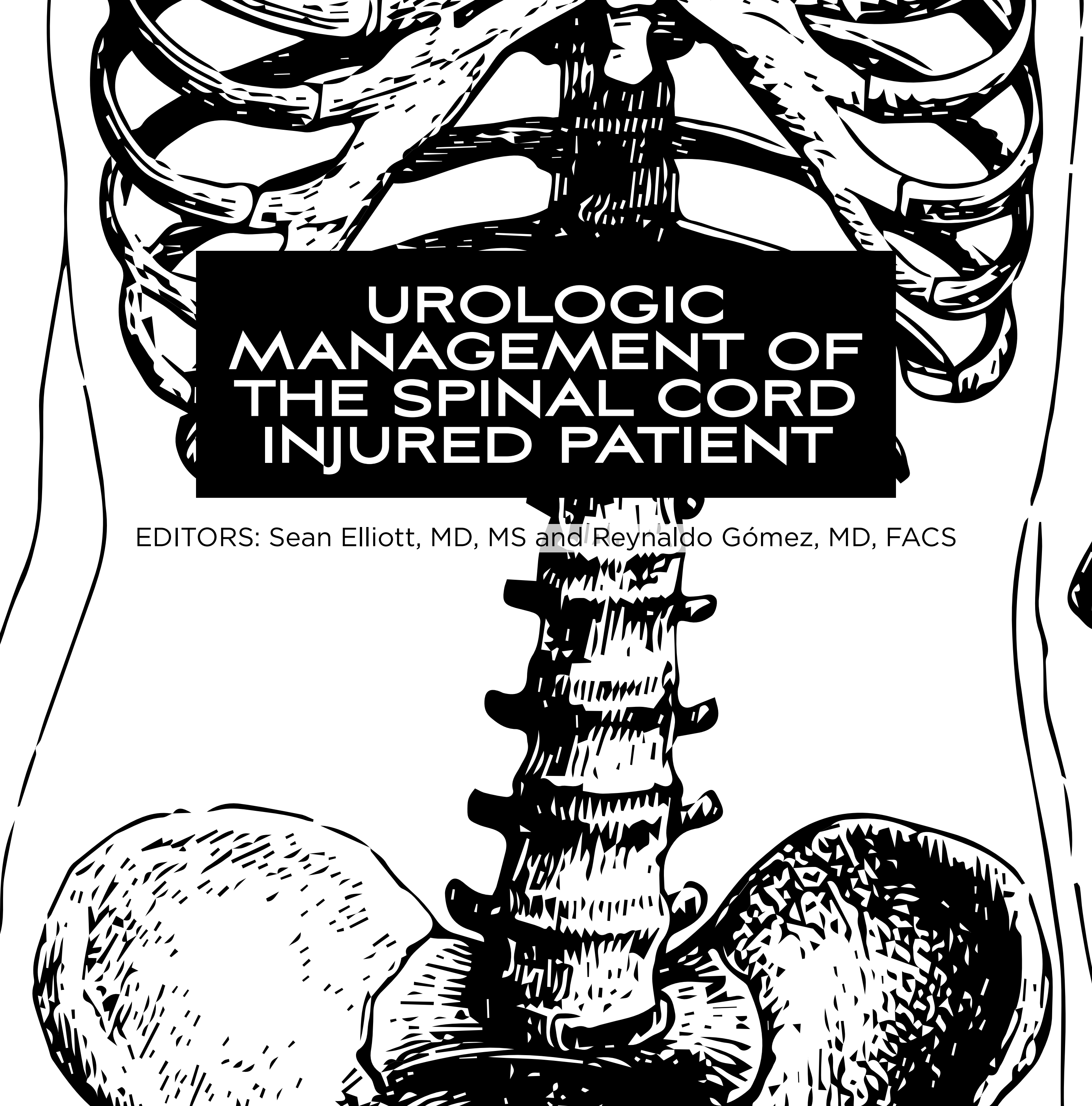

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SOCIÉTÉ INTERNATIONALE SIU D'UROLOGIE

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Abbreviations Used in the Text

AANS	American Association of Neurological Surgeons
AASECT	American Association of Sexuality Educators, Counselors and Therapists
aboBoNTA	abobotulinumtoxinA
AC	augmentation cystoplasty
ACI	Agency for Clinical Innovation, New South Wales
AD	autonomic dysreflexia
ADE	adverse drug reaction
ADL	activity of daily living
AFO	ankle-foot orthosis
AIS	American Spinal Injury Association Impairment Scale
AIS A	American Spinal Injury Association (ASIA) Impairment Scale A (complete) is defined by the absence of motor and sensory function in the sacral segments S4-S5. An AIS-A classification is made with a single observation.
ALARA	as low as reasonably achievable
AMS	American Medical Systems
ASAF	Autonomic Standards Assessment Form
ASIA	American Spinal Injury Association
ATLS	Advanced Trauma Life Support
ATP	adenosine triphosphate
AUA	American Urological Association
AUA-SI	American Urological Association Symptom Index
AUS	artificial urinary sphincter
BASCIS	British Association of Spinal Cord Injury Specialists
BID	twice a day
BiPAP	bilevel positive airway pressure
BMD	bone mineral density
BMI	body mass index
BN	bladder neck
BNC	bladder neck closure

BNI/ES	bladder neck incisions/external sphincterotomy
BoNT	botulinum neurotoxin (also written as botulinum toxin)
BoNT-AB	BoNT antibodies
BoNTA	botulinum neurotoxin A
BoNTA	botulinum neurotoxin type A intra-detrusor injection therapy
BSC	best supportive care
BTx	botulinum toxin (see also BoNT above)
BTX-A	botulinum A toxin (see also BoNTA above)
BWST	body weight–supported training
CAP	Continence Advisory Panel
CCC	continent catheterizable channel
CFU	colony-forming unit
CGRP	calcitonin gene-related peptide
CHD	coronary heart disease
CI	confidence interval
CIC	clean intermittent catheterization
CNS	central nervous system
CNS	Congress of Neurological Surgeons (chapter 2 only)
CPAP	continuous positive airway pressure
Cr-EDTA	Chromium EDTA
CrCL	creatinine clearance
CSM	cervical spondylitic myelopathy
CT	computed tomography
CTD	clitoral therapy device
CTPA	computed tomography pulmonary angiography
CUA	Chinese Urological Association
CUR	continent urinary reservoir
CVD	cardiovascular disease
DDAVP	Desmopressin
DESD	detrusor-external sphincter dyssynergia
DLPP	detrusor leak point pressure
DMSA	Technetium-99m (99mTc) dimercaptosuccinic acid
DO	detrusor overactivity

DRG	dorsal root ganglia
DRS	digital rectal stimulation
DSD	detrusor sphincter dyssynergia
DSID	detrusor internal sphincter dyssynergia
DVT	deep venous thrombosis
EAU	European Association of Urology
ECG	electrocardiogram
ECU	environmental control unit
ED	erectile dysfunction
EEJ	electroejaculation
eGFR	estimated glomerular filtration rate
EMG	electromyogram/electromyography
EMSCI	European Multicenter Study about Spinal Cord Injury
eNO	endothelium nitric oxide
ER	extended release
FDA	Food and Drug Administration (United States)
FES	functional electrical stimulation
FEV	forced expiratory volume
FI	fecal incontinence
FIM	Functional Independence Measure
fMRI	functional magnetic resonance imaging
Fr	French
FSFI	Female Sexual Function Index
FVC	forced vital capacity
GABA	gamma-aminobutyric acid
GFR	glomerular filtration rate
GOR	Grade of Recommendation
HN	hydronephrosis
HR	hazard ratio
HRQOL	health-related quality of life
I-QOL	Incontinence Quality of Life
IASP	International Association for the Study of Pain
IC	intermittent catheterization

ICI	International Consultation on Incontinence
ICIQ	International Consultation on Incontinence Questionnaire
ICS	International Continence Society
IDSA	Infectious Disease Society of America
IEF	incontinence episode frequency
IIEF	International Index of Erectile Function
IIQ-5	Incontinence Impact Questionnaire 5-item
IIQ-7	Incontinence Impact Questionnaire
ILUTBSD	International Lower Urinary Tract SCI Basic Data Set
IMMPACT	Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials
IMSOP	International Medical Society of Paraplegia
IPSS-QOL	International Prostate Symptom Score-QOL Index
IR	immediate release
ISAFSCI	International Standards to Document Remaining Autonomic Function After Spinal Cord Injury
ISC	intermittent self-catheterization
ISCIP	International Spinal Cord Injury Pain
ISCoS	International Spinal Cord Society
ISD	intrinsic sphincter deficiency
ISNCSCI	International Standards for Neurological Classification of Spinal Cord Injury
ISNFCSCI	International Standards for Neurological and Functional Classification of Spinal Cord Injury
IU	International units
IUC	indwelling urethral catheter
KAFO	knee-ankle-foot orthosis
KED	Kendrick Extrication Device
KHQ	Kings Health Questionnaire
LEMS	lower extremity motor score
LOE	Level of Evidence
LUT	lower urinary tract
LUTS	lower urinary tract symptom
M-ISI	Michigan Incontinence Symptom Index
MACE	Malone antegrade continent enema

MCC	maximal cystometric capacity
MDP	maximal detrusor pressure
MDRD	Modification of Diet in Renal Disease Study
MPA	medroxyprogesterone acetate
MPSS	methylprednisolone sodium succinate
MR	magnetic resonance
MRI	magnetic resonance imaging
MS	multiple sclerosis
MUP	maximal urethral pressure
mV	millivolt
MVA	motor vehicle accident
NBD	neurogenic bladder dysfunction
NBSS	Neurogenic Bladder Symptom Score
Nd:YAG	neodymium-doped yttrium aluminium garnet
NDO	neurogenic detrusor overactivity
NEMS	neuromuscular electrical stimulation
NEXUS	National Emergency X-Radiography Utilization Study
NGB	neurogenic bladder
NGF	nerve growth factor
NHS	National Health Service
NICE	National Institute of Health and Clinical Excellence
NIH	National Institutes of Health
NIS	Nationwide Inpatient Sample
NLI	neurological level of injury
NLUTD	neurogenic lower urinary tract dysfunction
nNO	neuronal nitric oxide
NO	nitric oxide
NPUAP	National Pressure Ulcer Advisory Panel
NPWT	negative-pressure wound therapy
NRN	NeuroRecovery Network
NRS	numerical rating scale
NSCID	National Spinal Cord Injury Database
NSRU	nonspecialist rehabilitation units

NSUI	neurogenic stress urinary incontinence
ntSCI	nontraumatic spinal cord injury
OAB	overactive bladder
onaBoNTA	onabotulinumtoxinA
OR	odds ratio
OSAS	obstructive sleep apnea syndrome
P2X3	purinergic receptors
Pabd	abdominal pressure
PDE5	phosphodiesterase type 5
P_{det} (also Pdet)	detrusor pressure
P_{detend}	end-filling detrusor pressure
P_{detmax}	maximal detrusor pressure
$P_{detmaxIDC}$	maximal detrusor pressure during first involuntary detrusor contraction
PE	pulmonary embolus
PET	positron emission tomography
PGA	Patient Global Assessment
PGI-I	Patient Global Impression of Improvement
PID	pelvic inflammatory disease
PLISSIT	Permission, Limited Information, Specific Suggestions, and Intensive Therapy
PNL	percutaneous nephrolithotomy
po	*per os* (orally)
PRB	pressure-regulating balloon
PRISM	Patient-Reported Spasticity Measurement
prn	*pro re nata* (i.e., as needed)
PROMIS®	Patient-Reported Outcomes Measurement Information System
PTNS	posterior tibial nerve stimulation
PVA	Paralyzed Veterans of America
PVC	polyvinyl chloride
Pves	intravesical pressure
PVR	postvoid residual
PVS	penile vibrostimulation
QALY	quality-adjusted life years

QLI	Quality of Life Index
Qmax	maximal urinary flow rate
QOL	quality of life
QOLP-PD	Quality of Life Profile for Adults With Physical Disabilities
QWB	Quality of Well-Being Questionnaire
RCT	randomized controlled trial
RHSCIR	Rick Hansen Spinal Cord Injury Registry
rimaBoNTB	rimabotulinumtoxinB
S-Cre	serum creatinine
SANS	Stoller Afferent Nerve Stimulator
SASCA	Southern African Spinal Cord Association
SCD	spinal cord damage
SCDy	spinal cord dysfunction
SCI	spinal cord injury
SCI-QOL	Spinal Cord Injury - Quality of Life
SCIM	Spinal Cord Independence Measure
SCIRE	Spinal Cord Injury Research Evidence
SCIRU	specialist spinal cord injury rehabilitation units
SD	standard deviation
SEER	Surveillance, Epidemiology, and End Results
SEP	somatosensory evoked potential
SF-12	12-Item Short Form Health Survey
SF-36	36-Item Short Form Health Survey
SF-36V	36-Item Short Form Health Survey for Veterans
SF-6D	Short Form 6 Disability
SF-Qualiveen	short-form Qualiveen
SIA	Spinal Injuries Association
SIP68	Sickness Impact Profile 68
SIS	small intestinal submucosa
SIU	spinal injury unit
SIUP	specific impact of urinary problems
SNARE	Soluble NSF Attachment Protein Receptor
SNM	sacral neuromodulation

SP	substance P
SPT	suprapubic tube
SRF	sexual rehabilitation framework
SSRI	selective serotonin reuptake inhibitor
STASCIS	Surgical Treatment for Acute Spinal Cord Injury Study
SUFU	Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction
SUI	stress urinary incontinence
SWBI	Sense of Well-Being Index
SWL	shock-wave lithotripsy
SWLS	Satisfaction With Life Scale
T½	half-life
TAI	transanal irrigation
Tc-99 DTPA	Technetium-99 diethylene-triamine-pentaacetate
TCA	tricyclic antidepressant
TENS	transcutaneous electrical nerve stimulation
THAQ	Tetraplegia Hand Activity Questionnaire
TID	three times a day
TOT	transobturator tape
TRPV1	transient receptor potential cation channel subfamily V member 1
tSCI	traumatic spinal cord injury
TVT	transvaginal tape
U-IIQ	Urge-Incontinence Impact Questionnaire
U-UDI	Urge-Urinary Distress Inventory
UDI	urodynamic investigation
UDI-6	Urinary Distress Inventory
UDS	urodynamic study
ULR	upper-limb reanimation
US	ultrasound
UTI	urinary tract infection
UUI	urgency urinary incontinence
UUT	upper urinary tract
VA	Veterans Affairs

VAP	vaginal pulse amplitude
VAS	visual analog scale
VB12	vitamin B12
V_{comp}	vesical compliance
VCUG	voiding cystourethrogram
Vd	volume of distribution
VED	vacuum erection device
VUD	videourodynamics
VUDS	video-urodynamic study
VUR	vesicoureteral reflux
WBC	white blood cells
WHO	World Health Organization
WHO-QOL	World Health Organization Quality of Life
WHOQOL-BREF	Short version of the WHO-QOL (World Health Organization Quality of Life) 100 questionnaire
YDL	Young-Dees-Leadbetter
ZPP	zone of partial preservation

Preface

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The occurrence of a spinal cord injury (SCI), and its sequela of paraplegia or tetraplegia, is undoubtedly one of the worst catastrophes a human being can suffer. The majority of these injuries are the result of trauma, which generally affects young and previously healthy people. The SCI not only compromises the physical sphere of the patient, but also severely affects the affective, social, economic, and occupational spheres, thus presenting a formidable challenge for rehabilitation.

A few decades ago, urologic pathology, including renal failure and urosepsis, accounted for the majority of chronic deaths after SCI. With the advent of urodynamics, intermittent catheterization, anticholinergic therapy, and, occasionally, surgical reconstruction of the bladder, we have dramatically altered the course of the disease. However, despite considerable advances, there is a worldwide lack of knowledge about the management of these patients with SCI, and the quality of care is deficient even in many developed countries. Indeed, this topic has been conspicuously neglected by our specialty, which is evident given the secondary attention that this problem has received in most international forums.

For this reason, we congratulate the Société Internationale d'Urologie (SIU) and the International Consultation on Urological Diseases (ICUD) for choosing this issue for the 2016 Consultation, and we are grateful for the opportunity to chair this project. This is a very wide and heterogeneous area, and is impossible to cover in its totality. Therefore, we elected to focus on the urologic management of the patient with *traumatic* SCI, because it is probably the most relevant scenario and because most of the principles applied with these patients can be extrapolated to other etiologies. The whole topic was divided into nine chapters to cover not only the management of urinary problems, but also the management of the bowel, fertility, and sexuality. Separate consideration was given to the management of children and elderly patients. In the last chapter, a global perspective of the current patterns of care and future directions is presented.

We invited a wide panel of experts, including urologists, neurologists, physiatrists, and therapists, to participate, with a global representation of continents, cultures, and socioeconomic statuses. We are grateful to our working group of almost 80 experts from around the world who immediately responded to our invitation with an impressive enthusiasm, reflecting our common feeling about the need for and utmost importance of this project.

Each chapter committee performed a comprehensive review of the pertinent literature, and conclusions and recommendations were produced based on the published evidence. This Consultation summarizes what is available at this time, and there is no question that it will have a strong impact on the management of patients with SCI in all countries. Despite the valuable information already available, high-quality studies are still lacking, and there are numerous areas in desperate need of research, so this work will also help to drive future research efforts.

A condensed form of each chapter will be submitted separately for publication as supplements in the *World Journal of Urology* for a more widespread dissemination of the contents.

Finally, we wish to express our gratitude to the SIU Executive Committee and to the ICUD Steering Committee, headed by Dr. Paul Abrams, for their wisdom and support. We are also equally grateful to the SIU editorial staff, led by Christine Albino, for their invaluable expertise and kind assistance.

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Co-Chairmen
Joint SIU-ICUD Consultation on Urologic Management
of the Spinal Cord Injured Patient

Introduction

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Chile

Bladder management has a great impact on the quality of life of the spinal cord injured individual. Their days can be dominated by issues of finding an accessible restroom and managing incontinence. There are added matters of medical importance such as recurrent urinary tract infections and renal dysfunction. We all encounter these patients in our practices, yet we lack a central repository for information on this topic. This SIU-ICUD Consultation on the Urologic Management of the Spinal Cord Injured Patient seeks to fill that gap.

This consultation summarizes a state-of-the-art literature review and its recommendations on the urologic management of patients after spinal cord injury (SCI).

After the nine committees were created, the committee chairs presented a summary of their exhaustive review during the 36th Congress of the Société Internationale d'Urologie (SIU) in Buenos Aires, Argentina, in October 2016. The discussions that ensued from those presentations were then incorporated into the final manuscript.

On behalf of the International Consultation on Urological Diseases (ICUD) and its steering committee representing the world's major urological associations (American Urological Association [AUA], Confederación Americana de Urología [CAU], European Association of Urology [EAU], International Continence Society [ICS], SIU, and the Urological Association of Asia [UAA]), it is a great pleasure to thank each of the nine committees' chairmen and members for their hard work in producing this impressive update. The urologic management of patients after SCI can be a poorly understood and oft-neglected topic. It is challenging since it crosses many disciplines, and thus much dedication and effort was required by all involved in this ICUD. As Consultation Chairs, we would like to express our immense gratitude to the SIU leadership, and in particular to Dr Paul Abrams and SIU support staff members, Christine Albino and Anna Johansen, for entrusting us with this important project.

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of the Spinal Cord Injured Patient

Evidence-Based Medicine Overview of the Main Steps for Developing and Grading Guideline Recommendations

P. Abrams, S. Khoury, A. Grant

Introduction

The International Consultation on Urological Diseases (ICUD) is a non-governmental organization registered with the World Health Organisation (WHO). In the last ten years, consultations have been organized on BPH, prostate cancer, urinary stone disease, nosocomial infections, erectile dysfunction and urinary incontinence. These consultations have looked at published evidence and produced recommendations at four levels: highly recommended, recommended, optional and not recommended. This method has been useful but the ICUD believes that there should be more explicit statements of the levels of evidence that generate the subsequent grades of recommendations.

The Agency for Health Care Policy and Research (AHCPR) have used specified evidence levels to justify recommendations for the investigation and treatment of a variety of conditions. The Oxford Centre for Evidence-Based Medicine have produced a widely accepted adaptation of the work of AHCPR. (June 5th 2001, www.cebm.net).

The ICUD has examined the Oxford guidelines and discussed with the Oxford group their applicability to the consultations organized by ICUD. It is highly desirable that the recommendations made by the consultations follow an accepted grading system supported by explicit levels of evidence.

The ICUD proposes that future consultations should use a modified version of the Oxford system which can be directly "mapped" onto the Oxford system.

1. First Step

Define the specific questions or statements that the recommendations are supposed to address.

2. Second Step

Analyze and rate (level of evidence) the relevant papers published in the literature.

The analysis of the literature is an important step in preparing recommendations and their guarantee of quality.

2.1 What papers should be included in the analysis?

- Papers published, or accepted for publication in the peer-reviewed issues of journals.
- The committee should do its best to search for papers accepted for publication by the peer-reviewed journals in the relevant field but not yet published.
- Abstracts published in peer-reviewed journals should be identified. If of sufficient interest, the author(s) should be asked for full details of methodology and results. The relevant committee members can then "peer review" the data, and if the data confirms the details in the abstract, then that abstract may be included, with an explanatory footnote. This is a complex issue – it may actually increase publication bias as "uninteresting" abstracts commonly do not progress to full publication.
- Papers published in non-peer-reviewed supplements will not be included. An exhaustive list should be obtained through:
  - I. The major databases covering the last ten years (e.g. Medline, Embase, Cochrane Library, Biosis, Science Citation Index).
  - II. The table of contents of the major journals of urology and other relevant journals, for the last three months, to take into account the possible delay in the indexation of the published papers in the databases.

It is expected that the highly experienced and expert committee members provide additional assurance that no important study would be missed using this review process.

2.2 How are papers analyzed?

Papers published in peer-reviewed journals have differing quality and level of evidence. Each committee will rate the included papers according to levels of evidence (see below).

The level (strength) of evidence provided by an individual study depends on the ability of the study design to minimize the possibility of bias and to maximize attribution.

It is influenced by:

The type of study, whose hierarchy is outlined below:

- Systematic reviews and meta-analysis of randomized controlled trials
- Randomized controlled trials
- Non-randomized cohort studies
- Case-control studies
- Case series
- Expert opinion

How well the study was designed and carried out

Failure to give due attention to key aspects of study methodology increases the risk of bias or confounding factors, and thus reduces the study's reliability.

The use of **standard checklists** is recommended to insure that all relevant aspects are considered and that a consistent approach is used in the methodological assessment of the evidence.

The objective of the checklist is to give a quality rating for individual studies.

How well the study was reported

The ICUD has adopted the CONSORT statement and its widely accepted checklist. The CONSORT statement and the checklist are available at www.consort-statement.org.

2.3 How are papers rated?

Papers are rated following a level of evidence scale.

ICUD has modified the Oxford Centre for Evidence-Based Medicine levels of evidence.

The levels of evidence scales vary between types of studies (i.e. therapy, diagnosis, differential diagnosis/ symptom prevalence study) the Oxford Centre for Evidence-Based Medicine Website: www.cebm.net.

3. Third Step: Synthesis of the Evidence

After the selection of the papers and the rating of the level of evidence of each study, the next step is to compile a summary of the individual studies and the overall direction of the evidence in an **Evidence Table**.

4. Fourth Step: Considered Judgment (Integration of Individual Clinical Expertise)

Having completed a rigorous and objective synthesis of the evidence base, the committee must then make a judgment as to the grade of the recommendation on the basis of this evidence. This requires the exercise of judgment based on clinical experience as well as knowledge of the evidence and the methods used to generate it. Evidence-based medicine requires the integration of individual clinical expertise with the best available external clinical evidence from systematic research. Without the former, practice quickly becomes tyrannized by evidence, for even excellent external evidence may be inapplicable to, or inappropriate for, an individual patient. On the other hand, without current best evidence, practice quickly becomes out of date. Although it is not practical to lay our "rules" for exercising judgment, guideline development groups are asked to consider the evidence in terms of quantity, quality, and consistency, as well as applicability, generalizability and clinical impact.

5. Fifth Step: Final Grading

The grading of the recommendation is intended to strike an appropriate balance between incorporating the complexity of type and quality of the evidence, and maintaining clarity for guideline users.

The recommendations for grading follow the Oxford Centre for Evidence-Based Medicine. The levels of evidence shown below have again been modified in the light of previous consultations. There are now four levels of evidence instead of five.

The grades of recommendation have not been reduced and a "no recommendation possible" grade has been added.

6. Levels of Evidence and Grades of Recommendation for Therapeutic Interventions

All interventions should be judged by the body of evidence for their efficacy, tolerability, safety, clinical effectiveness and cost-effectiveness. It is accepted that, at present, little data exists on cost-effectiveness for most interventions.

6.1 Levels of evidence

Firstly, it should be stated that any level of evidence may be positive (the therapy works) or negative (the therapy doesn't work). A level of evidence is given to each individual study.

Level of Evidence	Criteria

I	▪ Incorporates Oxford 1a, 1b
	▪ Usually involves:
	  ▪ meta-analysis of trials (randomized controlled trials [RCTs]) or,
	  ▪ a good-quality RCT or,
	  ▪ "all or none" studies in which treatment is not an option (e.g. in vesicovaginal fistula)

II	▪ Incorporates Oxford 2a, 2b and 2c
	▪ Includes:
	  ▪ ***low-quality RCT*** (e.g. <80% follow-up),
	  ▪ ***meta-analysis*** (with homogeneity) of ***good-quality prospective cohort studies***
	▪ May include a single group when individuals who develop the condition are compared with others from within the original cohort group.
	▪ There can be parallel cohorts, where those with the condition in the first group are compared with those in the second group

III	▪ Incorporates Oxford 3a, 3b and 4
	▪ Includes:
	  ▪ ***good-quality retrospective case-control studies***, where a group of patients who have a condition are matched appropriately (e.g. for age, sex, etc.) with control individuals who do not have the condition
	  ▪ ***good-quality case series***, where a complete group of patients, all with the same condition, disease or therapeutic intervention, are described without a comparison control group

IV	▪ Incorporates Oxford 4
	▪ Includes ***expert opinion***, where the opinion is based not on evidence but on "first principles" (e.g. physiological or anatomical) or bench research.
	▪ The ***Delphi process*** can be used to give expert opinion greater authority:
	  ▪ involves a series of questions posed to a panel
	  ▪ answers are collected into a series of "options"
	  ▪ these "options" are serially ranked; if a 75% agreement is reached, then a Delphi consensus statement can be made

6.2 Grades of recommendation

The ICUD will use the four grades from the Oxford system. As with levels of evidence, the grades of evidence may apply either positively (procedure is recommended) or negatively (procedure is not recommended). Where there is disparity of evidence, for example if there were three well-conducted RCTs indicating that Drug A was superior to placebo, but one RCT whose results show no difference, then there has to be an individual judgment as to the grade of recommendation given and the rationale explained.

Grade A recommendation usually depends on consistent level I evidence and often means that the recommendation is effectively mandatory and placed within a clinical-care pathway. However, there will be occasions where excellent evidence (level I) does not lead to a Grade A recommendation, for example, if the therapy is prohibitively expensive, dangerous or unethical. Grade A recommendation can follow from Level II evidence. However, a Grade A recommendation needs a greater body of evidence if based on anything except Level I evidence.

Grade B recommendation usually depends on consistent level 2/3 studies, or "majority evidence" from RCTs.

Grade C recommendation usually depends on level 4 studies or "majority evidence" from level 2/3 studies or Delphi processed expert opinion.

Grade D "No recommendation possible" would be used where the evidence is inadequate or conflicting and when expert opinion is delivered without a formal analytical process, such as by Delphi.

7. Levels of Evidence and Grades of Recommendation for Methods of Assessment and Investigation

From initial discussions with the Oxford group, it is clear that application of levels of evidence/grades of recommendation for diagnostic techniques is much more complex than for interventions. The ICUD recommends that, as a minimum, any test should be subjected to three questions:

1. Does the test have good technical performance? For example, do three aliquots of the same urine sample give the same result when subjected to dipstick testing?
2. Does the test have good diagnostic performance, ideally against a "gold standard" measure?
3. Does the test have good therapeutic performance, that is, does the use of the test alter clinical management? Does the use of the test improve outcome?

For the third component (therapeutic performance) the same approach can be used as for section 6.

8. Levels of Evidence and Grades of Recommendation for Basic Science and Epidemiology Studies

The proposed ICUD system does not easily fit into these areas of science. Further research needs to be carried out in order to develop explicit levels of evidence that can lead to recommendations as to the soundness of data in these important aspects of medicine.

Conclusion

The ICUD believes that its consultations should follow the ICUD system of levels of evidence and grades of recommendation, where possible. This system can be mapped to the Oxford system.

There are aspects to the ICUD system that require further research and development, particularly diagnostic performance and cost-effectiveness, and also factors such as patient preference.

Summary of the International Consultation on Urological Disease Modified Oxford Centre for Evidence-Based Medicine Grading System for Guideline Recommendations

Levels of Evidence	Description
I	Meta-analysis of RCTs or high-quality RCT
II	Low-quality RCT or good-quality prospective cohort study
III	Good-quality retrospective case-control study or cohort study
IV	Expert opinion

Abbreviation: RCT=randomized controlled trial

Summary of the International Consultation on Urological Disease Modified Oxford Centre for Evidence-Based Medicine Grading System for Guideline Recommendations

Grades of Recommendation	Description
A	Usually consistent with level I evidence
B	Consistent level II or III evidence or "majority evidence" from RCTs
C	Level IV evidence or "majority evidence" from level II or III studies
D	No recommendation possible because of inadequate or conflicting evidence

RCT=randomized controlled trial

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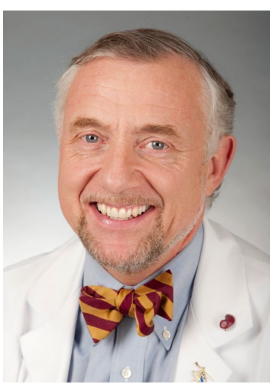

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Epidemiology and Pathophysiology of Neurogenic Bladder After Spinal Cord Injury

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1.1 Introduction

A spinal cord injury (SCI) is a devastating incident, quite often striking suddenly. A number of traumatic or nontraumatic events can lead to a fracture or dislocation of the spinal column, with resultant damage to the spinal cord leading to SCI. Traumatic causes of SCI include events such as vehicular or diving accidents, falls, gunshot injuries, disc prolapses, and sudden hyperextension injuries; infections and vascular events generally make up the nontraumatic causes.

The degree of neurological damage and consequent deficit depends on the level, severity, and extent of injury and whether the cord transection is complete or partial. Altered pelvic floor function, including genitourinary function, is a frequent occurrence following these injuries and can have a significant negative impact on both the quantity and quality of life in patients. The urological management of such patients involves protection of the upper tracts, prevention of complications, facilitating drainage of the bladder, and maintaining patient quality of life.[1]

1.2 Description of Search Methodology

A comprehensive literature review was undertaken for evidence gathering. The studies were identified by an electronic search of PubMed, Embase, MEDLINE, the Cochrane Database of Systematic Reviews, and by screening of reference lists and reviews. The search was conducted up to June 2016. A manual search of relevant references from the selected article was performed if needed. A wide variety of terms were searched for, including spinal cord injury, epidemiology, etiology, neuroanatomy, neurophysiology, and pathophysiology of spinal injuries. Additional terms searched for were neurogenic bladder, neuropathic bladder dysfunction, autonomic dysreflexia, classification of spinal cord injury and international standards of spinal cord injury classification. Additionally, a manual search of relevant urological textbooks was also undertaken.

1.3 Epidemiology of Spinal Cord Injury

The incidence and prevalence figures for SCI vary from region to region. Not surprisingly, most systematic reviews for this condition have been undertaken from the United States, Canada, and Australia with only a few from Asia. As a result, it is difficult to estimate the exact figures worldwide.

SCI is an injury to the spinal cord from traumatic or nontraumatic etiology, as defined by the International Spinal Cord Society (ISCoS).[2] Despite this, there is not a complete consensus to define some causes, such as iatrogenic lesions, as either traumatic or nontraumatic. This leads to considerable difficulty in properly assessing the epidemiology of SCI and the impact of risk factors in etiologic processes. Moreover, an accurate quantification of the worldwide prevalence and incidence of SCI is challenging and not entirely representative due to the lack of standardized methods of assessment across regions, limited information in the data collected, and a paucity of reliable data from developing countries and rural areas.

The causes of injury vary between countries, and among regions within a country, depending upon location (urban or rural). Overall, the incidence reported varies from 12 to more than 65 cases/million per year. Data from Olmsted county, Minnesota, United States, from 1975 to 1981 suggested an age- and sex-adjusted incidence rate of 71 spinal cord injuries/million.[3] More recent data showed that the incidence of SCI, excluding those who die at the scene, is 3.5 to 4.0/100,000 persons annually in the United States.[4,5] According to studies considered to be the most accurate, the annual incidence of SCI reported in a national system for the year 1991 was around 30.0 to 32.1 persons/million population in the United States. These rates correspond to between 7,500 and 8,000 new cases per year at that time.[6] Recent data from 2016 show that with a population size of 314 million people in the United States, the estimated annual incidence of SCI is approximately 54 cases/million population or approximately 17,000 new SCI cases each year.[7] As mentioned above, the annual incidence (per million persons) varies widely by country: from 27 in Japan,[8] to 13.4 in Switzerland,[9] 12.7 in France,[10] and 16.7 in South Africa.[11] The annual incidence varies within Europe, with 12.1 cases/million in the Netherlands compared to 57.8 in Portugal.[12,13] The reported incidence from other countries shows a similar trend, with 38 cases/million including traumatic and nontraumatic SCI in Saudi Arabia between 2000 and 2010.[14]

A systematic review in 2010 by Van den Berg *et al.* showed up to a three-fold variation in incidence rates between developed countries, with the highest rates reported in Canada and Portugal. Most traumatic spinal cord injury (tSCI) studies show a bimodal age distribution. The first peak was found in young men between 15 and 29 years of age and a second peak in older adults (mostly ≥65 years old and women).[15] A 2011 review article by Cripps *et al.* reported a prevalence ranging from 236 to 1009/million, but the authors noted that prevalence data are extremely scarce, especially from Asian, African, and South American countries. The same review found that North America (39/million) and Japan (40.2/million) had more than twice the incidence of Australia (15/million) and Western Europe (16/million).[16] Fitzharris[17] used a population-based regression model and estimated the overall incidence rate to be 27.5 traumatic SCI per million persons in the global population (population for 131 countries: 6.250 billion). The estimated tSCI incidence rate ranged from 18.3/million to 42.9/million.[17]

The National Spinal Cord Injury Statistical Center at the University of Alabama at Birmingham[7] reported approximately 12,000 new cases each year with 4:1 as the male-to-female ratio. The average age at injury was 40 years, with the most common injury being incomplete tetraplegia at 30%, followed by 25.6% for complete paraplegia, 20.4% for complete tetraplegia, and 18.5% for incomplete paraplegia. In the past, the leading cause of death among SCI patients was renal failure; however, improved urological management has changed this picture. Presently, pneumonia, pulmonary emboli, and septicemia supersede renal failure as the leading causes of death for SCI patients.

1.3.1 Traumatic SCI

A recent review by Singh *et al.*[18] noted the highest prevalence of tSCI at 906/million in the United States, and the lowest prevalence at 250/million in the Rhône-Alpes region, France. The crude annual incidence in the United States was highest in Alaska (83/million) and lowest in Alabama (29.4/million). The incidence in other parts of the world was found to be 58/million in Central Portugal, 19.5/million in Stockholm, Sweden, 16.9/million in southeastern Turkey, 14.6/million in Taipei, Taiwan, and the lowest incidence was 12.7/million, in the Rhône-Alpes region of France. Road traffic accidents remain the single most common factor, followed closely by falls; this is especially true in the elderly population. The United Arab Emirates reported the highest incidence of SCI due to work-related fall injuries, mainly involving the immigrant Indian population.[19]

1.3.2 Nontraumatic SCI

In contrast to traumatic causes, the epidemiology of ntSCI reveals somewhat different statistics about cause, incidence, and prevalence.[20] The authors report a prevalence rate of 2,310/million in Kashmir, India, and 1,120/million in Canada. Not surprisingly, in developing countries there was a higher proportion of infective causes (tuberculosis and HIV), while developed countries had a higher proportion of degenerative and neoplastic etiologies. The annual incidence of nontraumatic SCI in various regions of the world according to the World Health Organization (WHO) is 20/million in high-income parts of the Asia-Pacific region, 26/million in Australasia, 6/million in Western Europe, and 76/million in high-income parts of North America. Again, not surprisingly, the same figures are not available from the developing countries due to lack of adequate data collection. Nonadherence to minimum standards of data collection and a piecemeal approach to data collection were cited as the main causes for poor epidemiological information in this study.

1.3.3 SCI and the pediatric population

The estimated incidence of spinal injuries in the pediatric population was 24/million, with higher incidence of severe injuries among black adolescents.[21] Fortunately, the overall incidence of motor vehicular accidents leading to SCI seems to be coming down, primarily due to increased motor vehicular safety and improved traffic regulations.[22]

1.3.4 Conclusions

1. The incidence and prevalence figures of tSCI show a wide regional variation but the United States still has the highest incidence, with figures ranging from 83/million in Alaska to 29.4/million in Alabama.

2. Traffic accidents dominate as the most common cause of tSCI, with falls (especially in the elderly population) and violence coming a close second.

3. The male-to-female ratio for SCI is roughly 4:1, with the average age of injury being 40 years.

4. Globally, age distribution of tSCI is bimodal, with the first peak between 15 and 29 years of age with predominantly male patients, followed by a second peak, with an increased number of women, at age 65 years and above.

5. Among ntSCI cases, neoplastic and degenerative diseases are more prevalent in the developed world, while infective causes are more prevalent in the developing world.

6. Incomplete tetraplegia is the most common form of SCI presentation.

7. In addition to a paucity of data collection to adequately evaluate the true incidence and prevalence of SCI worldwide, there is a lack of adherence to minimum standards of data collection.

1.4 Etiology of Spinal Cord Injury

1.4.1 Traumatic causes

The major cause of tSCI in industrialized countries is motor vehicle accidents. On a global level, traffic accidents involving motor vehicles, bicycles, or pedestrians account for the greatest number of SCIs, typically 50% of all injuries. Some reliable data from Southeast Asia (Thailand and Vietnam) suggests the most common cause of tSCI was road traffic accidents with two- or three-wheeled vehicles. In Saudi Arabia, road traffic accidents are still the primary cause of SCI, particularly in young adults.[23] Alcohol appears to play a major role in adult SCI, especially given the predisposition in young men for injuries in traffic accidents. For approximately 25% of patients with acute SCI, alcohol played a major factor in their injury, with a much smaller percentage for other drugs.

As with incidence, the etiology of tSCI varies from one country to another. Violence/self-harm as a cause of tSCI was higher in North America (15% of all tSCI, almost all of which were firearm-related injuries) than in Western Europe (6%), Australia (2%), or Japan (2%).[16] Violence-related traumatic SCI occurred in regions of conflict or high availability of weapons: high rates of gunshot injuries linked to SCI were present in the United States and Brazil, with the highest proportion globally occurring in South Africa (35–40% in some areas), making violence the primary cause of SCI in this country.

Falls, especially from trees and rooftops, are the major causes of SCI in Southern Asia and Oceania. They remain the second most common cause of SCI worldwide after road traffic accidents. Although in some regions such as Nepal, they are the most common, with 75% of SCI due to falls from heights.[24] Older age is a known risk factor for falls. Not surprisingly, falls may exceed traffic accidents as a cause of SCI in the population over 65 years of age.[25] Lee *et al.* found that the incidence of traumatic SCIs from low falls in the elderly is increasing in developed countries with aging populations, while traumatic SCI resulting from high falls is more frequent in developing countries, commonly from trees, balconies, and construction sites. However, in some developing countries, low falls resulting in traumatic SCI occur in young people while carrying heavy loads on the head.[26] Japan and Western Europe had a higher rate of falls (42% and 37%, respectively) when compared with Australia and North America (29 and 20%, respectively).

About 10% to 15% of all of SCI cases are considered to be sports related.[27] This translates to roughly 1,200 new injuries per year with potential associated physical and psychological issues. The total direct costs for sports-related SCI in the United States is $694 million (USD) per year.[28] Diving-related injuries account for two-thirds of all sports-related SCIs, both in the United States and around the world.[29] Recreational diving accounts for the majority of cases. As one might expect, most of the diving injuries occur during the summer months, in men, and after the consumption of alcohol. The majority of diving-related injuries usually result in complete neurologic lesions, as opposed to injuries obtained in other sports, which result more often in incomplete deficits. The injury occurs almost exclusively in the cervical spine.

For the past 50 years, football-related SCIs have been studied. In the mid-1950s hard helmets were introduced. Later on, in the 1970s, the development of the tackling technique known as "spearing" took root, leading to an increase in SCIs on the football field. Hence, this technique was outlawed in 1976. This led to a 50% drop in the number of high school and college football quadriplegic injuries from 1976.[30,31] Approximately 40 sport-related cases of vertebral column damage without cord involvement and 7 cases of SCI were reported annually in the United States from 1977 to 2004.[32]

Significant risks of injury also occur in other contact sports such as hockey and rugby. The incidence of SCI injuries from these sports is significantly lower in the United States than the incidence of SCI from football, but in places such as Canada and South Africa where hockey and rugby are widely played, injuries from these sports comprise the majority of sports-related injuries.[33,34]

Hyperflexion of the spine is believed to be the predominant mechanism of injury during sporting activities. However, Torg *et al.* proved that axial loading caused by a blow to the top of the head was the most important factor.[35] The muscles of the neck and shoulder area normally absorb energy that is transmitted from the head to the spine. When enough pressure is generated, the bones, ligaments, and/or discs will fail, causing a cervical injury.[36] The types of injury typically seen at this junction are compression or "burst" fractures. It is generally accepted that primary SCI is most commonly a combination of the initial impact as well as subsequent persisting compression. The primary mechanism involves the initial mechanical injury due to local deformation and energy transformation, whereas the secondary mechanism encompasses a cascade of biochemical and cellular processes that are initiated by the primary process and may cause ongoing cellular damage and even cell death.

Stover *et al.*[37] reported, using data from the national database in the United States comprising data on more than 10,000 cases, that the most common cause of SCI was motor vehicle crashes (47.7%), followed by falls (20.8%), acts of violence comprising gunshot wounds and stabbings (14.6%), and sporting-related activities (14.2%).

1.4.2 Risk factors

1.4.2.1 Gender

Typically, young male patients comprise the majority of SCI victims, with the incidence rates peaking in the third and fourth decades in most countries. Men are also consistently at greater risk of morbidity and mortality from SCI across all age groups. The ratio of men to women with respect to SCI is typically 3:1 to 4:1.[4,37,38] The average age at injury has increased from 29 years during the 1970s to 42 years in 2015.

1.4.2.2 Race

In the United States, about 22% of injuries have occurred among non-Hispanic blacks since 2010, which is higher than the proportion of non-Hispanic blacks in the general population (12%).[7]

1.4.2.3 Comorbidities

In 2003, a cross-sectional, prospective survey was undertaken among the members of the Paralyzed Veterans of America. Respondents were mainly men (97%) and white (82%), and more than half had a paraplegic-level injury (52%), had been injured for an average of 24 years, and had an average age at injury of 36 years. Notably, SCI respondents reported a higher prevalence of several comorbidities than the general population including high blood pressure (49% vs. 26%, respectively), high cholesterol (47% vs. 30%), and diabetes (19% vs. 7%). Obesity was also a significant problem for individuals with SCI, with 25% reporting obesity. Of note, hypertension might have been overreported in those with SCI due to the presence of autonomic dysreflexia in this method of self-reporting.

Infection is a very common cause of rehospitalization, emergency room visits, and mortality in SCI patients.[39,40]

Individuals with SCI have an increased risk of bladder cancer; this cancer is more likely to be diagnosed at a later stage.

Cervical spondylosis is the most common preexisting abnormality of the spinal column in SCI patients, with a prevalence rate as high as 10% in some series. Spinal cord trauma may be superimposed on and exacerbated by the presence of congenital abnormalities, such as atlantoaxial instability, congenital fusions, or tethered cord, and may also occur in the presence of acquired disorders such as metastatic disease, or spinal arthropathies such as ankylosing spondylitis or rheumatoid arthritis. Typically, injuries are worsened or occur with a greater frequency in the face of these associated conditions, and, in some cases, would not have occurred had the associated anomaly not been present.

1.4.3 Causes of death

Hackler reported a death rate of 49% from a 25-year prospective follow-up of 270 SCI patients in the 1970s with renal disease as the major cause of death.[41] A decade later the leading causes of death switched to pneumonia, accidents, and suicides, as a consequence of improved urological care. An Australian review of mortality data from 335 individuals with tSCI between 1955 and 1994 reported suicide to be among the four leading causes of death for study subjects.[42] The estimated mortality rate was 2.3 times greater than in the general population and the suicide rate among SCI subjects was five times greater than among the general population. Most of the death occurred among subjects younger than 39 years old.[42] A US Department of Veterans Affairs study of SCI patients over a 25-year period reported suicide rates to be 10-fold greater than in uninjured people.[43] One Danish study of 888 individuals with SCI conducted from 1953 to 1990 found that the age-adjusted suicide rate was almost five times greater than that of the general population. The suicide rate was higher among those with less severe disabilities than among individuals with complete quadriplegia.[44]

These higher suicide rates were thought to be related to depression, which is more prevalent in this subset of the population. Kemp and Krause recorded a 31% prevalence rate of depressive disorder in the SCI community, twice the rate of the general population.[45]

The average remaining years of life for persons with SCI has not improved since the 1980s and remains significantly below life expectancies of persons without SCI. Mortality rates are significantly higher during the first year after injury than during subsequent years, particularly for persons with the most severe neurological impairments.[7]

The patients with SCI in the United States who have been enrolled in the National SCI Database since its inception in 1973 have now been followed for over 40 years. The causes of death that appear to have the greatest impact on reduced life expectancy for this population are pneumonia and septicemia. Mortality rates are declining for this population for cancer, heart disease, stroke, arterial diseases, pulmonary embolism, urinary diseases, digestive diseases, and suicide. However, these gains are being offset by increasing mortality rates for endocrine, metabolic, and nutritional diseases; accidents; nervous system diseases; musculoskeletal disorders; and mental disorders. There has been no change in the mortality rate for septicemia in the National SCI Database population during the past 40 years, and only a slight decrease in mortality due to respiratory diseases.[7]

1.4.4 Conclusions

1. Globally, age distribution of traumatic SCI is bimodal, with the first peak between 18 and 32 years old with predominantly male patients, followed by a second peak at 65 years and above, with an increased number of female patients.
2. The first peak of traumatic SCI cases mostly involves road accidents, while the second one predominantly involves falls.
3. Globally, road traffic accidents are the most common cause of traumatic SCI and occur primarily in younger people.
4. The second most common cause of SCI is falls, and these occur primarily in older people.
5. In developed countries, the percentage of people with SCI over the age of 60 years has sharply increased, and it is expected that these trends will continue to escalate in line with ongoing population aging.
6. In developed countries, the paraplegia-to-tetraplegia ratio for SCI is decreasing, and the frequency of incomplete lesions is increasing.
7. Due to improvements in urological care, the death rate from renal disease in individuals with SCI has decreased.

1.5 Classification of SCI

1.5.1 Overview of various classifications

Standardized terminology, evaluation methods, and neurological classification of SCI are very important for communication among medical professionals involved in patient care. Standardized classification is also important for achieving clinical care and accurate medical records, not only in initial evaluation of the patients with SCI but also for follow-up evaluations during the course of treatment. This standardized classification can also be used as a research tool for better understanding SCI pathophysiology and for indicating recovery of the patient. Historically, various attempts have been undertaken to set up a standardized classification system using those based on vertebral fracture and injury mechanisms; however, international consensus could not be achieved. The American Spinal Injury Association (ASIA) published the first version of the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) in 1982.[46] After several revisions, amendments, and redefining classification scales, the most recent standards were released in 2015.[47]

ASIA released the first standardized version using the Frankel Scale to define the neurological levels and the extent of injury. The Frankel Scale was originally developed in 1969[48] and it divided the degree of SCI into 5 scales, from A to E. ASIA used key muscle systems and 29 key sensory areas based on the

Frankel Scale. ASIA modified the Frankel Scale and renamed it as the ASIA Impairment Scale (AIS) in the fourth edition released in 1992. The concept of sacral sparing was applied to define completeness of the SCI in the same year. In 1992 ASIA collaborated with the International Medical Society of Paraplegia (IMSOP)—later renamed as the International Spinal Cord Society (ISCoS)—to endorse these standards. They were revised and renamed as the International Standards for Neurological and Functional Classification of Spinal Cord Injury (ISNFCSCI) in 1996.[49] In 2000, the term "functional" was removed from the name.[50]

1.5.2 International Standards for Neurological Classification of Spinal Cord Injury

1.5.2.1 Definition and terminology

The ISNCSCI are used to document the neurological examinations performed to measure neurological, sensory, and motor level on the right and left sides; sensory and motor scores; zone of partial preservation; and the ASIA Impairment Scale (AIS) for individuals with SCI (**Table 1-1**). AIS is a part of the ISNCSCI system.

There are several terms defined in the ISNCSCI; for example, "tetraplegia" should be used instead of "quadriplegia," a term used previously in the case of SCI individuals who have impairment in the trunk and lower extremities, including the upper limbs. Similarly, the term "paraplegia" should be used if there is no impairment at the spinal segments for the upper extremities, but damage may also include thoracic, lumbar, or sacral segments. Paraplegia is also used to describe cauda equina or conus medullaris lesions. Recently, the use of the traditional term "paresis" referring to incomplete lesions was abandoned, as incomplete lesions can be more accurately described using AIS.

The neurological level of injury refers to the most caudal region, the lowest normal segment of the spinal cord with normal sensory and motor function in both sides of the body. Completeness of neurological impairment should be decided by the presence of sacral sparing, regardless of partial or complete loss of sensory or motor function after an SCI lesion. Incomplete injury refers to the preservation of sensory or motor function at the lowest sacral segment (S4–5). However, in complete injury there is no sacral sparing at all. Similarly, when there is a partial preservation of sensory or motor function below the neurological level of injury in complete injury, the lowest level of preserved segments should be recorded for sensory and motor function bilaterally. This condition refers to the zone of partial preservation (ZPP), which is additionally defined only in complete injury. In the previous versions, clinical syndromes were described separately from incomplete injuries on the basis of clinical symptoms/features recorded. These clinical syndromes included central cord syndrome, Brown-Sequard syndrome, anterior cord syndrome, conus medullaris syndrome, and cauda equina syndrome. However, since the revised version was released in 2011, these are no longer included in the ISNCSCI system.

1.5.2.2 Neurological evaluation

Initial neurological evaluation in SCI individuals should be performed in the supine position and neurological impairment should be evaluated in a total of four different aspects: left, right, sensory, and motor functions. The level and severity of injury should be determined by function, regardless of level of injury of the vertebrae (**Figure 1-1**).[51]

Sensory examination should be performed in a total of 28 dermatomes in both right and left sides. Additionally, two different kinds of sensory exams should be undertaken to test sensitivity, which includes light touch and pinprick. Cotton is used for the light touch test and a safety pin for the pinprick test. Sensory function is graded on a three-point scale, from 0 to 2. Motor function is assessed in a key muscle in the upper extremities in the segment C5 to T1 and lower extremities in the segment L2 to S1. The strength of the key muscle is graded on a six-point scale, from 0 to 5. The test is performed on a total of 10 myotomes in each side, and therefore on a total of 20 when including both the right and left sides. In myotomes where there is no key muscle available in the segments C2 to C4, T2 to L1, and S2-S4-S5, injury at the motor level is considered the same as that at the sensory level.

To determine complete or incomplete injury, sensory and motor function of S4–5 should be tested to confirm sacral sparing phenomena. Sensory sacral sparing is evaluated using light touch, pinprick, and deep anal pressure sensation tests at the S4–5 dermatome, which corresponds to the perianal area, less than one centimeter lateral to the mucocutaneous junction of the anus. Deep anal pressure is performed by digital rectal examination where the second finger is inserted into the rectum to feel the pressure on the rectal wall against the thumb outside the anus. Motor sacral sparing is determined by the presence or absence of reproducible voluntary contraction of the anal sphincter around the examiner's finger upon squeezing the finger of the examiner. As previously mentioned, complete injury would be associated with no sacral sparing, meaning no sensory and motor function at S4–5, the lowest sacral segment.

1.5.2.3 Limitations of the current standard evaluation method

Nowadays, the ISNCSCI system is widely accepted as the standard evaluation method for SCI patients. However, there are several limitations. The ISNCSCI system has interexaminer variability since it depends solely on a physical examination. There should be clearer and more detailed definitions of thoracic segments in the future. In addition, one of the major flaws is that the ISNCSCI is used to evaluate the SCI patients with only sensory and motor function, and there is no assessment of autonomic functions in spite of their importance. To standardize the evaluation of the autonomic nervous system, ASIA and ISCoS recently collaborated to develop the International Standards to Document Remaining Autonomic Function after Spinal Cord Injury (ISAFSCI) in 2012[52] (**Figure 1-2**). The resultant Autonomic Standards Assessment Form (ASAF) is recommended to be completed during all evaluations for individuals with SCI. This ASAF is a separate worksheet from the ISNCSCI. ASAF consists largely of two parts: general autonomic function and the lower urinary tract/bowel/sexual function. In the evaluation of the lower urinary tract system, there are three categories to be scored: awareness of the need to empty the bladder, continence, and bladder emptying method. Since there are only very short categories for lower urinary tract evaluation, it is very difficult to describe complex situations in patients. Therefore, a separate form of the International Spinal Cord Injury Urodynamic Basic Data Set is available for documentation if the patient underwent a urodynamic test as a part of evaluation of the autonomic nervous system.

1.5.3 American Spinal Injury Association Impairment Scale (AIS)

This grading system is originally based on the Frankel Scale and there have been many modifications over the years to reach the most recent version. Currently, it is named the ASIA Impairment Scale and is incorporated as a part of the ISNCSCI system. The degree of impairment is recorded using AIS (**Table 1-1**) on a five-point grading system, from A (complete) to E (normal). Grade A is complete injury of both sensory and motor function as mentioned above. Grade B is incomplete injury where only sensory function is preserved below the neurological level of injury. In the most recent (2015) version of AIS, motor function should be preserved at least three segments below the neurological level of injury in both grades C and D. It should be emphasized that sensory and/or motor sacral sparing should be present in all incomplete injury categories. Grade E means normal sensory and motor function in patients who had previous impairment due to SCI.

1.5.4 Conclusions

1. The ISNCSCI classification system has been widely used for neurological evaluation and classification of SCI individuals since its establishment in 1982. Not surprisingly, it continues to evolve with improvement in understanding of SCI pathophysiology.
2. The ISNCSCI system describes neurological examination involving sensory and motor function tests to determine the neurological level, and sensory and motor function, and the ASIA Impairment Scale of individuals with SCI. **[LOE 4]**
3. The ISNCSCI depends only on physical examination to evaluate the SCI patients. Therefore, it may have limitations including interexaminer variability. **[LOE 4]**
4. There has been a lack of assessment regarding the autonomic nervous system.

1.5.5 Recommendations

2. Clinicians should use the ASAF for evaluation of autonomic function during all evaluations for individuals with SCI. **[GOR B]**
3. It is recommended to improve accuracy and reliability in the standardization of the lower urinary tract dysfunction secondary to SCI to facilitate diagnosis and management strategies.
4. Clinicians should use the ASIA impairment scale for evaluation of completeness of injury (sensory and motor). **[GOR B]**

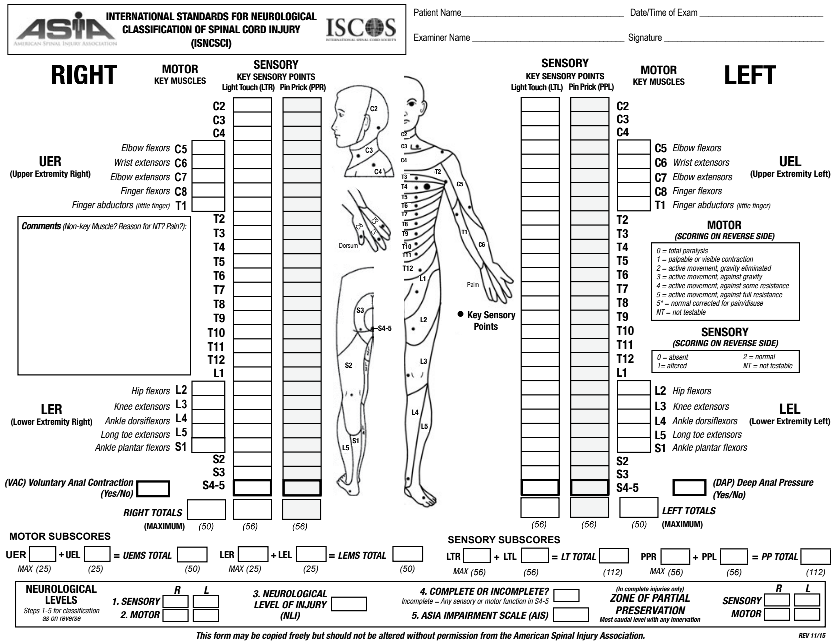
TABLE 1-1 American Spinal Injury Association Impairment Scale

A	Complete	No sensory or motor function is preserved in the sacral segments S4 and S5.
B	Sensory Incomplete	Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4 and S5 (light touch or pinprick at S4–5 or deep anal pressure) AND no motor function is preserved more than three levels below the motor level on either side of the body.
C	Motor Incomplete	Motor function is preserved at the most caudal sacral segments for voluntary anal contraction OR the patient meets the criteria for sensory incomplete status (sensory function preserved at the most caudal sacral segments [S4–S5] by light touch, pinprick, or deep anal pressure), and has some sparing of motor function more than three levels below the ipsilateral motor level on either side of the body. (This includes key or non-key muscle functions to determine motor incomplete status.) For AIS Type C—less than half of key muscle functions below the single nerve lesion have a muscle grade ≥3.
D	Motor Incomplete	Motor incomplete status as defined above, with at least half (half or more) of key muscle functions below the single neurological level of injury (NLI) having a muscle grade ≥3.
E	Normal	If sensation and motor function as tested with the ISNCSCI are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without an initial SCI does not receive an AIS grade.
Using ND		To document the sensory, motor, and NLI levels, the ASIA Impairment Scale grade, and/or the zone of partial preservation when they are unable to be determined based on the examination results.

Table courtesy of the American Spinal Injury Association (ASIA).

FIGURE 1-1
International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) Worksheet

Image courtesy of the American Spinal Injury Association: International Standards for Neurological Classification of Spinal Cord Injury, revised 2011; Atlanta, GA, Revised 2011, Updated 2015.


INTERNATIONAL STANDARDS FOR NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY (ISNCSCI)

Patient Name________ Date/Time of Exam________

Examiner Name________ Signature________

RIGHT — MOTOR KEY MUSCLES; SENSORY KEY SENSORY POINTS: Light Touch (LTR), Pin Prick (PPR)

C2, C3, C4

UER (Upper Extremity Right): Elbow flexors C5; Wrist extensors C6; Elbow extensors C7; Finger flexors C8; Finger abductors (little finger) T1

Comments (Non-key Muscle? Reason for NT? Pain?):

T2, T3, T4, T5, T6, T7, T8, T9, T10, T11, T12, L1

LER (Lower Extremity Right): Hip flexors L2; Knee extensors L3; Ankle dorsiflexors L4; Long toe extensors L5; Ankle plantar flexors S1

S2, S3, S4-5

(VAC) Voluntary Anal Contraction (Yes/No)

RIGHT TOTALS (MAXIMUM) (50) (56) (56)

LEFT — SENSORY KEY SENSORY POINTS: Light Touch (LTL), Pin Prick (PPL); MOTOR KEY MUSCLES

C2, C3, C4

UEL (Upper Extremity Left): C5 Elbow flexors; C6 Wrist extensors; C7 Elbow extensors; C8 Finger flexors; T1 Finger abductors (little finger)

T2, T3, T4, T5, T6, T7, T8, T9, T10, T11, T12, L1

MOTOR (SCORING ON REVERSE SIDE)
0 = total paralysis
1 = palpable or visible contraction
2 = active movement, gravity eliminated
3 = active movement, against gravity
4 = active movement, against some resistance
5 = active movement, against full resistance
5* = normal corrected for pain/disuse
NT = not testable

SENSORY (SCORING ON REVERSE SIDE)
0 = absent; 1 = altered; 2 = normal; NT = not testable

LEL (Lower Extremity Left): L2 Hip flexors; L3 Knee extensors; L4 Ankle dorsiflexors; L5 Long toe extensors; S1 Ankle plantar flexors

S2, S3, S4-5

(DAP) Deep Anal Pressure (Yes/No)

LEFT TOTALS (MAXIMUM) (56) (56) (50)

MOTOR SUBSCORES
UER ___ + UEL ___ = UEMS TOTAL ___ MAX (25) (25) (50)
LER ___ + LEL ___ = LEMS TOTAL ___ MAX (25) (25) (50)

SENSORY SUBSCORES
LTR ___ + LTL ___ = LT TOTAL ___ MAX (56) (56) (112)
PPR ___ + PPL ___ = PP TOTAL ___ MAX (56) (56) (112)

NEUROLOGICAL LEVELS (Steps 1-5 for classification as on reverse): R L — 1. SENSORY; 2. MOTOR
3. NEUROLOGICAL LEVEL OF INJURY (NLI)
4. COMPLETE OR INCOMPLETE? (Incomplete = Any sensory or motor function in S4-5)
5. ASIA IMPAIRMENT SCALE (AIS)
ZONE OF PARTIAL PRESERVATION (In complete injuries only) (Most caudal level with any innervation): R L — SENSORY; MOTOR

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FIGURE 1-2
International Standards to Document Remaining Autonomic Function after Spinal Cord Injury (ISAFSCI) Worksheet

Image courtesy of the American Spinal Injury Association: Autonomic Standards Assessment Form. Available at: http://asia-spinalinjury.org/committees/autonomic-standards/

Appendix I

Autonomic Standards Assessment Form

Patient Name: ____________________

General Autonomic Function

System/Organ	Findings	Abnormal conditions	Check mark
Autonomic control of the heart	Normal		
	Abnormal	Bradycardia	
		Tachycardia	
		Other dysrhythmias	
	Unknown		
	Unable to assess		
Autonomic control of blood pressure	Normal		
	Abnormal	Resting systolic blood pressure below 90 mmHg	
		Orthostatic hypotension	
		Autonomic dysreflexia	
	Unknown		
	Unable to assess		
Autonomic control of sweating	Normal		
	Abnormal	Hyperhydrosis above lesion	
		Hyperhydrosis below lesion	
		Hypohydrosis below lesion	
	Unknown		
	Unable to assess		
Temperature regulations	Normal		
	Abnormal	Hyperthermia	
		Hypothermia	
	Unknown		
	Unable to assess		
Autonomic and Somatic Control of Broncho-pulmonary System	Normal		
	Abnormal	Unable to voluntarily breathe requiring full ventilatory support	
		Impaired voluntary breathing requiring partial vent support	
		Voluntary respiration impaired does not require vent support	
	Unknown		
	Unable to assess		

Autonomic Diagnosis: (Supraconal ☐, Conal ☐, Cauda Equina ☐)

Lower Urinary Tract, Bowel and Sexual Function

System/Organ		Score
Lower Urinary Tract		
Awareness of the need to empty the bladder		
Ability to prevent leakage (continence)		
Bladder emptying method (specify)__________		
Bowel		
Sensation of need for a bowel movement		
Ability to Prevent Stool Leakage (continence)		
Voluntary sphincter contraction		
Sexual Function		
Genital arousal (erection or lubrication)	Psychogenic	
	Reflex	
Orgasm		
Ejaculation (male only)		
Sensation of Menses (female only)		

2=Normal function, 1=Reduced or Altered Neurological Function
0=Complete loss of control, NT=Unable to assess due to preexisting or concomitant problems

Date of Injury__________ Date of Assessment__________

This form may be freely copied and reproduced but not modified.
This assessment should use the terminology found in the International SCI Data Sets (ASIA and ISCoS - http://www.iscos.org.uk)

Examiner ____________________

1.6 Neuroanatomy

It is essential for any physician involved in the care of SCI patients to have an understanding of the structure and function of the normal spinal cord. The neuroanatomy of the spinal cord and lower urinary tract can be classified according to the type of impulses carried (e.g. parasympathetic, sympathetic, and somatic), or by the anatomical level from where it arises (e.g. cervical, thoracic, lumbar, and sacral). In this section, how the level of SCI affects the lower urinary tract function, and how the altered physiology and neural control[53] leads to the pathophysiology of SCI will be discussed. It is important to recognize the interplay between these factors to understand how an injury at a particular level affects the function of the lower urinary tract.

1.6.1 Gross anatomy

1.6.1.1 Spinal cord anatomy

The spinal cord is a tubular structure that originates below the foramen magnum and ends at the level of the first or second lumbar vertebra; it measures around 45 cm in length in men, and 42 cm in length in women. It has two enlargements, a cervical (C3–T2) one from where the nerves to the upper limbs emerge, and a lumbar (L3–S3) one for the legs and the pelvic viscera. The spinal cord is fixed at the bottom to the coccyx. Although it only comprises 2% of the nervous system, the spinal cord is of vital importance, as it contains tracts that are responsible for communicating between the brain and the rest of the body, carrying an enormous amount of information in both directions.

The spinal cord is covered by the same three meninges as the brain: the pia, arachnoid, and dura, and is attached to the brain by a series of lateral denticulate ligaments emanating from the pial folds. The tracts in the spinal cord are arranged in a precise order with each carrying a specific set of information (**Figure 1-3**). The emerging nerves are numbered in sequence as they exit from corresponding vertebrae as cervical, thoracic, lumbar, and sacral nerves. During the third month of embryonic development the spinal cord extends the entire length of the vertebral canal and both grow at about the same rate. As development continues, the body and the vertebral column continue to grow at a much greater rate than the spinal cord. This results in misalignment as to the spinal cord itself and the equivalent spinal nerve leading to the adult spinal cord, which terminates at the level of the first or second lumbar vertebrae, with the nerves extending down within the vertebral canal to exit through the same intervertebral foramina as they did during embryonic development. The resulting configuration gives the typical appearance of cauda equina on cross-sectional imaging.

The spinal cord has 31 segments, and each one of them has two dorsal and two ventral roots (except for the first cervical segment, which only has a pair of ventral roots). In the cervical segments, there are seven cervical vertebrae and eight cervical nerves (**Figure 1-3**). The C1 to C7 nerves exit above their vertebrae, whereas the C8 nerve exits below C7 and above the first thoracic vertebra. Then each subsequent nerve leaves the cord below the corresponding vertebra.

Each spinal nerve is composed of nerve fibres that are related to the region of the muscles and skin that develop from one body somite (segment). The spinal nerve roots are formed by the union of dorsal and ventral roots within the intervertebral foramen, resulting in a mixed nerve joined together and forming the spinal nerve. Spinal nerve rami include the dorsal primary ramus, which innervates the skin and muscles of the back, and the ventral primary ramus, which innervates the ventral lateral muscles and skin of the trunk, extremities, and visceral organs.[54]

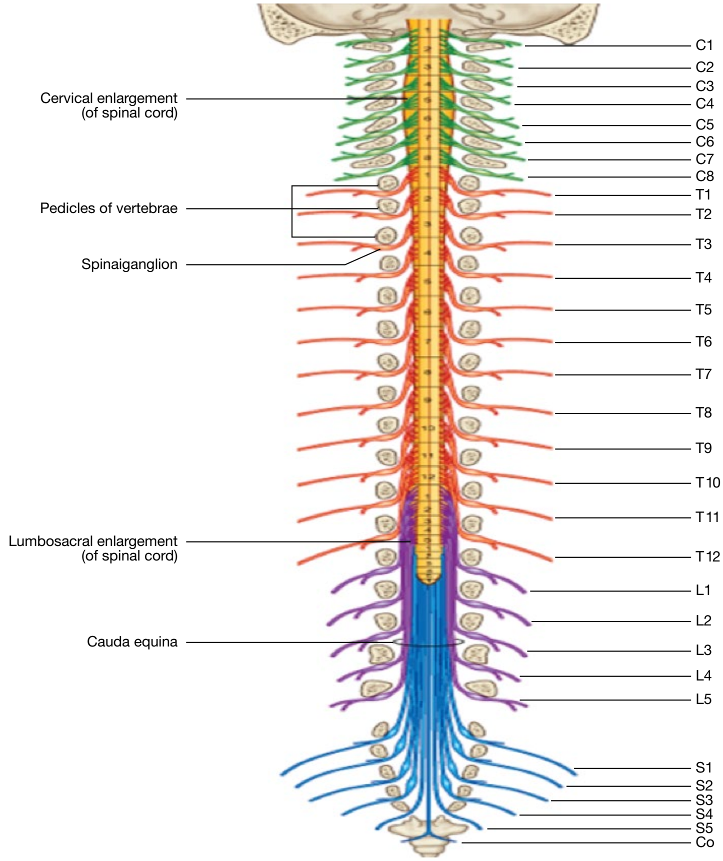

FIGURE 1-3
Spinal Cord General Neuroanatomy

Source: Dafny N. Anatomy of the spinal cord, in Neuroscience Online: An Electronic Textbook for the Neurosciences. *Department of Neurobiology and Anatomy, McGovern Medical School at UTHealth. Available: http://neuroscience.uth.tmc.edu/s2/chapter03.html.*[54]

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1.6.1.2 Cross-sectional anatomy

There is a distinct distribution of grey and white matter within the different segments of the spinal cord, with more grey matter in the lower segments. However, the tracts and the type of information carried in each is essentially the same throughout the length of the spinal cord. In the centre of the spine runs a central canal, filled with cerebrospinal fluid, which is surrounded by a single layer of cells, the ependymal cells. Around these is the grey matter, which contains cell bodies, and has an H-shaped structure. The grey matter is divided into four columns: dorsal horn, intermediate column, lateral horn, and ventral horn column (**Figure 1-4**). The dorsal horn is found at all spinal cord levels and comprises sensory nuclei that receive and process incoming somatosensory information. The ascending projections emerge to transmit the sensory information to the midbrain and diencephalon. The intermediate column and the lateral horn comprise autonomic neurons innervating visceral and pelvic organs. The ventral horn comprises motor neurons that innervate skeletal muscle. Another and more recent classification of neurons within the grey matter is based on function, and divides the neurons into three categories: root cells, column or tract cells, and propriospinal cells.

The root cells are located in the ventral and lateral grey horns and vary greatly in size. The root cells contribute their axons to the ventral roots of the spinal nerves and are grouped into two major divisions: somatic efferent root neurons and the visceral efferent root neurons, also called preganglionic autonomic axons, which send their axons to different autonomic ganglia.

The column or tract cells are confined entirely within the central nervous system (CNS). The axons of the column cells form longitudinal ascending tracts that ascend in the white columns and terminate upon neurons located rostrally in the brain stem, cerebellum, or diencephalon.

The propriospinal cells are spinal interneurons whose axons do not leave the spinal cord. They account for about 90% of spinal neurons.

The intermediolateral nucleus is located in the intermediate zone between the dorsal and the ventral horns, and extends from C8 to L3. It receives viscerosensory information and contains preganglionic sympathetic neurons, which form the lateral horn. A large proportion of its cells are root cells, which send axons into the ventral spinal roots via the white rami to reach the sympathetic tract as preganglionic fibres. Similarly, cell columns in the intermediolateral nucleus located at the S2 to S4 levels contain preganglionic parasympathetic neurons.

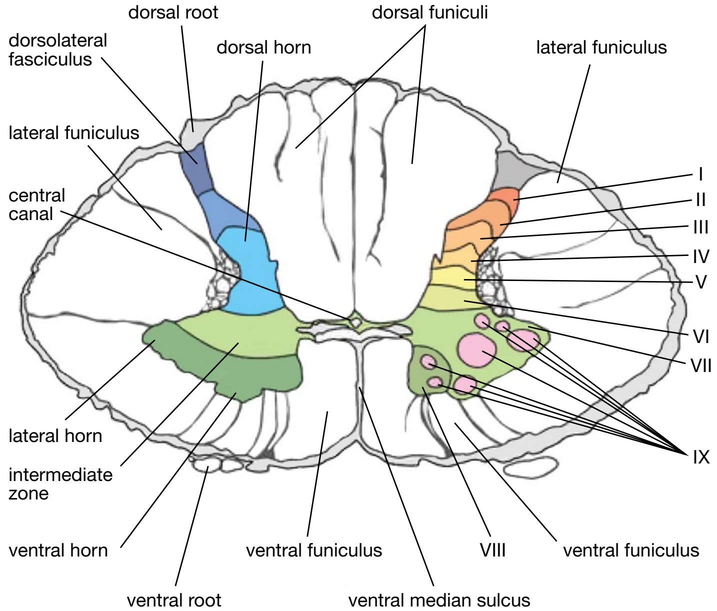
Lower motor neuron nuclei are located in the ventral horn of the spinal cord. They contain predominantly motor nuclei consisting of α, β, and γ motor neurons and are found at all levels of the spinal cord. They are root cells that innervate the visceral and skeletal muscles.

1.6.1.3 **Blood supply**

The arterial blood supply to the spinal cord in the upper cervical regions is derived from two branches of the vertebral arteries, the anterior spinal artery and the posterior spinal arteries. On the top, the two anterior arteries join and form a single artery that lies in the anterior median fissure of the cord. The posterior spinal arteries form an anastomotic chain over the dorsal aspect of the spinal cord. The arterial vasocorona lies on the surface of the cord, and forms a connection between the anterior and the posterior spinal arteries, which ensures an uninterrupted blood supply to the entire length of the spinal cord.

FIGURE 1-4
Cross-Sectional Anatomy

Source: Dafny N. Anatomy of the Spinal Cord, in Neuroscience Online: An Electronic Textbook for the Neurosciences. Department of Neurobiology and Anatomy, McGovern Medical School at UTHealth. Available: http://neuroscience.uth.tmc.edu/s2/chapter03.html.[54]



1.6.2 Lower urinary tract (LUT) innervation

The LUT is innervated by three sets of peripheral nerves from both the autonomic and somatic nervous systems. It is supplied by both parasympathetic and sympathetic components of the autonomic system. These nerves contain afferent (sensory) as well as efferent axons.

1.6.2.1 Autonomic system

Parasympathetic preganglionic neurons innervating the LUT are located in the lateral part of the sacral intermediate grey matter from the S2 to S4 levels in a region termed the sacral parasympathetic nucleus (**Figure 1-5**). Parasympathetic preganglionic neurons send axons through the ventral roots to peripheral ganglia, where they release the excitatory transmitter acetylcholine. They contract the bladder, and relax the urethra.[55]

Lumbar sympathetic nerves arise from lower thoracic and upper lumbar segments of the spinal cord. They inhibit the bladder body and excite the bladder base and urethra (**Figure 1-5**). Sympathetic outflow from the rostral lumbar spinal cord provides a noradrenergic excitatory and inhibitory input to the bladder and urethra. Activation of sympathetic nerves induces relaxation of the bladder body and contraction of the bladder outlet and urethra. This contributes to urine storage in the bladder. The peripheral sympathetic pathways follow a complex route that passes through the sympathetic chain ganglia to the inferior mesenteric ganglia and then through the hypogastric nerves to the pelvic ganglia (**Figure 1-5**).[56]

1.6.2.2 Somatic system

Pudendal nerves are derived from the somatic nervous system. They not only contract the external urethral sphincter but also supply somatic innervation to the whole of the pelvic floor (**Figure 1-5**). The somatic nerves come from the sacral roots of the spinal cord (S2–S4). The external urethral sphincter motoneurons are located along the lateral border of the ventral horn, commonly referred to as Onuf's nucleus. Sphincter motoneurons also exhibit transversely oriented dendritic bundles that project laterally into the lateral funiculus, dorsally into the intermediate grey matter, and dorsomedially toward the central canal.[57]

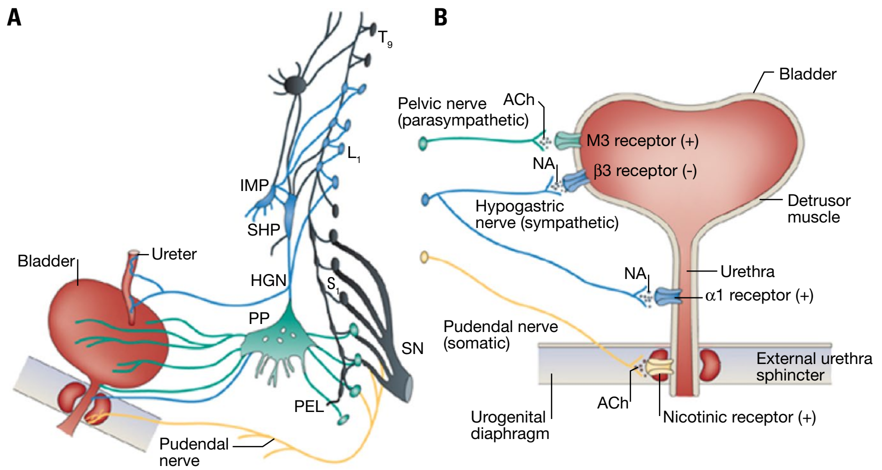


FIGURE 1-5
Innervation to the Lower Urinary Tract

Source: Dafny N. Anatomy of the Spinal Cord, in Neuroscience Online: An Electronic Textbook for the Neurosciences. Department of Neurobiology and Anatomy, McGovern Medical School at UTHealth. Available: http://neuroscience.uth.tmc.edu/s2/chapter03.html.[54]

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1.6.2.3 Afferents from the lower urinary tract

Afferent fibres innervate the LUT via pelvic, hypogastric (lumbar splanchnic), and pudendal nerves. These nerves are mixed nerves, and they also contain the efferent parasympathetic, sympathetic, and motor fibres supplying the bladder, urethra, sphincters, and the pelvic floor. The injected dyes from axons are taken up by afferent nerves and are transported to the afferent cell bodies in the lumbosacral dorsal root ganglia (DRG) where the afferent terminations are located, in the dorsal horn of the spinal cord. The primary afferent neurons of the pelvic and pudendal nerves are contained in sacral DRG, whereas afferent innervation in the hypogastric nerves arises in the rostral lumbar DRG (**Figure 1-5**). The central axons of the DRG neurons carry the sensory information from the LUT to second-order neurons in the spinal cord. These second-order neurons provide the basis for spinal reflexes and ascending pathways to higher brain regions involved in micturition, continence, and mediation of sensation (**Figure 1-5**). Pelvic nerve afferents, which monitor the volume of the bladder and the amplitude of the bladder contractions, consist of myelinated (Aδ) and unmyelinated (C) axons. During neuropathic conditions, including spinal cord injury and possibly some inflammatory conditions, there is recruitment of C fibres that form new functional afferent pathways leading to urgency incontinence and possibly bladder pain.[58]

1.6.2.4 Efferents from the lower urinary tract

There are three corresponding neural pathways that regulate LUT efferent activity involving both the autonomic and somatic nervous systems. Sacral parasympathetic (through the pelvic nerve) provide excitatory input to the detrusor; thoracolumbar sympathetic (through the hypogastric nerve) provide inhibitory input to the detrusor and excitatory input to the bladder neck and urethra; and sacral somatic (via the pudendal nerve) innervate the striated muscles of the sphincters and pelvic floor. Parasympathetic postganglionic fibres terminate predominantly at the detrusor muscle and release acetylcholine, resulting in detrusor contraction during voiding.[59,60]

1.7 Neurophysiology of the Lower Urinary Tract

1.7.1 Introduction

It is easier to understand the physiology of the lower urinary tract when described in the context of the micturition cycle. This allows for the practical understanding of the vesico-sphincteric complex.

Urine storage (continence) and emptying (micturition) depend on the integrated functioning of many components, including the central nervous system, the peripheral nervous system, the smooth muscle of the bladder, the stromal bladder cells, the suburothelial bladder cells, interstitial detrusor cells, the bladder urothelium, the smooth muscle of the urethra, the striated muscle of the pelvic floor, and the external urinary sphincter.[53] It immediately becomes apparent that the micturition cycle is a highly complex and integrated function and even a small interruption in the process somewhere can have a significant impact on the cycle. Hence, understanding the physiology of the LUT is essential for managing bladder dysfunction, be it of neurogenic origin or non-neurogenic origin.[61]

The process that controls the storing and emptying of urine is classically summarized as a complex of neural circuits in the brain and spinal cord that coordinate the activity of smooth muscle and striated muscle in the urethra and bladder in a reciprocal manner. These neural circuits act as a "flip-flop" switch[62] that enables the bladder to alternate between urine storage and emptying.[56,57,63,64] Although this is the basic concept of bladder function/dysfunction, the process is affected by other components as described above.

These components include the urothelium, lamina propria and vasculature, stromal wall collagen, elastin and matrix wall, and the smooth muscle and striated muscle of the bladder and urethra.

From the point of view of the neurological control of lower urinary tract function, it is intended to control the smooth muscle of the bladder and urethra and the striated muscle of the urethra and perineum in a reciprocal fashion.

1.7.2 Physiology of the bladder outlet

There is controversy about the relative role of the smooth and striated muscles of the circular sphincter and the contribution of the lamina propria to generate the closing pressure of the urethra.[65] Blocking striated sphincter musculature with nicotinic neuromuscular blocking agents has varying effects and urethral tone can be reduced by about 40%, suggesting that the smooth muscle is also important.

On the other hand, sympathetic blockade with adrenergic alpha-receptor blockers can also reduce urethral pressure by about 30%.[66]

The striated muscle constituting the sphincter complex in both sexes includes both slow-and fast-twitch fibres. Fast-twitch fibres and slow-twitch fibres are mainly characterized according to the basis of their functional and metabolic characteristics.[67] Slow-twitch fibres seem ideal to keep sphincter tone for extended periods, whilst fast-twitch fibres may be required to complement sphincter tone to maintain continence with sudden rises in intra-abdominal pressure. As in the case of smooth muscle, contraction of striated muscle fibres is governed by intracellular calcium through interactions with troponin. Fast-twitch fibres can be recruited quickly but also fatigue quickly. They perform predominantly anaerobic metabolism. In contrast, the slow-twitch fibres are found in a higher percentage in muscles that require sustained tension, such as the levator ani muscles and the urethral sphincter. These muscle fibres are recruited slowly and fatigue at a slower pace.[68]

1.7.3 Physiology of smooth muscle contraction of the bladder

Although recent evidence suggests that the normal bladder may be spontaneously active and exaggeration of spontaneous contractions could contribute to the development of detrusor overactivity, for the purposes of this paper, we consider that the contractile activity of the detrusor is mainly under neurological control.[69-72]

Using this view, we consider that muscarinic receptors induce detrusor contraction in response to release of acetylcholine from parasympathetic nerve terminals. There are five main types of muscuranic receptors. Although M2 receptors are more abundant, M3 receptors are the ones that are chemically active. The release of acetylcholine from nerve terminals and binding to M3 receptors will lead to phosphorylation of protein G, leading to increased activity of calcium channels (**Figure 1-6**) and suppressing adrenergic inhibitory mechanisms, which are mediated by β adrenergic receptors and stimulation of adenylate cyclase.[73] The principal neurotransmitter for the sympathetic system is noradrenaline.

FIGURE 1-6
Mechanism of Action and Interactions of M2 and M3 muscarinic, P2X1, and β_3 adrenergic receptors

Source: Ouslander JG. Management of overactive bladder. New Engl J Med. 2004;350(8):786–799.[74]

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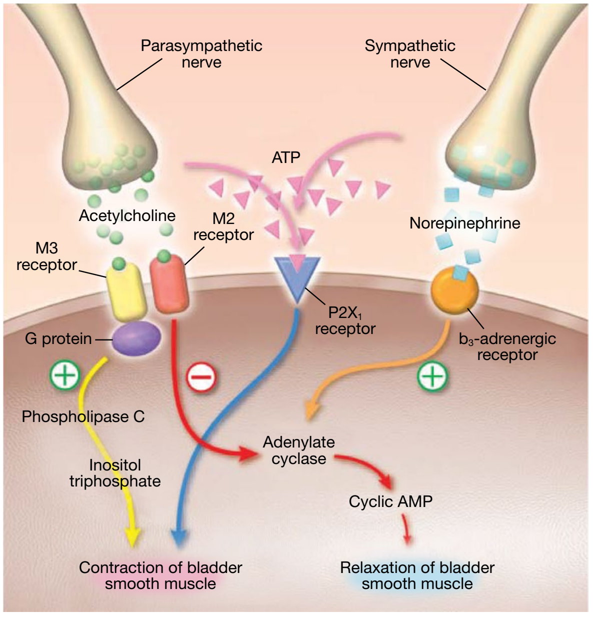


Although calcium serves as a trigger in all types of muscle, the activation mechanisms are different in the smooth muscle. Contractile response is slower and more durable than in skeletal muscle and cardiac muscle. In addition to smooth muscle, the human bladder contains approximately 50% of collagen fibres and 2% of elastin. Injury, obstruction, or denervation increases collagen content. The increased collagen in the bladder wall induces a decrease in compliance.[75-77]

1.7.4 Viscoelastic properties of the bladder

In the filling phase, the viscoelastic behavior of the bladder wall depends on neuromuscular characteristics and mechanical characteristics of the bladder wall. The accumulation of large amounts of urine without the significant increase of intravesical pressure is known as compliance. Bladder compliance is defined as the change in volume relative to the corresponding change in intravesical pressure. The volume/pressure curve during the filling of the bladder depends on several factors, including collagen, elastin, and smooth muscle as passive structures and smooth muscle as active. Hence, a decrease in compliance of the bladder can be a result of multiple factors, including changes in the composition of the bladder wall, such as more collagen or less elastin, hyperactivity of the smooth muscle, or a combination of these factors.[76,78]

It was previously thought that acute spinal cord section does not alter bladder compliance (but section of the pelvic nerves itself decreases accommodation). However, recent animal studies have suggested that central nervous system stimulation is required to maintain bladder compliance and this may involve an active afferent neural process.[79-81] The hypothesis is that signals from the bladder wall travel to the central nervous system during filling and could possibly inhibit spontaneous contractions of the musculature of the bladder that maintain accommodation during filling. Indeed, intravesical pressure reflects a combination of factors, including abdominal pressure surrounding the bladder and active detrusor pressure.

The principle of normal voiding involves a neurally mediated detrusor contraction leading to an increase of detrusor pressure without a significant change of abdominal pressure.

To demonstrate the force of contraction of the detrusor, measurement of detrusor pressure alone is insufficient. A muscle can use energy to generate power or to shorten its length. Since the bladder is a viscous hollow container, strength helps determine detrusor pressure while shortening velocity is related to urinary flow. Thus there is a trade-off between generating detrusor pressure and urinary flow.[82] If urethral resistance is low, then detrusor pressure can be almost undetectable; however, there may be a normal flow. This trade-off between detrusor pressure and flow resembles a constant power curve. This can be expressed in the equation: W (power) = Pdet (detrusor pressure) x Q (flow). This equation explains why a person can have a normal detrusor contraction and normal bladder power with low voiding pressure, as during micturition detrusor pressure reflects the outflow tract resistance. When the normal urethra is completely open with a high flow, only a small increase in detrusor pressure is needed to empty the bladder completely.

1.7.5 Emerging role of urothelium and suburothelium in bladder physiology

In addition to the traditional understanding of lower urinary tract sensory pathways, the emerging sensory role of the urothelium is an interesting field of research.[83,84] New information regarding cell interactions is emerging in this area.[85,86]

The urothelium (transitional epithelium of the urinary bladder) has been recently demonstrated to detect thermal, mechanical, and chemical stimuli. In response, urothelial cells secrete factors such as urinary proteins (e.g. urokinase) and signaling molecules such as adenosine triphosphate (ATP), acetylcholine, and nitric oxide.

Additionally, these cells express receptors (purinergic, cholinergic, and adrenergic) and mechanosensitive channels (transient receptor potential). The urothelium also responds to changes in bladder hydrostatic pressure by releasing factors such as ATP. This may interact with nerve terminals, interstitial cells, and urothelial purinergic receptors to transduce sensory information.

The distribution of anatomical components indicates that reciprocal communication is possible between urothelial cells located close to bladder nerves and smooth muscle cells. Evidence exists that ATP is released by the urothelial cells and binds to purinergic receptors on nerve cells in the bladder wall, stimulating afferent nerve activity, resulting in bladder sensation. All this information suggests that the urothelium may play a substantial role in urinary bladder sensory transduction.[83–86]

1.7.6 Micturition cycle

The lower urinary tract in adults is under both voluntary and involuntary neural control. This is different from other visceral organs innervated by the autonomic nervous system, whose regulation is only controlled by involuntary mechanisms.[87] The brain bladder control system is still poorly understood but is an area of current research.[88,89]

Following this schematic view, the micturition cycle could be understood as two relatively discrete phases: bladder filling/storage and bladder emptying/voiding. The micturition cycle normally displays these two modes of operation in a simple on-off fashion. The cycle involves switching from inhibition of the voiding reflex and activation of the storage reflexes to inhibition of the storage reflexes and activation of the voiding reflex and back again.[68,90–93]

1.7.6.1 Storage phase (filling):

- Storage of urine at low detrusor pressure (compliance) with appropriate sensation
- Bladder outlet closed at rest and during increases of intra-abdominal pressure
- Absence of detrusor contractions

1.7.6.2 Voiding phase (emptying):

- Contraction of the detrusor of adequate magnitude and duration
- Drop of the resistance of the smooth and striated sphincter
- Complete bladder emptying

1.7.6.3 **Bladder during the storage phase:**

The normal bladder response to filling should be an almost complete absence of change in intravesical pressure and detrusor pressure. At initial bladder filling, compliance of the bladder is due to the bladder's elastic and viscoelastic properties. Elasticity is the property that allows the bladder wall to stretch without an increase in tension. Viscoelasticity is the property that causes bladder stretch to induce an increase in tension. Viscoelastic properties of the bladder wall are due to the characteristics of the extracellular matrix of the bladder wall.[94]

In animal models, as bladder filling increases, spinal sympathetic reflexes facilitatory to bladder filling are evoked. It is thought the same mechanism occurs in humans. This active inhibitory effect is thought to be mediated by sympathetic modulation of cholinergic ganglionic transmission.[57,64,95–97] Based on this hypothesis two other possible effects promoting bladder filling may exist: a neurally mediated stimulation of α-adrenergic receptors (α1) in the smooth sphincter resulting in an increase in the resistance and a neurally mediated stimulation of β-adrenergic receptors (β3 inhibitory) in the bladder smooth musculature promoting a decrease in bladder wall tension.[71,81]

Many other neurotransmitters and signaling molecules such as ATP, purine, prostaglandins, nitric oxide, and cytokines have recently been involved in coordinating control of the lower urinary tract.[98,99]

1.7.6.4 **Outlet during the storage phase**

During bladder filling a progressive increase in proximal urethral pressure should occur. This is mediated by the striated sphincter and also by the smooth sphincter. This increase in urethral pressure follows an increase in efferent pudendal nerve impulse frequency and in electromyographic activity of the striated sphincter. This is the "guarding reflex" or the efferent limb of the spinal somatic reflex, which results in a gradual increase in striated sphincter activity during normal bladder filling. It has also been postulated that there is a sympathetically induced contraction of the smooth muscle sphincter with increase in resistance; however, it has been difficult to prove this experimentally or clinically.[90,94,100–102] In addition, passive properties of the urethral wall also play a role in the maintenance of continence but the exact nature remains unquantified.[100,103]

1.7.6.5 **Bladder during the voiding phase**

It is generally understood that the neural mechanisms in the storage phase are reversed in the voiding part of the cycle. It is thought that the inhibitory influences of the cerebral cortex are withdrawn. The pontine micturition centre then takes over to facilitate a coordinated void. This requires normal ascending and descending spinal cord pathways from pons to the sacral micturition centre. The voluntary bladder empting involves the inhibition of the somatic neural efferent activity to the striated sphincter and also the inhibition of the spinal sympathetic reflexes that were evoked during normal bladder filling. Finally, the parasympathetic neural impulses to the bladder travel through the sacral spinal cord and pelvic nerve (pelvic plexus) to the bladder and are responsible for leading to the contraction of the bladder smooth musculature.[104]

1.7.6.6 **Outlet during the voiding phase**

In order to achieve a low-pressure bladder emptying, a substantial drop in the resistance of the outlet is needed. This decrease in outlet resistance includes a funneling of the relaxed bladder outlet. This effect is mediated by the inhibition of the continence-promoting reflexes, which were active during bladder filling. In addition, there is evidence that the change in outlet resistance may also involve an active relaxation of the smooth sphincter area through a noradrenergic noncholinergic mechanism, possibly mediated by nitric oxide.[94,101,102] It seems that some of the changes at the outlet during voiding are probably at least in part due to the anatomic interrelationships of the smooth muscle of the bladder base and the smooth muscle of the proximal urethra.

1.7.7 Conclusions

1. Spinal nerves emerge from the corresponding vertebrae however, their origin is progressively higher since the spinal cord is shorter than the spine. This is of great importance when considering spinal cord injury.
2. The afferent and efferent tracts run along the spinal cord in an orderly fashion. This is of paramount importance when considering incomplete injuries.
3. The nerves that control the LUT emerge from different sites: the sympathetic branches come from the thoracolumbar portions, the parasympathetic from intermediolateral horn, and the somatic nerves from the S2 to S4 portion of the sacral roots.
4. The parasympathetic transmission is via cholinergic mechanisms, with acetylcholine as the principal neurotransmitter.
5. M3 receptors are the main active receptors, though M2 receptors are greater in number.
6. Noradrenaline is the main neurotransmitter for sympathetic pathways.
7. Bladder compliance is dependent on the elastic and viscoelastic properties of the smooth muscle of the bladder wall.
8. Passive outlet seal effect, based on the anatomical and histological architecture of the urethral submucosa, is responsible for continence in the storage phase with active contribution from the striated sphincter during end filling.
9. The emptying is facilitated by inhibition of spinal somatic and sympathetic reflexes and activation of vesical parasympathetic pathways.
10. There is a drop in outlet resistance caused by cessation of somatic and sympathetic spinal reflexes and funneling of relaxed outlet, due to smooth muscle continuity between the bladder base and proximal urethra.

1.8 Pathophysiology

The bladder function comprises two phases—storage and emptying. These phases are reliant on coordination between both the central and peripheral nervous systems. After SCI, either of these systems can be altered. The classic symptom in a suprasacral SCI is that of urinary incontinence, most often due to neurogenic detrusor overactivity (NDO). The pathophysiology of NDO can be described as an alteration in the micturition reflex.

1.8.1 Afferent pathways

The newly developed spinal reflex circuit, which is mediated by C fibres as a response to a reorganization of synaptic connections in the spinal cord, is thought to be responsible for the development of detrusor overactivity in response to low-volume filling after SCI. The direct evidence for this comes from animal experimental models (cats and rats).[105,106] However, a comparable process is thought to occur in humans following SCI, with some clinical evidence to support this view.[105]

1.8.2 Neurotrophic factors

This was first observed in a rat model. There appears to be some role of various neurotrophic hormones such as nerve growth factor (NGF) in the morphological and physiological changes of the bladder afferent neurons leading to the development of neuropathic bladder dysfunction.[106,107] The production of neurotrophic factors increases in the bladder after SCI.[108,109] It has been demonstrated that chronic administration of NGF into the rat bladder induces bladder hyperactivity and increases the excitability of dissociated bladder afferent neurons. On the other hand, intrathecal application of NGF antibodies suppressed neurogenic detrusor overactivity[109] and detrusor sphincter dyssynergia in SCI rats. Animal and human studies also support a role for the suburothelial expression of the transient receptor potential cation channel subfamily V member 1 (TRPV1), purinergic receptors (P2X3)[110] and/or the sensory neuropeptides substance P (SP), and calcitonin gene-related peptide (CGRP)[111] in the pathophysiology of human NDO. It has been shown that patients with SCI and NDO have increased TRPV1- and P2X3-immunoreactive suburothelial innervation compared with controls.[112]

1.8.3 Spinal cord and vertebral levels

Spinal control of micturition is located at sacral segments 2 to 4 (vertebral levels T12 to L2) and is described as the primary micturition centre.[113] A significant association exists between the level of a spinal cord lesion and the associated bladder dysfunction. In general, on a topographic and anatomical basis, when there is injury cephalad to the sacral spinal cord, one expects a voiding pattern consistent with upper motor neuron type injury with neurogenic detrusor overactivity. In contrast, injury to either the sacral cord or cauda equina segment should result in lower motor neuron type injury and detrusor hypo/areflexia. Patients with suprasacral spinal cord injuries are also at risk for detrusor-external sphincter dyssynergia (DESD) secondary to the loss of coordination from pons that can lead to incomplete bladder emptying, high postvoid residual, and increased bladder pressure, with resulting obstruction of kidneys leading to renal failure.[114]

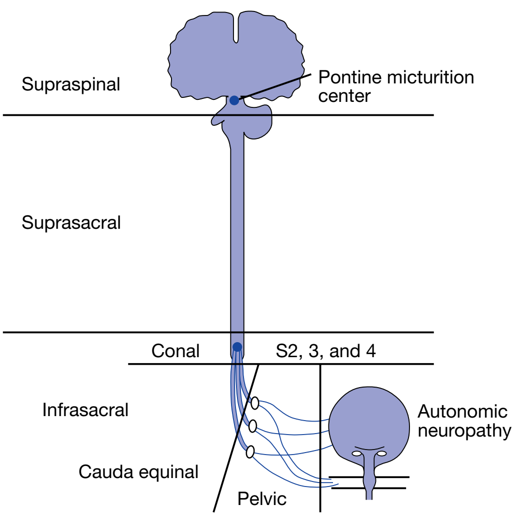
It would appear on the basis of the above categorization that the clinical expression should be clearly characterized. However, this is generally not the case, and the clinical manifestations of SCI quite often demonstrate a mixed picture. It has been demonstrated in some studies that there are multiple factors in this complicated situation leading to a mismatch between clinical presentation and presumed anatomical level of injury.[115] Some of these factors include:

- Degeneration and reorganization of crucial neural pathways distal to the lesion with or without neural sprouting at the level of injury that may affect the neurologic and urodynamic findings.
- SCI may be incomplete, thereby partially allowing the integration and modulation of complex micturition signals at multiple levels of the nervous system.
- Multiple injuries coexisting at different levels can result in unpredictable mixed voiding dysfunction. The multiplicity of levels of injury is occasionally unrecognized when based solely on urologic history and evaluation in patients with new SCI.[115]

For the purposes of description, if the sacral micturition centre (conus medullaris) is taken as a landmark for the convenience of clinical purposes, one can divide the patterns of bladder dysfunction as follows (**Figure 1-7**):

FIGURE 1-7
Levels of Injury in Neurogenic Lower Urinary Tract Dysfunction (NLUTD)

Source: Cardenas DD, Chiodo A, Samson G. Management of bladder dysfunction, chapter 28. Available: http://clinicalgate.com/management-of-bladder-dysfunction/.



- **Suprasacral lesion:** This is an injury anywhere above the level of sacral micturition centre but below the pons. The presenting features include detrusor overactivity with external sphincter dyssynergia.[114,116]
- **Sacral lesion:** This implies the lesion involving the sacral spinal micturition centre. This lesion is characterized by detrusor hypo/areflexia with a fixed underactive or denervated striated sphincter.
- **Infrasacral lesions including cauda equina:** These lesions involve the peripheral nervous system. These lesions include any injury below the level of sacral micturition centre and injury to cauda equina and all nerves leading to the bladder or sphincter.[117]

1.8.4 Video-urodynamics-based classification

Another way of describing the pathophysiology is based on urodynamics. The advantage is more precise categorization of the bladder/sphincter dysfunction. Urodynamics will demonstrate the lesion regardless of the site and degree of neurologic damage. The disadvantage is that urodynamics findings can be influenced by various factors such as urinary tract infections (UTIs), stones, etc.[91,117] The urodynamics will demonstrate neurogenic detrusor overactivity with sphincter dyssynergia in suprasacral SCI (**Figure 1-8**) and detrusor hypo/acontractility with sphincter weakness in sacral and subsacral lesions (**Figure 1-9**).

FIGURE 1-8
Detrusor Overactivity With Detrusor Sphincter Dyssynergia and Reduced Bladder Compliance Typical of a Suprasacral Spinal Cord Injury

Source: Persu C, Caun V, Dragomirițeanu I, Geavlete P. Urological management of the patient with traumatic spinal cord injury. J Med Life. 2009;2(3):296–302.

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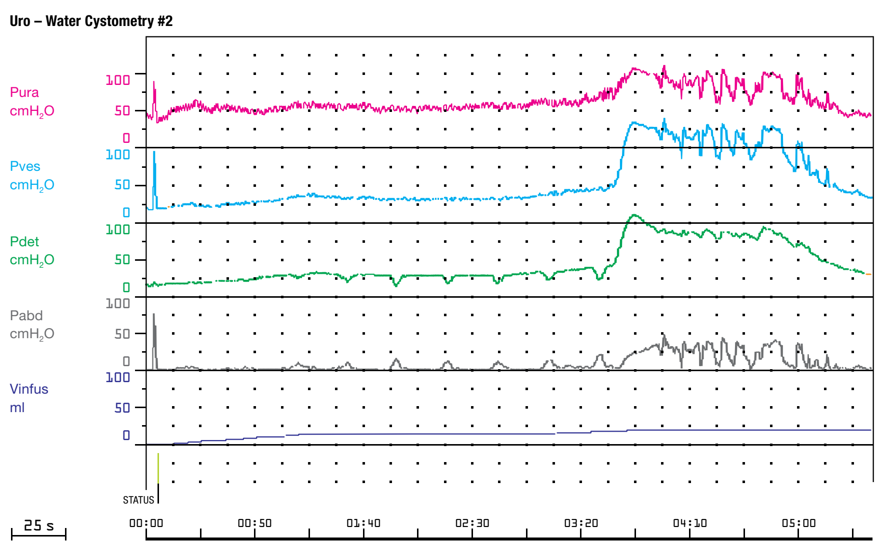
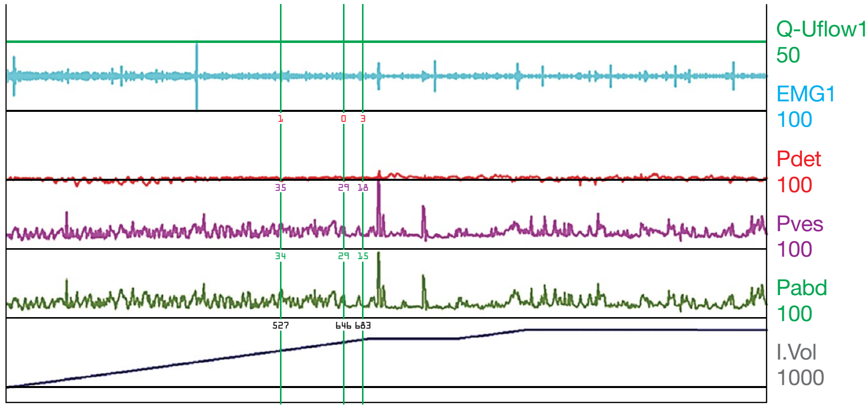


FIGURE 1-9
Detrusor Acontractility and Large Capacity Bladder Typical of a Sacral Spinal Cord Injury

Source: Allio BA, Peterson AC. Urodynamic and physiologic patterns associated with the common causes of neurogenic bladder in adults. Transl Androl Urol. 2016;5(1):31–38.



1.8.5 Clinically based classification

Wein *et al.*[91] classified voiding dysfunction after SCI based on symptoms as follows:

- **Storage failure:** This includes either an overactive bladder or underactive sphincter. It can also lead to loss of compliance. The symptoms will include frequency, nocturia, and urgency with/without incontinence.

  An underactive sphincter could lead to stress-related urinary incontinence.
- **Emptying failure:** This includes either a bladder that is underactive or a sphincter that is overactive.

Note that storage failure can occur in suprasacral SCI due to detrusor overactivity or reduced compliance, as well as in sacral SCI due to a weak sphincter. Similarly, emptying failure can occur in suprasacral SCI due to a fibrotic bladder or detrusor external sphincter dyssynergia (DESD), as well as in sacral SCI due to flaccid bladder.

1.8.6 Clinically based classification with urodynamics correlation

One can combine the symptoms and associated urodynamics findings to better understand the pathophysiology.[118,119]

- **Lesions above the brain stem:** The symptoms will include urinary frequency, urgency, with or without urge urinary incontinence. The bladder sensation can be normal or decreased. The urinary sphincters should be synergistic with the bladder and relax when the bladder contracts. The urodynamics will demonstrate NDO but no DESD with possible incomplete emptying, especially in the elderly.
- **Suprasacral spinal cord lesions:** The symptoms would be the same as with lesions above the brain stem but can be more severe with incomplete emptying and urinary infections, but most importantly DESD can lead to autonomic dysreflexia in lesions above T6 level. The accompanying urodynamics will demonstrate NDO but with DESD and incomplete emptying.

- **Sacral lesions:** The symptoms could be delayed sensations with stress-related urinary incontinence. The urodynamics will demonstrate poorly contracting detrusor with incomplete emptying. It might also show a weak sphincter.
- **Injury distal to the spinal cord:** The sensations to bladder filling could be normal to decreased. The urodynamics could show detrusor areflexia. The internal sphincter is likely incompetent, and the striated external sphincter may exhibit fixed residual tone that cannot be relaxed voluntarily.

1.8.7 Conclusions

1. SCI leads to NLUTD in about 70% to 84% of patients.
2. Two decades ago urinary tract mortality was ranked as the second leading cause of death in SCI patients, but with significant improvement in understanding and management of this condition, urinary disease now accounts for only ≈13% of deaths. **[LOE 3]**
3. It is postulated that a new spinal reflex circuit develops, which is mediated by C fibres as a response to a reorganization of synaptic connections in the spinal cord. This is thought to be responsible for the development of neurogenic detrusor overactivity in response to low-volume filling after SCI. **[LOE 4]**
4. Various neurotrophic hormones such as nerve growth factor affect the morphological and physiological changes of the bladder afferent neurons leading to the development of neuropathic bladder dysfunction. **[LOE 3]**
5. A suprasacral SCI usually results in a voiding pattern consistent with upper motor neuron type injury with neurogenic detrusor overactivity and DESD. **[LOE 3]**
6. Injury to either the sacral cord or cauda equina segment should result in lower motor neuron type injury and detrusor hypo / areflexia. **[LOE 3]**
7. The urodynamics will demonstrate neurogenic detrusor overactivity with sphincter dyssynergia in suprasacral SCI and detrusor hypo/acontractility with sphincter weakness in sacral and subsacral lesions. **[LOE 3]**
8. Suprasacral SCI may lead to incomplete emptying, urinary infections, and DESD; they are also associated with autonomic dysreflexia in lesions above the T6 level. **[LOE 3]**
9. Sacral SCI may lead to delayed sensation during bladder filling and to stress urinary incontinence. **[LOE 3]**
10. Injury distal to the spinal cord (cauda equina injury) may lead to a bladder with normal sensations with an incompetent internal sphincter and the striated external sphincter exhibiting fixed residual tone that cannot be relaxed voluntarily. **[LOE 3]**

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C2

Early Neurological and Urologic Care of Patients with Spinal Cord Injury

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Committee 2

CONTENTS

Early Neurological and Urologic Care of Patients with Spinal Cord Injury

2.1 Introduction

The care of patients with acute spinal cord injury (SCI) is rather complex. Care spans from the acute site to the scene of injury, involves emergency rescue teams and transportation for primary emergency hospital services, and requires triage activities to initiate timely treatment in the intensive care unit and eventual early surgical interventions. Patients with SCI are cumbered with very vulnerable clinical conditions, and require comprehensive and coordinated care. This includes not only addressing spine stability, requirements for transportation, and positioning of patients, but also sensitive monitoring and treating cardiovascular impairments. One of the leading pathophysiological conditions that exaggerates, or actually initiates, an SCI is associated with vascular conditions that can seriously affect the blood supply of the spinal cord. Therefore, maintaining stable vascular spinal cord perfusion, including a sufficient high systemic blood pressure (and consequently spinal cord perfusion), is of critical relevance. Blood pressure management should aim for a rather high mean arterial pressure (>80 mmHg). Due to the complexity of an acute SCI, it is advised that patients with SCI are immediately referred to primary acute care centres that are experienced and equipped to manage acute assessments of potential spine or spinal cord damage. For this purpose, multidisciplinary, as well as well-trained and coordinated teams are essential in recognizing the appropriate treatments and handling medical challenges.

This chapter will focus on concepts of early neurological and urological care in patients with SCI.

2.2 Description of Search Methodology

A semisystematic literature search was performed to provide a summary of all existing evidence of studies and reviews on the early neurological and urological care of patients with SCI. We searched the Embase® and MEDLINE® databases from 1946 to 2016 (November). No language restrictions were applied. We additionally searched the reference lists of all included studies and any relevant review articles. Important studies were included in the following chapter and summarized in a narrative fashion.

2.3 Neurological Management

2.3.1 Acute care management

2.3.1.1 Rescue and emergency care

The theoretical advantage of immobilization in both blunt and penetrating trauma is the prevention of displacement of unstable fractures that result in damage to a previously spared spinal cord. The three-column diagnostic approach for assessing injuries to the spine assumes that there is an underlying abrupt acceleration or deceleration mechanism to the spine, as occurs in blunt trauma. Therefore, when forces are applied to the spine, this results in disruption of the bony and ligamentous anatomy of at least two of the three columns.

The principles of the Advanced Trauma Life Support® (ATLS®) program by the American College of Surgeons advocate that a cervical spine injury should be assumed until proven otherwise in all trauma patients. The probability of a multilevel spinal injury in the setting of a known injury is approximately 20%, necessitating the need for complete spinal immobilization for any suspected SCI. The classic recommendations of the American College of Surgeons include a hard backboard, a rigid cervical collar, lateral support devices, and tape or straps to secure the patient, the collar, and the lateral support devices to the backboard.[1]

A rigid collar should be applied to the neck with manual in-line stabilization while minimizing cervical spine displacement. Spinal immobilization is a priority in the prehospital trauma algorithms and leads to improved outcomes.[2] However, patients with penetrating trauma who had prehospital spinal immobilization seem to have worse outcomes.[3] In one study, the process of immobilization delayed life-saving resuscitation; thus, patients who were immobilized had nearly twice the morbidity and mortality as those penetrating trauma patients who did not have full immobilization. While cervical collars and backboards are important tools in reducing further neurological injury, especially in blunt trauma, they have their own inherent risks and complications, such as high risk of aspiration, pressure sores, and increased intracranial pressure. Practitioners must recognize these risks and understand the need to remove immobilizing devices as soon as safety allows, particularly when concomitant head injury exists, in patients with ankylosing spondylitis, and in the setting of delayed resuscitation.[4–6]

Regarding penetrating trauma, Aryan *et al.* defined spinal stability as the ability of the patient to sustain physiological loads without incurring structural deformations, painful alterations, or neurological deficits. In their series of 60 patients, they noted two patients with radiologic two-column disruption who did not have spinal instability on dynamic radiographic imaging. The evidence seems to clearly suggest that the nature of a penetrating injury to the spine is to remain stable and not propagate, as the damage is done at the initial impact. Patients who demonstrate SCI after penetrating trauma do so at the moment of injury, whereas those who do not have neurological deficits do not subsequently develop signs of SCI.[7]

Clinical criteria to select appropriate patients for spinal immobilization have been studied and implemented.[8]

Prehospital spinal immobilization is required in the following circumstances:

- Spinal pain or tenderness, including any neck pain with a history of trauma
- Significant multiple system trauma
- Severe head or facial trauma
- Numbness or weakness in any extremity after trauma
- Loss of consciousness caused by trauma
- If mental status is altered (including drugs, alcohol, trauma) and no history is available, or the patient is found in a setting of possible trauma (e.g., lying at the bottom of the stairs or in the street), or the patient experienced near drowning with a history or probability of diving)
- Any significant distracting injury

Rescue is achieved through the use of appropriate transfer techniques, cervical spine collars (C-collars), lateral support, and spine boards and straps. Other devices used include a scoop stretcher with a rigid cervical collar and straps, a vacuum mattress in combination with a rigid cervical collar, and a Kendrick Extrication Device (KED®; also known as a short board) to assist with extrication following a motor vehicle crash or other confined-space rescues.[9]

ATLS guidelines recommend cervical spine immobilization in cases of suspected cervical injury or SCI, until excluded by radiology. Although these guidelines have been developed to protect patients with an unstable cervical spinal column, the guidelines have not been shown to benefit patients with penetrating injury.[10]

Prehospital selective immobilization protocols (also known as spinal clearance protocols) aim to identify trauma patients who are at very low risk of sustaining an SCI, and therefore could be transported without spinal immobilization. Hoffman *et al.*[11] have validated five criteria—National Emergency X-Radiography Utilization Study (NEXUS) criteria—where patients' cervical spine can be cleared without imaging; these include:

1. No midline cervical tenderness
2. No altered mental status
3. No evidence of intoxication
4. No painful distracting injuries
5. No focal neurological deficits

The role of paramedics is fundamental in improving the neurological outcome of the patients and in decreasing the time to spinal care units. Improved recovery and reduced mortality are associated with effective resuscitation efforts, prevention of hypoxia, and management of hypotension.[12] In an epidemiological study in Turkey, it was concluded that inadequately trained paramedics and lack of first aid care led to higher death rates following traumatic SCI.[13]

Although there is no definite timeline for early transfer to surgery for isolated cervical SCI, it is recommended that patients reach spinal units within 8 to 24 hours following injury, assuming that the patients are hemodynamically stable.[14] It has been reported that shorter times to spinal units lead to shorter lengths of hospital stay, decreased health care costs, decreased in-hospital mortality rates, and decreased dependence on mechanical ventilation. A cohort study in New South Wales, Australia, found that patients who reached a spinal unit after 24 hours, compared with patients who reached a spinal unit in less than 24 hours, were 2.5 times more likely to develop one or more secondary complications, including pulmonary embolism, deep vein thrombosis, and pressure ulcers.[15–17]

Patients with acute SCI, particularly those with high cervical spine injuries, are also at high risk for respiratory failure. Dysfunction of the muscles of inspiration and expiration caused by injury to the spinal cord may be exacerbated by pulmonary injury. Vigilance for signs of impending respiratory failure is imperative, and in such cases, definitive airway management with positive pressure ventilation should be strongly considered to ensure avoidance of hypoxemia. If airway protection is required in an urgent manner, rapid sequence induction with manual in-line spinal immobilization is generally considered the standard of care. Maintenance of spinal alignment is critical, particularly for those with cervical SCI.[18] An unobstructed airway, and adequate oxygenation and ventilation are the highest priorities. Patients with SCI often present with associated factors that may compromise airway protection, and establishment of a definitive airway should be considered early in the management of any patient with signs of impending airway compromise.

An injured spinal cord is particularly susceptible to systemic hypoperfusion. Sound preclinical evidence and numerous retrospective clinical studies report that prompt hemodynamic resuscitation and blood pressure support improve neurological outcomes.[19] Hypotension should be corrected as soon as possible, and mean arterial blood pressure should be maintained >80 mmHg.

Hypotension may be a result of neurogenic shock, but other potential causes of hemodynamic instability, such as hemorrhage, tension pneumothorax, cardiac tamponade, and sepsis, should be considered and managed appropriately if present. Adequate fluid resuscitation is essential, but can be particularly challenging in patients with SCI. Fluid overload needs to be avoided, as these patients are at high risk for pulmonary edema. Presently, there is no optimal algorithm to guide fluid resuscitation in an SCI patient, and further research in this area is greatly needed. Vasoactive agents should be considered early in the setting of hypotension that is not appropriately responsive to fluid resuscitation, but the optimal choice remains a matter of debate.[20] Patients with high cervical SCIs are especially at high risk for symptomatic bradycardia, which may lead to asystole, particularly with noxious stimulation. Symptomatic bradycardia should be treated upfront with atropine to ensure adequate cardiac output. Bradycardia that is refractory to atropine may respond to aminophylline, otherwise temporary pacing should be considered.

The use of methylprednisolone sodium succinate (MPSS) in acute SCI is greatly debated. Six randomized controlled trials (RCTs) have been conducted to study the safety and/or efficacy of MPSS; the most notable are the NASCIS II and III trials. No significant differences in motor, sensory, or functional recovery were found in any of the primary analyses. However, *post hoc* analysis of the NASCIS II data revealed that those receiving MPSS within 8 hours of injury had significant improvements in sensory and motor functions.[21] *Post hoc* analysis of the NASCIS III data demonstrated significantly greater motor recovery if the 48-hour MPSS protocol was used instead of the 24-hour protocol, when treatment was started within 3 to 8 hours of injury; however, there was a higher risk of infection.[22]

For a number of years, administration of MPSS within 8 hours of injury was commonplace, but there has been a recent shift away from the use of MPSS.[23] This can be attributed, in part, to the 2013 American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) *Guidelines for the Management of Acute Cervical Spine and Spinal Cord Injury*, which include a level 1 recommendation that states, "Administration of MPSS for the treatment of acute SCI is not recommended." This recommendation is a departure from the preceding guidelines, which suggested

MPSS as an option for patients with acute SCI.[24] This change is not supported by a commensurate shift in the body of evidence. In fact, recent evidence has emerged to suggest that surgery within 24 hours of injury in conjunction with 24 hours of MPSS treatment may improve neurological recovery and reduce adverse events.[25] MPSS should not be viewed as the standard of care; instead, it should remain as an option after balancing the benefits and risks for each patient. The complication profile and beneficial effect of MPSS appear to be optimal in cervical SCI. If MPSS is to be given, the 24-hour NASCIS protocol (30 mg/kg bolus at admission followed by 5.4 mg/kg/hour for 23 hours) should be utilized to minimize the adverse events that seem to cluster with the 48-hour protocol.

2.3.1.1.1 Recommendations

- Emergency health care providers must use the following criteria to determine the risk of SCI in a trauma patient: altered mental status, evidence of intoxication, suspected extremity fracture/distracting injury, focal neurological deficit, and spinal pain/tenderness. **[Level of Evidence (LOE) 1; Grade of Recommendation (GOR) A]**

- Emergency health care providers must determine if airway and ventilator support are needed in patients with high tetraplegia. **[LOE 4; GOR A]**

- Emergency health care providers must recognize and treat neurogenic shock. **[LOE 3; GOR A]**

2.3.1.2 Surgical spine management

Spinal compression and neurological deficit are two major principles used to decide on surgery. However, the surgical approach (anterior, posterior, or combined) varies depending on the patient. As a general principle, the main approach for patients without the presence of any pathology causing compression in the canal is posterior stabilization and fusion. Anterior decompression and fusion, as well as posterior stabilization are required for patients with spinal canal compression. In some cases, anterior and posterior surgical approaches are equivalent.

Early surgical decompression is playing an increasing role in the treatment of acute SCI. Although still controversial, evidence is mounting for its safety, clinical, and neurological outcomes. The definition of early surgery is not fixed, but most consider early to be less than 24 hours after SCI. In terms of safety, the treating surgeon must balance the potential benefits versus risks of early surgery. The benefits include relieving cord compression, and therefore limiting secondary injury. The risks include aggravating secondary injury by hypotensive episodes or blood loss. Several studies suggest patients should be treated with early surgery if they are medically stable enough for surgery. Clinical benefits of early surgery possibly include shorter length of both intensive care unit stay and overall hospital stay, and fewer medical complications (such as pneumonia and deep vein thrombosis). Preliminary results from the Surgical Treatment for Acute Spinal Cord Injury Study (STASCIS) suggest decompression of the spinal cord within 24 hours of injury is associated with improved neurological recovery in patients with cervical injury.[26–30]

2.3.1.2.1 Recommendations

- Spine surgeons should consider early surgical spinal canal decompression and spine fixation/stabilization, where indicated, and should promote early active rehabilitation to improve functional recovery. **[LOE 2; GOR B]**

2.3.2 Rehabilitation

The rehabilitation of patients with acute SCI is a multidisciplinary challenge. Close and immediate acute care (rescue, diagnostics, surgery, etc.) and early rehabilitation are needed to optimize outcomes.

In addition, rehabilitation requires a team of health care providers. Psychologists can help patients understand their injuries and cope with the loss of functional independence. Social workers may assist with vocational and financial concerns. Physiotherapists and occupational therapists are actively involved in the physical rehabilitation of patients in health care facilities and/or after discharge in the community. This complement of medical and allied care can have a significant impact on the long-term health of the SCI patient, as the team focuses on regaining function, enhancing preserved function, and preventing complications. Key components of physical rehabilitation are strength training, cardiovascular-focused exercise, respiratory conditioning, transfer/mobility training, and stretching to prevent contractures. The patient's progress helps to dictate the level of ongoing care needed in the community and the use of assistive devices for daily living. Usually, rehabilitation lasts about 6 months for a tetraplegic patient and about 3 months for a paraplegic patient. The whole rehabilitation process should, if possible, take place in specialized SCI centres.

2.3.2.1 Phases of rehabilitation

2.3.2.1.1 Early stages

In the early stages after an SCI, patients must be trained on how to position themselves in bed. SCI individuals should change positions every 3 to 6 hours to prevent pressure ulcers. In addition, the nurses and occupational therapists should instruct the patients to reach adequate independence. Low-level tetraplegics (C5–T1) and paraplegics without activity of the abdominal muscles (T1–T6/7) have to learn how to change positions in bed through compensatory movements (e.g., "arm swing" movement).

Paraplegics with lower lesions can turn themselves in bed with proper use of abdominal muscles.

In the early stages, it is important to prevent pressure wounds. After mobilization in the wheelchair, when the patient is back in bed, the skin has to be inspected carefully, so action can be taken very early if appropriate. Occupational therapists must be informed about every new skin lesion, and accordingly, modify the wheelchair or the seat (cushion) as well as the orthoses.

Physiotherapists and occupational therapists are involved in supporting and training for mobilization. It is important to prepare the patient for mobilization by offering mindful advice, preparing for the expected challenges (will help to reduce eventual fears), informing the patient about the steps involved in mobilization, supporting the circulation through pressure stockings and/or medication to avoid orthostatic hypotension, and using cervical collars or a corset if required.

For mobilization into an upright position (verticalization), especially in tetraplegia or in high paraplegia, it is important to gradually train the patient. Verticalization training should be at least 30 minutes every day and can be increased in a stepwise manner. Bedside verticalization is the first step in preparing the patient to sit in a wheelchair, and it is usually performed with the help of two people. If the patient can sit for at least 10 minutes without problems, a first transfer into the wheelchair can be performed (using a transfer board or a Hoyer® lift).

2.3.2.1.2 Rehabilitation of impairment

Good motor function (i.e., strength) is a prerequisite for training in activities of daily living (i.e., standing and walking). Besides individual physiotherapy—starting with passive-assistive movements and slowly increasing with active movements (first without and then with resistance) for the upper and lower extremities—the usage of training devices (specific devices for medical training therapy) and weightlifting can help to improve motor strength. For any movement, appropriate preparation of muscle tone, assessment of joint conditions (i.e., assessing for signs of joint contractures), and allowing for meaningful sensory feedback are requirements in relearning and training limb movements. Crutches, canes, and walkers can be integral tools in training for complex activities like standing and walking.

2.3.2.1.3 Rehabilitation of function

Before sitting in a wheelchair, it is important that the patient achieves enough trunk stability to allow for a controlled and safe sitting position. Optimal positioning in the wheelchair is especially important, and stability training should be performed as a first step. Being able to transfer from the bed to the wheelchair, and vice versa, is another important milestone in preparing the patient for wheelchair training. Eventually, if a patient has adequate body control and upper limb strength for a floor-wheelchair transfer, wheelchair training may be started. The patient must then learn to be as independent as possible with their wheelchair, as this is a prerequisite for later training to overcome curbs and wheeling downhill. Finally, training moves to the real world (outside of the hospital), and the SCI patient can reach independence in urban situations (e.g., tram, train, bus, etc.).

Walking training with a complete SCI becomes possible in patients with a lesion at least below the T11/12 level. In such cases, patients will have to compensate for the weakness of the lower limbs by using their arms to support their body weight. They may likely need to use two orthoses and two crutches, which would, however, put enormous strain on the shoulders.

Parallel bars or standing frames can be used in other conditions to train for standing. Training for patients with incomplete transversal paralysis begins with provisional tools: driven gait orthoses (e.g., Lokomat®; **Figure 2-1**), other various orthoses, treadmills, walkers, and special shoes and footwear. When walking, it is important to monitor the joint positions. Body weight–supported training (BWST) assists devices and therapists to dynamically support the patient's weight while they attempt locomotion on a treadmill or over ground. The therapy aims to enhance the remaining connectivity between the supralesional regions and the locomotor pattern generator in the spinal cord. BWST has been shown to improve assisted mobility and cardiorespiratory status in many patients. Furthermore, the relief of skin pressure and redistribution of blood flow help to prevent ulcers and joint-related complications of SCI.[31]

FIGURE 2-1
Driven gait orthoses (like the Lokomat) provide novel technical means to intensify training in patients with severe SCI when overground walking is not yet feasible.

2.3.2.1.4 Rehabilitation of independence

Rehabilitation of independence is an integral part of the rehabilitation program, as it defines the achieved level of outcome. While independence initially focuses on self-care issues (e.g., eating, dressing, toileting), it eventually covers areas of independent mobility, ranging from wheelchair use to independent and unsupervised walking. Eventually, independent living and living in the community require that many day-to-day activities can be achieved with either no or only limited support (technical or by caregivers). Thus, individual goals of living can be accomplished by the patients without dependence on other people for support.

2.3.2.1.5 Outcomes of independence

A patient with a complete lesion at C1–C4 has complete paralysis of the trunk, arms, and legs, and requires a mechanical ventilator, except in the case of C4 tetraplegia. Patients with C1–C2 tetraplegia may be candidates for phrenic stimulation and diaphragmatic pacing. Individuals with C4 tetraplegia may need continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) at night to assist with hypoventilation. These individuals are dependent for self-care, transfer, and bed mobility. Power wheelchairs and environmental control units (ECUs) can increase the independence of these patients (e.g., tape recorders, computers, telephones, page turners, automatic door openers, and other ECUs with mouth control [sip and puff], voice activation, chin control, head control, eyebrow control, or eye blink). However, they still require a 24-hour attendant for personal care and other homemaking tasks.

Patients with C5 tetraplegia have at least antigravity grade 3 (scale: 0–5) strength in the biceps and movement in the deltoid, rhomboid, supraspinatus, and infraspinatus muscles, but less than grade 3 movement in the wrist extensors. Movements gained include shoulder flexion, extension, and abduction; elbow flexion; forearm supination; and weak scapular adduction and abduction. There is paralysis of the trunk and legs, absence of elbow extension and pronation, and absence of all-hand movement. Patients are unable to perform independent transfers, but can operate a power wheelchair, including tilt backs, with appropriately placed controls/switches. Active elbow flexion allows for possible independent self-feeding, and with a ratchet tenodesis splint, it is possible to pinch without wrist extensors. C5 is the highest level of tetraplegia that permits driving, given specialized equipment and a wheelchair accessible vehicle. As most activities will require assistive devices, consideration may be given to tendon transfers for gross hand function once neurological recovery is considered complete.

Individuals with C6 tetraplegia have at least antigravity strength 3/5 in the radial wrist extensors (extensor carpi radialis longus and brevis). Additional muscles partially innervated include the supinator, pronator teres, clavicular head of pectoralis major, and latissimus dorsi. Movements gained include scapular abduction and radial wrist extension. With the addition of wrist extension, tenodesis grasp is possible, thereby allowing the fingers to pinch.[32]

C6 tetraplegics with at least 3/5 wrist extension may benefit from a wrist-driven flexor hinge splint (tenodesis splint) to create a three-jaw chuck pinch. In these individuals, upper-body dressing independence can be achieved, but some assistance will be required with lower-body dressing, and a hospital bed may be needed to elevate the head. Extensive training is needed for individuals with C6 tetraplegia to achieve independence for transfers. A sliding board and a trapeze over the bed may be necessary. Independent manual wheelchair propulsion is possible, but the wheelchair may require plastic-coated rims or knobs. A power wheelchair may be appropriate, especially if an individual is to return to work. With a tenodesis splint, some men can perform self-catheterization. However, they may need assistance with clothing, and are unable to apply a condom catheter. Women require continued assistance with catheterization. At the C6 level, tendon transfers can improve gross hand function. Tendon transfers of the pronator teres to the flexor digitorum profundus, the brachioradialis to the flexor pollicis longus, and the posterior deltoid to the triceps can provide finger and thumb movement and elbow extension.[33]

C7–C8 tetraplegia allows some function of the triceps, serratus anterior, pronator quadratus, extensor carpi ulnaris, flexor carpi radialis, flexor digitorum profundus and superficialis, interossei/lumbricals, and abductor pollicis. Movements gained at C7 include elbow extension of at least grade 3; scapular stabilization, protraction, and elevation; ulnar wrist extension; and wrist flexion. At the C8 level, digit flexion and extension and thumb flexion, extension, abduction, and circumduction allow for improved hand and finger function. Individuals with C7 tetraplegia will likely have enough upper extremity motor return to become independent in eating, grooming, dressing, and bathing, with appropriate assistive devices and durable medical equipment. Men are likely to achieve independent self-catheterization, but women may still require assistance, especially if leg spasticity is present. Independent transfers, weight shifts, pressure reliefs, and manual wheelchair use are feasible with extensive training. Most individuals with C7–C8 lesions have enough shoulder strength to operate a modified van with a standard steering wheel and a car with hand controls.

T1–T9 paraplegia excludes intrinsic hand muscles. The movement gained at T1 is fully functional upper limbs. With T2–T9 paraplegia, intercostal and erector spinae muscle function is added. Abdominal muscle innervation begins at T6. The recovery in traumatic sensorimotor complete SCI patients is very limited. Only patients with a low thoracic-level lesion recover some lower extremity motor scores (LEMSs), and sensory recovery is very limited. Independence is achieved in all self-care tasks, including bowel and bladder management and mobility. At lower thoracic levels, standing and ambulation are possible with bracing, but there must be adequate tolerance of vertical positioning. Standing frames, parallel bars, and bilateral leg orthoses help achieve vertical tolerance.

Individuals with T10–L1 paraplegia have fully innervated intercostals, external obliques, and rectus abdominis. With L1 paraplegia, there is also a partial innervation of the hip flexors, such as iliopsoas. Movements gained include trunk stability and improved potential for ambulation with orthoses. At L1, individuals will likely achieve household ambulation with bilateral knee-ankle-foot orthoses (KAFOs) using a four-point gait with crutches. Independence is achieved in all self-care tasks, including bowel and bladder management and wheelchair mobility.

L2–S4/5 paraplegia leaves fully intact abdominal muscles; most trunk muscles; partially to fully innervated hip flexors, extensors, abductors; knee flexors and extensors; and ankle dorsiflexors and plantar flexors. With L3 paraplegia, quadriceps and iliopsoas are fully innervated, and voluntary knee extension is improved. Ankle dorsiflexion is partially innervated at L4. Ankle plantar flexors are gained at S1. Individuals at these levels are fully independent in all self-care activities and functional mobility. Bowel and bladder management can be performed independently, but the methods are dependent upon lesion level.[34]

2.3.2.1.6 Recommendations

- Clinicians should refer patients with SCI to specialized SCI centres. **[LOE 4; GOR B]**

2.4 Management of nongenitourinary problems

2.4.1 Respiration

Respiratory complications represent the major cause of morbidity and mortality in SCI patients.[35] Complications include increased risk of pulmonary infection and death, as well as higher rates of symptoms of respiratory dysfunction. Inspiratory capacity is diminished in individuals with higher-level lesions, contributing to microatelectasis, dyspnea with exertion, and, in those with more severe impairment, respiratory insufficiency. Muscles of expiration are impaired in many individuals with SCI (e.g., injury >T8). This results in profound effects on cough effectiveness, and presumably on clearance of secretions, and in increased susceptibility to lower respiratory tract infections. In those with higher-level lesions, asthma-like disorders of airway function have been described; however, these are prevented by cholinergic antagonists. Such abnormalities have been attributed to the unopposed effects of parasympathetic innervation on respiratory smooth muscle resulting from disruption of sympathetic efferents.[36] A prospective study by Jackson and Groomes of 261 patients with acute SCI showed that the most frequent respiratory complications were atelectasis (36%), pneumonia (31%), and respiratory failure (23%). In addition, a total of 67% of the patients had respiratory complications in the acute phase.[37]

The two most important markers that predict the need for intubation are the level of the injury and the American Spinal Injury Association (ASIA) Impairment Scale (AIS) classification. Complete lesions above C5 require intubation. In these patients, elective intubation is recommended. Indications for emergent endotracheal intubation include respiratory distress, hypoxemia, and severe respiratory acidosis. Urgent intubation in patients who develop respiratory distress increases the risk of neurological damage, due to improper manipulation of the neck or hypoxia. Patients with cervical and high thoracic SCIs are at high risk of airway loss due to several factors, such as airway and neck edema or hematoma from direct trauma and local bleeding. All of these patients should be carefully observed, even if they have no immediate indication for intubation, as the progression of injury due to edema and ischemia may result in the worsening of respiratory function over minutes, hours, or days following injury. Patients with a high cervical SCI above the C5 level show the inability to maintain adequate oxygenation and ventilation as a result of the loss of diaphragmatic innervation (C3–C5 levels), as well as the loss of chest and abdominal wall strength. Patients with complete SCI above the C3 level will experience respiratory arrest in the prehospital environment as a result of absence of diaphragmatic function.

Prevention of respiratory complications must start immediately, irrespective of the level of the SCI. Secretion stagnation due to weakness of the expiratory musculature is treated with lung physiotherapy, postural drainage, suction, manual cough support, and mechanical insufflation-exsufflation. Mechanical insufflation-exsufflation employs positive pressure in the airway (insufflation) using a mechanical device (cough assist machine), and then immediately afterwards transforms this positive pressure into negative pressure (exsufflation). The high expiration flow causes secretions to be forced up into the upper airways. The cough device can be applied via a face mask or a tracheostomy tube.

Pulmonary embolism is a potentially life-threatening condition, and a significant cause of morbidity and mortality in patients with SCI, especially in cases of immobility. Diagnostic imaging of pulmonary embolism first involves a chest x-ray to rule out any conditions that mimic pulmonary embolism, including pneumonia and pneumothorax. The gold standard for imaging investigation is computed tomography pulmonary angiography (CTPA).[38] D-dimer levels may also be used to predict the likelihood of pulmonary embolism or, more generally, deep vein thrombosis development with high sensitivity and specificity. Prophylaxis is fundamental and includes anticoagulation, when there is no contraindication, and sequential compression devices.

2.4.2 Spasticity

Spasticity is a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex, as one component of the upper motor neuron syndrome.[39] Up to 80% of patients with SCI have spasticity. Of these patients, 41% report spasticity as a major obstacle to reintegration, and nearly 50%

report requiring pharmacologic treatment.[40] Spasticity often causes discomfort. Any trivial sensory stimulus may trigger painful spasms. Spasticity restricts joint motion and limits mobility. The asymmetric pull of overactive muscles can alter posture and cause deformities, such as kyphoscoliosis; flexion contractures of the elbow, hip, and knee; or equinovarus of the ankle. Untreated, spasticity leads to contractures, which are often difficult to correct. Spasticity affects positioning and pressure area care, resulting in pressure ulcers. It makes hygiene tasks, especially cleaning of hands, axillae, elbows, and genital areas, particularly difficult. Spasticity can interfere with bowel and bladder care and sexual relationships.

Treatment of spasticity is individualized, with the rational being that spasticity may not always have a negative impact on function. In some cases, it may provide some benefit. In such situations, treatment of spasticity has the potential to lead to further functional decline. The benefits of spasticity are seen in standing and gait, as well as in transfers. For instance, an ambulatory patient may find that the extensor spasm helps to control the knee flexion moment; thus, knee collapse is prevented because of the underlying weakness. Additionally, it seems that spasticity has some positive effects in regard to muscle mass, bone density, and circulation.

The most commonly used measures of spasticity with high reliability are the Ashworth Scale and Modified Ashworth Scale.[41,42] Additional clinical measures include the Penn Spasm Frequency Scale and the spasm frequency score, both of which can be used to monitor treatment efficacy.

2.4.2.1 **Treatments**

2.4.2.1.1 Stretching

Stretching remains the essential principle for management of all patients with SCI, and should form the base on which further treatments are added. Passive stretching decreases the excitability of motor neurons, and maintains the viscoelastic properties of muscles and joints. Stretching should be steady, continuous, and directional. Passive stretching activities are initially provided by a physical therapist, but the ultimate goal is education of the patient and caregivers, so the stretching activities can be performed on a daily basis. Prolonged passive standing through the use of a tilt table, standing frame, or standing wheelchair may also be used to promote stretching; however, this has been shown to at least temporarily reduce tone.[43,44]

2.4.2.1.2 Splinting and positioning

Although splinting with a device such as an ankle-foot orthosis (AFO) is most commonly used to improve function by preventing excessive plantar flexion during the gait cycle (either passive due to weakness or active due to tone), splinting may also improve spasticity and certainly reduce the risk of contracture. Proper positioning in the bed and in the wheelchair can reduce the risk of contracture and may influence the degree of spasticity. Certain postures should be avoided, like leg-scissoring posture (bilateral hip extension, adduction, and internal rotation). The affected joint can also be placed in a prolonged stretch position through serial casting, which involves placing the joint at the stretch through casting, and changing this every 5 to 7 days to achieve further stretch. Serial casting to provide prolonged stretch is often combined with botulinum toxin injection to reduce tone.

2.4.2.1.3 Physical modalities

Physical modalities used to treat spasticity include ultrasound, cryotherapy, vibration, shockwave therapy, magnetic stimulation, transcutaneous electrical nerve stimulation (TENS), and functional electrical stimulation (FES). These physical modalities work by modulating the viscoelastic properties of muscles and tendons (cryotherapy, ultrasound, and shockwave therapy), inducing long-term depression at the spinal level, stimulating cortico-cortical inhibitory pathways (magnetic stimulation), inducing short-term plasticity in injured spinal motor systems, or activating proprioceptive inputs (TENS). FES is designed to provide coordinated contraction of the muscle groups to produce purposeful movements, such as walking, usually with bracing; riding an exercise bicycle; or upper extremity activities (e.g., grasp). Although passive movements and stretching reduce spasticity, the addition of FES has been shown to be significantly more effective in patients with complete or incomplete SCI.[45,46]

2.4.2.1.4 Oral pharmacologic treatment

Oral medications are usually the first-line treatment, especially in conditions where spasticity is a generalized problem and does not involve just a specific muscle. A variety of medications from several classes can be used, but the effects need to be balanced against the potential for functional decline, reduced strength, and side effects. The list of proven medications is relatively limited at this time; however, using a single- or multiple-agent combination, an individualized regimen can usually be developed under close supervision. Inappropriate dose escalation often leads to side effects and, hence, to poor compliance. A “start low and go slow” policy limits unwanted functional effects. A combination of two agents should be tried if the spasticity does not respond to a single agent, or if the patient can only tolerate low doses. It is important to time the doses according to patient activity, care, and therapy. Ambulatory patients often require lower doses during the daytime, as they may be using spasticity to facilitate their walking. A dose may be required immediately after waking in the morning to facilitate care. The commonly used oral antispasticity drugs are those acting on the gamma-aminobutyric acid (GABA)ergic system (baclofen, gabapentin, and benzodiazepines) and the alpha-2 adrenergic system (tizanidine), and those that block calcium release into the muscles (dantrolene).

Baclofen

Baclofen is the most widely used oral antispasticity drug. The drug is a structural analog of GABA, with specific affinity for GABA B receptors. It is thought to reduce spasticity by enhancing inhibitory influences by increasing presynaptic inhibition through hyperpolarization, thus preventing the influx of calcium required for the release of neurotransmitters. Postsynaptically, baclofen likely acts by hyperpolarizing afferents. The net effect is inhibition of monosynaptic and polysynaptic spinal reflexes. With oral dosing, metabolism is 15% hepatic, with elimination primarily through the kidneys, and the half-life is approximately 3.5 hours. There are a variety of potential side effects, including sedation, drowsiness, and fatigue, which are generally the primary reason for discontinuation. Baclofen can reduce the seizure threshold, and should be used with caution in people with seizures. Stopping baclofen can provoke rebound spasticity within 48 hours, although rebound spasticity usually settles after another 48 hours. Sudden withdrawal may also cause seizures and hallucinations. Baclofen should be used with caution during pregnancy.

The usual starting dose is 5 mg thrice daily, and increased by 5 to 10 mg weekly until there is an optimal effect. The maximum dose is 90 to 120 mg/day.

Benzodiazepines

Diazepam is likely the oldest antispasticity agent still in use. Its mechanism of action is central, acting on the brainstem reticular formation and spinal polysynaptic pathways through GABA A receptors. Diazepam undergoes hepatic metabolism and is excreted through the kidneys as metabolites with a variable half-life ranging from 20 to 80 hours. The primary side effects are related to central nervous system (CNS) depression, leading to sedation and impaired cognition, attention, and coordination. Additional effects include intoxication and withdrawal, which may lead to symptoms ranging from anxiety to seizures and coma. This drug has somewhat fallen out of favour, given these adverse effects and the very long half-life, particularly in the elderly.

Clonazepam is a medication similar to diazepam, but has a shorter time of activity and is more easily discontinued. It may be used for suppression of myotonia and dystonia, and has shown some benefit in dystonia. Its half-life is also relatively long at 18 to 28 hours, but not as prolonged as that of diazepam, providing some advantage in regard to the degree of CNS depression. Clonazepam is particularly useful in the treatment of nocturnal spasms that interfere with sleep. Doses range from 0.5 to 2 mg.

Tizanidine

Tizanidine is an imidazoline derivative that acts centrally at the alpha-adrenergic receptor, both at the supratentorial and spinal levels. Its primary mechanism of action is blocking the release of excitatory amino acids (glutamate and aspartate) and facilitating glycine, which is an inhibitory neurotransmitter. Its half-life is approximately 2.5 hours, and the drug is hepatically metabolized to an inactive compound, which is subsequently cleared by renal mechanisms. Given these facts, dosing needs to be adjusted in those with hepatic failure, and this drug is a better choice in those with renal impairment, in contrast to baclofen. The most common side effects reported in clinical trials include drowsiness, sedation, and dizziness. As this drug acts at the alpha-2 receptors, hypotension is possible, especially when used in combination with other antihypertensive agents. Sudden stopping of tizanidine can lead to hyperadrenergic syndrome, characterized by anxiety, tremor, hypertension, and tachycardia. The usual starting dosage is 2 mg at bedtime, and increased by 2 mg weekly to a maximum of 36 mg, divided into three to four daily doses.

Clonidine

Clonidine can be provided in either oral or transdermal form. It acts primarily as an alpha-2 agonist, at both supraspinal and spinal sites. Its half-life is approximately 15 to 19 hours, with the drug metabolized primarily by hepatic mechanisms, but with a portion excreted renally in an active form. Dosing may thus need to be adjusted, especially in renal disease. The primary side effects are hypotension and bradycardia, both of which are concerns in SCI, given the autonomic instability. Clonidine is generally used in conjunction with either baclofen or tizanidine.

Dantrolene

Dantrolene blocks calcium release from the sarcoplasmic reticulum and interferes with excitation-contraction coupling of the skeletal muscle. Unlike other antispasticity drugs, it acts directly on the muscle and is less sedative. A major drawback of the medication is the potential for serious hepatotoxicity, with a reported overall incidence of 1.8%, of which 0.3% were fatal. This effect was more likely in women older than 30 years and those taking more than 300 mg for over 60 days.[47]

Gabapentin

Gabapentin was developed primarily as an anticonvulsant. It is commonly used as a neuromodulatory agent for neuropathic pain and may have some benefit in spasticity, but the evidence is limited. Gabapentin may be a reasonable medication to test in situations in which both neuropathic pain and spasticity are limiting, or in which it is suspected that the neuropathic pain is the primary noxious stimulus leading to increased spasticity. The side effects include weight gain, gastrointestinal disturbance, confusion, depression, hostility, and sleep disturbance. Gabapentin should start at 300 mg once daily on day 1, 300 mg twice daily on day 2, 300 mg thrice daily on day 3, and then increased according to the patient's response in steps of 300 mg every 2 to 3 days to maximum of 3,600 mg daily.

2.4.2.1.5 Local treatments

Local treatment with focal neurolysis or chemodenervation has been used as a spasticity management tool in a variety of upper motor neuron disorders. The agents generally used are phenol or, more commonly, botulinum toxin A or B. Chemodenervation has the advantage of providing local muscle relaxation without the systemic or central side effects. Botulinum toxin, in particular, is easy to administer, titratable, and reversible.

Botulinum toxin is effective in reducing tone with selected, graded weaknesses and can be used in conjunction with the previously discussed systemic treatments. The disadvantages of botulinum toxin are few, but include cost and a relatively short-lived effect of 3 to 6 months. Before considering botulinum toxin, it is important to address all trigger factors and to ensure that there are no significant contractures. The next step is for members of the multidisciplinary team to agree on the treatment goals, the target muscles, and the postinjection interventions.

Relative contraindications to botulinum toxin include fixed contractures, coexisting neuromuscular disorders, use of aminoglycosides, pregnancy, and bleeding disorders. Botulinum toxin A varieties include onabotulinumtoxinA (Botox®) and abobotulinumtoxinA (Dysport®). Botulinum toxin B is available as rimabotulinumtoxinB (Myobloc®). OnabotulinumtoxinA (Botox) dosing in individual muscles varies from as little as 10 units in small hand muscles to 200 units in large lower limb muscles.

Given the relative diffuse nature of spasticity in SCI, botulinum toxin use is more limited, but it may serve as an additional tool for very specific goals, such as reduced adductor tone to improve hygiene, gastrocnemius-soleus complex to reduce risk of contracture, and finger flexors to improve hygiene, improve cosmesis, and reduce pain. Functional gains in activities such as gait are limited, but reduction of lower extremity tone, particularly of hamstrings and ankle plantar flexors, may help improve stance, gait, and transfers. Adverse events of botulinum toxin include respiratory tract infections, muscle weakness, urinary incontinence, falls, fever, and pain, especially in children.[48]

Phenol injections may be used for motor nerve blocks or motor point blocks. The most commonly applied blocks are to the medial popliteal muscles to aid spastic foot drop, or to the obturator nerve either in patients with scissoring gait or to improve perineal hygiene and seating posture. Phenol injections should be done only under the guidance of an ultrasound scan or nerve stimulator. Nerve sprouting may lead to recurrence of spasticity. A single injection often has effects that last many months, and injection can be repeated if necessary. Phenol has the advantage of longer effect, lower cost, and better drug stability, but has the potential side effects of residual causalgia, edema, and skin sloughing. It also increases the risk of deep vein thrombosis.

Intrathecal baclofen

Intrathecal baclofen is indicated in patients with severe spasticity who are unresponsive to oral baclofen and have failed other conservative and pharmacologic therapies, and/or who experience unacceptable side effects at effective doses of oral medications.

Surgical procedures

Surgical procedures can be considered for patients who do not respond to typical physical, pharmacologic, and intrathecal options. However, these patients are quite uncommon in the adult population with spasticity of spinal origin. Laminectomy, cordectomy, and adhesiolysis can be considered, particularly the last one, when there is development of impaired cerebrospinal flow from spinal cord tethering and syringomyelia that leads to an increase in spasticity. Selective rhizotomy is commonly performed in the pediatric cerebral palsy population, but is rarely performed in adults with SCI. Many orthopedic procedures, such as lengthening (e.g., in Achilles tendon), releasing, or transferring a tendon, are helpful in optimizing function and preventing contractures. A tenotomy, the release of a tendon from a severely spastic muscle, may be performed in individuals with severe spasticity and without voluntary movement. Tendon lengthening serves to reduce the pull on spastic muscles, thereby positioning the joints at a more natural and useful angle. A tendon transfer, moving the tendon attachment to the bone closest to the muscle, is performed in muscles that have at least partial voluntary function, with the goal of allowing these muscles to produce useful movements. Osteotomy may be undertaken to correct deformity.[49,50]

2.4.3 Bowel dysfunction

Bowel dysfunction is a major physical and psychological burden for patients with SCI. Spinal cord lesions affect colorectal motility, anorectal sensation, and anal sphincter function. They can also cause neurogenic constipation. As with striated muscles, there are two distinct patterns in the clinical presentation of bowel dysfunction: injury above the conus medullaris and injury at the conus medullaris and/or cauda equina.[51] Bowel dysfunction caused by a lesion above the conus medullaris (hyperreflexic bowel) is characterized by increased colonic wall and anal tone. Voluntary (cortical) control of the external anal sphincter is disrupted, and the sphincter remains tight, thereby promoting retention of stool. The nerve connections between the spinal cord and the colon remain intact, and therefore, there is preserved reflex coordination and stool propulsion. The typical clinical presentation of bowel dysfunction is constipation and fecal retention, due, at least in part, to external anal sphincter activity. In these individuals, stool regulation occurs by reflex activity, caused by a stimulus introduced into the rectum, such as an irritant suppository or digital stimulation.

Bowel dysfunction caused by a lesion at the conus medullaris and/or cauda equine (areflexic/hyporeflexic bowel) is characterized by the loss of centrally mediated (spinal cord) peristalsis and slow stool propulsion. Clinically, it is commonly associated with constipation and a significant risk of incontinence due to the atonic external anal sphincter and lack of control over the levator ani muscle that causes the lumen of the rectum to open. Completeness of injury also has a significant impact on bowel function in individuals with SCI. Those with an incomplete injury may retain the sensation of rectal fullness and the ability to evacuate bowels, so no specific bowel program may be required. Individual variations in bowel routing prior to SCI and pre-existing conditions may also influence the pattern of bowel evacuation post injury.

It is important to underline that SCI patients usually do not perceive the normal desire for defecation, rather describing it as including abdominal distension, hardened or cool abdomen, hardening of the legs, abdominal pain, chills and dizziness, itching of the head, and pain at the sacrum level.[52]

An effective bowel management program for a person with a neurogenic bowel involves the modulation of stool consistency, promotion of stool transit through the bowel, and effective reflex or mechanical evacuation of stool from the rectum at an appropriate time and place. Such care is preemptive; bowel function is manipulated so that effective evacuation from the rectum occurs at a prespecified and predictable time, when appropriate resources, such as caregiver assistance, are available. By emptying the bowel at a chosen time, incontinence is avoided. In addition, regular emptying reduces the risk of impaction of stool due to constipation.[53]

2.4.4 Pain

Chronic pain is common in patients with neurological complications from a CNS insult such as SCI. Impaired sensory discrimination can make it challenging to differentiate central neuropathic pain from other pain types or spasticity. Some SCI-related impairments can be accommodated with compensatory strategies, whereas chronic pain, especially neuropathic pain associated with injury to the spinal cord, remains quite recalcitrant. In addition to the expected challenges in treating any chronic pain condition, SCI-related pain involves the disruption of the normal neural pathways that subserve pain transmission and attenuation. Central neuropathic pain may also begin months to years after the injury. The longest average latency in the development of central pain occurs in patients with SCI. In almost half of patients with SCI who have radiating neuropathic pain at the level of the injury (at-level pain), the pain develops within 3 months, but can present up to 5 years after SCI. The mean time to the development of at-level neuropathic pain is 1.2 years.[54] Before 2000, there was no consistent approach to the classification of SCI-related chronic pain. Three classification systems have since emerged as the leading systems based on their utility, comprehensiveness, validity, and reliability: the Cardenas SCI Pain Classification,[55] the International Association for the Study of Pain (IASP) Taxonomy,[56] and the Bryce-Ragnarsson SCI Pain Taxonomy.[57]

The International Spinal Cord Injury Pain (ISCIP) Classification has been adopted by many leading SCI and pain professional associations throughout the world.[58]

The first tier of this system comprises the nociceptive, neuropathic, other, and unknown categories. The distinction between the nociceptive and neuropathic categories is certainly approximate because the treatment approaches to these syndromes are often vastly different. As discussed later in this chapter, nociceptive pain can often be addressed by classic techniques (e.g., in musculoskeletal pain) or other medical interventions (e.g., in visceral and other nociceptive pain). This fact is in contradistinction to neuropathic pain, for which many treatment approaches are either pharmacologic or interventional. The ISCIP Classification also demonstrates the continued difficulty of even expert clinicians and scientists to categorize every single pain condition associated with SCI, as demonstrated by the other and unknown categories.

The relationship between spasticity and pain is complex. Spasticity can limit the range of motion of a joint and result in musculoskeletal pain. Reduction of spasticity may reduce biomechanical pain. It is also relevant to note that some spasticity interventions may modulate the pain transmission pathways. In addition, the sensory loss that occurs in many patients with SCI, especially those with AIS A neurological levels, may eliminate or substantially reduce the pain responses associated with noxious events. Increased spasticity may be the only harbinger of these events.[59] Common neuropathic pain descriptors include burning, uncomfortable cold, prickling, tingling, pins and needles, stabbing, shooting, lancinating, tight, swollen, and squeezing sensations that are distressing. Chronic itching in the region of the neurological deficit can also be considered a neuropathic pain equivalent. Importantly, although these descriptors suggest a neuropathic pain etiology, they are not specific to neuropathic pain and are frequently used in some common musculoskeletal pain syndromes. For example, burning is a common descriptor in both neuropathic pain and trochanteric bursitis. As a general law, below-level neuropathic pain represents central pain. At-level pain can stem from root and/or dorsal horn SCIs, and as such, represents peripheral (root) and/or central (dorsal horn) neuropathic pain.

The approach to SCI pain should commence in a manner similar to all chronic pain conditions—history, physical examination, and judicious use of diagnostic testing. Information should be obtained regarding the patient's initial SCI, including date; mechanism of injury; associated injuries, such as long bone and visceral trauma; description of vertebral column stabilization procedures; and comorbidities during the acute hospitalization and rehabilitation phases of injury. Descriptors should be attained regarding pain history, including time of onset from initial injury, time course, pain location, intensity and quantity, alleviating and aggravating factors, past evaluations, treatments (including effectiveness), and pharmacologic assessments. Inquiry into the presence or change in upper motor neuron signs, such as clonus or spasticity, is reasonable. Functional, occupational, and recreational history should be acquired for two reasons. First, these activities may contribute to the development of pain (e.g., development of shoulder pain in a wheelchair athlete). Second, the degree of pain interference with these activities will allow the clinician to judge the functional impact of the patient's pain condition. Some degree of psychological assessment is warranted, with exploration of possible depression, anxiety, personality disorder, concomitant brain injury, substance use, and cognitive impairment. In selected cases, a more formal psychological assessment, including psychometric testing, by either a psychologist or a psychiatrist may be appropriate. Furthermore, the patient should be queried as to what diagnostic tests have been previously undertaken.

Pain assessment should also include a patient self-report component, as this can supplement the information obtained during the clinical interview and provide a means of evaluating the success or failure of treatment strategies. The most commonly used measure of pain, for all types of pain, is a numerical rating scale (NRS). An NRS includes a range of numbers, generally starting from 0 (e.g. 0–10 or 0–100), anchored to descriptors (e.g., no pain at the lowest extreme of the range, and worst pain imaginable at the highest extreme). Several studies have established an NRS as a reliable measure of pain intensity.[60] Another typical measure of pain intensity is a visual analog scale (VAS). A VAS consists of a line (horizontal or vertical) anchored by two extremes, with one extreme (e.g., no pain) on one end and another extreme (e.g., worst pain imaginable) on the other end. Beyond pain intensity, it is reasonable to attempt assessment of pain according to daily activities. Of note, the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) recommended that measures of pain severity, physical functioning, and emotional functioning be included in all clinical trials of chronic pain interventions.[61] The impact of pain on physical functioning may be obtained by pain interference scales such as the Graded Chronic Pain Scale, the Brief Pain Inventory, and the Multidimensional Pain Inventory. These scales have demonstrated reasonable reliability and validity in SCI populations.[62]

Physical examination of an individual with SCI-associated pain should start with the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) neurological evaluation. This evaluation is supplemented by further neurological testing, including reflex testing, assessment of other sensory abnormalities (allodynia, hyperalgesia, and hyperpathia), and evaluation of muscle overactivity (spasms, spasticity, and clonus). Focal examination of a particular pain area would then proceed as a neuromusculoskeletal approach used for pain complaints in all populations. Items to be included are inspection, palpation, active and passive range of motion, and provocative maneuvers. Observation of wheelchair propulsion, posture, and gait may be appropriate in selected patients. Appropriate comfort and fit of assistive devices (cane, walker, and crutch) and orthotic devices should be undertaken if they seem to contribute to the pain syndrome. A survey of mood, behaviour, personality, and cognition is certainly reasonable.

Regarding diagnostic testing, above-level syndromes can be evaluated in a manner parallel to a non-SCI patient. Conditions associated with at-level and below-level lesions are more challenging. Imaging of the site of the initial spinal injury should be considered in these circumstances. Potential examples of pain generators that might be detected include segmental instability or compression at the site of injury, spinal nerve impingement, orthopedic hardware loosening, fluid collection, and syringomyelia. Discussion with the interpreting radiologist is recommended for assistance with the choice of imaging modalities. Potential discussion points could include the interference of hardware, the need for radiographic contrast (intravenous gadolinium for magnetic resonance imaging [MRI], subarachnoid ionic contrast for computed tomography [CT] myelogram, etc.), and the differentiation of acute from chronic changes. Given the possible unreliability of abdominal and pelvic examinations in a sensory-impaired patient, imaging may also be warranted if visceral pain is suspected. In addition to the traditional MRI and CT modalities, specialized techniques may be warranted for potential pain generators related to neurogenic bowel and bladder (i.e. colonoscopy, cystoscopy, urodynamic testing, etc.). Triple-phase bone scanning could be appropriate for evaluation of unsuspected fractures or complex regional pain syndrome.[63]

2.4.4.1 Treatments for Pain

The treatment of central neuropathic pain is very challenging. As a rule, pain resolution is unlikely. Like for spasticity, there are different approaches in pain management. The most used approach is pharmacologic therapy, with combination therapy consistently reported to be more efficacious than monotherapy.

2.4.4.1.1 Nonpharmacologic management

Nonpharmacologic management with a generalized exercise program in the form of global strength training, cardiovascular training, or recreational physical activities has the potential to be beneficial in several SCI-related conditions (e.g., spasticity, muscle atrophy, and bone health), but its effect on global pain in these conditions has not been greatly satisfactory. In addition to generalized and specified exercise programs, referral to physical or occupational therapy may be appropriate for patients with SCI with musculoskeletal pain, in an effort to address the biomechanical abnormalities that can be associated with mobility aids. Modification of orthotics, canes, walkers, crutches, and wheelchairs has the potential to influence detrimental ergonomics; the best example of this intervention is adjustment of the rear wheel of a manual wheelchair in an effort to modify the shoulder forces that can occur as a result of wheelchair propulsion.[64]

Acupuncture is popular in both general and SCI populations. Survey assessments have reported that between 15% and 35% of individuals with SCI have tried acupuncture for pain relief with a variable degree of effectiveness. Nayak and colleagues reported that approximately half of the patients who received 15 sessions of this modality experienced a clinically meaningful reduction in pain. This study suggested that acupuncture may be more effective in individuals with incomplete injuries or musculoskeletal pain than in those with complete injuries or neuropathic pain.[65] Obstructive sleep apnea syndrome also seems to have an impact on chronic pain. Recently, different studies have suggested the night-time CPAP as a possible solution to increase the pain threshold in normal and SCI patients.[66]

2.4.4.1.2 Pharmacologic treatments

Pregabalin remains the first choice of many physicians for pharmacologic treatment of neuropathic pain. It is a structural derivative of the inhibitory neurotransmitter GABA, which binds potently to the alpha-2/delta subunit of voltage-gated calcium channels. It is hypothesized that this binding reduces the influx of calcium into hyperexcited neurons, which, in turn, results in a reduction in the release of several neurotransmitters, including glutamate, noradrenaline, serotonin, dopamine, and substance P. The most common adverse events are mild or moderate, typically transient, somnolence and dizziness. Edema is also a reported side effect, and is more common in SCI patients. Dosing of pregabalin ranges from 150 to 600 mg/day, usually in two divided doses. It is always better to start with the lower dose and then control tolerability and adverse events before increasing the dose.

Before pregabalin release, and at present, gabapentin remains commonly used. This molecule is active at voltage-gated calcium channels. This agent has been considered effective in SCI-associated neuropathic pain in several smaller studies. The starting dose of gabapentin is 300 mg/day, and can be increased by 300-mg increments every 4 to 7 days, initially to three times daily, to a goal of 1,800 mg/day.

The use of antidepressants for below-level neuropathic SCI pain is a long-standing tradition. The substantial benefit of tricyclic antidepressants in neuropathic pain has led to this use.[67] Perhaps the most commonly used agent is amitriptyline. The initial dosage is 10 to 25 mg at bedtime with increases every 4 to 7 days to a goal of 75 to 100 mg at bedtime. Common side effects are sedation, dry mouth, orthostatic hypotension, confusion, weight gain, urinary retention, constipation, and blurred vision. Amitriptyline should be used carefully in patients with cardiac disease or history of dysrhythmia. Periodic electrocardiogram is required to reveal the presence of long QT syndrome. The most recent antidepressant additions for chronic pain are dual serotonin and norepinephrine reuptake inhibitors. Medications in this class include duloxetine, which has a US Food and Drug Administration (FDA) indication for chronic musculoskeletal pain, fibromyalgia, and diabetic neuropathy. Adverse effects are usually sedation, fatigue, nausea, hyperhidrosis, and dizziness. There is an increased risk of bleeding (use cautiously with anticoagulants) and of withdrawal syndromes with abrupt discontinuation. Duloxetine should be used with caution in patients with hepatic failure. The starting dose is 20 to 30 mg once daily, with weekly increments of the same dose to a goal of 60 mg/day.

Opioid medications have been suggested as a reasonable option for chronic nociceptive and, perhaps, neuropathic pain. In patients with SCI, concerns over the potential exacerbation of neurogenic bowel because of opioid-related constipation makes this decision even more challenging. Several developments within the opioid class of medications may be of specific interest to physiatrists treating SCI-related pain. Tapentadol is a centrally acting analgesic with a dual mechanism of action—agonist activity at the mu-opioid receptor and inhibition of norepinephrine reuptake. Another dual-acting product is tramadol, which is a combination of a mu-opioid agonist and a serotonin-noradrenaline reuptake inhibitor. This medication is noteworthy because its mechanism of action is distinct from those of other opioids. Tramadol has demonstrated benefit in osteoarthritis, fibromyalgia, and neuropathic pain; however, there is insufficient evidence to definitively consider tramadol as more effective compared with other opioids. A small RCT of patients with SCI-related neuropathic pain demonstrated a positive response to this medication.[68] There are new strategies for the management of opioid-related constipation, including peripheral opioid receptor antagonists and prokinetic agents.[69]

2.4.4.1.3 Other treatments

Given the refractory nature of central neuropathic pain states, multiple surgical interventions attempting to interrupt aberrant ascending nociceptive signaling or stimulation procedures attempting to modulate this signaling (neuromodulation) have been proposed to treat refractory central neuropathic pain. Surgical creation of destructive lesions ("lesioning") is most commonly applied to the spinal cord, and includes commissurotomy (i.e., midline myelotomy transecting the crossing fibres in the spinal cord), dorsal root entry zone lesioning, cordotomy (i.e., selective lesioning of the lateral spinothalamic tract pain pathways in the anterolateral cord contralateral to the side of pain), and cordectomy (i.e., transection of the spinal cord).[70]

2.4.5 Autonomic dysreflexia

Autonomic dysreflexia (AD) is a sudden and exaggerated autonomic response to various stimuli in patients with SCI or spinal dysfunction. It generally manifests in patients with SCI at or above T6, and is defined by an increase in systolic blood pressure >20 mmHg from baseline.[71] Furthermore, AD can have life-threatening consequences if not properly managed.[72] AD is caused by spinal reflex mechanisms that are initiated when a noxious stimulus enters the spinal cord below the level of injury. This afferent stimulus generates sympathetic overactivity leading to vasoconstriction below the neurologic lesion, along with involvement of splanchnic circulation causing vasoconstriction and hypertension. The excessive compensatory parasympathetic activity (and lack of sympathetic tone) leads to vasodilation above the level of the lesion and is thought to be responsible for headache, flushing, sweating, and nasal congestion. The reflex bradycardia is secondary to vagal stimulation. Bladder distension is the most common triggering factor for AD. The distension that can result from urinary retention or catheter blockage accounts for up to 85% of cases.[73] The second most common triggering factor for AD is bowel distension due to fecal impaction. Other potential factors include hemorrhoids and anal fissures, gastrointestinal precipitants (appendicitis, cholecystitis, etc.), pressure ulcers, ingrown toenails, fractures, heterotopic ossification, menstruation, pregnancy or labour, deep vein thrombosis, pulmonary embolism, and sexual activity. Medications, especially nasal decongestants and misoprostol, may also induce AD. Education of patients, caregivers, and family members regarding AD is vital to prevent it and to recognize its occurrence without delay.

If AD occurs, it is essential to find and eliminate the triggering stimulus (e.g., bladder distension or bowel impaction). Initial management also involves placing the patient in an upright position to take advantage of any orthostatic reduction in blood pressure, and loosening tight clothing and/or constrictive devices. Blood pressure should be monitored until the patient is stable. These steps will resolve the problem in most patients, but in some, pharmacotherapy (in general, antihypertensive agents that have a rapid onset and short duration of action) may become necessary.

2.4.5.1 **Treatment of AD**

2.4.5.1.1 Nitrates and nifedipine

In general, nitrates are the most commonly used therapeutics to lower blood pressure because they have a direct relaxant effect on vascular smooth muscles, leading to dilation of coronary vessels and peripheral veins. The topical application of 1 to 2 inches of 2% nitroglycerine (nitropaste) above the level of the lesion is effective, and can be removed when the hypertensive crisis subsides.[74] Alternatively, nifedipine is a dihydropyridine, L-type, voltage-sensitive calcium channel blocker. When it is administered in immediate-release form (10-mg capsules), it exerts coronary and peripheral vasodilator properties.[75] Although nifedipine significantly decreases resting mean arterial blood pressure in patients with SCI, and prevents dangerous blood pressure elevations during cystometry-evoked dysreflexic hypertension, there is a lack of well-controlled clinical trials on nifedipine use for the management of AD. If such antihypertensive compounds do not alleviate symptoms, then intravenous administration of sodium nitroprusside is indicated for rapid titration of blood pressure. Alpha-adrenergic receptor blocking agents (e.g., terazosin, a specific alpha-1 adrenergic antagonist) appear to prevent serious harm from AD. They are also efficacious in the first week of treatment in normotensive SCI patients with AD. Another alpha 1-adrenergic antagonist, prazosin (3 mg twice a day, given for 2 weeks), has been reported to reduce both the severity and duration of AD episodes in cervical and high thoracic SCI individuals. Prazosin is also well tolerated; however, it does not significantly lower resting blood pressure, yet it does reduce the severity of headaches.

2.4.6 Pressure ulcers

Pressure ulcers are a constant and costly problem in patients with SCI, typically resulting from partial or complete lack of control and sensation in sitting contact areas, as well as from varying degrees of incontinence. These factors lead to extended periods of immobility that may result in excessive tissue pressure and, ultimately, necrosis. Up to 95% of individuals with SCI will develop pressure ulcers in their lifetime.[76] Although preventable in most situations, pressure ulcers may disrupt rehabilitation, prevent individuals with SCI from working or attending school, and interfere with community reintegration.[77]

Tissue injury is related to both extrinsic and intrinsic factors. Extrinsic factors include pressure, shear, friction, immobility, and moisture due to urinary and fecal incontinence. Intrinsic factors relate to the condition of the patient, such as sepsis, local infection, decreased autonomic control, altered level of consciousness, older age, vascular occlusive disease, anemia, malnutrition, sensory loss, spasticity, contractures, smoking, and poor nutrition.[82]

In the immobilized patient, the most susceptible areas, in decreasing frequency, are the sacrum, trochanter, heels, scapula, coccyx, and posterior part of the middle thigh. In the mobilized patient, the most susceptible areas, in decreasing frequency, are the ischial tuberosity and the sacrum. Pressure ulcers occur when external pressure exceeds capillary pressure (12–32 mmHg), and ischemia of tissue begins to display a spectrum of injury patterns. The pathological sequelae of anoxia, ischemia, and necrosis can be reversed at the ischemic stage if the factors causing injury are identified and removed. It is also important to note that muscle is more susceptible to ischemia than skin, and fat has less tensile strength than skin, which explains the "tip-of-the-iceberg" phenomenon—when unimpressive skin changes can mask a significant, deep wound down to bone.[82]

Relieving skin pressure over a bony prominence for 5 minutes every 2 hours will allow adequate perfusion and prevent tissue breakdown,[78] emphasizing the relevance of regular patient repositioning.[82]

The most commonly used staging system for pressure ulcers was proposed in 1989 and updated in 2007 by the National Pressure Ulcer Advisory Panel (NPUAP) using a consensus conference model.[79]

- Stage I is defined as "intact skin with non-blanchable redness of a localized area usually over a bony prominence. Darkly pigmented skin may not have visible blanching; its color may differ from the surrounding area."
- Stage II is defined as "partial thickness loss of dermis presenting as a shallow open ulcer with a red pink wound bed, without slough. May also present as an intact or open/ruptured serum-filled blister."
- Stage III is defined as "full thickness tissue loss. Subcutaneous fat may be visible but bone, tendon or muscle is not exposed. Slough may be present but does not obscure the depth of the tissue loss. May include undermining and tunneling."
- Stage IV is defined as "full thickness tissue loss with exposed bone, tendon or muscle. Slough or eschar may be present on some parts of the wound bed. Often include undermining and tunneling."
- Unstageable is defined as "full thickness tissue loss in which the base of the ulcer is covered by slough (yellow, tan, gray, green or brown) and/or eschar (tan, brown or black) in the wound bed."

Recognizing that the terms unclassified/unstageable and deep tissue injury are generally graded as stage IV in Europe, the NPUAP has agreed to put them separately.

2.4.6.1 Treatment of pressure ulcers

2.4.6.1.1 Prevention

Prevention represents the first step in the management of pressure ulcers. Good positioning of the patient in the bed and/or wheelchair can make a difference. Prevention of pressure ulcers begins at the time of injury, and is a lifelong commitment for those living with SCI and/or their caregivers. Prevention recommendations include:[80]

- Examining skin daily to allow for early detection
- Minimizing moisture and incontinence
- Keeping skin clean and dry
- Having an individually prescribed wheelchair with a pressure redistribution cushion and regular pressure relief
- Ensuring that all equipment is functioning properly
- Decreasing or stopping smoking
- Limiting alcohol consumption, and eating a well-balanced, nutritionally complete diet, which includes monitoring of weight to detect undesirable trends.

Pressure relief should ideally be performed every 15 to 30 minutes for 30 to 120 seconds, depending on the technique.[81] Pressure relief is also the standard conservative treatment for a nonhealing pressure ulcer and has to be patient-tailored.

2.4.6.1.2 Dressing

Dressing of pressure ulcers can be characterized as passive action or active action, depending on the wound. The passive dressings vary widely:

- Transparent adhesive dressings are semipermeable, nonabsorptive, and occlusive. They allow gaseous exchange and transfer of water vapour from the skin to prevent maceration. They do not work well on wounds with excessive exudates.
- Hydrocolloid wafer dressings contain hydroactive particles that interact with wound exudates to form a gel. They provide absorption of minimal to moderate amounts of exudate and keep the wound surface moist.
- Gel dressings keep the surface of the wound moist as long as the gel does not dehydrate and provide atraumatic removal.
- Calcium alginate dressings are derived from brown seaweed and are semiocclusive, highly absorbent, natural, and sterile.

Finally, the active dressings have similar indications for moderate-to-heavy exudate wounds and have antimicrobial properties (e.g., dressings impregnated with silver) or collagen scaffold properties.[82]

2.4.6.1.3 Nutrition

Nutrition is essential for wound healing, and appropriate intake of proteins (1.25–1.5 g/kg) and nonproteins (30–35 kcal/kg) should be ensured. Clinicians and patients should be reminded that for surgical patients, the surgery itself will often depress the initial trend of nutritional parameters during the acute phase reaction following the procedure (7 days), but recovery is expected with adequate nutritional support.[82]

2.4.6.1.4 Negative-pressure wound therapy

In 1997, the plastic surgeons Dr. Louis Argenta and Dr. Michael Morykwas from the Wake Forest School of Medicine presented their 9 years of experimental and clinical experience using the vacuum-assisted wound closure device in a variety of chronic, subacute, and acute wounds, demonstrating enhanced granulation tissue and successful wound closure using this new technology.[82,83] Since then, negative-pressure wound therapy (NPWT) has become an important tool in the management of a wide spectrum of wounds. The vacuum-regulation device provides continuous or intermittent, controlled negative pressure to the wound through an airtight dressing, which is changed every second or third day. The use of NPWT has been described in chronic wounds, including pressure sores. The therapy is particularly beneficial in patients who are poor surgical candidates, require significant care, have failed previous operations, or develop areas of wound dehiscence following surgery.[82,84]

There are special considerations for using NPWT in patients with SCI. First, it is contraindicated to use NPWT in wounds with exposed vital structures, thick exudates, necrotic material, or significant purulence that would render therapy ineffective or lead to bleeding complications.[82,85]

Second, NPWT foam can irritate normal skin, and proper application in patients with SCI can be challenging. In some areas, it may be difficult to achieve an adequate seal due to fragile skin integrity. Finally, the application of the NPWT device in patients with SCI must be carefully monitored, so the device's foam and tubing do not generate any new pressure points on healthy skin that can lead to new ulcers. Despite these considerations, NPWT has been a revolutionary contribution to the wound care field and will continue to be an important option in pressure ulcer management, particularly as it simplifies chronic wound management in the aging population and is an outpatient treatment option.[82,86]

2.4.6.1.5 Electrical stimulation

Electrical stimulation has been used to enhance wound healing for more than 50 years. It has been postulated that electrical current attracts fibroblasts and macrophages, improves wound microcirculation by directly stimulating local cutaneous nerves, and orients and affects mesenchymal stem cell migration.[82,87,88] In 1996, Baker *et al.* reported their experience in identifying a biphasic waveform of electrical current as the optimal wound-healing protocol among 185 pressure ulcers in 80 patients with SCI who were treated for 45 minutes/day for 4 weeks. Based on these studies, the use of electrical stimulation as an adjunct to local wound care can be used in both the inpatient and outpatient settings, and is particularly helpful in accelerating the healing of small wound dehiscences that can develop in high-risk postsurgical patients.[82,89]

2.4.6.1.6 Treatment/prevention of infection and osteomyelitis

It is imperative that before a pressure ulcer is closed, the presence of infection has been investigated and eliminated. The removal of all nonviable tissue is the essential first step. After soft-tissue debridement, a specimen should be sent to the microbiology laboratory to assess not only for bacterial types and sensitivities, but also for quantitative culture. A result of more than 105 organisms per gram of tissue is diagnostic evidence of invasive infection and is predictive of failure of surgical closure. The most common organisms isolated from pressure ulcers are *Proteus mirabilis*, *Streptococcus* species (i.e., group D streptococci), *Escherichia coli*, *Staphylococcus* species, *Pseudomonas* species, and *Corynebacterium* organisms.[82,90] It is advisable to include an infectious disease specialist in the treatment of the often complex, multifactorial, multisource, and polymicrobial infections that occur in patients with SCI. Regarding the diagnosis of osteomyelitis, the first and easiest step is plain radiography, which can be confirmatory but is not very sensitive. Nuclear scintigraphy has a high false-positive rate and is therefore not very helpful. MRI has been found to have higher sensitivity and specificity rates.[91] The gold standard for the diagnosis of osteomyelitis remains the bone biopsy. The standard of care is the administration of intravenous antibiotics for 6 to 12 weeks if bone culture and sensitivity are positive for acute osteomyelitis with bacterial colonization.[82]

2.4.6.1.7 Surgical management

Surgical management of pressure ulcers involves a spectrum of options: simple debridement with direct closure, skin grafting, fasciocutaneous flaps, myocutaneous flaps, combination proximal femoral osteotomy and flap reconstruction (Girdlestone procedure), or end-stage lower extremity disarticulation and total thigh flap. There are several advantages to surgical closure of a pressure ulcer with muscle flaps in SCI, including definitive wound debridement with skin and soft-tissue coverage, elimination of dead space, improved vascularity, improved healing from underlying osteomyelitis, improved penetration of antibiotics, and restoration of resilient tissue to resist shearing, friction, and pressure. A comprehensive reconstruction will allow the patient to regain the activities of daily living more efficiently.[82]

Both musculocutaneous and fasciocutaneous flaps have their advantages. Flaps that include muscle have significant bulk and excellent blood supply. They, therefore, can be useful when a significant soft-tissue defect is present and when a history of infection is a consideration. On the downside, muscle is susceptible to ischemic injury and is not a good choice in ambulatory patients, as sacrificing muscle may lead to functional impairments. Fasciocutaneous flaps are durable, maintain a good blood supply (especially if they are axial in design), are closer to the normal anatomical tissue arrangement, and are less susceptible to ischemia. Thus, they are especially useful in wounds of limited depth, as are many in the sacral area. However, they become less useful if significant filling of dead space is required. Most flap coverage strategies use pedicled flaps. Common donors are the latissimus dorsi and serratus anterior muscles, and fillet flaps taken from an amputated lower extremity. In many cases, the gluteal vessels are used as the recipients.

The choice of flap reconstruction depends on the anatomical location of the pressure ulcer, and several options exist for the most common sacral, coccygeal, ischial, and trochanteric ulcers.[82,92]

In a recent systematic review, there was no statistically significant differences in complication and recurrence rates between musculocutaneous, fasciocutaneous, and perforator-based flaps for the treatment of pressure ulcers.[93,94]

2.4.7 Recommendations

- Clinicians must employ contemporary guidelines to manage pain in the SCI patient. **[LOE 1; GOR A]**

- Clinicians should employ methods to reduce the risk of pressure ulcers in the SCI patient. **[LOE 3; GOR B]**

- Clinicians must apply compression devices to prevent venous thromboembolism after SCI. **[LOE 1; GOR A]**

- Clinicians must begin low-molecular-weight heparin/unfractionated heparin immediately after SCI, when there is no contraindication. **[LOE 1; GOR A]**

2.5 Neuro-urological Management After Acute SCI

2.5.1 Assessment

2.5.1.1 Introduction

The urological evaluation of patients with SCI requires an understanding of the functional changes that occur in the urinary tract with spinal cord damage and the time frame in which these changes occur. It is also important to have some understanding of the potential for bladder recovery, as this may dictate the neuro-urological management.[95]

The initial phase following acute SCI is that of spinal shock.[96] In addition to the effects on skeletal muscle, spinal shock may result in an acontractile/hypocontractile detrusor. However, there is no generally accepted definition of spinal shock since there are no high-level evidence studies on this issue. The duration of spinal shock varies widely, from several days to several months. It is not an "all or nothing" entity, but depends on the extension and completeness of the spinal lesion. Nevertheless, Ditunno *et al.*[97] have proposed a spinal shock model, which is very helpful in understanding this phenomenon. It includes an initial phase of loss of reflexes and three subsequent recovery phases.[97]

Patients with injury at or above the T6 spinal cord level can develop AD. Recognition of dysreflexia is crucial as it can result in life-threatening sequelae.[98–100] From a urological perspective, this can be triggered by urinary tract infection, urinary retention, constipation, lower urinary tract intervention, and bowel or sexual activity.

During the initial evaluation of the SCI patient, it is important to consider the overall goals of management: (1) to achieve low-pressure storage of urine and efficient bladder emptying; (2) to achieve (social) continence, which is crucial to the patient being reintegrated into the community; (3) to minimize the risk of developing complications, including urinary tract infection, urethral stricture disease, calculus disease, hydronephrosis, and renal failure.[98]

2.5.1.2 History

In order to establish a patient's understanding of the long-term outcome, their potential for recovery, and counseling in regard to bladder function and management, it is ideal to see them in the early phase of injury. In the future, early intervention such as neuromodulation, may prevent the development of high-pressure overactive bladders.[101] This, however, is currently investigational.

Key information required when first assessing an SCI patient includes the mechanism of injury, the level of injury, and the completeness of injury. In addition, a standard urological history should be obtained, but the relevance of this information will be dependent on when the patient is seen in the timeline following SCI and the completeness of injury. Clinicians must ensure appropriate bladder emptying immediately after SCI. Initially, the patient may have an indwelling catheter or use intermittent catheterization (performed either by staff or by themselves). Important information includes the presence of potential red flags, such as symptoms of infection, hematuria, abdominal pain, and fever. History of bowel and sexual function should also be included in the urological evaluation.

Past urological history is relevant, especially if previous surgery has been undertaken, such as a transurethral resection of the prostate. In this situation, the loss of the bladder neck sphincter can result in urinary stress incontinence in a patient with a lumbar, sacral, or peripheral lesion.

Comorbidities that may influence management need to be elicited. This may include coexistent neurological diseases (e.g., Parkinson disease, traumatic brain injury, or dementia), which would potentially limit management options. Conditions such as narrow-angle glaucoma, uncontrolled hypertension, and cardiac arrhythmia may be relevant when considering medical therapy.

Current medications also need to be considered, especially with respect to interactions with either antimuscarinics or beta-3 agonists, both of which may be utilized in this cohort of patients. Certain medications can result in additive voiding dysfunction (e.g., opiates or agents with antimuscarinic properties, such as antidepressants and antipsychotics).[99]

Finally, an understanding of the social situation is crucial to the successful implementation of lower urinary tract management. This includes an understanding of the patient's cultural background and beliefs. It also includes knowledge of their usual lifestyle. The intake of alcohol and addictive drugs needs to be included in this discussion. In some circumstances, it may not be possible to change behaviours, despite SCI. An example is patients who regularly binge drink to the point of inebriation. Such patients may not be suitable for intermittent self-catheterization, nor would they be good candidates for bladder augmentation.

2.5.1.3 Questionnaires

Validated questionnaires are available for use in clinical assessment and research of patients with neurogenic lower urinary tract dysfunction secondary to SCI. The utilization of outside research is not mandated, but provides consistency in evaluating patients and monitoring progress. Validated questionnaires for the neurological population include the SF-Qualiveen, the Qualiveen, the neurogenic bladder symptom score, and the Incontinence Quality of Life (I-QOL).[102]

2.5.1.4 Examination

General physical examination of the patient with particular attention to body habitus, such as obesity, should be noted, as it could affect the ability to self-catheterize or the placement of a suprapubic catheter.

In addition to a standard urological examination, it is useful to complete a focused neurological assessment of the urogenital region. Included in this are anal tone, perianal sensation, and bulbocavernosus reflex. The interpretation needs to be done in conjunction with an understanding of time post injury and level of injury.

The bulbocavernosus reflex assesses the S2–S4 nerve roots and is a spinal cord–mediated reflex. It is assessed by feeling for anal sphincter contraction while squeezing the clitoris or glans penis. In the presence of a cervical or thoracic injury, absence of the bulbocavernosus reflex suggests the presence of spinal shock. Conversely, the presence of the reflex indicates the period of spinal shock is over. This has prognostic value, as absence of sensation or movement below the level of injury with presence of the bulbocavernosus reflex indicates a complete SCI and poorer prognosis. If the injury is lumbar, absence of the reflex may indicate a conus and/or cauda equina injury.

2.5.1.5 Bladder diary

The value of the bladder diary in the SCI cohort is not well studied, but it is highly recommended.[100] It aids in the management of patients, both in establishing a program of self-catheterization and as a monitoring tool, especially in those who may have ongoing urinary leakage after initial management.

2.5.1.6 Laboratory tests

Both dipstick urine analysis and formal microscopy and culture are important for the exclusion of urinary tract infection. The difference between asymptomatic bacteriuria and urinary tract infection is highly relevant. Asymptomatic bacteriuria must not be treated. Thus, routine urine testing is not recommended, unless patients are symptomatic, in an attempt to avoid overtreatment and subsequent development of resistant bacteria.

Renal function testing by way of serum creatinine and calculated glomerular filtration rate (GFR) is useful in the initial evaluation and for long-term monitoring. However, it must be recognized that changes in serum values may occur much later than anatomical changes, such as hydronephrosis, and testing will not detect mild renal dysfunction. Therefore, this cannot be used as an alternative to upper tract imaging. Creatinine clearance is more accurate, but is not routinely used due to the requirement to collect 24 hours of urine.

2.5.1.7 **Imaging**

Imaging is an essential part of long-term surveillance of patients with neurogenic lower urinary tract dysfunction.[103] The timing of the initial imaging assessment is not well established, but consensus is that it should occur within 3 months following SCI.[100,104] Its primary use is for evaluating if there is the presence of complications from neurogenic lower urinary tract dysfunction, such as hydronephrosis, renal stones, and bladder stone formation.

The modality used must avoid unnecessary radiation exposure, as imaging should be utilized repeatedly for long-term surveillance. It should be noninvasive, yet relatively accurate in providing the desired information. The most commonly utilized modality now is ultrasound.

The presence or absence of vesicoureteral reflux can be picked up on videourodynamics, which is also an essential part of the evaluation and monitoring of patients with SCI.[100]

Other imaging modalities such as abdominal CT/magnetic resonance (MR) and/or CT/MR urography or nuclear medicine renal scan may be used if an abnormality is picked up on routine ultrasound imaging.[104]

Noncontrast renal CT is useful for accurate delineation of renal stones and exclusion of ureteric stones in the event that unilateral hydronephrosis is identified, with or without loin pain. CT/MR urogram is utilized for detailed imaging of the collecting system in a patient with hematuria and may be used as a functional test in the presence of presumed obstruction.

Nuclear medicine renal scan can be utilized to assess renal function as well as confirm the presence of obstruction.

2.5.1.8 **Cystoscopic evaluation**

The benefit of routine urethrocystoscopy in the acute SCI patient is not proven.[105] However, it is mandatory if there is suspicion of other pathologies, such as bladder tumour, bladder calculus, urethral stricture, etc. In this situation, patients may have had hematuria, recurrent or persistent urinary tract infection, or difficulty with catheterization. The main concern is development of bladder cancer. Although the prevalence may be slightly higher in the SCI cohort, it does not necessarily justify routine urethrocystoscopy in patients with acute SCI.[106]

2.5.1.9 Recommendations

- Clinicians must ensure appropriate bladder emptying immediately after SCI. **[LOE 3; GOR A]**

- Clinicians must perform an initial neuro-urological assessment within the first 3 months after SCI. **[LOE 3; GOR A]**

- Initial neuro-urological assessment should include history, validated questionnaires, bladder diary, physical examination, measurement of renal function, and urinary tract imaging. Urodynamics should be performed after the resolution of spinal shock. **[LOE 4; GOR B]**

2.5.2 Urodynamic investigation

2.5.2.1 Introduction

Urodynamic investigation (UDI) is the gold standard to evaluate lower urinary tract function in patients with SCI.[100] UDI allows for patient-tailored management, and regular follow-up with UDI seems beneficial.[107] Remarkably, ambulatory and nonambulatory patients with acute SCI have a similar risk for unfavourable urodynamic measures. Therefore, complete neuro-urological assessment including UDI is strongly recommended in all acute SCI patients, regardless of the ability to walk.[108] Same session repeat UDIs are crucial in clinical decision-making since repeat measurements may yield completely different results.[109] Any technical source of artefacts must be critically considered, and all urodynamic findings have to be reported in detail:

- Maximum storage detrusor pressure (Pdet)
- Bladder compliance
- First sensation of bladder filling
- First and strong desire to void
- Urgency
- Urinary leakage or maximum cystometric capacity (reflects the storage phase and maximum flow rate)
- Voided volume
- Voiding time or average flow rate (mirrors the voiding phase)
- Pelvic floor electromyography (EMG; assesses both the storage and voiding phases)

Urodynamic parameters, in combination with the bladder diary and the medical history, allow for diagnosis and treatment. Special attention should be given to appropriate standardization of the urodynamic technique since this is the prerequisite for reproducible and reliable results. Hence, UDI has to be performed and reported in accordance with the standards of the International Continence Society (ICS).[110,111]

2.5.2.2 Cystometry and pressure-flow studies

Cystometry (cystomanometry) is performed to assess the storage (filling) phase. A double-lumen transurethral or suprapubic (6–10 French) catheter (the catheter lubricant should be without anesthetic additive to avoid an impact on bladder sensation) is used. The bladder has to be emptied with intermittent catheterization before each UDI. A physiological filling rate (ideally, should not exceed body weight in kilograms divided by four)[111] should be used. The fill medium can be physiological saline, or a mixture of a contrast medium and saline at body temperature. A fast fill rate, nonphysiological ion concentrations, and low temperature of the filling fluid may all negatively affect urodynamic results.[100] During filling, provocation tests, including coughing, change of position from supine or sitting to standing, or handwashing, can be used to demonstrate inducible detrusor overactivity, urgency or stress, and urinary incontinence.

It is highly recommended to repeat UDI at least once since repeat measurements may yield completely different results.[109] Ice water testing can be used to test for temperature-sensitive reflex detrusor contraction mediated by afferent C fibres. Detrusor overactivity may be demonstrated, even if there is no detrusor activity in the standard UDI, thereby helping to unmask a putatively acontractile detrusor. Since the ice water test is a nonphysiological investigation that may relevantly bias subsequent UDIs, it should be performed at the end of, and not precede, more physiological standard UDIs.[112] Bladder sensation during UDI is assessed on the basis of the volume in the bladder at the patient's first sensation of bladder filling, first desire to void, and strong desire to void. Urgency is defined as the sudden, compelling desire to void.[110]

A pressure-flow study is performed to assess the voiding (emptying) phase, and reflects the coordination between the detrusor and urethra/pelvic floor during micturition. Possible pathological findings include detrusor external acontractility/hypocontractility and bladder outlet obstruction, including detrusor external sphincter dyssynergia (DESD) and postvoid residual. It has to be considered that many patients with SCI will not be able to void spontaneously; that is, maximum cystometric capacity and postvoid residual will be identical.

2.5.2.3 **Surface electromyography**

EMG of the pelvic floor, including urethral and anal sphincter activity, is an established method for the diagnosis of bladder sphincter dysfunctions. Pelvic floor EMG and videourodynamics are the most acceptable and widely agreed upon methods for diagnosing DSD, and they are superior to external urethral sphincter pressure measurement.[113] The pelvic floor EMG is usually simultaneously measured with cystometry. Surface electrodes should be placed ventral and close to the anus. The EMG amplitude is measured in millivolts and provides a simple semiquantitative tracing of the muscle activity over time. After changing the positions of the electrodes (e.g., UDI at a follow-up visit), the amplitudes of the different EMG measurements cannot be compared because of the different electrode impedances and the different muscle masses. However, the shape of the tracing remains the same, and thus is comparable. Surface electrodes are therefore highly vulnerable to artefacts, and the signal should be monitored throughout the measurements (e.g., by zoom tracing on the tracking software, oscilloscope, or audio signal). Urine leakage (especially in the supine position) can lead to misinterpretation of EMG findings, as fluid contact with the surface electrodes may mimic DSD (defined by the ICS as a detrusor contraction concurrent with an involuntary contraction of the urethral and/or periurethral striated muscles).[110]

2.5.2.4 **Videourodynamics**

Videourodynamics is the combination of cystometry and pressure-flow study (when spontaneous voiding is possible) with imaging. It is the gold standard for UDI in neuro-urological disorders,[100] especially in patients with SCI. If videourodynamics is not available, then cystometry continuing into a pressure-flow study should be performed with cystography. Videourodynamics can detect vesicoureteral reflux, bladder trabeculation, pseudodiverticula, diverticula, detrusor internal sphincter dyssynergia (bladder neck dyssynergia), detrusor external sphincter dyssynergia, and reflux into the seminal vesicles and prostate. However, ionizing radiation should be kept to a minimum according to the as low as reasonably achievable (ALARA) principle.

2.5.2.5 **Safety**

The main risks of UDI are associated with urethral catheterization. If the patient's sensation is preserved, dysuria is quite common in the first days following UDI. Patients with impaired bladder and urethral sensation are at risk for more severe complications since catheterization problems may not be recognized promptly due to impaired urogenital sensation.

Prophylactic antibiotics reduce the risk of bacteriuria, but not of urinary tract infection after UDI.[114] Thus, antibiotic prophylaxis is not generally recommended, especially when taking into account the alarming prevalence of antibiotic resistance worldwide.

A relevant issue in SCI patients, particularly in those with a lesion at or above T6, is UDI-induced AD;[115] overall incidence is up to 73%.[116] Thus, if available, continuous cardiovascular monitoring during UDI is strongly recommended. In the case of AD during examination, stopping UDI and immediate emptying of the bladder is mandatory to avoid a life-threating situation, and further treatment (e.g., with nifedipine) may be necessary.[100,116]

A history of potential allergies is important, especially considering the allergic potential of latex gloves, catheters, and contrast media.

2.5.2.6 **Description of urodynamic findings**

UDI measures the parameters of the storage (filling) and voiding (emptying) phases. Filling rate, temperature, different sensation qualities, urological medications, former treatments, and position of the patient during examination have to be reported. Considering the urodynamic tracings and all previously mentioned observations/values, a urodynamic diagnosis can be established, consisting of bladder sensation, bladder capacity (low: approximately <350 mL; normal: approximately 350–550 mL; high: approximately >550 mL), bladder compliance (low: <20 mL/cm H_2O; normal: >20 mL/cm H_2O), detrusor function, and sphincter function (see **Table 2-1**).

TABLE 2-1 Urodynamic Characteristics and Findings[110]

Urodynamic Observations	
Pves (cm H_2O)	
Pabd (cm H_2O)	
Pdet (cm H_2O)	
Filling rate (mL/min)	
Bladder sensation (first sensation of bladder filling, first desire to void, strong desire to void; normal, increased, reduced, absent, nonspecific bladder sensation, bladder pain, urgency)	
Storage	**Voiding**
Maximum cystometric capacity (mL)	Voided volume (mL)
Bladder compliance (volume change divided by the change in Pdet [mL/cm H_2O])	Voiding time (s)
Abdominal leak point pressure (cm H_2O)	Maximum flow rate (mL/s)
Detrusor leak point pressure (cm H_2O)	Average flow rate (mL/s)
Maximum Pdet during storage phase (cm H_2O)	Maximum Pdet during voiding phase (cm H_2O)
	Maximum Pdet at maximum flow rate (cm H_2O)
	Postvoid residual (mL)
Urodynamic Diagnosis	
Detrusor function	**Outlet/urethral function**
Normal detrusor function	Normal urethral function
Detrusor overactivity	Abnormal urethral function
▪ Phasic detrusor overactivity	▪ Bladder outlet obstruction
▪ Terminal detrusor overactivity	▪ Detrusor sphincter dyssynergia
▪ Detrusor overactivity incontinence	▪ Nonrelaxing urethral sphincter obstruction
Acontractile/hypocontractile (underactive) detrusor	
Bladder compliance (low, normal)	
Bladder capacity (low, normal, high)	
Stress urinary incontinence	

Abbreviations: Pabd: abdominal pressure; Pdet: detrusor pressure; Pves: intravesical pressure.

2.5.2.7 Indication for urodynamics in SCI patients

It is important to note that early UDI may be useful, even in patients with incomplete SCI who have preserved/recovered significant function, as early treatment (if indicated) may improve long-term outcomes. Indeed, patients who are ambulatory after SCI also have high-risk urodynamic changes on UDI.[108,117] Thus, the first UDI should be performed within 3 months of SCI. In patients with unfavourable urodynamic parameters[108] (i.e., high maximum Pdet during the storage phase [>40 cm H_2O],[118] low-compliance bladder [<20 mL/cm H_2O],[119] detrusor overactivity, DSD, and vesicoureteral reflux), follow-up UDI should be considered 1 to 3 months after initiation of treatment (e.g., antimuscarinics, intradetrusor onabotulinumtoxinA injections, etc.) to assess the treatment effects.

2.5.2.8 Troubleshooting and good urodynamic practice

Abdominal, rectal, and/or detrusor contractions can increase intravesical pressure (Pves) in a similar way. Thus, to improve quality and reliability of urodynamic assessments, it is essential to monitor both the Pves and the abdominal pressure (Pabd), which are used to calculate the Pdet (Pves – Pabd = Pdet). Pressure changes of the detrusor are smooth, whereas artefacts from Pabd are usually sharp; this occurs as a consequence of the sudden pressure increase from coughing, which is used to check for proper pressure transmission and should be frequently repeated (if the SCI patient is able to cough).[120] Initial Pabd and Pves should be in an expected range, and initial Pdet should be close to zero. Resting values are vulnerable to patient position changes. Fast filling can mimic a low-compliance bladder; hence, use physiological speed and stick to the formula for calculation of filling speed.[111]

Other common problems are a negative Pdet,[111] potentially due to the one of following:

- Too high Pabd: Consider gently repositioning the rectal balloon or draining some of the rectal balloon filling.
- Too low Pves: First check for potential air bubbles trapped in the catheter, or catheter may be kinked and blocked. Test by slow flushing of the catheter, or by repositioning the catheter.
- Too high initial Pdet: As normal empty Pdet is between 0 and 5 cm H_2O, any value higher than 10 cm H_2O needs to be checked.[111] Thus, check if Pves and Pabd are in the expected range, the zero balance, and the proper signal response to coughing:
  - If Pabd is too low, very slowly flush the rectal balloon with 1 to 2 mL.
  - If Pabd is too high, repeat the same procedure as explained above.
  - If Pves is too high, check catheter placement and for kinking. The solution may be catheter repositioning or slowly flushing the catheter.

2.5.2.9 Recommendations

- For UDI, if available, videourodynamics must be performed to detect and specify lower urinary tract function and dysfunction after the resolution of spinal shock. **[LOE 1; GOR A]**

2.5.3 Initial urological management

SCIs are often associated with severe concurrent head, thoracoabdominal, and skeletal injuries that require urgent management.[121] The SCI, any associated injuries, and cardiovascular stabilization are the primary priority. As such, the bladder is usually managed with an indwelling urethral catheter at the time of presentation to the emergency department.[121] Even in the absence of serious concurrent injuries, spontaneous voiding is often not possible due to the neurological injury, and catheterization is required to decompress the acontractile/hypocontractile bladder.

Acute presentation of a complete SCI can also be accompanied by priapism in the hours following injury.[122] This is generally high-flow priapism, which results from unopposed parasympathetic input, which increases penile arterial flow. It is also usually associated with a worse prognosis for neurological recovery, and generally can be managed conservatively. Spontaneous resolution is seen in most cases within 6 to 24 hours. Urethral catheterization can still be carried out in the presence of priapism.

Based on data from the 1,250 SCI patients included in the European Multicenter Study about Spinal Cord Injury (EMSCI; www.emsci.org), two models have been derived and validated to predict urinary continence and complete bladder emptying 1 year after injury.[95] The full model is based on the LEMS, light-touch sensation in the S3 dermatome, and Spinal Cord Independence Measure (SCIM) subscale respiration and sphincter management within the first 40 days of SCI. The simplified model is based on the LEMS only.[95] Early prediction of bladder outcomes may optimize counseling and patient-tailored rehabilitative interventions, and improve patient stratification in future clinical studies.

Intermittent catheterization is generally considered a better long-term method of bladder emptying (compared with indwelling catheters), based on low-to-moderate quality evidence demonstrating reduced complications and better preservation of renal function.[99,123,124] The time to consider a trial of intermittent catheterization is based largely on local practice patterns, expert opinions, and the clinical status of the patient.[121] Once the patient is medically stable and can regulate their own fluid intake, intermittent catheterization may be considered.[104,125] Often intermittent catheterization teaching is introduced during the inpatient rehabilitation program. Earlier conversion to intermittent catheterization may avoid the risk of catheter-related complications and reduce the incidence of bacteriuria,[126] although other small series have not shown any long-term differences based on initial bladder management.[127] Patients with adequate hand function should try to learn how to do intermittent catheterization themselves, and those without adequate hand function may still be able to do intermittent catheterization with appropriate caregiver or nursing support.

In cases where the patient is able to resume spontaneous voiding with the removal of the indwelling catheter, the patient's postvoid residual should be monitored, either with occasional intermittent catheterization or with bedside ultrasound measurements. Periodic bladder diaries may also be used to assess bladder function. In patients with persistent voiding dysfunction who are unsuitable for intermittent catheterization, conversion of a urethral to a suprapubic catheter may decrease the risk for urethral erosion over time.[104,128] Patients with poor hand function or cognitive impairment and no full-time attendant, urethral abnormalities, bladder capacity below 200 mL, or significant incontinence may be better managed with a continued indwelling urethral or suprapubic catheter in the initial period after SCI, until the bladder can be assessed with urodynamics.[123] A Cochrane review did not find any high-quality studies to suggest that special types of indwelling catheters (silver or antibiotic impregnated) can reduce urinary tract infections over the short term in non-SCI patients, and more research is needed on these catheters to define any potential role in patients with acute SCI.[129] Educational interventions early after SCI that attempt to reduce urological complications, such as urinary tract infections, have yielded mixed results.[130,131]

The same conservative, medical, and surgical options discussed in Chapter 4: Nonsurgical Urological Management of Neurogenic Bladder After Spinal Cord Injury and Chapter 5: Surgical Management of the Neurogenic Bladder After Spinal Cord Injury are applicable, especially antimuscarinics[132,133] as first-line pharmacologic treatment for neurogenic detrusor overactivity and intradetrusor botulinum toxin A injections[134,135] for refractory neurogenic detrusor overactivity. Although given the potential for bladder function to change over time,[136] and especially for patients' functional capabilities to improve during the initial year after injury,[137] irreversible surgical interventions should usually be delayed until 1 year after SCI.

There has been considerable interest in trying to prevent the development of bladder complications with interventions early after SCI. In one small case series, 10 patients with complete suprasacral SCI were treated with early sacral neuromodulation (1–4 months after injury). In a subsequent follow-up, there was preservation of bladder compliance, no detrusor overactivity, and improved bowel and erectile function compared with untreated SCI patients.[101] Similarly, animal studies have demonstrated that early medications, intradetrusor onabotulinumtoxinA, and neuromodulation can modify long-term bladder function after SCI.[138–140] There have been registered clinical trials further evaluating the ability of early neuromodulation (ClinicalTrials.gov: NCT01043848) and intradetrusor onabotulinumtoxinA injections (ClinicalTrials.gov: NCT00711087, NCT01698138) to preserve bladder function and prevent the development of complications associated with neurogenic bladder.

2.5.3.1 Conclusions

- Urinary continence and complete bladder emptying can be predicted using the EMSCI models (LEMS, light-touch sensation in the S3 dermatome, and SCIM subscale respiration and sphincter management [full model], or LEMS only [simplified model]) within the first 40 days after SCI. **[LOE 2]**

2.5.3.2 Recommendations

- Clinicians must consider spontaneous voiding and/or intermittent catheterization in appropriate patients once they are medically stable. **[LOE 3; GOR A]**
- Clinicians should delay irreversible surgical interventions until 1 year after SCI due to the potential for neurological recovery. **[LOE 4; GOR B]**
- Clinicians must consider antimuscarinics as first-line pharmacologic treatment for neurogenic detrusor overactivity. **[LOE 1; GOR A]**
- Clinicians must consider intradetrusor botulinum toxin A injections for treatment of refractory detrusor overactivity. **[LOE 1; GOR A]**

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C3

Surveillance and Management of Urologic Complications After Spinal Cord Injury

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Committee 3

CONTENTS

Surveillance and Management of Urologic Complications After Spinal Cord Injury

3.1 Surveillance of Neurogenic Bladder Patients

Background of Urologic Surveillance in Neurogenic Bladder Patients

The rate of renal failure–associated mortality in neurogenic bladder (NGB) patients was approximately 50% prior to the development of regular surveillance examinations and upper and lower tract monitoring by clinicians.[1] Regular surveillance evaluations include a detailed history and physical examination, lab testing for kidney function assessment such as blood creatinine and creatinine clearance (CrCl), cystoscopy when necessary, and upper and lower urinary tract imaging and examinations. However, no consensus guidelines exist on how often NGB patients should be evaluated, much less what type of studies or imaging should be included in a routine surveillance protocol. Renal failure in NGB patients is usually a sequel associated with high intravesical pressure, vesicoureteral reflux, infection, and hydronephrosis, all of which can be assessed on upper and lower tract imaging such as ultrasound and video-urodynamics. Unfortunately, these sequelae often go unidentified, as NGB patients may not be able to sense bladder distension, dysuria, or flank pain, depending on level and completeness of injury, until upper urinary tract damage has already occurred and becomes irreversible. Thus, it is important to establish cost-effective and reliable urologic surveillance and follow-up protocols for these patients. Unfortunately, evidence-based medicine has provided minimal guidance and information on the urologic surveillance of NGB patients.

3.1.1 Serum creatinine and other markers of renal function

Patients with spinal cord injury (SCI) have an increased risk of renal insufficiency.[2] Furthermore, kidney disease is an independent risk factor for mortality in SCI patients.[3] This combination warrants aggressive and lifelong monitoring of renal function.[2] However, the ideal method of monitoring renal function in the SCI patient population is not well established. There is no best test that is well accepted, and the frequency of assessment is not known. The *Guidelines on Neurogenic Lower Urinary Tract Dysfunction* established by the European Association of Urology (EAU) recommend annual biochemistries, but specifics as to which tests should be completed are not provided. Clinical practice guidelines for the *Bladder Management of Adults With Spinal Cord Injury*, established by the Consortium for Spinal Cord Medicine and the Paralyzed Veterans of America (PVA), confirm that there is no consensus on the frequency or the range of tests that should be included.[4]

Options for monitoring of renal function include: serum creatinine, CrCl, cystatin C, and radioisotope studies such as Tc-99 DTPA Nuclear Renal Scans or Cr-51 EDTA plasma clearances. Indeed, testing that utilizes an exogenous marker such as Tc-DTPA or Cr-EDTA is considered to be the gold standard.[5] However, such testing is often labour intensive and costly, resulting in infrequent use.

Serum creatinine is probably the easiest and most commonly used measure to obtain. With the serum creatinine, glomerular filtration rate (GFR) can then be estimated using several equations such as the Cockroft-Gault and Modification of Diet in Renal Disease Study (MDRD) equations. These equations take into account variables including age, gender, and weight, in addition to the serum creatinine.

However, creatinine has been confirmed to be inaccurate in the SCI patient population. The basis for this is the fact that creatinine is derived from the breakdown of creatine and phosphocreatine, both of which are derived from muscle. However, because SCI patients have reduced muscle mass, their serum creatinine is often lower. This may result in an overestimation of the true renal function.[6] Indeed, serum creatinine in SCI adults may not become abnormal until there is a severe loss of renal function, such as a GFR of <51%.[7] Hence, assessment of renal function using serum creatinine for the calculation of GFR is not accurate.

On the other hand, measurement of CrCl is not affected by differences in muscle mass or creatine production when calculated from measurements of urine and plasma.[8] When comparing estimated CrCl (by Cockroft-Gault calculation) to measured CrCl, the Cockroft-Gault equation overestimated GFR by 20% in paraplegics and by 40% in quadriplegics.[9] Hence, direct measurement of CrCl is more accurate, but is often more labour intensive and may still entail limitations such as incomplete urine collections.

Cystatin C is considered to be superior to serum creatinine as a marker of renal function,[10] especially in SCI patients.[11] It is produced by nucleated cells at a stable rate and is not affected by muscle mass, age, or gender.[10] In SCI adults, when compared to Cr-EDTA, cystatin C and serum creatinine had correlation coefficients of 0.72 and 0.26, respectively; the area under the curve was 0.912 for cystatin C compared to 0.507 for serum creatinine.[11] Cystatin C is clearly an accurate marker for renal function; however, cost concerns may still limit its use.[12]

Conclusions

1. Patients with SCI are at increased risk of renal insufficiency. **[Level of Evidence (LOE) 1]**
2. Serum creatinine is an inaccurate measure of renal function in SCI patients. **[LOE 2]**
3. There is no consensus in regard to the optimal test to evaluate renal function in patients with SCI or the frequency at which these tests should be obtained. **[LOE 2]**

Recommendations

1. Clinicians must monitor renal function in patients with SCI on at least an annual basis. **[Grade of Recommendation (GOR) A]**
2. Clinicians should not rely on serum creatinine alone when monitoring renal function in patients with SCI. **[GOR B]**
3. Clinicians may consider using CrCl, cystatin C, and radioisotope studies such as Tc-99 DTPA Nuclear Renal Scans or Cr-51 EDTA plasma clearances when monitoring renal function in patients with SCI. **[GOR C]**

3.1.2 Urinalysis and urine culture

3.1.2.1 Definition and detection of UTI

Despite advances in care, urinary tract infections (UTIs) continue to be a major reason for morbidity and mortality in SCI patients. Risk of death attributed to urosepsis is higher in SCI patients compared to the general population. In SCI patients, the frequency of UTI is approximately 2.5 infections per patient per year,[13] which is also substantially higher than the general population.[14] Risk factors include urinary stasis, high bladder pressures, vesicoureteral reflux, bladder stones, and catheter use.[15]

Bacteriuria is an extremely common finding in NGB patients, regardless of the method of bladder management. In the vast majority of these patients, the bacteriuria is not associated with symptoms (i.e. asymptomatic bacteriuria). Treatment of asymptomatic bacteriuria is not beneficial to the patient, and may result in significant medication side effects.[16]

Symptomatic UTI in the SCI patient is defined as urinary culture with $\geq 10^2$ colony-forming unit (CFU) bacteria/mL and symptoms. NGB patients with UTIs often present differently than the general population. Symptoms are frequently nonspecific, and can include spasticity, autonomic dysreflexia, urinary incontinence, and pelvic discomfort.[17] Given the high baseline rate of bacteriuria, it is very important to confirm the presence of UTI symptoms before obtaining a urine culture. Furthermore, it is often prudent to defer antimicrobial therapy until the urine culture results are available. If the symptoms resolve while waiting for the culture results, this indicates that the symptoms were likely not caused by a UTI.

3.1.2.2 Follow-up

Patients with NGB, in general, and SCI, in particular, have a higher risk of developing UTI than individuals without NGB or SCI. Reasons are multiple and include the use of catheters (intermittent or indwelling), frequent instrumentation for urodynamic testing, detrusor sphincter dyssynergia (DSD) with high bladder pressures that may push bacteria to the upper urinary tract, and prostatic ducts or incomplete emptying with elevated residuals. Hydronephrosis, stones, and bladder diverticula may also contribute to increase the risk of UTI in SCI patients.

The 2016 version of the EAU neuro-urology guidelines (https://uroweb.org/guideline/neuro-urology) and the 2013 version of the CUD Incontinence guidelines 5th edition (http://www.icud.info/incontinence.html) give only vague information regarding the best way to detect UTI when following SCI patients with NGB. The recommendation to perform urinalysis every 6 months to every 3 years reflects the consensus opinion of the panel members based on common sense and good clinical practices. Series reporting the urological follow-up of neurogenic-impaired patients for several decades do not indicate any specific frequency for urinary investigation for the presence of bacteria during the period under scrutiny.

3.1.2.3 When should a urine culture be obtained?

Three studies that described cohorts of patients with NGB followed during several decades did not describe the frequency or the moment urinalyses were performed, despite the fact that recurrent UTI was recognized as an adjuvant cause for the progressive deterioration of renal function in several patients.[18–20]

Asymptomatic bacteriuria in SCI patients is more frequent than in the general population. Rates depend on the method of bladder management: 23% to 39% in patients doing intermittent catheterization (IC) and 57% in patients using a condom. Bacteriuria will be present in virtually all patients using an indwelling catheter or a subrapubic tube.[21] Therefore, routine urinary testing for bacteriuria is not recommended in this population if asymptomatic. However, urinalysis and urine culture should be obtained if there are classic UTI-like symptoms (more likely to be seen in a patient with an incomplete injury) or if less-specific symptoms are noted, such as cloudy or malodorous urine, sudden change in the voiding pattern (e.g. increasing frequency and/or incontinence), increased muscle spasticity, or increased autonomic dysreflexia, lethargy, hypotension, or malaise.[22]

3.1.2.4 Urinary evaluation and botulinum toxin A treatment

In the pivotal randomized controlled trial (RCT) of onabotulinum toxin A injection in the bladder wall, administration of some type of antibiotic prophylaxis was allowed on the presumption that bacteriuria might impair efficacy of the toxin. However, many injected patients rely on some type of catheterization and present with chronic bacteriuria.

In a consecutive series of 154 patients undergoing a total of 273 treatments with onabotulinum toxin A for refractory neurogenic detrusor overactivity, urine samples were collected by sterile catheterization for urinalysis and culture. Patients with no clinical signs of UTI underwent injections without antibiotic prophylaxis. Bacteriuria was found in 73% of all patients pretreatment. Following treatment, symptomatic UTI occurred in 7% (5/73) of cases with sterile urine culture and in 5% with bacteriuria.[23] These results not only raise the question of whether routine antibiotic prophylaxis is required prior to botulinum toxin A injection, but also raise the question of whether urinalysis is even necessary in asymptomatic patients, as the results may not impact the decision to proceed with treatment.

Urinary evaluation after intradetrusor botulinum toxin A injection depends upon patient symptoms and type of bladder management. Pooled analysis of two large randomized studies showed that the incidence of bacteriuria in the first 3 months after intradetrusor onabotulinum toxin A 200 U was 49.5%,[24] which is not substantially different from the incidence of bacteriuria in a clean intermittent catheterization (CIC)-managed population. However, in multiple sclerosis (MS) patients voiding normally per urethra and treated with the same dose, the proportion of patients with *de novo* bacteriuria was 53.5%. This high incidence of bacteriuria was attributed to an increased postvoid residual (PVR) urine or urinary retention requiring *de novo* CIC.[24] However, the incidence of bacteriuria in MS patients may be decreased to 25.8% if the dose of onabotulinum toxin A is reduced to 100 U.[85] Overall, these data suggest that urinalysis after botulinum toxin A injection is not required in patients doing IC unless a symptomatic UTI emerges.

Conclusions

1. Patients with SCI have a higher risk of developing UTI than the general population. **[LOE 1]**

2. Asymptomatic bacteriuria in SCI patients is more frequent than in the general population; the rates depend on the method of bladder management. **[LOE 2]**

3. Cloudy and foul-smelling urine may represent bacteriuria without UTI and, by itself, may not warrant a urine culture. **[LOE 4]**

Recommendations

1. Clinicians should not obtain routine urinalysis in asymptomatic SCI patients. **[GOR B]**

2. Clinicians should not obtain routine urinary culture in asymptomatic SCI patients. **[GOR B]**

3. The clinician should obtain a urinary culture in SCI patients with clinical evidence of a symptomatic UTI. **[GOR A]**

4. Clinicians should be aware that SCI patients with a UTI may present with atypical symptoms, including a change in the voiding pattern, increased muscle spasticity, increased autonomic dysreflexia, lethargy, hypotension, or malaise. **[GOR A]**

3.1.3 Imaging

There is currently no consensus on the optimal type of imaging for surveillance of the upper tracts in patients with NGB secondary to SCI. The current literature would indicate that routine iodinated contrast studies and computed tomography (CT) are no longer indicated as part of routine surveillance protocols. Similarly, routine renal function studies (renal scans) are rarely used during surveillance follow-up visits.[25] A comparative study of 162 NGB patients at the Miami Veterans Affairs (VA) Medical Center with 478 matched renal ultrasound and renal scan studies performed within 48 hours of each other as part of a surveillance protocol showed a nearly perfect correlation of results from either modality. In other words, the results of the functional study (renal scan) correlated with the renal ultrasound in nearly all cases.[26] As renal ultrasound is significantly less expensive, less invasive, and easier to perform, it was adopted as the sole imaging modality of choice for upper tract surveillance of NGB patients at the Miami VA. This is consistent with the observation by two studies indicating that 80% of urologists prefer a renal ultrasound during routine surveillance of NGB patients (see **Table 3-1**).[1,27,28]

A recent review article from *Urologic Clinics of North America* details a scenario involving 1 follow-up visit a year to discuss symptoms, conduct blood testing, and perform a renal ultrasound and abdominal x-ray. The article states that repeat urodynamic study (UDS) testing should be performed solely based on the premise that the outcome of the tests may change patient management.[26] This clinical principle leaves a direct parameter for follow-up at the discretion of the urologist. In order to determine the opinions and discretions of most urologists, a literature search was performed involving the method and timing of follow-up surveillance protocols for NGB patients. Several studies were found involving questionnaires polling urologists about their normal follow-up patterns; other studies involved directing management of NGB patients based on the results of their surveillance testing. These results are summarized in **Table 3-1**.

TABLE 3-1 Follow-up Surveillance Protocols for NGB Patients

Author/ date published	Number of doctors queried or number of patients studied	Follow-up visit	Lab tests	Upper tract imaging	Lower tract imaging	Cystoscopy
Razdan *et al.*[1]	160 urologists queried		93% creatinine yearly	80% renal US yearly, 20% renal scan yearly	65% UDS every 12–24 months, 35% no regular UDS	25% yearly cystoscopy; 75% cystoscopy only if long-term catheter, hematuria, or recurrent UTI
Bycroft *et al.*[28]	12 urologists surveyed	1 did exams every 6 months, 7 did exams every 12 months, 1 did exams every 1–2 years, 1 did exams every 1–5 years		Renal U/S done every 12 months in 9, every 18 months in 1, every 6 months in 1, every 3 years in 1	UDS done every 12 months in 2, only once in 1, every 12 then every 24 months in 1, every 12 months (reflex voiders only) in 1, every 2–3 years in 1, and only if indicated in 6	
Blok *et al.*[46]	105 urologists surveyed	58% did exams every 12 months, 34% did exams every 3–6 months		Mostly renal U/S done every 12 months in 78%, every 24 months in 17%, every 3–6 months in 34%	75% UDS done every 12–24 months, 11% VUDS done every 12–24 months, 14% no regular UDS	

Abbreviations: CrCl: creatinine clearance; CT: computed tomography; MRI: magnetic resonance imaging; PVR: postvoid residual; UDS: urodynamic study; U/S: ultrasound; UTI: urinary tract infection; VCUG: voiding cystourethrogram; VUDS: video-urodynamic study.

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TABLE 3-1 Follow-up Surveillance Protocols for NGB Patients, *Cont'd*

Author/ date published	Number of doctors queried or number of patients studied	Follow-up visit	Lab tests	Upper tract imaging	Lower tract imaging	Cystoscopy
Kitahara *et al.*[47]	314 urologists surveyed	68% did exams every 12 months, 29% did exams every 12–24 months	1% creatinine every 12 months	72% renal U/S; 26% intravenous pyelogram; 1% renal scan done, 73% did every 12 months, 30% did every 12–24 months	52% UDS, 10% VUDS done, 73% did every 12 months, 30% did every 12–24 months	7% cystoscopy done yearly
Nosseir *et al.*[258]	80 patients studied over years	Every 6 months	CrCl once every 2 years, urinalysis every 6 months	Renal U/S every 6–12 months	UDS every 12 months	
Hadji *et al.*[259]	59 patients studied over 13 months	Yearly exam completed	Creatinine, CrCl, and urinalysis done every 12 months	Renal U/S every 12 months	UDS every 12 months	
Khanna *et al.*[260]	100 patients studied over 3 years	Yearly exam completed	Creatinine done every 12 months	Renal U/S or voiding cysto-urethrogram done every 3 years	UDS every 3 months for 1 year after spinal shock, then every 6 months for 1 year, then yearly	
Denys *et al.*[261]	205 urologists surveyed	5% did exams every 3 months, 48% did exams every 6 months, 46% did exams every 12 months, 1% did exams every 24 months		All did renal U/S; 24% did every 6 months, 70% did every 12 months, 6% did every 24 months	All did UDS; 3% did UDS every 6 months, 23% did UDS every 12 months, 23% did UDS every 24 months, and 44% did NOT do UDS in follow-up	
Linsen-meyer[241]	96 patients studied over 2 years	Yearly exam completed	Urinalysis done every 12 months	Renal scan every 12 months	UDS every 12 months	

Abbreviations: CrCl: creatinine clearance; CT: computed tomography; MRI: magnetic resonance imaging; PVR: postvoid residual; UDS: urodynamic study; U/S: ultrasound; UTI: urinary tract infection; VCUG: voiding cystourethrogram; VUDS: video-urodynamic study.

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TABLE 3-1 Follow-up Surveillance Protocols for NGB Patients, *Cont'd*

Author/ date published	Number of doctors queried or number of patients studied	Follow-up visit	Lab tests	Upper tract imaging	Lower tract imaging	Cystoscopy
Burki *et al.*[262]	12 urologists surveyed	7 did exams every 12 months		12 renal U/S done mostly every 12 months	10 VUDS done every 12 months, 1 UDS done every 12 months	
Cameron *et al.*[45]	7,210 patients studied over 2 years	36% every 12–24 months	91% Creatinine every 12–24 months, 80% urinalysis every 12–24 months	35% renal U/S Every 12–24 months, 40%CTscanevery 12–24 months, 2.5% MRI every 12–24 months, 1.5% renal scan every 12–24 months	7% UDS every 12–24 months, 9% PVR every 12–24 months	12% cystoscopy every 12–24 months

Abbreviations: CrCl: creatinine clearance; CT: computed tomography; MRI: magnetic resonance imaging; PVR: postvoid residual; UDS: urodynamic study; U/S: ultrasound; UTI: urinary tract infection; VCUG: voiding cystourethrogram; VUDS: video-urodynamic study.

By examining the number of patient-cases and urologists queried in all these studies, a fairly common pattern of surveillance can be illustrated. Overall, most urologists and their patients are being seen in follow-up at least once per year. These follow-ups usually include, at a minimum, a history and physical, creatinine level, and some form of upper and lower urinary tract visualization. Occasionally these visits are supplemented with real-time anatomical imaging of the bladder and urethra in the form of office-based cystoscopy, as necessary. In addition to regular surveillance visits, urologic evaluation should be performed sooner (as needed) based on a variety of signs and symptoms, such as new-onset urinary incontinence, recurrent UTI, hematuria, etc.

Conclusions

1. Renal ultrasound is the preferred imaging study for both the initial evaluation and subsequent routine surveillance of patients with NGB secondary to SCI. **[LOE 3]**

2. Iodinated contrast studies, CT scans, and nuclear function studies (renal scan) are not part of a routine surveillance protocol for patients with NGB secondary to SCI. **[LOE 3]**

Recommendations

1. Clinicians should obtain upper urinary tract imaging (such as a renal ultrasound) at least every other year. **[GOR A]**

2. Bladder ultrasound may be combined with renal ultrasound as a noninvasive means of providing information about bladder stones and bladder wall thickness. **[GOR C]**

3.1.4 Urodynamics

Urodynamics findings cannot always be predicted based on the level of SCI.[29] Therefore, it is important to always ascertain a baseline urodynamics study in all newly diagnosed SCI patients. Urodynamics should be performed after spinal shock has ended. The average period of spinal shock in patients is approximately 90 days or, more exactly, when the bulbocavernosus reflex returns.[26] Once a baseline urodynamics study has been completed, clinicians can then base their treatment protocols on the urodynamics findings instead of assuming a treatment protocol based on level of SCI.[30]

Multichannel urodynamics defines the variables of compliance and detrusor leak point, which are the most important predictors of upper urinary tract damage. Video-urodynamics carries with it the added benefit of real-time fluoroscopic anatomical information during both a filling and voiding stage. However, video-fluoroscopy puts the patient at risk for regular radiation exposure on a repeated and chronic basis.

A 2014 International Consultation on Incontinence Research Society meeting examined the risks and benefits of using video-urodynamics over traditional urodynamics studies in neurologically intact patients, and determined that only low-level evidence was present for the benefit of adding video-fluoroscopic imaging to urodynamics studies.[31] It remains controversial whether the video portion of the UDS is always necessary for every patient with NGB.[31]

Conclusion

1. The addition of fluoroscopy to urodynamics allows for evaluation of anatomical pathology in the bladder such as trabeculations, diverticuli, and vesicoureteral reflux. **[LOE 2]**

Recommendation

1. Clinicians should perform urodynamic assessment at the time of initial evaluation, and repeat studies when dictated by new clinical, laboratory, or radiographic findings. **[GOR B]**

3.1.5 Screening cystoscopy

There is a body of literature recommending cystoscopy for bladder cancer screening in SCI, as these patients have a higher risk of bladder cancer than the general population. This review will examine the evidence for this practice.

3.1.5.1 Definition and utility of screening

In routine urologic practice, cystoscopy for diagnostic purposes is commonly performed in response to signs or symptoms related to a bladder-related condition. Cystoscopy for surveillance purposes is generally limited to those persons with certain treated malignancies of the upper and lower urinary tract. Surveillance cystoscopy as a screening tool is not generally performed, as it does not fulfill the criteria for a screening test. Screening for disease, such as a malignancy, is a means of accomplishing early detection of disease in a large number of asymptomatic people, to reduce the complications and mortality rate from that disease among the persons screened.[32] In order to have such an effect, the screening tool should identify diseases that a) cause substantial morbidity and mortality in the population at risk, b) have a high prevalence in a detectable preclinical state, and c) are amenable to effective and improved treatment because of early detection. The screening test must be safe, specific, sensitive, rapidly and easily administered, inexpensive, and reproducible.[32,33]

3.1.5.2 Conditions for screening at-risk populations

In the SCI population, cystoscopy is often used as a screening tool for bladder cancer. This is based on historical literature showing a markedly higher incidence of bladder cancer than in the general population, particularly in chronically catheterized SCI patients (0.1%–10%).[34,35] It is important to note that the older literature (e.g. prior to 1985) reflected a time when bladder management of SCI patients was generally less rigid than it is today. The introduction of clean IC in 1972 by Lapides[36] and subsequent developments of medications and procedures impacting the hygiene and compliance of the lower urinary tract contributed dramatically to the improvement of bladder health, which has likely decreased the risk of developing bladder cancer.

More recently, bladder cancer incidence rates in SCI patients appear to be trending downward, but do not yet match those of the general population, based on two studies with large numbers of SCI patients. Studying the records of more than 3,000 SCI patients, and comparing them to a cohort from the Surveillance, Epidemiology, and End Results (SEER) database, Groah *et al.* found that the risk of bladder cancer was higher in the SCI population when compared with the general population (with age and sex adjustment) and that bladder management with an indwelling catheter independently conferred a significant risk of bladder cancer.[37] Pannek reviewed the charts of more than 43,000 SCI patients in Germany, Switzerland, and Austria over a 5-year period (1995–1999) and found a 0.11% risk of developing bladder cancer.[38] This was lower than earlier rates reported by West *et al.* of 0.39%, also over a 5-year period (1988–1992), and Bickel *et al.* of 0.32%.[39,40] Of note, most of the early studies reporting the incidence of bladder cancer in SCI patients were small studies in which the denominator was very small or not clearly defined.

Chronic indwelling catheterization in SCI patients is regarded as a risk factor for bladder cancer development, and appears to increase with increasing time of catheterization.[37] Bladder stones and recurrent UTI appear also as independent risk factors for the development of bladder cancer.[41,42]

These factors, which are significantly more prevalent in the SCI population, in addition to the most common risk factors established for the general population (i.e. advancing age, smoking, chemical exposure), put the SCI population at greater risk for bladder cancer. Thus, there is continued advocacy for cystoscopy as a screening tool, presumably corroborated when abnormal histologic findings and the occasional urothelial malignancy are still being reported in screened SCI patient populations.[43,44]

3.1.5.3 Current practices and evidence

There is no consensus at this time regarding screening cystoscopy in SCI patients. This is manifested in the variation of urologic practices reported in SCI populations. Authors from the United States, Canada, the United Kingdom, Ireland, and Japan report a variable range of screening cystoscopy rates.[28,45–47] The lack of consensus results from a dearth of consistent data to support recommendations on the optimal time interval between screening cystoscopy procedures, risk factors to take into account (e.g. number of years of chronic catheterization, smoking history, UTI rate), the apparent decrease in risk of bladder cancer in SCI patients over the last 3 decades, and the overall utility of screening for bladder cancer (see below). If screening cystoscopy is conducted, it is generally done on a yearly or biannual basis.

Recommendations to perform screening for any disease must be based on adherence to the accepted principles of screening, as well as evidence for the efficacy of the screening test to achieve its goals. These will be reviewed below:

1. Does the disease have significant morbidity and mortality?

Bladder cancer, particularly in advanced stages, is highly morbid and fatal. It is the fourth most commonly diagnosed cancer in men and the ninth most commonly diagnosed cancer in women in the United States. It is the seventh leading cause of solid cancer–related deaths.[48] Furthermore, the morbidity of bladder cancer in SCI patients appears to be higher than in the general population.[37]

2. Does the disease have a high prevalence in a preclinical state?

Two small studies of screening cystoscopy revealed a very low yield of bladder cancer. Hamid *et al.* found no bladder tumours in 36 patients with indwelling catheters for at least 5 years. The patients had a mean follow-up of 12 years.[49] Yang and Clowers identified no bladder tumours in 59 patients who were chronically catheterized for >10 years, or for >5 years and actively smoking cigarettes, who were undergoing annual cystoscopy over a 6-year period.[50] Other studies that did not specify a standard screening program for bladder cancer in SCI patients, but had patients undergo at least intermittent cystoscopy, also reported low rates of cancer detection. No cancers were found in 262 SCI patients, many of whom were on a screening program.[43] Only 2 cancers were found in a study of 3,670 SCI patients who had at least 2 cystoscopies during an extended follow-up (range: 1–47 years).[37]

Many of the bladders cancers that develop in SCI patients are reported to be of high grade and advanced stage at the time of diagnosis, even in screened populations. Squamous cell carcinoma of the bladder is an aggressive, rapidly progressing malignancy, and is found in a much greater proportion (25%–50%) in SCI patients compared with the 2% to 5% of all bladder malignancies in Western countries.[38,51–53] Urothelial carcinomas are also typically diagnosed at a high stage and grade in SCI patients, and at a younger age.[40,41] Several authors argue that the biology of these rapidly progressing tumours precludes detection in a preclinical state, particularly on a schedule of annual cystoscopy.[38,41,50]

3. Is the disease amenable to effective and improved treatment because of early detection?

Identification of urothelial carcinoma of the bladder in earlier stages (Ta, T1, and some T2) generally results in more effective treatment/higher cure rates, even with high-grade disease. Squamous cell carcinoma of the bladder is also likely to better respond to treatment when it is diagnosed at an earlier stage,[53] but is felt to be a more aggressive and rapidly progressing malignancy compared with urothelial carcinoma.

4. Is the screening test safe, rapidly and easily administered, inexpensive, and reproducible?

Cystoscopy is generally safe, although it is an invasive procedure. Scheduling SCI patients for cystoscopy generally requires more planning than with ambulatory patients. Cystoscopy is a straightforward procedure. However, when being performed in conjunction with bladder biopsy, particularly in an SCI patient prone to autonomic dysreflexia, it may require anesthesia and an operating room setting, which dramatically increases the risk and costs of the procedure. The reproducibility of cystoscopy is considered to be high.

5. Does the screening test have adequate sensitivity, specificity, and predictive value?

While cystoscopy is the gold standard for identifying a neoplasm within the bladder, limiting cystoscopy to the chronically catheterized and, in particular, to the long-standing chronically catheterized would significantly impact the sensitivity and specificity of the test. Inflammatory changes secondary to catheterization could mask the earliest stages of the disease (decreasing sensitivity), and paradoxically could also lead to false-positive results in others (decreasing specificity), leading to unnecessary biopsies. There are several studies that identify the development of bladder cancer in SCI patients who were not chronically catheterized.[50,51] Performing annual cystoscopy on all SCI patients to improve the test's sensitivity would be prohibitive from a cost and feasibility standpoint.

6. Is there evidence that the screening test decreases morbidity and mortality in an asymptomatic and at-risk population?

There is currently no high-quality evidence that demonstrates the superiority of screening cystoscopy over no cystoscopy in SCI. There is scant evidence in the general population for screening, even in those at high risk for the development of bladder cancer.[48] The factor generally considered as being the most significant in conferring bladder cancer risk is smoking. In a recent evaluation of the association between tobacco smoking and bladder cancer including men and women in the National Institutes of Health-AARP (NIH-AARP) Diet and Health Study cohort, former smokers (119.8 per 100,000 person-years; hazard ratio [HR], 2.22; 95% confidence interval [CI], 2.03–2.44) and current smokers (177.3 per 100,000 person-years; HR, 4.06; 95% CI, 3.66–4.50) had higher risks of bladder cancer than never smokers (39.8 per 100,000 person-years).[54] In SCI patients, the reported risk of bladder cancer was 86.8 per 100,000 person-years in those who used indwelling catheters 10 to 19 years, and increased to 398.1 per 100,000 person-years in those who used indwelling catheters for 20 years or more (relative risk 4.6; 95% CI, 1.5–14.0).[37] Thus, persons with SCI who used catheters for fewer than 19 years were at lower risk for bladder cancer than former and current smokers in the general population. With insufficient evidence that screening would be beneficial to those at higher risk in the general population, it would be difficult to advocate for screening in the SCI group with a lower risk. Whether there is a valid argument to be made for screening in persons with indwelling catheters for >20 years remains to be seen but, as noted earlier, there has been no high-quality evidence directly addressing the efficacy of screening in any SCI cohort.

Two recent systematic reviews concluded that surveillance cystoscopy should not be performed to screen for bladder cancer in the asymptomatic SCI patient.[55,56] The disease is morbid and prevalent in SCI patients and, generally speaking, treatment early in the disease can decrease its morbidity and mortality. However, the presence of a preclinical state during which a reasonable screening schedule can be useful is questionable; the invasiveness, cost, and inconvenience of the screening procedure is significant; and the decreasing incidence of the disease in SCI patients and low yield of reported bladder cancer in screening studies all argue against screening cystoscopy in this population.

Conclusions

1. Based on one contemporary study, bladder cancer risk is higher in chronically catheterized SCI patients than in the general population, but persons with SCI who used catheters for fewer than 19 years were at lower risk for bladder cancer than former and current smokers in the general population. **[LOE 3]**

2. Cystoscopy does not fulfill the criteria for an appropriate screening test for bladder cancer in asymptomatic SCI patients. **[LOE 3]**

Recommendations

1. Clinicians should not perform cystoscopy to screen for bladder cancer in asymptomatic SCI patients. **[GOR B]**

2. Clinicians should not perform cystoscopy to screen for bladder cancer in chronically catheterized SCI patients, no matter the duration of catheterization. **[GOR B]**

3.1.6 Urinary cytology

As reviewed above, patients with SCI have a substantially higher risk of bladder cancer than the general population, and cytology has been evaluated as a screening tool. However, the use of screening cytology or diagnostic cytology in the spinal cord population is not clear. Interpretation of the urine cytology in this patient population is challenging for the cytopathologist due to the common presence of bacteriuria and inflammatory changes present in the urothelium of patients with chronic indwelling catheters or on IC. Interpretation is also challenging due to the atypical bladder cancer subtypes,[39] including squamous cell carcinoma and adenocarcinoma, which may be less associated with positive urine cytologies. In addition, there is sparse literature to strongly refute or support its use, and no studies were identified that included NGB patients other than those with a diagnosis of SCI.

In an early retrospective study of spinal cord patients diagnosed with squamous cell carcinoma of the bladder cancer,[34] cytology was obtained in 4 of 6 patients. None had positive cytology for cancer, and one was found to have squamous metaplasia on cytology. This study did identify indwelling catheter as a risk factor, but found cytology not to be diagnostic of cancer in this small series.

Three later prospective studies of spinal cord populations resulted in no positive cytologies in patients screened. Broecker *et al.*[35] evaluated 81 patients with an indwelling catheter for at least 10 years or an external collection device for at least 15 years; in no patient was urine cytology positive for cancer, though several patients had squamous metaplasia. Esrig *et al.*[57] prospectively evaluated 37 SCI patients with indwelling catheters with bladder barbotage. No patient in this cohort had a positive cytology, including 2 that were diagnosed with bladder cancer on biopsy. In an additional study of 152 cytology specimens in the SCI population (various bladder management types), 1 case of bladder cancer was detected; however, this patient's cytology was read as normal.[58] None of 8 patients with atypical cytologies were diagnosed with cancer.

Other authors have found cytology more beneficial. Stonehill *et al.*[59] recommended yearly screening cytology in patients catheterized for more than 5 years. This was based on a retrospective review of 208 patients who underwent a screening protocol and had at least 1 cytology in the 3 months prior to planned bladder biopsy. Seventeen patients were diagnosed with cancer, and 12 had at least 1 cytology that the authors called positive. The definition of positive cytology included not only a positive reading for cancer, but also a cytologic reading of any of the following: (1) atypical suspicious, (2) keratinizing squamous metaplasia, (3) suspicious for cancer, or (4) dysplasia. In addition, of the 20 patients who did have a positive result, only 8 were found to have malignancy confirmed on biopsy. The authors do state that only 2 patients had cancer diagnosed based on repeat biopsy due to positive cytology result alone. Likewise, Locke *et al.*[60] found positive cytology in 2 of 25 patients with more than 10 years of indwelling catheter management, and both were confirmed to have squamous cell cancer on biopsy.

Several more recent studies do not support the use of cytology in this setting. Davies *et al.*[61] performed a prospective study of a variety of urine markers for bladder cancer, including urine cytology for the detection of bladder cancer in patients with SCI. A total of 1,075 urine samples were collected from 457 patients over 5 years. The methods of bladder management in these 457 patients were: 79 indwelling catheter, 368 IC, and 10 methods not specified. Two patients were diagnosed with bladder cancer during the study period, and no patient had urine cytology reported as positive for cancer. Likewise, in a retrospective review of 32 SCI patients by Kalisvaart *et al.*,[51] only 1 of 19 patients with a known method of detection of bladder cancer was diagnosed by positive cytology; the histologic type of cancer was not reported for this patient.

Conclusion

1. There is insufficient evidence to support the use of routine urinary cytology in the evaluation of the asymptomatic SCI patient. **[LOE 4]**

Recommendation

1. Clinicians should not use urinary cytology in asymptomatic SCI patients. **[GOR D]**

3.1.7 Quality of life measures

SCI is a dramatic, life-changing experience with multiple adverse effects in many body systems. Living with SCI presents challenges in most aspects of daily living, including health-related aspects, of which urinary tract issues play a major part. Life expectancy for patients with SCI has increased substantially. How well patients with SCI live, or their quality of life (QOL), is very important. There are unique problems that these patients face, which means that QOL measures that are not designed for patients with SCI, or not validated for this population, may be inaccurate. Even those measures designed for other neuropathic conditions such as MS may not truly reflect the QOL of the SCI patient. Questionnaires addressing health-related quality of life (HRQOL) must be valid (i.e. they measure what is intended), responsive (i.e. they are able to detect a change, even a small one), and interpretable (i.e. those using it must understand the results and find them useful).

There are many indicators of QOL in SCI. This document looks at the measures available for the impact of urinary symptoms and complications, including incontinence, and how they can be used to assess outcomes of treatment.

3.1.7.1 SCI, urinary problems, and QOL questionnaires

The Spinal Cord Injury Research Evidence (SCIRE) website (https://www.scireproject.com/outcome-measures) has a valuable resource that summarizes the outcome measures available for patients with SCI. There are 105 outcome measures (although these are not all QOL measures). This review includes all the questionnaires with continence and QOL domains from this source. A review of urologic questionnaires related to the management of SCI and NGB has been done. Also, a full literature review was performed in PubMed and Scopus for all papers published in peer-reviewed journals over the past 10 years looking at QOL measurement as related to urinary dysfunction and its impact in SCI patients. The search criteria used were: urinary incontinence OR urinary bladder, neurogenic AND QOL OR patient reported outcomes AND SCIs.

There are a number of symptom and QOL scoring tools available for use in SCI that have a component that measures the impact of urologic symptoms. A recent review of questionnaires for NGB[62] identified 18 questionnaires; however, the focus of a majority of the questionnaires was on patients with MS. In addition, there are several questionnaires that do evaluate patients with SCI that were not included in the review.

The SCIRE group identified 13 QOL instruments specific to SCI in its review in 2010:[63]

Patient-Reported Spasticity Measurement (PRISM), Quality of Well-Being Questionnaire (QWB), Qualiveen, Sickness Impact Profile 68 (SIP68), 36-Item Short Form Health Survey (SF-36), 36-Item Short Form Health Survey for Veterans (SF-36V), 12-Item Short Form Health Survey (SF-12), Short Form 6 Disability (SF-6D), Quality of Life Index (QLI), Quality of Life Profile for Adults With Physical Disabilities (QOLP-PD), Satisfaction With Life Scale (SWLS), Sense of Well-Being index (SWBI), World Health Organization Quality of Life short version of the WHO-QOL 100 (WHO-QOL-BREF) and Incontinence Quality of Life scale (I-QOL).

Only SF-36, WHO-QOL-BREF, Qualiveen, and the I-QOL are presently listed on the SCIRE website. SF-36 and WHOQOL-BREF do not contain a specific urologic component, but they are widely used and validated for measuring QOL in SCI. The Spinal Cord Injury - Quality of Life (SCI-QOL) measurement has been developed since the review; it is also validated but, unlike the other two, it does have a urologic component.

SF-36[64] is a generic health status measure that was introduced in 1992 and has been translated into various languages and used worldwide. It is designed to be applied to all health conditions, assesses health concepts that represent basic human values, and is relevant to a person's functional status and well-being. It contains 36 questions covering 8 domains: physical functioning, role limitations due to physical health problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems, and mental health. The responses are based on a Likert scale. Both standard (4 week) and acute (1 week) recall versions are used. Version 2 of the SF-36 was released in 1996 and some modifications were made to the format, the wording of the questions, and the response options. It has shown reliability and validity as a measure of mood in people with SCI.[65]

WHO-QOL-BREF[63] conceptually fits with the World Health Organization (WHO) definition of QOL. There are 4 domains of QOL: physical health (raw score range: 7–35), psychological health (raw score range: 6–30), social relationships (raw score range: 3–15), environment (raw score range: 8–40). Two items measure overall QOL and general health. This QOL instrument was reported as being the most acceptable and established instrument to assess QOL after SCI in a systematic review by the SCIRE group in 2010.

SCI-QOL is a questionnaire specifically looking at QOL in patients with SCI. It has 3 major domains and 18 subdomains. The major domains are physical-medical health, emotional health, and social participation.[66,67] When developing the questionnaire, pain was the most frequently mentioned complication (by 16% of respondents) within the physical-medical section, followed by issues related to bladder and bowel management (12%). There are 5 bladder questions in this domain relating to UTIs and bladder issues.

We have identified 6 other questionnaires that assess aspects of QOL in patients with SCI that include a bladder or incontinence domain as part of the overall questionnaire. They are summarized below:

Spinal Cord Independence Measures (SCIM)[68] consists of 16 questions devoted to level of dependence after SCI, with higher scores denoting less dependence (full independence scores 100). The bladder domain is scored from 0 to 15; a score of 0 is given to those with indwelling catheters, 5 for those requiring assistance with IC or voiding with a residual >100 mL, 10 for those performing their own IC, and 15 to those with continence, not requiring IC, and with a residual <100 mL.

The Tetraplegia Hand Activity Questionnaire (THAQ)[69] is a measure of arm and hand function in tetraplegics that consists of 9 subclasses, one of which is continence and relates to bladder management. Lower scores indicate higher levels of independence and items are scored: 1) Performance or doing (0=without difficulty to 3=help from others); 2) Use of an aid (0=never to 3=always); and 3) Importance of performing activity independently (0=not important to 2=very important).

The Abruzzese scale[70] is based on the **Norton** and **Gosnell** scales and designed to assess the risk of pressure sore development in acute and long-term phases. It has 9 domains, of which one is continence. This is measured on a 4-point scale, and high scores denote greater incontinence and higher risk of pressure sores.

The Waterlow Scale[71] is used to assess the risk for pressure ulcer development. It was created to provide better sensitivity and specificity than the Norton by increasing the number of items used. Every patient is evaluated on 8 items: age, sex, body build, appetite, continence of urine and feces, mobility, skin appearance in risk areas, and special risks (disorders associated with tissue malnutrition, neurologic deficits, medication, recent surgery or trauma).

The **SCI-Health Questionnaire Complications (SCI-HQ: Compl)** contains 21 domains with different complications, including 2 related to bladder management: UTI and stones. Three questions are asked for each complication, and scoring is on a 6-point scale for each question: 1) Have you experienced this problem? 2) Have you sought or received treatment? 3) To what extent did it limit your activity?

The Rick Hansen Spinal Cord Injury Registry (RHSCIR) community follow-up questionnaire[72] is a questionnaire for follow-up in the community of patients enrolled in the RHSCIR. It includes questions on both UTI and incontinence taken from the SCI-HQ: Compl questionnaire.

There are a number of scoring tools evaluating the impact of urologic symptoms on QOL. However, there are only 4 validated for use in NGB or SCI. These are I-QOL, Qualiveen, short-form Qualiveen (SF-Qualiveen), and Neurogenic Bladder Symptom Score (NBSS).

I-QOL[73] measures the effect of urinary incontinence on QOL and is divided into 3 subscales: avoidance and limiting behaviour, psychosocial impact, and social embarrassment. It is a 5-point response scale ranging from 1 (extremely) to 5 (not at all). It has been validated for patients with NGB, but not specifically in SCI.

Qualiveen[74] is a disease-specific QOL measurement for patients with SCI who have urinary disorders. It was originally developed for French-speaking men and women with SCI, and it has subsequently been validated for the MS population; culturally adapted validated versions are available in English, German, Dutch, Turkish, and Italian. It has 30 items that examine 4 domains: bother limitations (9 items), frequency of limitations (8 items), fears (8 items), and feeling (5 items). Responses are done with a 5-point Likert-type scale, and scores range from 0 (no impact) to 4 (high adverse impact). Each domain score is computed as an average of the scores for the items it contains. Individual items are equally weighted. An overall QOL score also can be calculated from the mean of the 4 domains, with lower scores indicating better QOL (i.e. no limitations constraints or negative feelings). It takes less than 30 minutes for completion. The Qualiveen was validated in 281 patients with SCI with urinary difficulties.

SF-Qualiveen[75,76] was devised to shorten the original Qualiveen, decreasing the time and financial cost of data collection and the risk of total nonresponse or item nonresponse. It consists of 8 questions regarding bother, restriction, worry, and feelings related to urinary problems. It is scored 0 to 4 for each of the 8 questions, with higher scores indicating worse symptoms. However, it was developed for the MS population specifically.

NBSS[77] was developed specifically to assess symptoms and bladder-related consequences for NGB in SCI, MS, and spina bifida. It contains 24 questions, and 22 of these cover incontinence, storage and voiding symptoms, and urinary complications associated with NGB. Two additional questions address bladder management and urinary-specific QOL. These questions include the frequency and quantity of urine leakage, the impact on health and every day activities, the frequency and severity of UTIs, and the frequency of bladder and kidney stones. The median score is 19 out of a possible 74, with higher scores relating to worse symptoms.

Other questionnaires found in the literature review that evaluate QOL in SCI with urologic problems and their treatments include:

- Both **Urge-Incontinence Impact Questionnaire (U-IIQ)** and the **Urge-Urinary Distress Inventory (U-UDI)**[78] have been validated for use in a population that includes those with neurogenic incontinence associated with disease or injury, but they are not validated for use in the SCI population.
- The **Kings Health Questionnaire (KHQ)** is a 24-item scale designed to assess HRQOL associated with lower urinary tract symptoms (LUTS) and urinary incontinence, but it is not designed for use in the neuropathic population.
- The **International Lower Urinary Tract SCI Basic Data Set (ILUTBSD)**[79] is one of the Basic Data Sets that have been created in the areas of lower urinary tract function, urodynamics, urinary tract imaging, bowel function, pain, female sexual and reproductive function, male sexual function, cardiovascular function, pulmonary function, endocrine and metabolic function, and QOL.
- The **Patient Global Impression of Improvement (PGI-I)** and **Wuolle questionnaire**[80] look at activities of daily living and QOL.
- The **Michigan Incontinence Symptom Index (M-ISI)**[81] is a validated instrument for assessing severity and bother related to urinary incontinence, but it is not validated for use in the SCI population.
- The **Overactive Bladder Patient Satisfaction With Treatment Questionnaire (OAB-PSTQ)** is for patients with overactive bladder, but it is not specific for NGB.

- The **Patient Global Assessment (PGA)** is a nonspecific assessment tool that can be used for a wide range of physical disorders.
- The **American Urological Association Symptom Index (AUA-SI)** is widely used as a symptom score, but it is not validated for use in the SCI population.
- The **International Prostate Symptom Score-QOL Index (IPSS-QOL)** is widely used as a symptom score, but it is not validated for use in the SCI population.

Conclusion and Recommendations

Assessment of urinary symptoms or the impact of treatments in patients with NGB often uses measures such as urinary frequency, pad usage, urodynamic parameters, and QOL measures that are not specific to SCI patients, and often not specific to urinary symptoms. They therefore may not be a true reflection of the impact of symptoms or treatments in these patients. We have identified all of the papers published in the past 10 years assessing QOL in SCI patients undergoing urologic treatments.

There are a lot of questionnaire options, most of which are not specific for SCI. There is a wide variety of QOL measure used, probably inappropriately, for this population. There are 4 validated QOL measures for urologic problems in SCI, which are I-QOL, Qualiveen, SF-Qualiveen, and NBSS. In addition, SF-36 and WHO-QOL-BREF, although not containing a urologic component, are valid measures of overall QOL in this population.

Table 3-2 summarizes 45 papers pertaining to SCI and QOL related to urinary problems and bladder management over the past 10 years. A large proportion of these papers pertain to intravesical botulinum toxin A injection and assessing the toxin's effect on QOL. There are a number of QOL tools used that are shown in the table. Eight studies used I-QOL, 5 used Qualiveen (or SF-Qualiveen), and 6 used SF-36. All the others used QOL measurements that were not validated for the SCI population, so one could question the validity of the outcomes in regard to QOL. At this point, there is no evidence of which validated questionnaire is the most appropriate to use in this patient population.

TABLE 3-2 Urologic Problems and Quality of Life in Spinal Cord Injury

Author	Study type	Number	QOL tools	Evidence grade	SCI type	Subject
Abdel Meguid[263]	RCT	38	IPSS-QOL	2	SCI	BTx A, Do you include trigone?
Abdul Rahman *et al.*[264]	Therapy case series	12	UDI, IIQ-7	4	A variety of spinal cord pathologies	Tension-free vaginal tape in neuropathic bladder
Adelved *et al.*[265]	Prospective, longitudinal, single cohort	31	SF-36	3	Sacral fracture	Sacral fractures and QOL including bladder dysfunction
Adriaansen *et al.*[266]	Cross-sectional multicentre	282	ILUTBSD, SF-Qualiveen	3	SCI >10 years	Bladder emptying method and QOL
Akkoc *et al.*[267]	Cross-sectional, multicentre	195	KHQ	2	SCI	Bladder management spontaneous vs ISC
Anquetil *et al.*[268]	Cross-sectional	30	Qualiveen 30	3	SCI	Botox vs cystoplasty
Bernuz *et al.*[269]	Case series	152	Patient Global Impression of Improvement, Wuolle Questionnaire, Verbal Rating Scale	3	C5–C7 tetraplegic	Tetraplegic patients and QOL in those that could and couldn't do ISC
Böthig *et al.*[270]	Retrospective	56	International Consultation on Incontinence Questionnaire Short Form		High respiratory dependent tetraplegic	Suprapubic catheter vs ISC
Cameron *et al.*[271]	Inception cohort	24,762	Psychosocial factors, not QOL measurements		SCI	Complications associated with bladder management
Cameron *et al.*[272]	Cross-sectional analysis of prospective database	175	M-ISI, AUA-SI, Fecal Incontinence Severity Index		SCI and MS	Comparing bowel and bladder dysfunction

Abbreviations: AUA: American Urological Association; AUA-SI: American Urological Association Symptom Index; BTX-A: botulinum toxin A; DESD: detrusor external sphincter dyssynergia; HRQOL: health-related quality of life; IIQ-7: Incontinence Impact Questionnaire; I-LUTBSD: International Lower Urinary Tract SCI Basic Data Set; IPSS-QOL: International Prostate Symptom Score Quality of Life; I-QOL: Incontinence Quality of Life Scale; ISC: intermittent self-catheterization; KHQ: Kings Health Questionnaire; M-ISI: Michigan Incontinence Symptom Index; MS: multiple sclerosis; NDO: Neurogenic Detrusor Overactivity; QLI: Quality of Life Index; QOL: quality of life; RCT: randomized controlled trial; SCI: spinal cord injury; SF-36: 36-Item Short Form Health Survey; Qualiveen-SF: Qualiveen short-form; TOT: transobturator tape; UDI: urodynamic investigation; UDI-6: Urinary Distress Inventory.

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TABLE 3-2 Urologic Problems and Quality of Life in Spinal Cord Injury, *Cont'd*

Author	Study type	Number	QOL tools	Evidence grade	SCI type	Subject
Chartier-Kastler *et al.*[273]	Review of ISC as a treatment of neuropathic retention		Not specified		SCI, MS, SB	ISC
Chen *et al.*[274]	Single-arm clinical trial	38	UDI-6	2	Suprasacral SCI	BTx
Chen *et al.*[275]	Observational	72	I-QOL	3	SCI	Repeated BTx
Chen *et al.*[276]	RCT	100	I-QOL	1	SCI	Role of percutaneous tibial nerve stimulation
Cruz *et al.*[277]	Multicentre, double-blind RCT	275	I-QOL	1	SCI, MS	BTx
Ge *et al.*[278]	Observational	24	I-QOL	3	SCI	BTx
Giannantoni *et al.*[279]	Prospective observation	17	I-QOL	3	SCI	BTx
Ginsberg *et al.*[280]	2 double-blind RCT	691	I-QOL	1	SCI, MS	BTx
Grise *et al.*[281]	RCT	77	Qualiveen	1	NDO	BTx (Dysport)
Gurcay *et al.*[282]	Cross-sectional	54	SF-36 (Turkish version)	3		Bladder incontinence effects QOL
Gurung *et al.*[283]	Retrospective analysis	19	Questionnaire survey	3	SCI	Cystoplasty after 10 years
Hagan and Rekand[284]	Postal survey of bladder management and satisfaction	248	Questionnaire	3	SCI	Bladder management and satisfaction of life
Hollingworth *et al.*[285]	Prospective cohort	59	I-QOL, Short-Form 6-Dimension	3	SCI, other neurogenic patients	Maps urinary incontinence to QOL

Abbreviations: AUA: American Urological Association; AUA-SI: American Urological Association Symptom Index; BTX-A: botulinum toxin A; DESD: detrusor external sphincter dyssynergia; HRQOL: health-related quality of life; IIQ-7: Incontinence Impact Questionnaire; I-LUTBSD: International Lower Urinary Tract SCI Basic Data Set; IPSS-QOL: International Prostate Symptom Score Quality of Life; I-QOL: Incontinence Quality of Life Scale; ISC: intermittent self-catheterization; KHQ: Kings Health Questionnaire; M-ISI: Michigan Incontinence Symptom Index; MS: multiple sclerosis; NDO: Neurogenic Detrusor Overactivity; QLI: Quality of Life Index; QOL: quality of life; RCT: randomized controlled trial; SCI: spinal cord injury; SF-36: 36-Item Short Form Health Survey; Qualiveen-SF: Qualiveen short-form; TOT: transobturator tape; UDI: urodynamic investigation; UDI-6: Urinary Distress Inventory.

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TABLE 3-2 Urologic Problems and Quality of Life in Spinal Cord Injury, *Cont'd*

Author	Study type	Number	QOL tools	Evidence grade	SCI type	Subject
Ke and Kuo[286]	Retrospective cohort	22	AUA/IPSS-QOL index	3	SCI at or above mid thoracic	Transurethral incision of bladder neck
Krassioukov *et al.*[287]			Standardized Autonomic Function Questionnaire	3	SCI athletes	Catheterization practices
Kuo[288]	Prospective cohort	33	UDI-6, IIQ-7	3	SCI	Urethral injection of BTx
Kuo and Liu[289]	Prospective cohort	33	UDI-6, IIQ-7	3	Suprasacral, SCI	Repeat BTx
Kuo[290]	Prospective cohort	55	UDI-6, IIQ-7	3	SCI	QOL between detrusor, BTx and urethral BTx
Lima *et al.*[291]	Prospective cohort	67	SF-36, Qualiveen	2	Neurogenic bladder	QOL before and after cystoplasty
Linsenmeyer[292]	Review of BTx in NDO				SCI, MS	BTx
Liu *et al.*[293]	Cross-sectional study	142	SF-36, KHQ	3	SCI	Bladder management and QOL
Lombardi *et al.*[294]		75	SF-36	3	Incomplete SCI	Sacral neuromodulation
Losco *et al.*[295]	Retrospective review of TOT in SCI	27	Patient satisfaction no method identified	3	SCI	TOT
Martens *et al.*[296]	Cross-sectional study	93	Qualiveen, SF-36	2	Complete SCI	Brindley bladder stimulator
Merenda *et al.*[297]	Descriptive retrospective	16	Thematic analysis of QOL	3	SCI	Mitrofanoff
Noonan *et al.*[298]	Cross-sectional	70	SF-36	3	SCI >2 years post-injury	Impact of associated conditions on QOL

Abbreviations: AUA: American Urological Association; AUA-SI: American Urological Association Symptom Index; BTX-A: botulinum toxin A; DESD: detrusor external sphincter dyssynergia; HRQOL: health-related quality of life; IIQ-7: Incontinence Impact Questionnaire; I-LUTBSD: International Lower Urinary Tract SCI Basic Data Set; IPSS-QOL: International Prostate Symptom Score Quality of Life; I-QOL: Incontinence Quality of Life Scale; ISC: intermittent self-catheterization; KHQ: Kings Health Questionnaire; M-ISI: Michigan Incontinence Symptom Index; MS: multiple sclerosis; NDO: Neurogenic Detrusor Overactivity; QLI: Quality of Life Index; QOL: quality of life; RCT: randomized controlled trial; SCI: spinal cord injury; SF-36: 36-Item Short Form Health Survey; Qualiveen-SF: Qualiveen short-form; TOT: transobturator tape; UDI: urodynamic investigation; UDI-6: Urinary Distress Inventory.

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TABLE 3-2 Urologic Problems and Quality of Life in Spinal Cord Injury, *Cont'd*

Author	Study type	Number	QOL tools	Evi-dence grade	SCI type	Subject
Nwadiaro *et al.*[299]		125	"significant satisfaction"	3	SCI	Urethral catheter vs suprapubic cystostomy
Pannek and Kullik[300]	Prospective	41	Qualiveen	3	SCI	Urodynamics correlation with QOL
Patki *et al.*[301]	Prospective	37	International Consultation on Incontinence Questionnaire	3	SCI	BTx
Sánchez *et al.*[302]	Prospective observational	91	KHQ	3	SCI	Bladder management and QOL
Sorokin and De[303]	Review of patients unable to do ISC			3	SCI unable to do ISC	Review of patients unable to do ISC
Sussman *et al.*[304]	Prospective, double-blind, placebo controlled	92	I-QOL, HRQOL, Overactive Bladder Patient Satisfaction With Treatment Questionnaire, Patient Global Assessment	1	SCI, MS	BTx, specific QOL improvement measures with treatment
Tsai *et al.*[305]	Prospective open label	18	QLI	2	SCI	BTx transperineally for DESD
Utomo *et al.*[306]	Cochrane Review		Concluded that studies with QOL measurement needed		SCI, MS	Surgical management of functional bladder outlet obstruction
Zhang *et al.*[307]	Search of 8 databases		QOL method not stated	3		Acupuncture, systematic review protocol

Abbreviations: AUA: American Urological Association; AUA-SI: American Urological Association Symptom Index; BTX-A: botulinum toxin A; DESD: detrusor external sphincter dyssynergia; HRQOL: health-related quality of life; IIQ-7: Incontinence Impact Questionnaire; I-LUTBSD: International Lower Urinary Tract SCI Basic Data Set; IPSS-QOL: International Prostate Symptom Score Quality of Life; I-QOL: Incontinence Quality of Life Scale; ISC: intermittent self-catheterization; KHQ: Kings Health Questionnaire; M-ISI: Michigan Incontinence Symptom Index; MS: multiple sclerosis; NDO: Neurogenic Detrusor Overactivity; QLI: Quality of Life Index; QOL: quality of life; RCT: randomized controlled trial; SCI: spinal cord injury; SF-36: 36-Item Short Form Health Survey; Qualiveen-SF: Qualiveen short-form; TOT: transobturator tape; UDI: urodynamic investigation; UDI-6: Urinary Distress Inventory.

Conclusion

1. There are 4 validated QOL measures for urologic problems in SCI: I-QOL, Qualiveen, SF-Qualiveen, and NBSS. **[LOE 2]**

Recommendation

1. Clinicians aiming to measure QOL associated with urologic problems in SCI should be aware of which tools are validated for this specific patient population and should use these tools appropriately. **[GOR B]**

3.1.8 Timing and strategies of surveillance

The importance associated with regular surveillance is to guide, alter, or maintain treatment regimens. Just as patients make follow-up visits for catheter supplies or medication refills, so should these visits involve regular upper and lower tract imaging. The imaging studies determine the benefits or harms of current treatment regimes. Routinely scheduled visits for planned surveillance allow the clinician and the patient to re-evaluate their current treatment and detect new symptoms or clinical problems. New clinical issues should dictate the need for unplanned further diagnostic testing and modifications of the established protocol. **Thus, any surveillance protocol should be flexible and tailored to the patient's clinical evolution over time**. Furthermore, the clinician should determine what works for the patient, as well as the patient's willingness and ability to follow the treatment protocol. Regular surveillance allows for real-time visualization of progress in treating a complex and challenging disease state.

The frequency and type of upper and lower tract imaging in SCI patients should consist of (at a minimum) a renal ultrasound completed at yearly intervals. In addition, urodynamics should be performed at baseline after spinal shock, and follow-up studies should be at the discretion of the clinician. These diagnostic examinations may be performed in conjunction with a yearly urologic visit that consists of a detailed history and physical, creatinine, and urinalysis measurements by an experienced clinician trained in the diagnosis and treatment of neurologic voiding dysfunction patients. It is not simply enough to perform these tests in NGB patients; the clinician must also be able to interpret, diagnose, and formulate treatment plans based on their results.

3.1.8.1 Recommendations from medical societies

There are several societies that have previously published, with varying degrees of intensity, surveillance protocol recommendations. These include the following: 1) The **International Continence Society (ICS)** states that the following should be performed when evaluating a neurologic injury patient: detailed history and physical, urinalysis, PVR, blood testing, imaging of the upper tracts, and urodynamics.[82] Unfortunately, they do not give a time frame nor follow-up for these procedures; 2) The **American Urological Association (AUA)/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU)** recommended work-up for NGB patients includes urodynamics in follow-up at "appropriate intervals;" however, they do not give an example or time frame for these intervals;[83] 3) The **European Association of Urology (EAU)** guidelines on neurogenic lower urinary tract dysfunction are more definitive overall, and state that a urologic exam should be done annually in NGB patients; the annual exam should consist of a history and physical, blood testing such as creatinine, and a urine culture. Upper tract imaging and PVR should be performed in conjunction with a urinalysis every 6 months. The EAU guidelines also state that video-urodynamics is the gold standard in lower tract evaluation, and should be performed annually in those neurogenic patients with detrusor overactivity and decreased compliance;[84] 4) The **Paralyzed Veterans of America (PVA)** state that a urologic evaluation should be done yearly in SCI patients; they define this evaluation as consisting of an upper tract study, a lower tract study, and cystoscopy to define bladder anatomy. While no exact society-wide definition of appropriate follow-up protocols for NGB patients has been established, many published works detail that most urologists follow their NGB patients at least every 2 years and, at most, every 3 to 6 months.[85]

3.1.8.2 Deviation of surveillance protocols

If patients develop complications or experience increased LUTS within these yearly follow-up periods, it may be necessary to intercede with decreased intervals between surveillance visits. **Thus, any surveillance protocol should be flexible and adapted to the patient's clinical evolution over time**. This determination should be made by the experienced clinician and tailored to the patient's history of compliance to medical recommendations and treatment successes and failures. Surveillance also allows the physician to determine how well a particular treatment is working. Upper and lower tract imaging may alert a clinician as to when to change to a more (or less) invasive treatment as the anatomy and physiology of the lower urinary tract evolve from the initial injury and diagnosis. Some patients may regain control of volitional voiding, while others may have decompensation of their bladder control over time. Oftentimes these changes are silent (especially with insensate individuals) and may only be noted during real-time imaging of the bladder anatomy and function.

Conclusions

1. Patients with NGB secondary to SCI benefit from initial urologic evaluation and subsequent follow-up (including detailed history, physical examination, labs, and possible urodynamic testing) on a regular basis. **[LOE 3]**
2. While no exact definition of appropriate follow-up protocols for NGB in SCI patients has been established, many published works detail that most urologists follow their NGB patients at least every 2 years and, at most, every 3 to 6 months. **[LOE 2]**

Recommendation

1. Clinicians should regularly evaluate SCI patients with a urologic history, physical exam, and upper tract evaluation. **[GOR A]**

3.2 Management of Urologic Complications

3.2.1 Urinary tract infection and colonization

Despite advances in care, UTIs continue to be a major reason for morbidity and mortality in SCI patients. Risk of death attributed to urosepsis is higher in SCI patients compared with the general population. In SCI patients, the frequency of UTI is approximately 2.5 infections per patient per year,[84] which is also substantially higher than the general population.[86] Risk factors include urinary stasis, high bladder pressures, vesicoureteral reflux, bladder stones, and catheter use.[87] The bacteria implicated in UTIs in SCI patients are different than those in healthy adults. While *E. coli* remains the most common cause of UTIs, there is a tendency to find other organisms such as *Pseudomonas* (15%), *Acinetobacter* (15%), *Enterococcus* (6%), and multiorganismic infections (26%).[88] SCI patients are typically exposed to multiple antibiotics for various reasons, resulting in a high prevalence of antibiotic-resistant bacteria in the urine.

When a UTI is suspected, it is important that the urine specimen be obtained in an appropriate manner in order to prevent contamination and a potential false positive result.

For patients with indwelling catheters (either urethral catheter or suprapubic tube [SPT]), the indwelling catheter should be changed to a new catheter, and the specimen should be obtained from the new catheter after capping the catheter for a few minutes to allow a small amount of urine to collect in the bladder. The urine specimen should then be collected by uncapping the catheter. For patients with external catheters or who perform IC, the specimen should be collected by catheterization with a new sterile catheter.

3.2.1.1 Asymptomatic bacteriuria

Bacteriuria is an extremely common finding in NGB patients, regardless of the method of bladder management. In the vast majority of these patients, the bacteriuria is not associated with symptoms (asymptomatic bacteriuria). Treatment of asymptomatic bacteriuria is not beneficial to the patient, and may result in significant medication side effects.[89]

NGB patients with UTIs often present differently than the general population (see section 3.2.1..). Therefore, it is often prudent to defer antimicrobial therapy until the urine culture results are available. If the symptoms resolve while waiting for the culture results, this indicates that the symptoms were likely not caused by a UTI.

Although routine treatment of asymptomatic bacteriuria is not recommended, it is important to treat bacteriuria prior to urologic procedures in order to prevent the development of a symptomatic UTI or sepsis. Therefore, antibiotic therapy is recommended for SCI patients prior to cystoscopy procedures and urodynamic testing, whereas in most patients it is not.[90] In addition, standard antibiotic recommendations should be followed for more invasive procedures such as shock-wave lithotripsy (SWL), ureteroscopy, percutaneous renal surgery, and open or laparoscopic surgical procedures.

3.2.1.2 Symptomatic UTI

Symptomatic UTI in the SCI patient is defined as urinary culture with $\geq 10^2$ CFU bacteria/mL and symptoms including, but not limited, to LUTS, urinary incontinence, increased spasticity, autonomic dysreflexia, pelvic discomfort, fever, and decreased energy level. UTIs in SCI patients are considered complicated due to the presence of structural and functional urinary tract abnormalities. Therefore, an extended course (7–14 days) of antibiotics is recommended.[89] As noted above, the prevalence of resistant bacteria is high in SCI patients, and urine cultures should be obtained in all SCI patients with suspected UTIs in order to guide therapy. Recurrent UTIs are defined as 3 or more UTIs within 12 months.[91] In SCI patients with recurrent UTIs, upper urinary tract imaging should be obtained to evaluate for abnormalities such as urinary tract stones or hydronephrosis. The presence of UTIs in SCI patients can reflect an underlying functional abnormality of the bladder. Therefore, urodynamic testing should be considered, especially in patients with hydronephrosis and those who are voiding or who are performing IC. Cystoscopy should be performed if significant hematuria is present or if imaging suggests the presence of a bladder abnormality.

3.2.1.3 **UTI prevention**

3.2.1.3.1 Oral antibiotics

Daily oral antibiotic prophylaxis has been proposed as a method of preventing UTIs in SCI patients. A meta-analysis of 15 trials found that this therapy reduced asymptomatic bacteriuria but not symptomatic UTIs, and caused an increase in antibiotic resistance.[92]

3.2.1.3.2 Intravesical antibiotics

Although commonly utilized, there is very little literature addressing the use of intravesical antimicrobials for recurrent bacteriuria or UTIs. One case report described 2 patients with multidrug resistant *E. coli* who performed IC and remained infection- and bacteria-free for 8 to 9 months of follow-up.[93] In 2 RCTs involving SCI patients, daily aminoglycoside instillation (kanamycin with colistin, neomycin, and polymyxin B) decreased bacteriuria.[94,95] However Haldorson *et al.* randomized 108 adults with NGB to instillation of 0.1% of neomycin or no treatment, and no significant difference was seen in the incidence of bacteriuria.[96] In a prospective case series of 10 children with NGB who performed IC, daily instillation of 28.8 to 57.6 mg of gentamicin successfully reduced bacteriuria, and all patients had sterile urine after 1 week.[97] When a low-dose gentamicin solution was instilled daily in a different study, it was not effective for preventing bacteriuria or UTIs.[98]

3.2.1.3.3 Cranberry

Proanthocyanidin is the active ingredient in cranberry supplements and is thought to block the adherence of bacteria to uroepithelial cells, particularly *E coli*. D-mannose is thought to function in a similar manner. Several small studies have looked at the efficacy of cranberry in preventing UTIs in SCI patients, and results are mixed. However, the numbers are too small to draw conclusions and concentrations of proanthocyanidin were not standardized across preparations or studies.[99] Hess *et al.* looked at 47 patients with SCI, the majority with condom catheter drainage, randomized to 6 months of cranberry extract or placebo followed by the alternate for 6 months. No differences were seen in bacteriuria, but the rates of UTI and symptoms were lower when the patients were taking cranberry.[100] In a different crossover study by Linsenmeyer *et al.* there was no difference in bacteriuria or UTIs.[101] A Cochrane review did not find sufficient evidence to recommend cranberry preparations in the prevention of UTIs in the general population.[102] An independent review of the evidence by the Infectious Disease Society of America (IDSA) concluded that cranberry products should not be routinely used to reduce catheter-associated bacteriuria or UTIs in patients with NGB managed with intermittent or indwelling catheterization.[103]

3.2.1.3.4 Methenamine salts

Methenamine salts act through the production of formaldehyde from hexamine, which is a bacteriostatic agent. Urinary acidification also occurs, and it is unclear which of these mechanisms is responsible for the action of methenamine salts.[104] A meta-analyses of 7 trials demonstrated that, in patients without upper tract abnormalities, there is good evidence of benefit for prevention of UTIs.[93] However, a double-blind RCT in 305 SCI patients found no benefit in reducing UTIs, regardless of bladder management approach.[93]

3.2.1.3.5 Other agents

Small studies have demonstrated benefit of bladder inoculations with *E. coli* HU2117 and 83972 in SCI patients who were able to achieve successful colonization with the probiotic strains.[105,106] However, larger studies are needed to confirm these results. Ascorbic acid irrigations has not been shown to be efficacious in the prevention of UTI in SCI patients with indwelling catheters.[107]

3.2.1.4 Catheter type and UTI risk

In a randomized multicentre trial comparing the rate of UTIs in IC patients using hydrophilic-coated and noncoated catheters, there was a delay to time of first symptomatic UTI in the patients who used hydrophilic-coated catheters, and the incidence of antibiotic-treated symptomatic UTIs was reduced by 21% ($p<0.05\%$) in the acute phase (within 3 months of SCI). However, with longer follow-up there was no difference between the groups.[108] A recent meta-analysis looked at 5 studies comparing hydrophilic-coated to noncoated catheters and concluded that there was a significant decrease in the incidence of UTIs when using hydrophilic catheters.[109] In another randomized crossover trial, 45 patients were randomized to 24 weeks using single-use hydrophilic-coated catheters versus multiple-use polyvinylchloride catheters (washed with soap and water and air dried after every use). No differences were seen in febrile UTIs or antibiotic use.[110]

A recent crossover cohort study in acute stroke patients managed with standard indwelling silicone catheter or silicone catheter coated with an ultrathin layer of gold, palladium, and silver demonstrated no benefit to the coating.[111] In a Cochrane review of hospitalized patients with indwelling catheters, silver alloy was found to reduce the risk of catheter-acquired UTI in the short term. However, there was not enough evidence to suggest whether any standard catheter was better than another in patients catheterized for longer than 1 week.[112] In 2013, a Cochrane systematic review examined catheter policies for the management of long-term voiding problems in adults with NGB disorders. A total of 400 studies were examined, but none met inclusion criteria.[113]

3.2.1.5 Special situations

3.2.1.5.1 External sphincterotomy

Certain male patients with quadriplegia may be managed with an external sphincterotomy (to reduce detrusor leak point pressure) and condom catheter drainage. If such patients develop UTIs, assessment of PVR should be obtained to ensure adequate bladder emptying. Urodynamic testing should also be considered to assess the efficacy of the sphincterotomy. If there is evidence of urethral obstruction, repeat sphincterotomy may be indicated.

3.2.1.5.2 Urinary diversion

Following supravesical urinary diversion, pyelonephritis may occur. This is typically accompanied by fever, chills, leukocytosis, nausea, and vomiting. Upper tract imaging should be performed to rule out urinary obstruction. If obstruction is present, the system should be drained via percutaneous nephrostomy, and a urine culture should be obtained from the nephrostomy tube. Urine specimens from the urostomy bag or from the stoma are contaminated by skin flora, and findings from such specimens should be interpreted accordingly.

3.2.1.5.3 Continent catheterizable channel

The majority of patients with augmentation cystoplasty or continent urinary diversion will have mucus production that can act as a nidus for infection. Irrigation of the bladder or pouch at regular intervals with normal saline has been show to decrease the incidence of symptomatic UTI.[114]

Conclusions

1. Urinary specimens obtained from drainage bags or urostomy bags are often contaminated. **[LOE 4]**
2. Bacteriuria is an extremely common finding in patients with SCI and is not associated with symptoms (asymptomatic bacteriuria) in the vast majority of these patients. **[LOE 3]**
3. The bacteria infecting the urinary tract in patients with SCI may vary from those infecting able-bodied patients. **[LOE 2]**
4. Antibiotic resistance is commonly noted in the bacteria infecting patients with SCI. **[LOE 3]**
5. Recurrent UTI in an SCI patient may be a sign of an anatomical or functional abnormality. **[LOE 2]**
6. Cranberry does not prevent bacteriuria or UTIs in SCI patients. **[LOE 2]**
7. Methenamine salts do not prevent UTIs in SCI patients. **[LOE 2]**
8. Intravesical antibiotic instillation may reduce bacteriuria, but does not reduce the incidence of UTI in SCI patients on IC. **[LOE 2]**
9. Long-term IC using a hydrophilic coating does not prevent bacteriuria or UTIs. **[LOE 2]**
10. The use of antimicrobial-coated catheters does not reduce UTI risk in SCI patients managed with indwelling catheters. **[LOE 3]**
11. Regular irrigation with normal saline (or even tap water) in patients with continent urinary reconstruction or diversion may prevent recurrent UTIs. **[LOE 4]**

Recommendations

1. Clinicians should change to a new catheter when obtaining a urine specimen in patients with indwelling catheters. One can then obtain the urine specimen after capping the new catheter for a few minutes to allow a small amount of urine to collect in the bladder. **[GOR B]**

2. Clinicians should obtain urine specimens by catheterization with a sterile catheter for patients who manage their lower urinary tract with external catheters or IC. **[GOR B]**

3. Clinicians should not obtain urine specimens from urostomy bags, in patients with a urostomy, due to the risk of skin contamination. **[GOR B]**

4. Clinicians should not treat asymptomatic bacteriuria in SCI patients, except prior to urologic procedures. **[GOR B]**

5. Clinicians should base antibiotic therapy on urine culture results, even in SCI patients with recurrent infections. **[GOR A]**

6. Clinicians should evaluate patients with recurrent UTIs (≥3/year) with urinary tract imaging and UDSs. **[GOR B]**

7. Clinicians should not use daily antibiotic prophylaxis for preventing UTIs in SCI patients. **[GOR A]**

8. Clinicians should not routinely use cranberry, methenamine salts, or intravesical antibiotics to prevent bacteriuria or UTI in SCI patients. **[GOR C]**

9. Clinicians should not use hydrophilic-coated catheters to prevent bacteriuria or UTIs for patient who manage their lower urinary tract with IC. **[GOR B]**

10. Clinicians should not use antimicrobial-coated indwelling catheters to prevent UTI. **[GOR B**]

11. Clinicians may recommend regular irrigation with normal saline or tap water in patients with continent urinary reconstruction or diversion to prevent recurrent UTI. **[GOR C]**

3.2.2 Renal stones

Renal stone disease is an important source of urologic morbidity among SCI patients. Due to impaired autonomic sensation, particularly in those with SCI lesions above T6, classic symptoms of renal colic may be absent, making the diagnosis more challenging. Atypical symptoms such as generalized abdominal pain, frequent urinary infections, or autonomic dysreflexia may be the presentation of renal colic in this patient population. In addition, the presentation of renal stone disease is more frequently associated with infection or potentially serious obstructive urosepsis and has a high rate of serious complications, as demonstrated by the higher than expected need for poststone procedure intensive care unit admission.[115–117] Furthermore, there is a risk of chronic renal dysfunction[118,119] and mortality[117,120] associated with the presentation and treatment of renal stones among SCI patients.

3.2.2.1 Epidemiology

Renal stone disease occurs at a higher rate among patients with SCI compared to the general population. Rates 7 to 8 times higher than the general population have been reported,[121] and the risk of renal stone disease increases over time after the SCI.[122] Review articles that have synthesized the available evidence have estimated the proportion of SCI patients that develop renal stone disease is approximately 7% to 20% over a 10-year time period.[123-125] Prior research examining the rate of stone disease over time did not demonstrate a significant change in the number of renal stones diagnosed in SCI patients between 1973 and 1999;[121] however, additional large-scale studies are necessary to evaluate the incidence and prevalence in more contemporary time periods. Patients have the highest risk of developing renal stone disease during the initial 3 to 6 months after an SCI, likely due to hypercalciuria as a result of calcium mobilization from the bones of the lower limbs.[121-126]

3.2.2.2 Risk factors

Several intuitive risk factors for renal stone disease are associated with SCI. First, UTI and chronic bacteriuria (particularly with urea-splitting organisms such as *Proteus, Pseudomonas, Klebsiella, E. coli,* and some *Staphylococcus* species) have a well-established relationship with renal stone disease in SCI patients. There is a preponderance of struvite and calcium phosphate stones in SCI patients, and a higher than expected association between stone disease and positive urine cultures or postoperative urosepsis.[127–129] However, the role of UTI in the etiology of renal stone disease may be changing among SCI patients, as metabolic-based stones seem to be more common in recent years.[130] Second, metabolic changes relevant to renal stone disease are present in SCI patients. Historical studies have demonstrated that SCI patients often have hypercalciuria and hypocitraturia; however, there are not consistent differences between SCI patients with versus without a history of stone disease.[131–134] Third, reduced urine output may be a result of a conscious fluid restriction to reduce IC frequency or urinary incontinence, or due to autonomic alterations in perspiration.[118] Fourth, a history of renal stone disease prior to the SCI is a potent risk factor for renal stone disease after SCI.[115] Fifth, residing in the "geographic stone belt" (similar to the general population) is also a risk factor for renal stone disease among SCI patients, likely as a result of warmer temperatures and increased sun exposure.[135] Other potential risk factors for renal stone formation include complete cervical SCI, vesicoureteral reflux, and indwelling catheter usage. However, these risk factors have data with conflicting conclusions about their impact on renal stone formation, and analysis of their independent effects is not possible due to inadequate adjustment of confounding factors.[123–125]

3.2.2.3 Treatment

Like in the general population, in SCI patients, treatment of renal stone disease is now almost exclusively endourologic, and options such as conservative/medical management, SWL, ureteroscopy, and percutaneous nephrolithotomy (PNL) are all valid options. There are currently no comparative studies in the SCI population that assess safety, stone-free rates, or long-term outcomes among these treatment options. As in non-SCI patients, interventions for renal stone disease should be based on the patient's clinical condition, stone characteristics, stone location, and the physician's endourology experience and comfort level. Special considerations in the treatment of SCI patients include preoperative identification and treatment of bacteriuria, consideration of body habitus and any positioning limitations as a result of leg contractures or spinal curvature, thoracic spinal implants that may compromise fluoroscopic imaging, prior lower urinary tract reconstruction that may hinder retrograde endoscopic access, and the need for flexible instruments during PNL in a kidney scarred in place due to multiple prior percutaneous procedures.

A conservative approach to the management of renal colic (with or without medical expulsive therapy) is an acceptable option in the general population, and endorsed by numerous urologic societies, such as the AUA and EAU.[136,137] However, there is little research examining the safety or effectiveness of conservative management or medical expulsive therapy in SCI patients. One case series reported that a large proportion of SCI patients were successfully managed with conservation measures, although the details associated with this were not reported.[138]

SWL is the least invasive intervention for renal stone disease. The literature reporting the results of SWL in SCI patients is limited to small heterogeneous case series from the 1980s and 1990s. Stone-free rates were reported at between 44% and 73%.[117,139–146] These stone-free rates are lower than in the general population; however, this comparison is challenging, given the large stone burdens that were treated with SWL in SCI patients. Other factors that may reduce stone-free rates are impaired ureteral peristalsis due to chronic infection and the lack of post-SWL mobility. Specific potential considerations for SCI patients include a higher likelihood of ureteral stents or percutaneous drainage[141,144] at the time of (or prior to) SWL due to urinary infection, reduced anesthetic requirements for many patients,[140] and the potential need to treat small retained stone fragments that may be clinically relevant in SCI patients.[143]

The use of ureteroscopy in SCI patients was traditionally limited due to the inability to position patients for rigid ureteroscopy. However, with the advent of flexible ureteroscopy, this limitation has been significantly reduced and it is now a commonly used treatment modality.[115] In a matched cohort study, patients with NGB (including SCI patients) undergoing ureteroscopy had a longer operative procedure, a high rate of complications (including death), and a lower stone clearance rate.[147] Similar results were seen in 2 small case series of SCI patients treated with flexible ureteroscopy, with a higher than expected proportion of serious complications (including death), and a lower proportion of patients being rendered stone free after a single procedure.[148,149]

PNL is a more invasive treatment option; however, it is the preferred procedure for large stones (>2 cm). The literature reporting on the results of PNL in SCI patients is also limited to small, heterogeneous case series. While eventual stone-free rates are acceptable (80%–90%), most series require multiple procedures, higher risk (supracostal approach), or multiple renal punctures.[120,150–154] These series report that the risk of serious complications (including death) associated with PNL in SCI patients is approximately 6% to 20% (and in one series was determined to be 3-fold higher than in non-SCI patients[151]). In general, there seems to be a higher risk of blood transfusion, perirenal abscess, urosepsis, and intensive care admission than would be expected in the non-SCI PNL population.

Conclusions

1. SCI patients are at an increased risk of renal stone disease. **[LOE 2]**
2. Risk factors for renal stone disease among SCI patients include UTI, metabolic changes, reduced urine output, prior history of renal stone disease, and environmental conditions. **[LOE 3]**
3. SCI patients treated with SWL, ureteroscopy, or PNL generally have lower post-procedure stone-free rates, and higher risk of serious procedural and infectious complications compared with non-SCI patients. **[LOE 3]**

Recommendations

1. Clinicians may consider a metabolic evaluation for SCI patients with a history of significant renal stone disease; measures to reduce bacteriuria and increase fluid intake should be considered. **[GOR C]**
2. Antibiotic prophylaxis (guided by preoperative urine culture results) must be administered prior to interventions for urinary stone disease in SCI patients. **[GOR A]**
3. Elective stone treatment in SCI patients should involve the least invasive modality with the highest likelihood of success; informed consent should include a discussion of the increased perioperative risks associated with renal stone treatment in SCI patients. **[GOR C]**

3.2.3 Bladder stones

3.2.3.1 Epidemiology

The overall incidence of bladder calculi in patients with SCI has been variable, with rates ranging from 3.3% to 29%.[155,156] A longitudinal cohort study by Chen *et al.* has shown a decreasing incidence of bladder calculi over time, with a 29% incidence in 1973, decreasing to 8% by 1996.[156] This study also demonstrated that the highest incidence in stone formation was seen in white patients who were injured at a younger age, as well as those with a complete SCI. The time to stone formation is also reportedly variable. Hansen *et al.* report that the greatest risk of stone formation is in the first year after injury, with rates as high as 14% in this time period.[157] Other studies have shown a longer time period to stone formation, with the mean time to first stone formation of 95 months.[155] Once a patient develops their first stone, recurrence rates are high, with 16% to 23% of patients developing more stones in the future.[155,158]

The incidence of stone formation has been shown to be variable based on type of bladder management. The highest-risk patients are those managed with an indwelling catheter (i.e. urethral or SPT), with as high as a 9-fold increase in stone formation in these patients compared with continent patients who are catheter free.[156] The rates of stone formation with a urethral catheter have been reported to be 4% to 6.6%,[155,158] compared with an SPT, which have been reported at between 4% and 25%.[158,159] Patients who perform IC have an overall risk of stone formation of approximately 2%, or an annual risk of 0.2%.[155,158] Patients who use condom catheters or reflex void are also at risk of stone formation, albeit at a lower risk than those who have indwelling catheters or do clean intermittent catheterization (CIC), with rates as low as 1.1%.[155]

3.2.3.2 **Risk factors**

The risk factors for bladder stone formation in SCI patients are well known. As already described, the risk of stone formation increases significantly in patients with indwelling catheters. Catheter encrustation has been shown to have a positive correlation with bladder stone formation, with up to 85% of patients with encrustation found to have bladder stones on cystoscopy.[160] Indwelling catheters can also lead to bacterial colonization of the urinary tract. Colonization with urea-splitting organisms such as *Proteus, Pseudomonas,* and *Klebsiella* also leads to stone formation. SCI patients have been shown to trend toward alkalotic urine and hypocitraturia even without colonization with bacterial colonization, putting them at higher risk of stones.[161]

SCI patients are also at higher risk of stone formation due to immobility, particularly in the first 3 to 6 months after injury when they are the least mobile. Immobility can lead to demineralization of bone and subsequent hypercalciuria.[162]

Urinary stasis also leads to stone formation, despite the best attempts at complete bladder emptying. Patients with prior history of bladder outlet obstruction or those who develop obstruction as a result of their injury are at risk to develop bladder diverticuli. Stone formation can occur in these diverticuli. Patients who undergo outlet resistance procedures to improve continence are also at risk for stone formation, as stones can often lead to incomplete emptying and urinary stasis. This is demonstrated by the pediatric and adult populations of patients with bladder augmentation.[163,164] Augmentation patients also develop mucus from the bowel segment of the augmentation, leading to stones. Furthermore, patients with history of continent cutaneous diversion are at even higher risk of bladder calculi, with rates of intervention as high as 25%.[164]

3.2.3.3 **Consequences**

The consequences of bladder stone formation are similar to upper tract calculi. If stones are colonized by bacteria, the patients are at risk of developing symptomatic UTIs or sepsis from a UTI. SCI patients are at particularly high risk of developing sepsis because they do not always present with typical symptoms of UTI and treatment is more often delayed.

The other major consequence of developing bladder calculi is the need for recurrent procedures to attempt to rid the patient of his or her stone burden. With high recurrence rates, these patients often undergo multiple procedures during their lifetime to manage stones.

3.2.3.4 Treatment

Treatment of bladder calculi in patients with SCI is the same as in the general population. Options include endoscopic, percutaneous, or open approaches. As the stone size and burden increase, the tendency toward a percutaneous or open approach increases, but this is ultimately surgeon dependent. The goal of treatment is to remove all stone fragments. This is particularly important for patients with very limited mobility and those with bladder augmentations, as they are at very high risk of forming recurrent stones if fragments are left in the bladder.

Patients are often colonized with bacteria, so it important to obtain a urine culture prior to any treatment to ensure appropriate antibiotic coverage. Antibiotic prophylaxis in this population is not appropriate, as it promotes bacterial resistance.

It is important to consider the etiology of stone formation in the long-term management of stones. Patients with bladder outlet obstruction from prostatic enlargement, detrusor sphincter dyssynergia, or urethral strictures may benefit from treatment of the obstruction to allow for improved bladder emptying. This could result in a change to the overall bladder management, so it is imperative to discuss the expected outcome of a procedure to treat outlet obstruction with the patient.

Prevention of stone formation is key to decreasing recurrent stones. In the pediatric augmentation population, Kronner *et al.* described the importance of adequate oral fluid intake, timely IC, bladder irrigation, and eradication of urea-splitting bacteria.[163] These techniques have been implemented over the past 40 years and have played a key role in the overall decreased incidence of bladder stones in SCI patients.

Conclusions

1. Patients at highest risk of bladder stone formation are those with indwelling catheters. **[LOE 3]**
2. Other risk factors for bladder stone formation include urinary tract colonization with urea-splitting organisms, immobility, bladder augmentation, urinary stasis, or incomplete emptying. **[LOE 3]**
3. Treatment of bladder stones can be performed with an endoscopic, percutaneous, or open approach. **[LOE 3]**
4. Treatment of bacteria at the time of a procedure is important, but antibiotic prophylaxis should be avoided. **[LOE 3]**
5. Prevention of stone formation by various techniques, including increasing physical activity, ensuring adequate oral fluid intake, timely IC, bladder irrigation, complete bladder emptying, and eradication of urea-splitting bacteria, can decrease recurrence of stone formation. **[LOE 3]**

Recommendations

1. Clinicians must remove bladder stones (using an endoscopic, percutaneous, or open approach) in patients with SCI. **[GOR A]**

2. Clinicians should treat bacteriuria prior to intervention for bladder stones. **[GOR B]**

3. Clinicians may consider treating the outlet in patients with bladder stones and bladder outlet obstruction. **[GOR C]**

4. Clinicians should encourage techniques to prevent stone formation in SCI patients, including increasing physical activity and ensuring adequate oral fluid intake, timely IC, bladder irrigation, complete bladder emptying, and eradication of urea-splitting bacteria to decrease recurrence of stone formation. **[GOR B]**

3.2.4 Urethral trauma

3.2.4.1 Incidence, etiology, and risk factors

Urethral complications are recognized in patients post-SCI. A number of papers have looked at the incidence of urethral complications in specific subsets of patients post-SCI.

A radiology paper reported on urethral findings in 200 men with SCI.[165] The report does not state why the men underwent urethrography. It reported 16 urethral diverticula, 5 strictures and 1 false passage. The diverticula were said to occur at the penoscrotal junction most commonly followed by the membranous urethra and rarely at the fossa navicularis. The penoscrotal junction is particularly susceptible in patients with an indwelling catheter that is improperly worn. Similarly, another paper reviewed video-urodynamics and urethrography studies over 1 year and reported urethral diverticula in 4.2% to 9.8% of patients depending on the appearance of the diverticulum, as assessed by 3 independent physicians.[166]

A study consisting of 1,418 video-urodynamic studies in SCI men revealed a 25% prevalence of urethral strictures in men who performed CIC compared with 14% in men who used other methods of bladder emptying.[167] The median time to stricture was reported at 5.9 years. Interestingly, only 1 in 3 strictures underwent urethrotomy; stricture recurrence posturethrotomy was 100%. In general, radiological studies suggest a risk of urethral trauma in SCI patients of about 20%, depending on how patients were selected for the investigations and the time from injury.

Risk factors for urethral diverticula were assessed in 55 patients with SCI.[168] The risk factors for diverticula in the bulbomembranous urethra were found to be the prior sphincterotomy, use of condom catheter drainage, history of UTI, and detrusor external sphincter dyssynergia; the only risk factor noted for diverticula at anterior urethra was CIC.

A retrospective case series reviewed complications in 142 men with SCI who managed their lower urinary tract with and without indwelling catheters. The following complications were noted in the 56 men with indwelling catheters: 5 fistulae, 12 erosions, 13 strictures, and 5 periurethral abscesses. Of the 86 noncatheterized men, the following complications were noted: 10 fistulae, 6 erosions, and 4 strictures. This result would suggest that catheter-related complications such as erosions and strictures are more prevalent in men with indwelling catheters.[169] The other risk of long-term indwelling catheters in men is formation of a hypospadias (**Figure 3-1**). In another study of 123 patients, 12 developed urethral strictures after a mean 8 years of follow-up.[170] Two strictures occurred in 5 patients (40%) with an indwelling catheter and in 8 patients out of 79 patients (10%) performing IC. From 400 cases of indwelling catheters, 2 strictures were found. In addition, 4 abscesses were noted that subsequently ruptured and developed into urethral diverticula.[171]

FIGURE 3-1
Example of a male patient with SCI with a urethral indwelling catheter for many years who has spatulated the entire shaft of the penis with pressure from the catheter. He was successfully managed with a suprapubic catheter.

Photo courtesy of Anne P. Cameron, MD.

The primary issues that can be seen in women with indwelling urethral catheters include leakage of urine around the catheter (either from urethra erosion or detrusor overactivity) and urethral erosion, which can be significant enough that a catheter is unable to be maintained in the bladder. A prior review of long-term indwelling catheters in women with NGB noted urinary leakage around the catheter in 92% of women.[172] The time between catheter insertion and leaking due to urethral erosion can be between 6 months and 30 years.[173] The incidence of urethral trauma with an indwelling urethral catheter is variable and will depend on the length of time with the catheter, frequency of catheter change (it should be changed every 4–6 weeks), catheter size (sizes 14–16 Fr are generally recommended with a 10-cc balloon), and how well the patient cares for the catheter, as it will intermittently pull against the bladder neck. Larger catheters increase the risk of urethral erosion or discomfort and are not effective at (initially) decreasing pericatheter leakage, which is almost always due to detrusor overactivity (unless this evolves to a state of urethral erosion). In addition, increasing balloon size when catheters are spontaneously expelled is not advised, as this can result in urethral erosion and the catheterization method needs to be changed, not simply upsized.

Urethral erosion occurs due to prolonged urethral catheterization. This can result in an incompetent, patulous urethra in women (**Figure 3-2**). Careful assessment needs to be made of the urethral damage in women, as often the bladder neck and urethra are destroyed and, if the damage is severe enough, 1 or 2 fingers can be directly inserted into the bladder. In addition, there is sometimes no tissue between the finger and inferior pubic ramus, which can impact decisions regarding management.

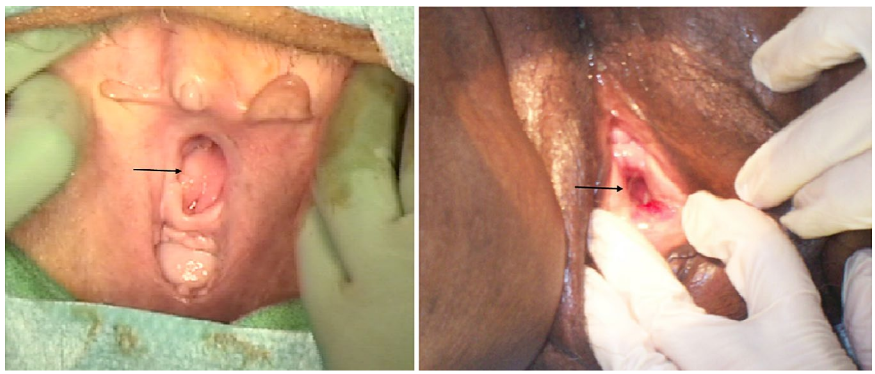

FIGURE 3-2
Example of two female SCI patients where catheter upsizing and balloon over-inflation were used to manage incontinence around a catheter, resulting in profound urethral erosion with palpable pubic bone via the urethra in both cases.
Black arrows indicate the urethra.

Photos courtesy of Anne P. Cameron, MD.

CIC is an established method of bladder emptying in SCI. The risk of creating a false passage in the urethra is not reported in the literature, as some false passages will remain undetected and eventually form a stricture or diverticulum. In a series of 9 patients with a false passage in the urethra, all patients were stented either after transurethral incision, fulguration, or stenting alone. All had a catheter left *in situ* for 2 to 3 weeks postoperatively. Two of these strictures recurred and these patients ultimately required urinary diversion.[174]

The risk of urethral stricture in patients who empty their bladder with urethral IC is reported to be less than 3.2% in some studies.[175,176] In the study by Asfar *et al.*, 164 patients performing CIC were followed up for a mean of 84 months, and only 1 patient developed a urethral stricture. Other papers on long-term IC, however, report a higher stricture rate of approximately 10% to 20%.[177–179] With the long-term rate of urethral stricture being higher, methods to reduce this risk by changing catheter design have been attempted.

An RCT found no significant difference in stricture rate or hematuria with the use of a hydrophilic-coated catheter versus a polyvinyl chloride (PVC) catheter, but the trial unfortunately had a high drop-out rate and so was inconclusive.[180] In another study of 30 patients with the use of low friction hydrophilic catheters, 4 (13%) strictures were noted at a median of 7 years of follow-up.[181] A prospective crossover study of 18 patients comparing a nelaton catheter with a prelubricated nonhydrophilic catheter found lower urethral cell count on the surface of the nonhydrophilic catheter, suggesting that this catheter causes less trauma.[182] Another report of 14 patients who crossed over from a LoFric® catheter (Astra Tech AB, Mölndal, Sweden) to an EasiCath® (Coloplast A/S, Espergærde, Denmark) had a dynamometer study that showed less friction with the former.[183] It is entirely reasonable that a low friction catheter would cause less urethral trauma, but it is unlikely that one size fits all patients, and causes of false passages may also be related to individual anatomy and flexibility of the catheter.

In developing countries, as well as in some first-world countries, patients may not be able to afford multiple IC catheters; thus, many reuse catheters. A study showed that reusable silicone catheters did not lead to increased urethral complications in 23 men, but did lead to increased UTI.[184] The average length of use of a single catheter was 3 years. Therefore, the use of reusable silicone catheters could be an economical method of bladder management when resources are limited.

There are no RCTs comparing the outcomes of indwelling urethral catheter with other forms of bladder management in patients with SCI specifically.[113] A recent meta-analysis noted the following complications to be more commonly found with indwelling urethral catheters compared with other forms of bladder management:[185] urethral erosion (catheter-induced hypospadias),[186] urethrocutaneous fistula, epididymitis, and periurethral abscess.[187] Catheter blockages and encrustation are common.[188,189] Multiple reports indicate that the rates of complications are higher in patients with indwelling urethral catheters compared with CIC.[187,190,191]

Several methods to minimize the risks associated with indwelling urethral catheters have been suggested. In addition to good hygiene and care of equipment, increased fluid intake (>2 L/day) is recommended to decrease catheter blockage.[188] Silicone catheters are recommended over latex catheters.[192] Anticholinergic medication may be beneficial to help protect the upper urinary tracts.[193] Use of an anchoring device (e.g. StatLock device) may be helpful to decrease the risk of UTI and urethral erosion.[186,194] Weekly catheter changes have been suggested to decrease infections,[195] but this is often not feasible from a practical perspective. The benefit of catheter irrigation is unknown. Daily prophylactic antibiotics are not recommended for routine use in patients with indwelling urethral catheters. Despite these efforts, indwelling urethral catheters are associated with a high rate of genitourinary complications, and routine surveillance is recommended.[196–198]

3.2.4.2 Investigation and management

The investigation and management of urethral complications has been described by a number of case series and reports. There are no randomized trials in this area. The reports describe the surgical outcomes of managing urethral trauma for specific conditions such as diverticula, erosions, fistulae, and false passages, or surgeons have reported combined outcomes of urethral surgery for all the types together to provide a larger data set.

With regard to urethral diverticula, most case series describe the use of cystoscopy to diagnose the condition. For diverticula in the posterior urethra, appreciation of the surrounding anatomy would also be considered useful, and some form of cross-sectional imaging would be advised. In a study of 8 patients with diverticula, ultrasound was used during intraurethral injection of saline, and all diverticula were defined morphologically on ultrasound.[199] Ultrasound is not a substitute for endoscopy or for CT/magnetic resonance imaging (MRI), but can be used if there is a contraindication to CT/MRI.

The original description of urethral diverticulum repair was by Monseur.[200] Little has changed since, and a case series of 48 patients where 90% were bulbar and 10% penile reported no diverticular recurrences, although strictures occurred in 3 patients. Ten patients with previous fistulae also recurred, but half of these resolved with catheterization for 4 to 5 weeks.[201] Another smaller case series of 4 patients with urethral diverticula advocated 1-stage repair with suprapubic diversion and reported no failures.[202]

False passages commonly occur due to catheterization in the SCI population. The false passage is easily diagnosed with cystoscopy. Management of the false passage in the first instance should involve catheterization with a 14- to 16-Fr catheter for 3 to 6 weeks. In one study, this was performed for 3 to 6 weeks, with 5 days of antibiotics in 6 patients. All false passages disappeared, and there were no recurrences at a mean 10 months of follow-up.[203] Another study reported on 8 patients with a urethral false passage treated with a 12-Fr catheter inserted under endoscopic control.[204] If a patient refuses a catheter, then a stent may be inserted instead. In 5 male patients who refused indwelling catheter for false passage due to interference with sexual intercourse, nitinol stents were inserted for 3 to 6 months, allowing the false passages to heal.[205] If the false passage track has matured and fails to heal, then an urethroplasty may be indicated.

A report of 14 women with a patulous urethra reported good success in all at 6 to 60 months follow-up with pubovaginal sling repair, and all women were able to catheterize through the urethra.[206] A sufficient amount of urethral length is necessary (at least 1 cm), or a sling should not be considered.[206] When the urethra will not sustain a sling, urethral closure may be undertaken either abdominally or transvaginally, or via a combined approach. Six women who underwent transvaginal closure were reported to be dry at 6 years of follow-up.[207] Also, another report of 11 women operated on via a transvaginal approach reported on 1 failure at 6 weeks.[208] However, another series reported only 40% success from 5 transvaginal closures, but 100% success from 10 combined abdominal and transvaginal closures.[209] Another series stated that the retropubic approach to bladder neck closure in 26 patients had no complications compared with the transvaginal approach undertaken in 2 women.[210] Similarly, in another study, 4 patients who underwent transabdominal urethral closure were dry, whereas 4 of 8 patients who underwent urethral closure transvaginally developed urethral fistulae.[173] The benefits of transvaginal closure include the reduced morbidity of the less invasive procedure, but this method is unlikely to be suitable for all patients. Currently, there is insufficient evidence to say when to use either approach.

For catheter-induced erosion causing hypospadias deformity in men, urethroplasty is often undertaken. A report of 11 men who had urethroplasty with a median length of erosion of 6 cm reported a success of 64%.[211] All 4 recurrences occurred within the first month. In men with significant loss of urethral tissue, transperineal closure of the membranous urethra may be undertaken along with a form of urinary diversion. In one study of 8 men and 4 women, urethral closure was achieved in all men and 3 women.[212] Some patients, however, required multiple procedures to gain continence control.

Fistulae in the SCI population may be complex. Where possible, cross-sectional imaging such as MRI maybe useful in determining the anatomy of the fistula.[213] A fistula may occur due to urethral obstruction, catheterization, infection from poor bladder management, and pressure ulcers. The underlying problem needs to be managed just as carefully as the fistula. Occasionally, a fistula may heal if the underlying problem is initially addressed.[214] However, surgical intervention focused on the urethra is often required and, if the underlying problem (and urethral injury) is severe enough, urinary diversion may be necessary. For an infected fistula, abscess drainage and treatment of any osteomyelitis is necessary. In patients with prior sphincterotomy, a urinary diversion is a good option.[215]

In a report of 21 patents with urinary-cutaneous fistulae, 7 fistulae were due to decubitus ulcers, 5 to wound infections, 4 to condom catheter complications, 4 to traumatic catheterizations, and 1 to pelvic trauma. Thirteen of 21 patients underwent fistula repair, with 7 eventually requiring an ileal conduit or suprapubic catheter.[216] In a similar report of urethral reconstruction performed in 17 patients (among them 6 urethral strictures, 4 erosions, 3 fistulae, and 1 diverticula), 11 patients eventually required urinary diversion.[217] Only 4 of the 17 patients had a patent urethra at 3.7 years of follow-up. In severe cases of decubitus pressure ulceration, both fecal and urinary diversion may be required.[218]

Another small case series reported 4 patients with urethral stricture, fistula, or diverticula who had urethral reconstruction successfully with an adapted Monseur's technique.[219] A prospective database of 23 patients consisting of 10 erosions, 7 strictures, 3 diverticula, 2 urethrocutaneous fistula, and 1 combined diverticulum and stricture were treated surgically.[220] Successful reconstruction was possible in 60% of the erosions, 86% of the strictures, and 67% of diverticula and fistulas. Patients with severe urethral erosion associated with deficiency or deterioration of the penile skin are likely not candidates for urethroplasty with penile or preputial skin flaps. In such patients, a urinary diversion may be warranted.

Management of urethral stricture in men performing regular CIC is a challenge. Prior to considering any intervention, the urethral stricture should be adequately assessed with urethrocystoscopy, urethrography, voiding cystourethrography, and/or ultrasound of the urethra.[221] Urethrotomy is often the initial therapy; however, long-term success is not optimal, and further intervention is often required.[167,222] Part of the challenge is the definition of success. A urethra may not be patent on radiographic evaluation, but may be open enough to allow for regular CIC. In one study of 105 men undergoing internal urethrotomy for urethral stricture, 8 patients still had radiographic evidence of a urethra stricture but were able to perform CIC without an issue.[167] However, the risk of repetitive urethral microtrauma due to CIC raises the risk of recurrent stricture in this patient population.[223] For those patients with recurrent stricture, disease options would include repeat urethrotomy, urethral reconstruction, and urinary diversion.

Conclusions

1. Urethral complications occur in approximately 20% of SCI patients over the long term. **[LOE 3]**
2. Intermittent catheterisation is associated with urethral strictures, diverticula, and false passages. **[LOE 3]**
3. Indwelling urethral catheterization is associated with a high rate of urethral complications, including urethral stricture, erosion, fistula, and periurethral abscess. **[LOE 3]**
4. Urethral damage in the female SCI patient may occur as early as 6 months with an indwelling urethral catheter. **[LOE 3]**
5. Reusable catheters do not increase the risk of urethral trauma compared with single-use catheters. **[LOE 3]**
6. There is insufficient evidence for whether a transvaginal, abdominal, or combined approach is better for urethral closure of an eroded female urethra. **[LOE 3]**
7. Surgery to correct urethral complications carries a higher risk of failure in the SCI population than in the non-SCI population. **[LOE 3]**
8. Urinary diversion is sometimes needed to deal with urethral complications in SCI patients. **[LOE 3]**

Recommendations

1. Clinicians should encourage women with SCI to limit indwelling urethral catheter use to less than 6 months in order to avoid the risk of urethral atrophy and erosion. **[GOR B]**

2. Clinicians should consider treating female urethral erosion with an autologous pubovaginal sling, if sufficient urethral tissue is present. **[GOR B]**

3. Clinicians should consider bladder neck closure to treat the destroyed female urethra. **[GOR B]**

4. Clinicians may consider a period of catheterization for the initial management of a male urethral false passage. **[GOR B]**

5. Urologists may consider initial management of male urethral stricture with dilation or urethrotomy. **[GOR B]**

6. Urologists may consider repeat dilation, urethrotomy, urethroplasty, and lower urinary tract reconstruction as options for male SCI patients with recurrent urethral stricture disease. **[GOR C]**

7. Urologists should avoid ventral graft urethroplasty in male SCI patients due to concerns about urethral diverticulum and difficulty performing IC. **[GOR C]**

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C4

Non-Surgical Urologic Management of Neurogenic Bladder After Spinal Cord Injury

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Non-Surgical Urologic Management of Neurogenic Bladder After Spinal Cord Injury

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Methods

A literature review was performed using PubMed to collect relevant publications for each individual section in this chapter. The search was limited to human data and patients with spinal cord injury, unless data was only available for other similar neurological conditions. All publications including original research, systematic reviews, meta-analyses, review articles, and case reports were included. Only articles published in English were included, and when multiple articles discussed a similar condition or question, the most relevant or highest evidence was referenced.

4.1 Introduction

After spinal cord injury (SCI), patients suffer from several disabilities and are almost universally affected by neurogenic bladder. Before the advent of modern urologic care, those who survived their initial injury died of urologic complications of renal failure or urosepsis.[1] Thankfully, with the introduction of proper catheter drainage and antibiotics, survival changed dramatically, and urologic causes have fallen from the most common cause of death to the fifth.[2,3] Now that patients are surviving to near-normal life expectancy, quality of life (QOL) and social participation of the patient have become some of the urologist's biggest roles in the management of these patients. Clearly, a top-down approach of management first involves preserving renal function; but with the rarity of renal failure in this population, the new priorities have become continence and a feasible bladder management plan that allows patients to leave the house and participate in society independently. With the advent of advanced catheter technology, modern medical therapy and botulinum toxin (BoNT) working together to preserve the upper tract, continence and independence are now feasible for more patients.

4.2 Intermittent Bladder Catheterization

4.2.1 Introduction

Despite little high-quality data to examine all methods of bladder drainage in patients with SCI,[4,5] intermittent urethral catheterization (IC) is generally recommended as the preferable method of bladder drainage in patients with SCI.[6,7] Intermittent urethral catheterization has also been found to be the preferred method of management for SCI patients from a urologist's perspective.[8] Although no large, high-quality, randomized controlled trials (RCTs) exist to examine which bladder drainage mechanism is best,[5] several studies report higher rates of complications with an indwelling catheter compared with IC, including higher rates of stones, urinary tract infections (UTIs), urinary tract fistulae, strictures, and cancer.[9–12]

There is, however, difficulty in determining exactly what bladder management is being performed in SCI patients around the globe. A recent Turkish study reported the types of bladder management techniques in 337 SCI patients who had had their injury for a minimum of 2 years. The authors found that IC was used in 77.9% of patients while only 3.8% had indwelling catheters, 13.8% voided spontaneously, 2.9% used voiding manoeuvres, 1.3% wore diapers, and only 0.6% used condom drainage.[13] Although the use of IC has been increasing over time, in the United States Spinal Cord Injury Model System registry, from 12.6% in 1972 to 56.2% in 1991, only 20% of those discharged from hospital on IC will continue this method of bladder drainage in the long term. The use of indwelling catheterization has fluctuated over time, from 33.1% in 1972 down to 16.5% in 1991 and back up to 23.1% in 2001. In this same group, 70% of patients discharged from hospital with an indwelling catheter remained on this form of management in the long term.[14]

Weld *et al.* reviewed 316 patients (313 men) in the American Veteran population followed for 18.3 ± 12.4 years. They found that 92 (29%) patients performed IC, 114 (36%) had an indwelling urethral catheter (IUC), 74 (23%) voided spontaneously, and 36 (11%) had an indwelling suprapubic tube (SPT). Most patients changed their method of bladder drainage at least once during the follow-up period. Most commonly, quadriplegic patients changed from IC to indwelling catheter due to incontinence and lack of independence.[11]

Unfortunately, IC is not possible in all patients with SCI. In a recent Turkish survey study of patients with SCI, Yilmaz *et al.* found that 26% of patients reported being unable to perform IC. Reasons included insufficient hand function, inability to position properly, and spasticity.[15] Similarly, Zlatev *et al.* reported that 23.3% of patients with SCI were unable to complete IC based on a retrospective analysis of upper extremity function in more than 4,000 SCI patients in the United States.[16] Yavuzer *et al.* in Turkey assessed compliance with the initial bladder drainage method and found that 52% of patients discharged with IC reverted to an indwelling catheter by an average of 24 months following discharge. Reasons for not maintaining IC included dependence on caregivers, spasticity, incontinence between catheterizations, and lack of external collection devices for women.[17]

In developing countries, however, access to IC supplies or even the requisite sanitation with running water to perform the skill is unavailable. Hence the rate of indwelling catheter use, which only requires monthly changes, is much higher, with reports of indwelling catheters of 76% in Nigeria[18] and 84% in Turkey,[17] but in countries with high-quality medical care and access to supplies, the rate of indwelling catheter is as low as 37% in Bosnia,[19] 38% in South Korea,[20] and 13% to 37% in the UK.[21,22]

Resultant of this poor care, mortality after SCI is also much higher in developing countries. The 1-year mortality after SCI in Nigeria is 34%, South Africa 13%, Zimbabwe 49%, and Latin America 21%, with Sierra Leone having an astounding 83% mortality after 28 months. Developed nations have substantially better survival after SCI, with 10-year mortality approaching that of the general population, from 11% to 16% in the United States, Canada, Australia, and Western Europe.[23] The majority of deaths in developing countries are due to pressure ulcers and renal complications. Although indwelling catheter usage or even the lack of access to this basic urologic treatment cannot be deemed the cause of this mortality, it is clear that without basic urologic care mortality is very high.

Although IC is recommended as the optimal form of bladder management in patients with SCI, it may not be feasible to perform or maintain in all patients for a variety of reasons. Additional options include condom catheter drainage, or indwelling catheters such as urethral catheters or SPT. In addition, and beyond the scope of this discussion, other surgical options exist, including continent catheterizable stoma or urinary diversion such as an ileal conduit.

Factors to consider when choosing an appropriate method of bladder drainage in SCI patients include: age, gender, comorbidities, level and completeness of injury, hand function, availability and desire for caregiver assistance, body habitus, spasticity,[6] and in the developing world access to running water, sanitation, and catheter supplies.

Intermittent urethral catheterization is usually indicated for assisted bladder emptying in SCI patients, providing benefits, such as preservation of the upper urinary tract function and improvement of urinary continence. In addition, self-IC (when able) provides more independence to the patient and consequently a better quality of life.[24] Nevertheless, IC may be associated with specific complications.

The purpose of this section is to review the indications, technique, classification, benefits, and complications of intermittent bladder catheterization in spinal cord–injured patients.

4.2.2 Intermittent catheter options

"Sterile" IC was originally proposed by Guttmann and Frankel (1966).[25] The sterile technique implied the use of sterile materials, handled with sterile gloves. At that time, sterile technique was complex and costly, with limited indication outside the hospital environment.

These limitations opened the way to the introduction of "clean" IC, described by Lapides in the beginning of the 1970s,[26,27] where he proposed that a "sterile" or "strictly aseptic" technique was not necessary and that the use of the "clean" catheterization technique could be employed. This revolutionary concept proved to be easily employable and reduced urologic complications in SCI patients. Still, sterile IC does somewhat reduce the risk for associated urinary infection and/or bacteriuria compared with clean IC.[28–31]

More recently, hydrophilic catheters have been introduced with the objective of facilitating IC techniques, improving patient comfort, and reducing complications associated with catheterization. Hydrophilic catheters have a polymer layer, which coats the surface of the catheter and has high affinity for water. These characteristics form a slippery surface, which facilitates the catheter's entrance into the urethra. The development of such catheters came with a new IC technique, called the "no touch" technique, providing benefits in terms of less external contamination.[31] A pull-in aid or special package is used to handle the catheter without directly touching the sliding surface of the hydrophilic catheter.

There is conflicting evidence suggesting that the use of lubricated hydrophilic catheters is associated with less risk for symptomatic urinary infections in SCI patients.[32] However, the costs of the hydrophilic catheters can still limit their broad use in different communities.

4.2.3 Complications of intermittent catheterization

One of the main drivers of the success of IC is the reduction of symptomatic UTIs and preservation of renal function compared with indwelling catheters. However, this management method is life-long, and all long-term complications need to be considered, as there are possible delayed complications.

The more common complications of IC are recurrent symptomatic UTIs, lesions of the urethral mucosa, urethral stenosis, and false passages.[33,34] Wyndaele and Maes conducted a retrospective study with a mean follow-up of 7 years, demonstrating that 20% of the patients who perform clean IC with conventional non-coated polyvinyl chloride (PVC) catheters with lubricant had some sort of complication. Urethral lesions were the most frequent of these, including urethral stenosis/stricture or false passage.[33] Perrouin-Verbe *et al.* also assessed the incidence of long-term clean IC complications. Twenty-eight percent of the patients developed symptomatic UTIs. At a 5-year follow-up, the rate of epididymitis was 28.5%, and the rate of urethral stenosis was 19%.[34]

Adequate frequency of catheterization, good education on hygiene, avoidance of bladder overfilling, and maintenance of a low-pressure bladder are among the most important factors for preventing UTI.[35]

4.2.4 Studies comparing hydrophilic versus conventional catheters

Several authors have compared catheter types for IC, but most have noted only small differences in complications. Data on patient preference also needs to be interpreted with caution, as consumer-directed advertising of single-use catheters is heavily promoted. De Ridder *et al.* conducted a prospective, randomized study, including 123 SCI patients, comparing the intermittent bladder catheterization with hydrophilic catheters versus conventional catheters with lubricant. There was no statistically significant difference between the groups regarding the occurrence of bacteriuria or leucocytes. However, after 1-year follow-up, there were more symptomatic urinary infections in the group using a conventional catheter with lubricant (82% vs 64%, respectively; p=0.02).[32] Only 57 (46%) of 123 patients completed the 12-month study.

Bjerklund Johansen *et al.* assessed patients' satisfaction with changing to hydrophilic catheters for IC. Of 409 patients recruited, 378 (283 men, 95 women; mean age: 43.5 years; 65% with SCI) completed a 12-day trial of the hydrophilic catheter and then completed a satisfaction questionnaire. At baseline, 74% used standard PVC catheters and 36% pre-lubricated PVC catheters. Mean duration of IC was 4.6 years. Of the 378 patients, 55.2% were happy to continue with the hydrophilic device. No individual patient factors were found to be significant in catheter choice.[36]

Prieto *et al.* reviewed the evidence on strategies to reduce UTI, other complications, or improved satisfaction in IC users by comparing: (1) one catheter design, material, or technique versus another; (2) sterile technique versus clean; or (3) single-use or multiple-use catheters. Thirty-one trials (13 RCTs and 18 randomized crossover trials) addressed the inclusion criteria comparing method or design and UTI/bacteriuria, other complications, or participant-assessed outcomes. Studies varied widely in follow-up, UTI definition, and attrition; in some, data could not be combined. Where there were data, confidence intervals were wide, and hence clinically important differences could be neither reliably identified nor ruled out. The authors concluded that current research evidence is weak and study design issues are significant.[37] It has not yet been established whether the incidence of UTI, other complications such as hematuria, and user satisfaction are affected by sterile or clean technique, coated or uncoated catheters, single- or multiple-use catheters, or by any other strategy. It is important to emphasize that this systematic review included not only SCI adults, but also children with neurogenic bladder dysfunction (NBD) due to myelomeningocoele, men with prostatic obstruction, and women with multiple sclerosis (MS). Studies varied in setting, length of follow-up, definitions of outcomes, and participants. There were a variety of settings—acute care neurology units, community, and long-term care.

Li *et al.* conducted a systematic review and meta-analysis of RCTs comparing the use of hydrophilic and non-hydrophilic catheters for IC in patients with SCI.[38] Five studies involved 508 subjects; 462 subjects completed the study and were included in this meta-analysis. There was a significantly lower incidence (odds ratio [OR]: 0.36; 95% CI: 24%–54%; $p<0.0001$) of reported UTIs in the hydrophilic-treated group compared with the non-hydrophilic–treated group. Hematuria was also reported significantly less in the hydrophilic-catheter group than in the non-hydrophilic–catheter group (OR: 0.57; 95% CI: 35%–92%; $p=0.001$). This meta-analysis supports the benefit of hydrophilic catheters over non-hydrophilic ones in patients with SCI. The odds reduction of UTI was cited at 64%, and 43% for hematuria. Most of the evidence came from men, and so it does not seem that these data can be generalized to women with SCI without further evidence.[39] Also, it must be noted that much of the literature comparing intermittent catheter brands is industry sponsored and must be interpreted cautiously. A realistic approach in clinical practice would be to allow patients to try several brands and types of catheters, and allow them to choose the preferred catheter for their own needs.

4.2.5 Intermittent catheterization technique and strategies to avoid complications

Intermittent urethral catheterization patients should be instructed to wash their hands well, use non-contaminated (clean) catheters and lubricants, as well as clean the region of the urethral meatus before introducing the catheter. The cleaning of the hands and the urethral meatus can be done with water and soap.[40] The patient should slowly withdraw the catheter at the end of the procedure in order to ensure that all urine is emptied from the floor of the bladder.

The patient may adopt different positions to perform the catheterization (sitting, lying, or standing), depending on his/her physical limitations and the place where the procedure is carried out.[41] Women may use a projected mirror for better visualization of the urethral meatus, which is especially important in the patient's rehabilitation. Care provided by a multidisciplinary team is recommended to check the technique and educate the family members and/or caretakers about the importance of avoiding external contamination. Printed information leaflets and educational videos can help with adequate comprehension of the technique. In the case of motor deficit, which makes auto-catheterization impossible, family members or a caretaker can undertake the responsibility of performing the procedure.[41]

The number of catheterizations indicated per day mostly depends on oral liquid intake, but it is usually 4 to 6 times within 24 hours. A lower number of IC procedures in 24 hours may result in urinary infections, while very frequent catheterizations may increase the risk for urethral complications.[41,42]

Intermittent urethral catheterization frequency may vary according to urodynamic parameters (bladder complacency and detrusor pressure). Bladder distension should be avoided (>400 mL) in order to prevent urinary infections.[42]

Asymptomatic bacteriuria is a frequent finding in SCI patients on IC.[33,34] There is no indication to perform routine urine culture exam in these patients. Asymptomatic bacteriuria should not be treated, except in cases when the patient must undergo surgical or endoscopic manipulations,[43,44] which is also the recommendation of the Infectious Disease Society of America (IDSA).

Routine antibiotic prophylaxis is not justified. Although it reduces the incidence of asymptomatic bacteriuria, there is no evidence that it reduces symptomatic UTIs.[45] On the other hand, non-specific symptoms, such as exacerbation of spasticity (and difficulty in inserting the catheter in the urethra due to the spasms of the pelvic floor), worsening of incontinence, fever, and abdominal and back pain, may suggest occurrence of urinary infection in SCI patients. In these cases, urine culture may be useful to guide antimicrobial treatment.[45] Whenever an SCI patient presents episodes of symptomatic UTI, the IC technique must be reinforced.[41,42] Hydrophilic catheters and the no-touch technique may also be offered to patients on IC and recurrent complications.

The introduction of IC represented a cornerstone in the urologic management of SCI patients. Currently, the most used technique is "clean" IC, which provides evident benefits in terms of preservation of renal function.[37] Recent advances include pre-lubricated catheters, hydrophilic catheters, and the no-touch technique, which could potentially minimize the risk for complications, such as UTIs and urethral injuries.[32,46–48] However, the costs of hydrophilic catheters can still be a limiting factor for the dissemination of this technique. A 2008 national survey in Canada reported the reuse of catheters by 47% of spinal cord–injured patients.[49] Although policy changed in the United States in 2008, resulting in an increased provision of single-use catheters, a 2013 survey indicates that 56% of patients reuse their catheters a median of 20 times.[50] It is not possible to make evidence-based recommendations on the most appropriate method for cleaning and storing the reusable catheters.

Factors that may help in the prevention of recurrent UTIs include education strategies (reinforcement of the IC technique), prevention of bladder overdistension, and the use of aseptic technique (no-touch technique). For SCI patients, choice of catheter will depend on personal preference, cost, portability, and ease of use.[37] Future research strategies must consider cost-effectiveness analysis and use of the standard definition for symptomatic UTIs.

4.2.6 Complications of intermittent catheterization compared with indwelling catheters

Chronic indwelling catheterization is associated with similar types of complications as IC; however, the frequency of many of these complications is much higher with indwelling catheters. Complications include cystitis, pyelonephritis, hydronephrosis secondary to bladder wall thickening and fibrosis, urethral trauma and bleeding, urethritis, and bladder stones.[6] Other potential morbidities include a higher risk for pressure ulcers as well as more frequent and longer hospitalizations among those treated with indwelling catheters.[51] The presence of an indwelling catheter has also been associated with a higher risk for major depressive disorder compared with IC.[52]

Shekelle *et al.* performed a systematic review of risk factors for UTI in adults with SCI that included 22 studies.[53] These authors found increased bladder residual volume as a risk factor that was supported by evidence from two studies. They found that patients on IC had fewer UTI episodes than those with an indwelling catheter. Fortunately, urinary sepsis was rare, but management with an indwelling catheter represented a risk of developing sepsis. Several authors have also reported similar findings of up to a 6-fold rate of UTI in patients with indwelling catheters compared with IC.[9,11,54] In a Cochrane Review,[55] 14 trials were reviewed comparing the evidence for UTI in indwelling urethral catheterization with intermittent catheterization. Due to evidence of clinical and statistical heterogeneity, the results were inconclusive with a very low quality of evidence.

In a retrospective study of 140 patients with SCI, Ku *et al.* found that IC was an independent risk factor for the development of epididymo-orchitis compared with indwelling catheters.[56] Men on IC had a rate of 67% compared with 25% in the indwelling group over the 17 years of the study. Urethral strictures were more common in the men on IC, but these were not an independent contributing factor for the development of epididymo-orchitis. In contrast, in another long-term study of 316 men post-SCI,[11] indwelling urethral catheterization had a far greater risk for urethral stricture, epididymitis, and peri-urethral abscess than for those performing IC. Of note, the patients with suprapubic tubes had a very low rate of urethral complications.

Kidney stones are more common in patients with SCI compared with the general population. The rate of kidney stones based on bladder management has been variable in the literature. Chen *et al.*[57] found that approximately 7% of persons with an SCI experienced the first kidney stone within 10 years of injury, and any form of bladder instrumentation (indwelling catheterization, IC, or condom catheterization) resulted in more kidney stones compared with spontaneous voiding. Among 140 men followed for 17 years with SCI, Ku *et al.*[20] found that renal stones were more common in patients managed with indwelling catheters compared with those with spontaneous voiding or IC. Complete injury was also an independent risk for renal stone formation. Several other long-term follow-up studies[11,58,59] have also found an increased risk for upper tract stones with indwelling catheter management compared with IC, but others[60] have found the opposite result.

A very high incidence (up to 30%) of bladder stones has been reported in patients managed with long-term indwelling catheters.[11] In a group of 457 SCI patients,[21] the absolute annual risk for bladder stone formation with an indwelling urethral or suprapubic tube was 4% compared with 0.2% on IC, and having formed a stone in the past year quadrupled the risk for stone formation in the indwelling catheter group to 16%. There was no difference in the stone formation rate between suprapubic and urethral catheters. Other studies have shown a 3-fold increase in bladder stones with an indwelling catheter,[54] or even higher.[11]

Hydronephrosis and vesicoureteric reflux have also been shown to be more common in patients with indwelling catheters, with rates as high as 30% to 38% for upper tract changes and 22% to 28% reflux for indwelling urethral and suprapubic tubes, respectively, compared with IC with rates closer to 18% and 8%.[11] These changes are likely due to bladder wall thickening and the resulting loss of bladder compliance associated with indwelling foreign bodies.[61]

Weld *et al.* assessed bladder compliance in 316 SCI patients based on bladder management technique and found those with indwelling catheters to be at higher risk for decreased compliance compared with those on IC ($p<0.01$). This retrospective review also found that those with abnormal bladder compliance were at an increased risk for vesicoureteral reflux (VUR), imaging abnormalities, pyelonephritis, and upper urinary tract stones ($p<0.01$, <0.01, 0.04, and <0.01, respectively).[61] Chao *et al.* reported a higher rate of upper urinary tract scarring and caliectasis in catheterized versus non-catheterized SCI patients.[62]

Some studies report the incidence of bladder cancer in the SCI population to be similar to that of the non-SCI population (0.11%–0.39%).[12,63] However, the presence of an indwelling catheter (urethral or SP tube) has been found to be an independent predictor for the development of bladder cancer, after controlling for risk factors such as age, gender, and smoking status (relative risk [RR]: 4.9; 95% CI: 1.3–13.8). This historical cohort study also found the risk for bladder cancer to be higher in the SCI population compared with a sample of the general population.[10] West *et al.* associated the presence of an indwelling catheter with a higher rate of squamous cell carcinoma.[12] A recent meta-analysis found a rate of bladder cancer as high as 1.0% (95% CI: 0.0–5.0) in catheterized SCI patients.[64] In a retrospective review of catheterized SCI patients, no significant difference was noted in the rates of bladder cancer in patients with indwelling urethral catheters compared with suprapubic catheters.[65] In the only population-based study of bladder cancer in SCI from Taiwan, the rate of cancer was not different than the general population despite a large percentage of these patients being managed with indwelling catheters, adding more controversy to this subject.[66]

A summary of the comparison of complications between catheters is presented in **Table 4-1**.

TABLE 4-1 Complications Associated With Intermittent Catheter Compared With Indwelling Urethral or Suprapubic Catheter

Complication	Intermittent catheter	Urethral catheter	SPT
Symptomatic urinary tract infections	↑	↑↑↑↑	↑↑↑↑
Bladder cancer	↑	↑↑	↑↑
Bladder stone	↑	↑↑↑↑	↑↑↑↑
Worsening bladder compliance	↑	↑↑	↑↑
Urinary incontinence	↑↑	↑↑	↑↑
Urethral strictures	↑↑	↑↑	=
Epididymitis	↑↑	↑↑	=
False passages/hematuria	↑↑	=	=
Upper tract stones	↑	↑↑	↑↑
Hydronephrosis	↑	↑↑↑	↑↑↑

↑: increased risk compared with general population; =: no clear increase in risk
SPT: suprapubic tube.

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TABLE 4-1 Complications Associated With Intermittent Catheter Compared With Indwelling Urethral or Suprapubic Catheter, *Cont'd*

Complication	Intermittent catheter	Urethral catheter	SPT
Vesicoureteric reflux	↑	↑↑↑	↑↑↑
Urethral erosion	=	↑↑↑↑	=

↑: increased risk compared with general population; =: no clear increase in risk
SPT: suprapubic tube.

4.2.7 Quality-of-life data

Several studies have compared QOL in SCI patients with different forms of catheter drainage. Mitsui *et al.* compared 34 SCI patients with SPT with 27 patients on IC. More SPT patients reported being "fully" or "almost" satisfied than IC patients. Seventy-four percent of SPT patients were rarely bothered with daily activities compared with 37% of IC patients.[59] Sherrif *et al.* reported that 56% of patients with SPT felt that SPT had positively impacted their QOL.[67] In a survey of ventilator-dependent tetraplegic patients, a preference for SPT was found over IC, although not statistically significant.[68] Despite a high rate of catheter-related problems, up to 84% of patients with SPT are satisfied.[69]

Cameron *et al.* also found the worst scores in terms of psychosocial outcome measures in patients with indwelling catheters compared with spontaneous voiders, IC, or condom drainage.[51] Sánchez Raya used the Kings Health Questionnaire to assess QOL in patients with SCI based on bladder management technique. The physical role domain was the only area where a difference in QOL was detected based on bladder management technique. Those patients on condom drainage had lower physical limitation scores (better QOL). Sexuality was the main concern for the majority of patients.[70]

Study results are conflicting in terms of QOL improvement in SCI patients based on bladder drainage technique. An individualized approach to selecting the appropriate method of bladder drainage will likely lead to the best chance at improved QOL in this patient population.

4.2.8 Conclusions

- The most commonly used intermittent catheterization technique is "clean" intermittent catheterization. **(Level of Evidence [LOE] 3)**

- Asymptomatic bacteriuria is a frequent finding in SCI patients on IC. **[LOE 3]**

- The most frequent urologic complications related to IC in the long term are recurrent UTIs and urethral trauma. **[LOE 3]**

- Kidney stones are more common in patients with SCI than in the general population. **[LOE 3]**

- UTI, bladder stones, poor bladder compliance, upper tract deterioration, bladder cancer, and urethral erosion are far more common in patients treated with indwelling catheters compared with IC. **[LOE 3]**

4.2.9 Recommendations

- Clinicians should stress to patients the following methods to prevent UTI: adequate frequency of catheterization, good education on hygiene, avoidance of bladder overfilling, and maintenance of a low-pressure bladder. **(Grade of Recommendation [GOR] B)**

- Clinicians should recommend IC as the preferred method of bladder management in patients with retention due to a lower risk for complications. **[LOE 3; GOR B]**

- Clinicians must not treat asymptomatic bacteriuria except in cases when the patient must undergo surgical or endoscopic manipulations. **[LOE 1; GOR A]**

- Clinicians should reinforce proper IC technique whenever an SCI patient presents with episodes of symptomatic UTI. **[LOE 3; GOR B]**

- Clinicians should not ignore non-specific signs and symptoms of UTI in this population, such as exacerbation of spasticity, difficulty in inserting the catheter into the urethra due to spasms of the pelvic floor, worsening of incontinence, fever, and abdominal and back pain, which may suggest presence of urinary infections in SCI patients. **[LOE 3; GOR B]**

- Clinicians should offer hydrophilic catheters and no-touch technique to SCI patients with recurrent complications on IC using standard catheters. **[LOE 2; GOR B]**

4.3 Indwelling Catheters

Permanent indwelling catheters are another option for bladder drainage in patients with SCI who are not candidates for IC. Indwelling catheters may be trans-urethral or suprapubic (SPT).

Indwelling catheters are placed with the intent to maintain adequate bladder drainage and low intravesical pressures to help protect the upper urinary tract. However, some evidence suggests that despite continuous bladder drainage and low urinary volumes, spikes in intravesical pressures (>40 cm H_20) occur, and some patients will still develop renal scarring and abnormal ultrasound findings.[71] In an effort to minimize upper tract damage in patients with SPT, some authors suggest the use of anticholinergic medications in patients with neurogenic detrusor overactivity.[67,72,73] In 1997, Kim *et al.* reviewed 109 patients with indwelling catheters (80 urethral, 29 SPT) and found better bladder compliance and a lower rate for hydronephrosis in patients using oxybutynin.[74] Conversely, Pannek *et al.* retrospectively evaluated the urodynamics study (UDS) findings in 85 patients with chronic SPT and found no difference in bladder compliance, irrespective of anticholinergic use.[75]

As indwelling catheterization is not the "gold standard" or ideal form of bladder management for patients with SCI, an individualized approach to the decision for SPT versus urethral catheter is required to maximize patient satisfaction and minimize morbidity.[17]

4.3.1 Suprapubic catheters

If IC is not feasible, SPT is one option for bladder management in SCI patients. Common indications for SPT include inability or unwillingness to perform IC, urethral damage or stricture disease, obesity preventing urethral access, lower extremity spasticity, inability to wear condom catheter, persistent incontinence despite IC, and neurological disease progression.[69,72,76,77]

Benefits of SPT include: enhanced independence, avoidance of urethral trauma and splaying (catheter erosion of urethra), lack of need to pass a catheter multiple times in a day, improved body image, and improved sexual function.[73,77,78] In a contemporary retrospective review study, Krebs *et al.* reported that SPT drainage was the bladder management of choice in 11.8% of neurogenic bladder patients, 93.5% of whom had SCI. In a large US population, factors associated with higher use of SPT drainage included male gender, high level of American Spinal Injury Association (ASIA) Classification A SCI, and age >45 years.[79]

Unlike IC, urethral catheter, or condom catheter drainage, SPT drainage requires a surgical procedure. This may be done under local anesthetic in some cases, but often in patients with neurogenic bladders, a general or spinal anesthetic is required to adequately distend the bladder for safe placement of the SPT. Multiple techniques have been reported.[80-82]

In addition to the risks of anesthetic, risks of SPT insertion include: infection, bleeding, autonomic dysreflexia (AD), injury to bladder neck, injury to surrounding structures such as bowel or blood vessels, and failure to pass the catheter into the bladder.[83] Ahluwalia *et al.* reported an intra-operative complication rate of 11%, but most were minor. Patients with neurogenic bladders have an increased risk for complications compared with other indications for SPT.[84] To minimize complications, cystoscopy can be performed simultaneously with or without the addition of transabdominal ultrasound.[82]

Postoperative complications occur in up to 23% of patients, but are mostly minor such as catheter clogging or UTIs.[84] Challenges with catheter changes may include: pain, autonomic dysreflexia, retained catheters, loss of SP tract due to catheters falling out and not being replaced in a timely fashion, UTI, and injury to bladder neck or prostatic urethra.[85] To minimize SPT complications, some authors recommend frequent catheter flushing and catheter changes. Communication with caregivers and patient education regarding catheter care are necessary as well.[76]

The majority of data regarding outcomes of SPT in patients with SCI comes from retrospective case series and focuses on reporting the long-term complications of chronic SPT drainage such as UTI, lower and upper tract calculi, incontinence, catheter blockage, gross hematuria, cancer, and renal deterioration.[11,59,65,76–78] **Table 4-2** demonstrates results from contemporary studies reporting the outcomes of SCI patients with SPT. No RCTs have been conducted to compare the outcomes of SPT with other forms of bladder management in SCI patients.[5]

TABLE 4-2 Complications: Suprapubic Catheterization

Reference	N (*N*= SCI patients in study)	Follow-up	UTI*	Bladder stone	Upper urinary tract stones	Epididymitis	Urethral stricture	Incontinence	Gross hematuria	Cancer	Renal deterioration
Katsumi *et al.*[65]	46	10.9 yr	97.9%†; 10.9% urosepsis	41%	26%	4%	0	/	20%	4%	/
Sugimura *et al.*[78]	149	68 mo	27%	22%	8%	2%	/	7%	/	0.7%	6% renal scarring; 14% VUR
Ahluwali *et al.*[84]	219 (9)	50 mo	26%	/	/	/	/	/	/	/	/
Weld and Dmochowski[11] (from graphs)	36	18.3 ± 12.4 yr	3% pyelonephritis	22%	35%	6%	0%	/	/	/	28% VUR; 39% abnormal imaging
Nomura *et al.*[77]	118 (90)	/	2.5% pyelonephritis	25%	/	/	/	10%	/	/	4%
Mitsui *et al.*[59]	34	8.6 yr	12%	65%	9%	0%	0%	26% (21% mild; 5% moderate)	0%	0%	0%
MacDiarmid *et al.*[76]	44	58 mo	43%	41%	7%	2%	/	11%	5%	0%	0%

*Variable definitions used for each study.
†Defined as at least one symptomatic UTI (requiring treatment with antibiotics).
Abbreviations: mo: months; SCI: spinal cord injury; UTI: urinary tract infection; VUR: vesicoureteral reflux; yr: years.

Few retrospective series have compared the outcomes of patients with SPT versus other forms of bladder drainage. In 2000, a retrospective review of 316 SCI patients with a mean follow-up of 18.3 ± 12.4 years was reported. Complications occurred in 27.2%, 44.4%, and 53.5% of patients treated with IC, SPT, and indwelling urethral catheter, respectively. A lower risk for epididymitis (p=0.001), urethral stricture (p=0.002), and peri-urethral abscess (p=0.006) was found with SPT compared with indwelling urethral catheter.[11] Most recently, Katsumi *et al.* reported the complication rates of 179 male SCI patients with SPT compared with patients with indwelling urethral catheter. They found no statistically significant difference in the rates of: UTI, urosepsis, pyelonephritis, bladder stones, upper urinary tract calculi, and hematuria. Urethral strictures, fistulae, and scrotal abscesses, however, occurred only in the indwelling urethral-catheter group and led to a change to SPT drainage in 13 patients. Penile urethral erosion occurred only with indwelling urethral catheters (23%).[65]

4.3.2 Indwelling urethral catheters

An indwelling urethral catheter is another option for bladder management in patients with SCI. Indwelling catheters involve insertion, under sterile conditions, of a trans-urethral catheter, which is worn continuously. Catheters are changed approximately every 4 to 6 weeks, and multiple products are available. Factors to consider when selecting a catheter product include: cost, latex allergy, lumen size, and balloon size. Size 14–16 Fr is generally recommended with 10-cc balloons. The patient and caregiver should be educated regarding appropriate hygiene and care of the catheter and associated drainage bags.[6] Larger catheters increase the risk for urethral erosion or discomfort and are not effective at decreasing peri-catheter leakage, which is almost always due to detrusor overactivity. Also, increasing balloon size when catheters are spontaneously expelled is not advised, as this is a sign of urethral erosion and the catheterization method needs to be changed, not simply upsized.

Indwelling urethral catheters are generally reserved for patients unable or unwilling to perform IC, and who have a contraindication to other options such as condom drainage or SPT. Urethral catheterization is typically indicated in patients during the acute phase (0–2 weeks) following SCI due to the need for fluid balance monitoring.[4] Indwelling urethral catheterization is also beneficial in SCI patients with acute medical conditions.[6] In general, urethral catheterization is considered the last option for chronic urinary drainage, but it is the most appropriate method for certain SCI patients. Few patients (1.3%–3.8%) chose indwelling urethral catheters as a bladder management immediately after injury in contemporary studies.[13,79] However, many SCI patients who are initially managed with IC often switch to urethral catheter over time.[14]

The rates of common complications seen with indwelling urethral catheters have been summarized in **Table 4-3**. A comprehensive discussion of urethral complications is discussed in Chapter 3, Surveillance and Management of Urologic Complications After Spinal Cord Injury.

TABLE 4-3 Complications: Indwelling Urethral Catheter (IUC)

Reference	N (*N*= SCI patients in study)	Follow-up	UTI*	Bladder Stone	Upper urinary tract stones	Epididymitis	Urethral stricture	Urethral erosion	Gross hematuria	Cancer	Renal deterioration
Hollingsworth *et al.*[64‡]	/		/	27.2% (CI: 12.8–40.9)[†]	/	/	8.7% (CI: 0.0–18.7)	/	13.5% (CI: 3.4–21.9)	1.0% (CI: 0.0–5.0)	/
Katsumi *et al.*[65]	133	10.9 yr	93.2%[§]; 15% urosepsis	38%	32%	10%	3%	23%	20%	0.8%	/
Weld and Dmochowski [11] (extrapolated from graphs)	114	18.3 ± 12.4 yr	8% pyelonephritis	28%	54%	35%; 8% peri-urethral abscess	22%	/	/	/	22% VUR; 30% abnormal imaging
Larsen *et al.*[54]	56 (54 IUC; 2 SPT)	7 yr	75%[◊]; 21% urosepsis	61%	32%	9% peri-urethral abscess	23%	21%	41%	/	23% parenchymal thinning

*Variable definitions used for each study.
†Studies of primarily male patients.
‡Meta-analysis of non-infectious complications of SCI patients with IUC, so each outcome included a different number of studies and patients.
§Defined as at least one symptomatic UTI requiring treatment with antibiotics.
◊More than one symptomatic UTI.
Abbreviations: CI: confidence interval; IUC: indwelling urethral catheter; SCI: spinal cord injury; SPT: suprapubic tube; UTI: urinary tract infection; VUR: vesicoureteral reflux; yr: years.

Several methods to minimize the risks associated with indwelling urethral and suprapubic catheters have been suggested. In addition to good hygiene and care of equipment, increased fluid intake (>2 L/day) is recommended to decrease catheter blockage.[86] Silicone catheters are recommended over latex catheters.[87] Anticholinergic medication may be beneficial to help protect the upper urinary tracts.[74] Use of an anchoring device (e.g. StatLock® device; C. R. Bard, Inc; Murray Hill, New Jersey, USA) may be helpful to decrease the risk for UTI and urethral erosion.[88,89] Weekly catheter changes have been suggested to decrease infections,[90] but this is often not feasible from a practical perspective. The benefit of catheter irrigation is unknown. Daily prophylactic antibiotics are not recommended for routine use in patients with indwelling urethral catheters. Despite these efforts, indwelling urethral catheters are associated with a high rate of genitourinary complications, and routine surveillance is recommended.[4,6,7]

4.3.3 Conclusions

- Indwelling catheter drainage (SPT and urethral catheters) is associated with several potential complications such as infections, stones, and deterioration of the upper tract. **[LOE 3]**
- Although SPT has the added surgical risk over indwelling urethral catheter, it prevents potentially irreversible urethral injury and is overall better tolerated by patients. **[LOE 3]**
- Indwelling urethral catheterization is an option for SCI patients but should be used as a last-resort option due to a high rate of complications including: urethral erosion, fistula, epididymitis, and peri-urethral abscess. **[LOE 3]**
- Ongoing urologic follow-up of SCI patients using indwelling catheters drainage is necessary. **[LOE 3]**

4.3.4 Recommendations

- In SCI patients unable or unwilling to perform IC or who decline an SPT, clinicians may offer indwelling urethral catheterization as a last resort, due to a higher rate of complications. **[LOE 3; GOR B]**
- Ongoing urologic follow-up of SCI patients using indwelling catheter drainage is necessary, as upper tract deterioration, urolithiasis, and other urinary complications are not rare. **[LOE 3; GOR B]**
- Further research in the form of prospective trials or RCTs is required to further assess the outcomes of indwelling catheters in SCI patients. **[LOE 3; GOR B]**

4.4 Condom Catheter Drainage

4.4.1 Condom catheter

Condom catheter drainage, or external sheath drainage, is an option for bladder drainage, or more specifically a urine collection system for male SCI patients who are incontinent or use reflex voiding or bladder expression. There is a lack of appropriate external drainage devices for female patients given the anatomical differences. Condom drainage may be appropriate for men with incontinence due to SCI, but several factors need to be considered. This form of bladder management should not be used in patients with a retracted penis, broken or excoriated skin, confusion/dementia who may remove sheath, or a presence of urinary retention,[91] and the majority of men require a sphincterotomy to decrease detrusor leak point pressure (DLPP) to a safe level to prevent upper tract deterioration.

Several studies have compared various condom catheter drainage devices. In 2001, Fader *et al.* compared 6 devices in a randomized, crossover trial in 58 men. However, this study was not limited to men with SCI. A preference was found for the Aquadry Clear Advantage™ (Bard Medical Covington, GA, USA) product in the overall opinion question ($p<0.01$). Sheaths that required an applicator were found to be less desirable than those with no applicators ($p<0.001$).[92] A second RCT in 2006 compared the Conveen® Optima (Coloplast, Minneapolis, MN, USA) with the Clear Advantage urinary sheath. Both were one-piece, silicone, self-adhesive devices. The Coveen Optima was found to be preferred, in terms of security and ease of use, by 67% of the 36 participants who reported a preference. Again, this study was not limited to men with SCI.[93]

Multiple devices are available, including single- and double-piece sheaths. Clear devices allow for monitoring of the skin. BioDerm® external continence device (BioDerm, Largo, FL, USA) is a product that applies to the glans only. Only one size is necessary, and it is used for patients with a retracted penis; however, it should not be used in patients with phimosis, catheter-induced hypospadias, or inflammation/ulceration of glans.[94,95]

The use of penile implants to facilitate condom catheter drainage has been reported. In 1992, Perkash *et al.* completed a retrospective review of 79 SCI patients with semi-rigid penile implants. The main reason for the implantation was the inability to wear an external urinary sheath due to a small retracted penis. Of the 79 participants, 81% had success wearing a condom catheter postoperatively. The penile implant improved quality of life due to better continence, sexual function, self-esteem, and mobility. There was an 8% failure rate and an infection rate of less than 2%.[96]

There is a lack of high-quality evidence assessing the efficacy of condom drainage versus catheter bladder drainage in patients with SCI. In 2013, a Cochrane Review was conducted to assess the evidence for catheter policies in patients with neurogenic bladder. The study sought to assess whether condom drainage was better than urethral catheterization or SPT drainage. The meta-analysis included RCTs and quasi-RCTs. Unfortunately, no studies were found that met inclusion criteria for this meta-analysis.[5] In 2006, Saint *et al.* performed an RCT to compare condom catheter drainage with indwelling urethral catheterization, but this population did not consist of SCI patients.[97]

The majority of the research regarding the use of condom catheters focuses on complications and risks as opposed to clinical trials to assess efficacy. The use of condom catheters has been associated with: penile edema/injury/necrosis,[98–101] fibroepithelial polyps,[102] and urethral diverticulum.[103] Some studies have suggested that condom drainage may be associated with poor emptying and hydronephrosis.[104,105]

The rate of UTI with condom catheter drainage has been well assessed. Esclarin de Ruz found an overall UTI incidence of 0.68 per 100 person-days in an inpatient population of SCI patients. The risk of UTI was highest for patients with indwelling Foley catheters, 2.72 compared with 0.36 for those with condom catheter drainage. Those undergoing IC had a risk of 0.41 per 100 person-days of developing a UTI. Undergoing invasive procedures and cervical SCI were also found to be risk factors for UTIs in this study. This was not a randomized trial, and it assessed patients in the acute phase of their SCI.[9] Overall, condom catheter in the appropriate patient may be associated with a lower risk for UTI than indwelling urethral catheterization.

To minimize the risks associated with the use of condom catheter drainage, ongoing monitoring is recommended. Condom catheters can be worn continuously and the product should be changed every 24 to 48 hours.[106] Devices must be properly measured for length and circumference. Approximately

3.8 cm of penile length is required for application. Four hours after application, the device should be assessed to ensure it is on correctly and that there is no damage.[107] Due to lack of sensation, some patients with SCI may not be aware of problems with the device not adhering or causing penile injury. Physical examination of the penis, assessment of postvoid residuals, bladder pressure monitoring, and upper tract imaging should be done routinely,[91,108] although an evidence-based follow-up schedule is yet to be determined. Any problem should warrant medical attention.[100,101,107–109]

In patients with suprasacral SCI, detrusor sphincter dyssynergia (DSD) may occur, leading to incomplete bladder emptying, UTI, autonomic dysreflexia, elevated voiding pressures, and upper urinary tract demise if a condom catheter is chosen as a bladder management method.[110] The outlet resistance must be reduced in patients managed with condom catheter drainage to prevent these complications, which may occur only over time. OnabotulinumtoxinA, or botulinum toxin A, is not yet approved for the indication of treating DSD, but it has been studied in a few small RCTs with variable results.[111]

External sphincterotomy is the permanent and effective option for patients with DSD who want to wear a condom catheter.[73] Pan *et al.* reported on the long-term outcomes following sphincterotomy, showing a success rate of 32% following a single sphincterotomy at a median follow-up of 71 months. Failure following sphincterotomy, defined as urosepsis, recurrent DSD, upper tract dilatation, or renal failure, developed in 57 (68%) of 84 patients at a median follow-up of 36 months. Repeat sphincterotomy was performed in 30 of 57 patients with a median duration of success of 68.5 months. Renal failure did not occur in any of the patients.[112]

More recently, Vainrib *et al.* reported on the outcomes of 97 patients undergoing bladder neck incisions/external sphincterotomy (BNI/ES) over a period of 40 years. Condom catheter drainage (± IC) was used in 80.4% of patients in this study. Forty-seven percent of patients required a repeat BNI/ES due to elevated bladder pressures, UTIs, elevated postvoid residual urine volumes (PVRs), hydronephrosis, or impaired renal function. Success rates ranged from 50% to 85.7% for up to 3 repeat procedures over a mean follow-up of 119 months.[113] These studies indicate good long-term success despite a high need for repeat procedures. Repeat procedures are safe and effective.

4.4.2 Conclusions

- Condom catheter drainage is associated with complications such as poor bladder emptying, hydronephrosis, upper tract deterioration, UTI, and skin and penile injury. **[LOE 3]**

- Patients with DSD who opt for condom catheter drainage require treatment to allow for safe bladder drainage; usually this is accomplished with sphincterotomy. Sphincterotomy often requires repeat procedures over time. **[LOE 3]**

4.4.3 Recommendations

- Clinicians may offer condom catheter drainage to SCI patients who are unable or unwilling to perform IC. Patients with high-pressure voiding due to DSD must be willing to undergo sphincterotomy. **[LOE 3; GOR C]**

- Clinicians must monitor SCI patients who are using condom drainage with routine physical examination of the penis, assessment of postvoid residuals, bladder pressure monitoring, and upper tract imaging. **[LOE 3; GOR B]**

4.5 Reflex Voiding and Bladder Expression with Valsalva or Credé

Most patients after SCI are in retention and are unable to void, requiring some mechanical form of bladder drainage. However, there are patients who are occasionally able to void spontaneously despite the neurologic injury. According to the National Spinal Cord Injury Database (NSCID), from 2001 to 2006, about 19% of subjects with an SCI in the United States were able to void, and this trend has been similar in the past 30 years.[14] When evaluating a patient with an SCI, it is very important to assess how he or she is emptying the bladder, and distinguish between spontaneous voiding and bladder expression or bladder reflex triggering.

Bladder function will be impacted depending on the type and area of the neurologic injury or lesion. The acute phase (spinal shock) can interrupt supraspinal pathway function, resulting in temporary urinary retention with underactive or acontractile detrusor that may last for a few weeks to months. Incomplete injuries (ASIA categories B through D) with intact or partial sensation below the level of the spinal lesion can manifest with coordinated physiologic voiding because this relies on Aδ afferent nerves responsible for the spino-bulbospinal reflex.[114]

Supraspinal injury is commonly associated with bladder involuntary contractions, also called neurogenic detrusor overactivity (NDO), and normal sphincter function. Suprasacral spinal lesions are associated with impairment of both bladder and sphincter functions, resulting in NDO and detrusor sphincter dyssynergia. Lower complete injuries such as *conus* lesions or sacral injuries present with acontractile detrusor, but the sphincter function can be overactive or acontractile. Lower incomplete injuries such as *cauda equina* or peripheral nerve lesions have a variable presentation with NDO and acontractile sphincter or *vice versa*.[115]

Direct compression over the suprapubic area can facilitate bladder emptying in two different pathways: bladder reflex triggering and bladder expression.

4.5.1 Bladder reflex triggering

Based on the standardization of terminology by the International Continence Society, bladder reflex triggering refers to the different manoeuvres necessary to elicit an exteroceptive reflex bladder contraction.

Reflex voiding is a non-physiologic mechanism that induces a bladder contraction through activation of C-fibres and an intact peripheral reflex arc that are unveiled after a suprasacral injury or lesion. Bladder reflex triggering can be induced by rhythmic suprapubic percussions (7–8 taps) delivered every 3 seconds until voiding occurs. Contraction would hopefully be limited to detrusor fibres in the bladder to facilitate voiding. However, bladder neck fibres, activation of pelvic floor muscles, or simultaneous contraction of the external sphincter DSD can also occur and would prevent voiding.[116] Other manoeuvres to induce reflex voiding include thigh scratching, ano-rectal manipulation, pulling pubic hair, touching the penile skin, or squeezing the clitoris and would be different for every patient.[117]

4.5.2 Bladder expression

Bladder expression achieves voiding through a mechanical forceful increase in the intravesical pressure to overcome the outlet resistance; this typically generates a low flow. The most commonly used manoeuvres are the Valsalva and Credé manoeuvres. The Valsalva manoeuvre was named after Antonio Valsalva, who described this approach to assess the patency of the ear canal by increasing both intra-thoracic and intra-abdominal pressure while applying closing lips and nostrils.[118] The Credé manoeuvre was described by Carl S.F. Credé as a mechanical downward compression over the suprapubic area to facilitate expulsion of the placenta.[119] Although the detrusor pressure is not physiologically high, this is commonly associated with reflux to seminal vesicles, prostate, and upper tracts.[116]

Patients who are candidates for bladder reflex triggering should have: (1) a suprasacral neuropathic lesion, (2) the ability to follow up to confirm safe bladder parameters, and (3) an open outlet after treatment (drug therapy, onabotulinumtoxinA injection, sphincterotomy, or bladder neck incision).[115]

Bladder expression can be considered in patients with neurogenic bladder with sacral SCI in whom safe urodynamic parameters can be confirmed and followed up.[115,120]

There are no meta-analyses or RCTs assessing this therapy. Four recent systematic reviews were identified6,[115,120,121] and they all concluded and recommended clean intermittent catheterization (CIC) as the primary method for bladder management before considering bladder reflex triggering or bladder expression. The International Consultation on Incontinence (ICI 2013) formed a neurologic incontinence committee to address and update recommendations on bladder management in neurogenic lower urinary tract dysfunction (NLUTD). The authors emphasized evaluating symptoms and investigating both bladder and sphincter function in the presence of a neurogenic lesion. Bladder reflex triggering and bladder expression were recommended as a conservative bladder management in specific scenarios where safe bladder parameters could be confirmed and followed.[115]

The European Association of Urology (EAU) updated the Guideline on Neuro Urology and provided no evidence-based recommendations on reflex voiding and bladder expression, and only highlighted similar statements as the ICI regarding safety. The authors stressed caution when managing high-pressure voiding and autonomic dysreflexia; one should monitor for adverse events affecting the upper tracts.[120]

The Consortium for Spinal Cord Medicine published a clinical practice guideline for health care providers in 2006 to address bladder management for adults with SCI. Recommendations from this Guideline were also similar and do not differ from the ICI statement. The authors provide indications and exclusions for reflex voiding and bladder expression, as well as list possible complications associated with these.[6]

In 1968, Golding reported good outcomes and no adverse events in 25 patients with SCI managed with bladder expression after 8 weeks,[122] and this method was adopted for patients with myelodysplasia or SCI with concomitant stress urinary incontinence.[123–125] In contrast, a concerning finding in another retrospective study of bladder expression was that synchronous bladder contraction and open bladder neck occurred in only 2% (4/207) of the patients.[126] This event was previously reported by McGuire and Wagner, when they demonstrated that even after complete sacral injury and loss of the sympathetic nerve supply to the proximal urethra, the bladder neck remains closed during bladder expression.[127] In a small study, Smith and colleagues compared early severe adverse events in 6 SCI patients managed with bladder expression versus 6 patients managed with intermittent or indwelling catheterization. All patients managed with bladder expression had upper tract dilatation on intravenous pyelogram by 2 months, and 50% (3/6) sustained a deep venous thrombosis (DVT) compared with 1 DVT (1/6) and no dilatation in the group of patients managed with catheterization.[128] The authors speculated on possible urinary retention as the possible etiology for DVT as previously described by Young and Mitchell in a case of massive urinary retention and associated iliac vein obstruction.[129]

Since the publication of Lapides *et al.* of clean intermittent catheterization in the treatment of urinary tract disease in 1972,[27] several studies have described the benefits of this method and the associated lower adverse event burden compared with any other bladder emptying method in the patient with SCI. Intermittent urethral catheterization is associated with less bacteriuria,[130] UTIs,[130–132] lithiasis,[131,133] and less dilation of the upper urinary tract[131] compared with bladder reflex triggering and bladder expression. Bladder reflex triggering has also been associated with a higher risk for symptomatic autonomic dysreflexia after controlling for SCI level in a Japanese, multicentre, retrospective study on 571 SCI patients with level T6 or higher SCI.[134]

Longer follow-up studies have confirmed the deleterious effect on renal function when using bladder reflex triggering and bladder expression. Chang and colleagues performed a cross-sectional study on SCI patients from the 1976 Tangshan earthquake. There were 74 patients who used bladder expression regularly after discontinuing indwelling catheter. Bladder expression (Valsalva) was performed 5 to 7 times per day and voided volumes were reported as 300 mL to 400 mL. The authors reported that half of these patients had a residual volume larger than 300 mL, pyuria was present in 82%, urinary lithiasis in 31%, ureteral dilatation in 60%, hydronephrosis in 35%, and renal damage in 16%. Risk for ureteral dilation, hydronephrosis, and renal damage was higher in men compared with women.[135]

A Danish retrospective review of SCI patients reported on renal function using renography and 51Cr-EDTA plasma clearance while assessing on multiple variables including bladder management with a mean of 45 years of follow-up. One hundred and sixteen patients were included in the study, wherein the bladder-emptying methods used for the longest period were reflex triggering (63%), bladder expression (22%), indwelling catheter (5%), normal voiding (4%), ileal conduit (3%), and IC (2%).

The cumulative risk for moderate renal deterioration was 58% and severe deterioration 29%, with no difference among different bladder management techniques; however, almost all patients used triggering or expression. Renal deterioration risk was increased in patients with dilated upper tracts and those with nephrolithiasis requiring surgical intervention. Although the authors were not able to investigate the effect of hypertension and diabetes mellitus as contributors to renal deterioration, 85% of these patients performed either bladder reflex triggering or compression.[136]

4.5.3 Risks and complications

Bladder reflex emptying and bladder expression are considered conservative bladder management that is associated with increased complications in the lower urinary tract and upper tracts, and with renal function with possible deleterious systemic effects.[115] Safety parameters on these bladder-emptying methods rely on a low intravesical storage pressure environment to avoid damage to the upper tracts and preserve renal function with a satisfactory emptying of the bladder.

Although IC is the gold standard for bladder management in the acute and chronic phases of neurogenic bladder, reflex bladder emptying and expression are still commonly used[131] despite their chronic deleterious effects previously described[135,136] and acknowledged in prior systematic reviews.[6,115,120,121] Bladder expression and triggered bladder voiding are associated with adverse events including upper tract urinary damage, renal deterioration, urinary tract infections, lithiasis, autonomic dysreflexia, worsening urinary incontinence, and loss of bladder compliance.[6,115,120]

High bladder pressure is not only a problem that occurs sporadically at the time of voiding but also a serious common effect that could be present during the storage phase or every time the patient leaks. In 1981, McGuire and colleagues in a landmark publication reported the association between a high DLPP and serious adverse urologic events. They reported that 81% of patients with DLPP >40 cm of water had ureteral dilatation and 68% had vesicoureteral reflux, whereas only 10% of those with low DLPP had ureteral dilatation and none of them had vesicoureteral reflux.[137] The duration of bladder contraction and overall cumulative time of high detrusor pressure potentially transmitted to the upper tracts are also an important variable when evaluating bladder expression or reflex trigger contraction.[138]

High bladder pressures can be generated if the outlet fails to open; there are several methods to address this in select patients where catheter management is not possible. Alpha-blocker medication, BoNT injection to the bladder neck or external sphincter, bladder neck incision, or sphincterotomy can promote low-pressure voiding in patients using bladder reflex triggering, with varying success.[139] OnabotulinumtoxinA sphincter injection was found to decrease PVR, improve maximal urethral pressure (MUP), and decrease DSD compared with lidocaine injection in a small, randomized, double-blind study by de Sèze and colleagues.[140] Pharmacotherapy with alpha blockers has also proven to improve symptoms based on a validated questionnaire and MUP at 8 weeks compared with placebo in a randomized, double-blind, placebo-controlled trial in 244 patients with suprasacral injury. At 1 year, about half of the patients had follow-up data, and this showed that 71% had a significant improvement in their symptoms compared with baseline.[141] Urodynamic parameters and follow-up with imaging are fundamental to guaranteeing safe bladder pressures and assessing the outlet when using bladder expression or bladder reflex triggering. Even patients with sacral SCI with a non-contractile bladder and open bladder neck can present with a contraction at the level of the external sphincter (membranous urethra). This has been described at the time of bladder expression during fluoroscopic imaging of the voiding phase.[142]

Adequate emptying is not always achieved when using bladder reflex triggering or bladder expression even without outlet obstruction, and a large postvoid residual can be associated with recurrent UTIs, urinary lithiasis, and overflow urinary incontinence. Urinary incontinence is frequently a problem with this bladder management method due to the presence of involuntary bladder contractions resulting from other unplanned stimulus, and thus men often need an external device such as a condom catheter, making this a less favourable approach for female patients, who have no equivalent option.

Other rare severe adverse events such as rupture have been described in particularly vulnerable patients. Reinberg *et al*. published a case report of renal rupture associated with bladder expression.[143]

4.5.4 Conclusions

- Bladder expression and triggered bladder voiding are associated with adverse events including upper tract urinary damage, renal deterioration, UTIs, lithiasis, autonomic dysreflexia, worsening urinary incontinence, and loss of bladder compliance. **[LOE 2 and 3]**

- Bladder expression has some role in those patients with sacral SCI when there is confirmed compliant, non-contractile bladder and urethral sphincter with an open bladder neck. **[LOE 3]**

4.5.5 Recommendations

- Clinicians should recommend intermittent catheterization as the preferred method of bladder management rather than bladder expression or triggered bladder voiding. **[LOE 3; GOR B]**

- Clinicians should not recommend bladder expression (in sacral SCI) or triggered bladder voiding (in suprasacral SCI) if any of the following urodynamic findings are present: small bladder capacity, high leak point pressure, low bladder compliance, vesicoureteral reflux at any point of the study, closed bladder neck during voiding, or high voiding pressure. **[LOE 3; GOR B]**

- Clinicians should ensure that patients opting for a program of bladder expression or reflex voiding have the physical and mental capacity as well as the social support to accomplish this program and follow up reliably for continuous renal and bladder assessment. **[LOE 4; GOR B]**

- Clinicians should counsel patients who are considering bladder expression or triggered bladder voiding about adverse outcomes including upper tract urinary damage, renal deterioration, UTIs, lithiasis, autonomic dysreflexia, worsening urinary incontinence, and loss of bladder compliance. **[LOE 3; GOR B]**

- Surgeons should offer medical or surgical intervention to open the bladder neck when there is high voiding pressure, in a patient interested in pursuing bladder expression or triggered bladder voiding. [**LOE 3; GOR B]**

4.6 Medical Management of the Spinal Cord–Injured Bladder

Medical management with the use of oral pharmacotherapy is the mainstay of symptomatic and pressure management in neurogenic bladder dysfunction (NBD). Despite its importance, there have been few changes in the agents available, and there is sparse literature applicable to the neurogenic population in general or the SCI population in particular. Most evidence is from the overactive bladder (OAB) population, who are neurologically intact. Indeed, in many countries, these medications have approval by regulatory authorities only in the OAB group, and physicians frequently employ off-label use of these medications for SCI patients.

4.6.1 Medications promoting storage

4.6.1.1 Anticholinergics

The most commonly used pharmacotherapy in NBD is anticholinergic therapy. Anticholinergic (or antimuscarinic) agents are the most widely cited therapy in international guidelines[144–146] and have been used for the longest, in both the adult and pediatric populations. Commonly used agents are summarized in **Table 4-4**.

TABLE 4-4 Common Medications Promoting Storage

Class	Drug	Dose	Pharmacology	Side effects
Non-selective anticholinergics	Propantheline	Up to 90 mg daily	Non-selective antimuscarinic	Constipation, dry mouth, tachycardia, hypersensitivity to light
	Oxybutynin	IR 5–30 mg divided TID	Non-selective antimuscarinic	Dry mouth, dry eyes, constipation, headache, sleep disturbance, diarrhea, worst cognitive
	Oxybutynin	ER	Slower breakdown of the capsule allows slower release	Dry mouth, dry eyes, constipation, headache, sleep disturbance, diarrhea, worst cognitive
	Oxybutynin	Patch	Bypasses first-pass hepatic metabolism	Skin irritation, dry mouth, dry eyes, constipation, headache, sleep disturbance, diarrhea, worst cognitive
	Tolterodine	IR 2–8 mg divided BID; ER 2–8 mg/day	Non-competitive antimuscarinic	Dry mouth, dry eyes, constipation, headache, sleep disturbance, diarrhea
	Propiverine	Up to 90 mg daily	Calcium agonist with moderate anticholinergic effects	Dry mouth, dry eyes, constipation, headache, sleep disturbance, diarrhea, restlessness, dizziness, vertigo, speech disorders
	Trospium	Up to 60 mg daily	Quaternary ammonium derivative with antimuscarinic action	Dry mouth, dry eyes, dry nose, constipation, headache, sleep disturbance, diarrhea
Selective anticholinergics	Solifenacin/ Darifenacin	Up to 10 mg daily/ up to 15 mg daily	M3 antagonist	Constipation, headache, dizziness, dry eyes, dry mouth
Beta 3 agonists	Mirabegron	Up to 100 mg daily	Beta 3 agonist	Increase in HR (typically 1–2 bpm) increase in BP, rarely severe hypertension
Alpha blockers	See **Table 4-5**	See **Table 4-5**	Alpha-receptor blockade at alpha 1a receptor and alpha 1d	Postural hypotension, retrograde ejaculation, floppy iris syndrome
Tricyclic anti-depressants	Imipramine	Up to 45 mg daily	Anticholinergic and serotonin reuptake inhibitor	Dizziness, drowsiness, constipation, vision disturbance, sleep disturbance, dyspepsia

BID: two times a day; BP: blood pressure; bpm: beats per minute; ER: extended release; HR: heart rate; IR: immediate release; TID: three times a day.

Anticholinergics are now formulated in a selective form, with greater potency for the M3 muscarinic receptor. This has improved the side-effect profile. Pharmacologically the contraction of the bladder is driven by parasympathetic stimuli and more specifically, the acetylcholine stimulation of muscarinic receptors. These receptors are found in both the mucosa and the detrusor muscle.[147] M2 and M3 receptors are the predominant antimuscarinic receptors found in the bladder, with the M3 receptors playing a larger part in bladder contraction, despite being outnumbered in quantity.[148] Hence, it is the M3 receptor that is targeted. Antimuscarinics exert their action by competitively competing for the

M1 (found extravesically) and M3 receptors at their post-ganglionic sites. This leads to impairment or diminution of the involuntary contractions of the bladder through blockade of this acetylcholine-stimulated receptor.

Anticholinergic medications have been shown to improve subjective symptoms of urgency, frequency, and incontinence or lead to cure in patients with SCI (RR: 2.80; 95% CI: 1.64–4.77; anticholinergic 63% vs placebo 22%).[149,150] They have also been proven to change objective urodynamic measures, by increasing cystometric capacity (by 49.79 mL; 95% CI: 15.38–84.20[150,151]), increasing the mean volume at first detrusor contraction by 50 mL and lowering the detrusor pressure at the strongest contraction by 38.3 cm H_20.[149,150] These alterations in urodynamic parameters are critical to neurogenic bladder management in the prevention of upper tract deterioration by maintaining the detrusor leak point pressure and bladder compliance within safe limits.

Patients performing IC with neurogenic bladder also show significant improvement with the use of anticholinergic medications. This has been demonstrated by improvements in urodynamic bladder compliance, and decreases in hydronephrosis (23% vs 3%) and febrile UTIs (27% vs 11%).[152]

Anticholinergic medications often come in extended-release and immediate-release preparations. The efficacy of extended-release preparations is slightly better, but where these have the advantage is in greatly decreased side effects.[153]

There are many types of anticholinergic medications available worldwide. We will discuss oxybutynin, propantheline, tolterodine, fesoterodine, trospium, solifenacin, and darifenacin. Dosing, pharmacology, and side-effect profile of these commonly used preparations are presented in **Table 4-4**.

Oxybutynin is the most widely available anticholinergic agent. It acts on the M1, M2, and M3 receptors.[154] Oxybutynin is formulated in immediate-release, extended-release, and transdermal patch and gel preparations. Immediate-release oxybutynin (5-mg tablets given three times a day) is rapidly absorbed from the gut and reaches peak tissue levels in 30 to 60 minutes. Extended release (ER) relies on slow breakdown of the capsule and hits peak tissue levels in 11 to 13 hours (5–30 mg, tablet form).[155]

Transdermal applications bypass the gastrointestinal system and hit a steady-state level after the first application after about 3 days. The transdermal and extended-release applications are not more efficacious in treatment, but are better tolerated and have fewer side effects. Intravesical oxybutynin, which is prepared by crushing the tablets and dissolving them in sterile solution by the patient or caregiver, has been proven to work at 5 mg/30 mL three times a day.[154] The use of botulinum toxin A has largely superseded intravesical use of oxybutynin, but in some centres, the intravesical option represents a cost-effective method of oxybutynin administration with an improved side-effect profile.

The evidence for the efficacy of oxybutynin is excellent.[156,157] It has been proven to help symptoms, urodynamic parameters (compliance and bladder pressures), catheter blockages if catheter dependent, and continence. Many other antimuscarinics have been used, all with an aim to improve the side-effect profile of oxybutynin. Common side effects experienced by patients using oxybutynin in oral immediate release (IR) form are dry mouth (up to 70%), dry eyes, constipation, headache, sleep disturbance, and diarrhea. Cognitive side effects are a particular issue with oxybutynin ER.

Individual anticholinergic agents have their own specific pharmacological properties (**Table 4-4**). Propantheline blocks both the muscarinic and nicotinic receptors of acetylcholine. It does not appear to affect the central nervous system. Cognitive side effects are prominent with oxybutynin. The half-life of propantheline is 2.2 to 3.7 hours, and it can cause neuromuscular blockade in high doses.[158] The dose of propantheline is 7.5 mg to 30 mg three times a day.

Tolterodine and fesoterodine are selective for the M2 and M3 receptors and have a greater affinity for the bladder and a lower affinity for the parotid gland compared with oxybutynin.[159] Fesoterodine is the first metabolite of tolterodine. Tolterodine has both an immediate-release formulation and an extended-release formulation. The dosing is 2 mg to 8 mg BID for IR and 2 mg to 8 mg daily for ER. Prolonged QT interval found on electrocardiogram (ECG) monitoring is a significant side effect and is dose dependent for tolterodine, which has limited its approval in some countries. But the newer fesoterodine does not have this side effect, hence dosage can be increased safely from 4 mg to 8 mg.

Trospium is unique, in that as a quaternary amine, it should not cross the blood-brain barrier. This limits the adverse cognitive effects usually associated with anticholinergic agents. Trospium is primarily renally excreted (80%), and it works on muscarinic receptors to acetylcholine with no nicotinic activity. It should be taken on an empty stomach and peaks in concentration at 6 hours. It is equivalent in efficacy to oxybutynin when assessing the maximum cystometric bladder capacity, maximum voiding detrusor pressure, bladder compliance, and residual volume.[155]

The introduction of selective agents for the M3 receptor, solifenacin and darifenacin, has improved tolerability, but not always with improvements in efficacy. These agents are extremely selective for the M3 receptor compared with traditional antimuscarinics. The SONIC trial[156] compared 4 weeks of solifenacin against placebo or active treatment (oxybutynin). It was not powered to look for superiority over oxybutynin, but it demonstrated modest benefit over placebo in efficacy endpoints and improvements in patient-reported outcomes and side effects, compared with oxybutynin.

4.6.1.2 **Beta 3 agonists**

The only non-anticholinergic bladder relaxant to improve storage available is mirabegron (Myrbetriq™ in USA and Betmiga™ in Europe) (**Table 4-4**). Mirabegron works on the beta 3 adrenergic receptor and enhances bladder relaxation via the sympathetic pathway. It has a slower onset of action than agents that competitively inhibit contraction, as anticholinergic drugs do. Of the adrenergic receptors in the bladder, 97% are beta 3.[160] Stimulation of this receptor has been demonstrated to show relaxation of the detrusor muscle.[161] Doses between 25 mg to 50 mg per day of mirabegron have been shown to improve symptoms in patients with non-neurogenic OAB.[162] There are currently no RCTs for mirabegron in neurogenic bladder patients. A recent retrospective series in the SCI population has shown improvements in urodynamic parameters including bladder capacity (from 365 mL to 419 mL) and compliance and decrease in catheterization frequency (from 8.1 to 6.4 per 24 hours) and incontinence episodes.[157] Further studies are imminent.

Hence mirabegron has advantages in terms of side-effect profile, but there is as yet limited evidence as to its efficacy in NBD. In the SCI population, there is insufficient current evidence to recommend mirabegron over agents such as oxybutynin. Mirabegron has a distinctive advantage in those neurogenic patients with a movement disorder, such as Parkinson's disease, where anticholinergic use is best avoided.

4.6.1.3 Alpha blockers

Alpha blockers also have a role in treating storage symptoms in patients with neurogenic bladder. They cause relaxation of the trigonal bladder and bladder neck.[158] They have been demonstrated to decrease the intravesical pressure at the maximum capacity of the bladder by 36 cm H_20.[159] Alpha blockers have also been shown to decrease detrusor overactivity on urodynamic studies.[158] Tamsulosin is becoming a key player in multi-pharmaceutical treatment of NBD. Tamsulosin has the dual action of blocking both alpha 1a receptor and alpha 1d. McGuire and Savastano initially postulated the potential for such combination treatment in primates many years ago.[159]

4.6.1.4 Other relaxing agents

Tricyclic antidepressants have been shown to work as both an antimuscarinic and a serotonin reuptake inhibitor. There is good evidence for their use in the pediatric population, but their side-effect profile and cardiac toxicity makes them less useful in the adult population.[161]

Dantrolene and baclofen, agonists of the GABA B receptor and facilitators of storage, have limited use due to their side-effect profile. The severity of the side effects of these drugs has limited their use for neurogenic bladder. However, when used for other indications, there may be some corresponding improvement in bladder symptoms.

4.6.1.5 Combination treatment

In attempting to maximize bladder relaxation via multiple pathways, combination therapy with an alpha blocker and anticholinergic,[163] or using a tricyclic, such as imipramine as a bladder relaxant with anticholinergic,[164] or even using triple therapy of imipramine with anticholinergic and alpha blockers[165] may improve pressure and symptoms.

The evidence for this is based on the improvement of symptoms in patients with non-neurogenic bladder outflow obstruction treated with both alpha blockers and anticholinergics,[162] as opposed to alpha blockers alone. There is also an SCI primate model[159] demonstrating the efficacy of combination therapy. Using different pharmacological pathways has the advantage of not increasing side effects that would be seen with increasing doses of anticholinergics in particular.

Whether this approach is warranted and tolerable in the era of botulinum toxin A injections is questionable. However, in situations where moving to chemical denervation is unwanted or unachievable, there may now be a role for a new triple-combination therapy for pressure management using an anticholinergic, beta agonist, and alpha blocker.

This approach has not been extensively studied, though it is in use in many SCI units worldwide. There is animal data supporting the role of antimuscarinics and beta agonists in improvement of bladder parameters including elevating the bladder elastin level, reducing nonvoiding contractions, and increasing bladder compliance in SCI rats.[163]

It should be noted that there is a high risk for iatrogenic injury in these SCI patients with medications. Combinations such as beta agonists and alpha blockers have vasoactive side effects, and caution needs to be exercised where other agents such as phosphodiesterase inhibitors may also be in use. Many of these patients have a considerable polypharmacy. Cognitive impairment has been linked with the long-term use of anticholinergics.[166] Simple and safe medical therapy is crucial.

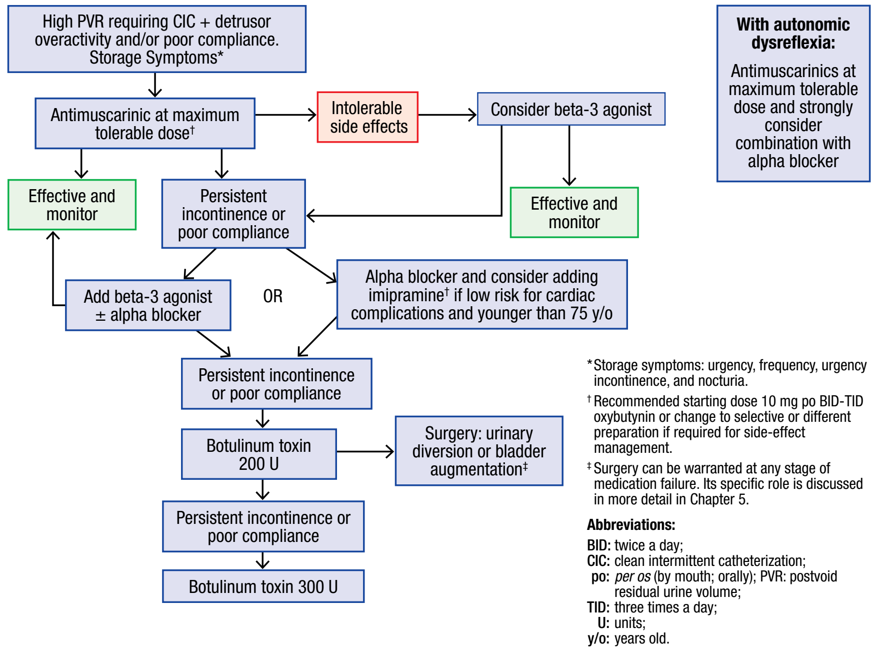
4.6.1.6 New/investigational agents

Owing to the side-effect profile of anticholinergic agents, there is much ongoing research into more efficacious and better-tolerated bladder relaxants. Vardenafil has been demonstrated in animal data to reduce nonvoiding contractions in spinal cord–injured rats.[164] Tadalafil has been shown in an experimental model using strips of donated human bladder and prostate to further enhance the tamsulosin-induced reduction of contraction.[165] Vardenafil has been shown to improve cystometric capacity and lower maximum detrusor pressures.[167] Inosine *in vitro*, probably via a sensory mediated mechanism, improves neurogenic overactivity in a rat model.[166]

4.6.1.7 Medication failure in bladder pressure management

Medication can fail due to intolerable side effects, not achieving reductions in urodynamic parameters, or failure to resolve symptoms. When oxybutynin fails, the side effects typically limit it being prescribed in higher doses, and hence changing to a different preparation or different medication is required. Depending on local availability and cost, options include using the oxybutynin patch, using the slow-release oral formula, or changing to a selective agent such as solifenacin. If the side-effect profile is predominantly anticholinergic (dry mouth, dry eyes, constipation), then changing to a beta agonist can be trialed, but in the presence of adverse urodynamic parameters this would need to be closely monitored with urodynamics, given there is as yet sparse data on the effective use of beta agonists in NBD. A schema for management of medication failure is presented in the algorithm for management of neurogenic bladder dysfunction in SCI (see **Figure 4-1**).

FIGURE 4-1
Algorithm for Medical Management of SCI.



For patients with failure to control urodynamic parameters or symptoms, combination therapy with addition of a beta agonist to an anticholinergic, with or without an alpha blocker, can be tried, but ultimately, they may be best served with treatment with botulinum toxin A.

4.6.2 Medications facilitating emptying

4.6.2.1 Facilitating emptying by reducing outlet resistance

The role of medical therapy for DSD and decreasing sphincter tone is likely to be insufficient to preserve upper tract function or produce voiding in the SCI patient who cannot void. However, some advantage can be obtained in patients who void without mechanical assistance. There may also be instances where lowering outlet resistance helps facilitate catheterization, but there is no specific data demonstrating the use of agents such as alpha blockers in this instance. Alpha blockers may play a role in facilitating emptying by reducing outlet resistance. Tamsulosin has been shown to decrease postvoid residuals and increase flow rate in a population with MS.[167,168] There are many alpha blockers available and the common ones are presented in **Table 4-5**. It is noteworthy that symptoms of autonomic dysreflexia improve in the SCI population with the use of alpha blockers. Of individuals with injuries above T6, 44% had improvement in AD symptoms on terazosin.[168]

TABLE 4-5 Alpha-Blocker Medications

Medication	Dose range	Common side effects
Alpha blockers:		Rhinitis, postural hypotension, dizziness, abnormal ejaculation, floppy iris syndrome
Alfuzosin	5–10 mg daily	Less ejaculatory problems and less dizziness/postural hypotension
Doxazosin	2–8 mg daily	Most dizziness and postural hypotension—need dose escalation
Tamsulosin	0.4–0.8 mg daily	High rate of ejaculatory problems
Terazosin	2–10 mg daily	Most dizziness and postural hypotension—need dose escalation
Silosodin	8 mg daily	Lowest rate of ejaculatory problems and hypotension

4.6.2.2 Facilitating bladder emptying by promoting contraction

No agent (e.g. Bethanecol) has been shown to effectively facilitate bladder emptying by promoting contraction,[145] and these agents can have cardiovascular side effects and could potentiate autonomic dysreflexia, as they do not promote coordinated voiding.

4.6.2.3 Increased sphincter tone

There is a very limited role for pharmacotherapy in prompting continence in patients with intrinsic sphincter deficiency secondary to NBD. Duloxetine and alpha agonists have been tried in the non-neurogenic population with some success but at the expense of side effects.[169] Estrogen may be used to reverse any coincident atrophic changes in post-menopausal women with SCI, but even in the non-neurogenic population its role in stress incontinence is limited.[170]

4.6.2.4 Decreased urine production

Desmopressin (DDAVP) has been used to minimize the amount of nocturia in patients with neurogenic bladder. Patients with nocturnal polyuria were shown to decrease the need for catheterization overnight. This has only been shown in small numbers and requires close monitoring.[171]

4.6.3. Conclusions

- Anticholinergics improve bladder capacity, incontinence, lower urinary tract symptoms, bladder compliance, and reduce upper tract complications in patients with SCI who manage their bladder with either IC or indwelling catheters. These are the mainstay of symptom and pressure management in SCI neurogenic bladder dysfunction. **[LOE 1]**

- Oxybutynin has been the most studied in SCI, but all anticholinergics have been proven to be non-inferior to oxybutynin, and the extended-release formulations have fewer side effects. **[LOE 1]**

- The use of mirabegron as an alternative or its addition to anticholinergics shows promise that requires validation. **[LOE 3]**

- Alpha-adrenergic blockers have been used with some modest success in SCI patients to not only facilitate those already voiding, but also increase capacity and compliance in combination with anticholinergics. **[LOE 3]**

- Nocturnal polyuria has been treated successfully with desmopressin in small studies with SCI patients, but further studies are warranted. **[LOE 3]**

- There are no pharmaceutical agents available to aid bladder contraction in patients with flaccid bladder. **[LOE 4]**

4.6.4. Recommendations

- Clinicians must consider the use of anticholinergics in all SCI patients with NBD symptoms or worrisome urodynamic findings. **[LOE 1; GOR A]**

- Clinicians should consider the use of mirabegron as an alternative in patients who fail anticholinergics; or it may be used in combination. **[LOE 2; GOR B]**

- Less frequently used agents such as tricyclic antidepressants may have a role in specific scenarios and in combination therapy. **[LOE 3; GOR C]**

- Tamsulosin or other adrenergic blockers may be used to improve capacity and compliance in combination with anticholinergics. **[LOE 3; GOR C]**

- All medications, particularly combination therapy, should be prescribed with care due to the risk for polypharmacy and cognitive impairment in this group of patients. **[LOE 3; GOR B]**

- When oral medical therapy fails, clinicians should avoid drug "cycling"; rather, clinicians must consider alternative treatment such as botulinum toxin **[LOE 2; GOR A]** or surgical reconstruction. This schema is represented in **Figure 4-1**.

4.7 Botulinum Toxin

4.7.1 Botulinum toxin for the spinal cord–injured bladder

Failure of anticholinergic medications in SCI neurogenic bladder dysfunction management has spurned the development of second-line treatments, including the use of BoNT. It should be remembered that the majority of data on botulinum toxin injection for NDO is from the two groups of patients, SCI and MS, included in the registry trials for regulatory approval.

4.7.1.1 Formulations

Various commercial formulations of botulinum toxin (BoNT) are being used worldwide, both on- and off-label (**Table 4-6**). Only four commercial preparations are licensed for use in the United States: onabotulinumtoxinA (onaBoNTA), abobotulinumtoxinA (aboBoNTA), incobotulinumtoxinA, and rimabotulinumtoxinB (rimaBoNTB). Each has a revised name designation to reinforce the concept that each BoNT product has an individual efficacy and potency that is unique from other formulations. In fact, the US Food and Drug Administration (FDA) mandates a "black box warning" on all BoNT products, attesting that each preparation is unique and not interchangeable.

TABLE 4-6 Available Commercial Formulations of Botulinum Toxin

Generic name	Trade name	Company, country	Toxin isotype
OnabotulinumtoxinA	Botox®	Allergan, USA	Botulinum toxin A
AbobotulinumtoxinA	Dysport®	Ipsen, UK	Botulinum toxin
IncobotulinumtoxinA	Xeomin®	Merz Pharma, Germany	Botulinum toxin
BTX type A	Prosigne®	Lanzhou, China	Botulinum toxin A
RimabotulinumtoxinB	Myobloc®	Solstice Neurosciences, USA	Botulinum toxin B

4.7.1.2 Mechanism of action

The primary effect of BoNT on the bladder is to inhibit acetylcholine release from parasympathetic nerves, resulting in a decrease in neurogenic detrusor overactivity and incontinence episodes, and an increase in bladder capacity (**Figure 4-2**). A more complete neuromuscular blockade of the detrusor results in impaired voiding and/or urinary retention if relatively larger doses of BoNT are used.[172] The efficacy of BoNT in conditions of detrusor overactivity not only may result from an inhibitory effect on the detrusor muscle, but also some effects of the drug may be mediated by altering the afferent (sensory) input. Acetylcholine released from urothelium and acting on nearby muscarinic receptor populations (i.e. urothelium or afferent nerves), or neuronal sources of acetylcholine binding to muscarinic receptors within urothelium or afferent nerves could have a significant impact on bladder sensory input to the central nervous system and may be impacted by BoNT treatment.

FIGURE 4-2
Parasympathetic nerve terminal within the bladder depicting mechanism of action of botulinum toxin:

A: binding of toxin heavy chain to specific receptor and internalization of toxin within the nerve terminal;

B: translocation of light chain into cytosol;

C: inhibition of neurotransmitter release by cleavage of specific SNARE (Soluble NSF Attachment Protein Receptor) proteins. A to G, botulinum toxin serotypes.

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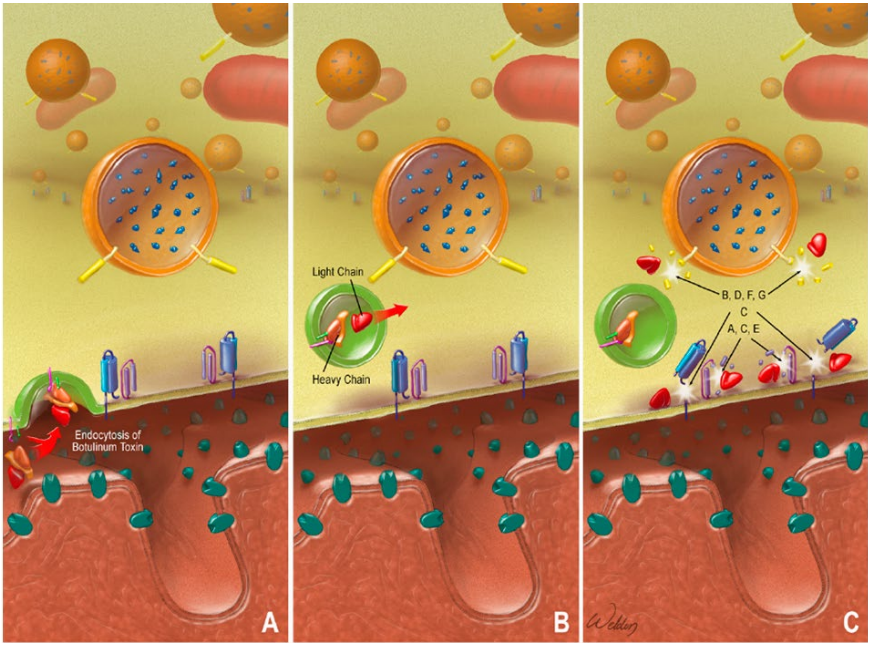

In addition, recent basic and clinical evidence suggests that BoNT may have sensory inhibitory effects unrelated to its actions on acetylcholine release. For example, an *in vitro* model of mechanoreceptor-stimulated urothelial adenosine triphosphate (ATP) release was tested in SCI rat bladders to determine whether intravesical botulinum toxin A administration would inhibit urothelial ATP release, a measure of sensory nerve activation.[173] The results demonstrated that hypo-osmotic stimulation of bladder urothelium evoked a significant release of ATP that was markedly inhibited by BoNT. This suggests that impairment of urothelial ATP release may be one mechanism by which BoNT reduces detrusor overactivity. Botulinum toxin has also been shown to inhibit release of neuropeptides such as calcitonin gene–related peptide, a substance thought to play a role in overactive bladder conditions such as sensory urgency or chronic bladder inflammation (i.e. interstitial cystitis).[174,175]

Successful BoNT treatment for overactive bladder is associated with a significant decrease of transient receptor potential vanilloid 1 (TRPV1) and/or P2X3 in suburothelial sensory nerve fibres.[176] These changes may reflect a direct effect of BoNT on the afferent innervation of the bladder or may occur as a secondary effect to the action of BoNT on the efferent innervation of the detrusor. Intravesical BoNT injection has even been shown to reduce nerve growth factor content in the bladder tissue of patients with NDO.[177] The result of this action of BoNT could decrease the hyperexcitability of C-fibre bladder afferents, thereby reducing neurogenic detrusor overactivity.

In summary, the exact mechanism by which BoNT acts in conditions of NDO has not been fully elucidated. It likely modulates bladder function by acting on multiple transmitter/growth factor/receptor systems that all use SNARE (Soluble NSF Attachment Protein Receptor) protein–dependent pathways for release or expression.

4.7.1.3 **Injection technique**

Sterile cystoscopic preparation should be performed with standard antibiotic coverage for a minor cystoscopic procedure. Urinalysis should be negative at the time of the procedure (if the patient has a history of chronic bacteriuria, appropriate preoperative antibiotic coverage is indicated). Anticoagulation medicine should be stopped for at least 3 days before injection when possible. Both rigid and flexible cystoscopic techniques work well without an apparent difference in clinical outcomes; however, most male patients cannot tolerate rigid cystoscopy in the office due to discomfort. Surgeon preference and institutional practice usually decide which technique is used. Flexible cystoscopy is most commonly performed in the office for the majority of cases to minimize cost to patients. However, the rigid scope allows for easier orientation within the bladder compared with a flexible cystoscope.

The FDA approved 200 units (U) of onaBoNTA for NDO. Based on our experience, if the results are suboptimal, we will increase the bladder injection dosage to 300 U in select cases before considering augmentation. In cases of impaired muscle contraction/respiration, our starting dose of onaBoNTA is lowered to 100 U. Pediatric patients start with a 100 U dose of onaBoNTA, although others have described doses up to 12 U/kg, similar to doses given in other neuropediatric populations.[178] Typical doses in adult patients treated with aboBoNTA range from between 500–1,000 U, and for rimaBoNTB range from between 2,500-15,000 U (5,000 U is most common).

It should be emphasized that no standardized injection technique exists for botulinum toxin A (BoNTA) injection in lower urinary tract tissues. Different bladder injection paradigms have been described (i.e. trigone vs trigone sparing), although none has been proven by a large, randomized clinical trial to be superior to the other. All **LOE 1** studies have avoided trigone injection presumably because of the inherent risk of developing vesicoureteral reflux, although several studies have disproven this risk.[179–181] We usually inject 1 mL per site (10 U onaBoNTA/mL); therefore, for example, if we are using 200 U, there will be approximately 20 injection sites. In this case, we would take two bottles of 100 U of onaBoNTA and dissolve each bottle in 10 mL of preservative-free saline.

The bladder volume is typically kept at 150 mL to 200 mL, and blood vessels are avoided during injection. The first observable change is in urgency, frequency, and incontinence after 4 to 7 days, and all variables improve significantly after 4 weeks.[182]

4.7.1.4 **Clinical results**

The use of onaBoNTA in the urinary bladder was first described in manuscript form by Schurch and colleagues, who demonstrated a significant increase in mean maximum bladder capacity (296–480 mL, $p<0.016$) and a significant decrease in mean maximum detrusor voiding pressure (from 65 to 35 cm H_2O, $p<0.016$) in 21 patients with detrusor overactivity who were injected with onaBoNTA.[183] Seventeen of nineteen patients were completely continent at 6 weeks' follow-up and were very satisfied with the procedure. Interestingly, baseline improvement in urodynamic parameters and incontinence persisted at 36 weeks in the follow-up of 11 patients. In the largest clinical series presented to date, a multicentre retrospective study examined 200 patients with neurogenic bladder treated with intravesical onaBoNTA injections.[184] At both 3- and 6-month follow-up, mean cystometric bladder capacity increased and mean voiding pressures decreased significantly.

A strong impetus driving industry-sponsored clinical trials examining the effects of BoNTA on NDO was provided by the first randomized, placebo-controlled trial examining the effects of two doses of onaBoNTA (i.e. 200 or 300 U) versus saline injection on various parameters, including urodynamic measurements and urinary incontinence episodes.[172] Significant decreases in incontinent episodes (~50%), significant increases in maximal cystometric capacity (~170–215 mL), and significant improvements in QOL scores were demonstrated in both onaBoNTA treatment groups compared with controls. Beneficial effects lasted the duration of the study (6 weeks). The study was not powered to detect statistical differences between the two onaBoNTA doses injected. Importantly, no safety concerns related to adverse events from onaBoNTA treatment were reported.

Since that time, five other **LOE 1** studies have demonstrated clinical efficacy of onaBoNTA for neurogenic detrusor overactivity in NBD patients (MS and/or SCI).[185–189] The primary efficacy is described in **Table 4-7**. Three studies showed an approximately 60% reduction in urge incontinence episodes with 200 U of onaBoNTA and significant improvements over the placebo group.[185–187] There were no significant differences between the 200 U and 300 U groups regarding primary efficacy. A recent *post-hoc* analysis found that the beneficial effects of onaBoNTA were similar between both MS and SCI patients, except that a larger placebo effect was observed in MS patients and a greater magnitude of reduction in maximum detrusor pressure was found in SCI patients.[190] The larger reduction in bladder pressure in SCI patients was attributable to their higher baseline values. Median duration of response with onaBoNTA from a long-term extension trial was 9 months for the 200 U dose.[191] Fifty-two percent of patients responded for 6 to 12 months, 22% for less than 6 months, and 26% of patients had clinical benefit for more than 1 year. The lone **LOE 1** study examining the effects of aboBoNTA versus placebo found much greater reductions in incontinence episode frequencies (IEFs) in both aboBoNTA injection groups, but the difference between each aboBoNTA group and its comparable placebo group did not reach statistical significance.[189]

TABLE 4-7 Changes in Primary Efficacy From Botulinum Toxin Bladder Injection in 6 LOE 1 Studies

Reference	Patient population	Treatment	Primary efficacy	Results
Schurch *et al.*[172]	59 pts (53 SCI, 6 MS)	Placebo, 200 U onaBoNTA, 300 U onaBoNTA	Reductions in UI compared with baseline at weeks 2, 6, 12, 18, 24	**Significant reductions in UI** compared with baseline in all time points of both onaBoNTA groups except 200 U group at weeks 12 and 18
Herschorn *et al.*[185]	57 pts (38 SCI, 19 MS)	Placebo, 200 U onaBoNTA	# of daily UI on 3-day diary at week 6	**57% decrease** in median daily UI episodes in 300 U onaBoNTA group compared with 12.5% increase in UI episodes in placebo group
Cruz *et al.*[186]	275 pts (121 SCI, 154 MS)	Placebo, 200 U onaBoNTA, 300 U onaBoNTA	Mean weekly UI episodes at week 6 compared with baseline	**59.7% decrease** in 200 U and **69.9% decrease** in 300 U onaBoNTA groups, significantly greater than 36% decrease in placebo group

aboBoNTA: abobotulinumtoxinA; IEF: incontinence episode frequency; MS: multiple sclerosis; onaBoNTA: onabotulinumtoxinA; pts: patients; SCI: spinal cord injury; U: units; UI: urinary incontinence.

continued on **page 186**

TABLE 4-7 Changes in Primary Efficacy From Botulinum Toxin Bladder Injection in 6 LOE 1 Studies, *Cont'd*

Reference	Patient population	Treatment	Primary efficacy	Results
Ginsberg *et al.*[187]	416 pts (196 SCI, 227 MS)	Placebo, 200 U onaBoNTA, 300 U onaBoNTA	Mean weekly UI episodes at week 6 compared with baseline	**63.9% decrease** in 200 U and **73% decrease** in 300 U onaBoNTA groups, significantly greater than 31.1% decrease in placebo group
Apostolidis *et al.*[188]	73 pts with SCI	Placebo; 50 U, 100 U, or 200 U onaBoNTA	Weekly UI at week 6 compared with baseline	**No significant difference in UI between any onaBoNTA groups versus placebo at week 6.** Significant difference between 200 U group and placebo at week 30
Denys *et al.*[189]	42 pts (22 SCI, 20 MS)	Placebo 15 or 30 injections and aboBoNTA 750 U 15 or 30 injections	Mean daily IEF on day 84 compared with baseline	**No significant difference in IEF between 15- or 30-injection aboBoNTA and placebo.** 76.2% decrease in IEF in 15-injection aboBoNTA, 51.6% decrease in IEF in 15-injection placebo, 100% decrease in IEF in 30-injection aboBoNTA, 59.1% decrease in 30-injection placebo

aboBoNTA: abobotulinumtoxinA; IEF: incontinence episode frequency; MS: multiple sclerosis; onaBoNTA: onabotulinumtoxinA; pts: patients; SCI: spinal cord injury; U: units; UI: urinary incontinence.

Complete continence (dry rate) following BoNTA injection varied between toxin dosage and toxin formulation, as well as the time point measured from the injection. At 6 weeks following injection, a 100% reduction in incontinence episodes from the FDA label dose of 200 U onaBoNTA ranged from 23.1% to 38%.[186–188] Two of three studies reported significant differences between 200 U onaBoNTA dry rates and placebo dry rates. For 300 U onaBoNTA, dry rates ranged from 36% to 39.6% at 6 weeks in two studies,[186,187] while another study found a dry rate from 300 U onaBoNTA of only 10.7% at 24 weeks following injection.[185] The single **LOE 1** study comparing aboBoNTA with placebo found no statistical significant difference between complete continence rates in either 15-injection aboBoNTA (64%) or 30-injection aboBoNTA (63%) and corresponding placebo groups (33% and 17%, respectively) on day 84 after injection.[189]

The beneficial effects of onaBoNTA are limited not only to symptomatic improvements. Patients with NBD often have high-pressure neurogenic detrusor overactivity that places their upper tracts at risk for deterioration (hydronephrosis, reflux, or renal failure). Changes in urodynamic measures from **LOE 1** studies are listed in **Table 4-8**.[172,185–189] Maximal cystometric capacity (MCC) increased by approximately 60% in the 200 U onaBoNTA groups and increased by approximately 69% in the 300 U onaBoNTA groups. Significant reductions in detrusor pressure, whether measured as maximal detrusor pressure (MDP) or maximal detrusor pressure during first involuntary detrusor contraction ($P_{detmaxIDC}$) were also reported following injection with both doses of onaBoNTA. AbobotulinumtoxinA also demonstrated significant increases in MCC and significant reductions in MDP compared with placebo, with greater changes observed with the larger injection template (30 vs 15 injections).

TABLE 4-8 Changes in Urodynamic Parameters From Botulinum Toxin Bladder Injection in 6 LOE 1 Studies

Reference	Treatment	Change in MCC	Change in MDP	Change in $P_{detmaxIDC}$
Schurch *et al.*[172]	Placebo, 200 U onaBoNTA, 300 U onaBoNTA	Increased by **57.6% in 200 U, 72.4% in 300 U** onaBoNTA (increases of 169 mL and 182 mL, respectively) compared with 17.7% increase in placebo	Reduced by **57.7% in 200 U, 67.2% in 300 U** onaBoNTA (decreases of 44.4 cm H_2O and 62.2 cm H_2O, respectively) compared with 10.1% decrease in placebo	N/A
Herschorn *et al.*[185]	Placebo, 200 U onaBoNTA	Increased by **75.3% in 300 U** onaBoNTA (increase of 224 mL) compared with 10.7% decrease in placebo	Reduced by **45.8% in 300 U** onaBoNTA (decrease of 27.5 cm H_2O) compared with 18.1% increase in placebo	N/A
Cruz *et al.*[186]	Placebo, 200 U onaBoNTA, 300 U onaBoNTA	Increased by **63.5% in 200 U, 63.7% in 300 U** onaBoNTA (increases of 157 mL and 157.2 mL, respectively) compared with 2.6% increase in placebo	N/A	Reduced by **55.1% in 200 U, 63.9% in 300 U** onaBoNTA (decreases of 28.5 cm H_2O and 26.9 cm H_2O, respectively) compared with 15.4% increase in placebo
Ginsberg *et al.*[187]	Placebo, 200 U onaBoNTA, 300 U onaBoNTA	Increased by **59.9% in 200 U, 65.6% in 300 U** onaBoNTA (increases of 151 mL and 168 mL, respectively) compared with 6.3% increase in placebo	N/A	Reduced by **68.4% in 200 U, 70.7% in 300 U** onaBoNTA (decreases of 35.1 cm H_2O and 33.3 cm H_2O, respectively) compared with 4.7% decrease in placebo
Apostolidis *et al.*[188]	Placebo; 50 U, 100 U, or 200 U onaBoNTA	No clear dose-response relationship, largest increases in 100 U and 200 U groups	N/A	Linear dose response: decreased by 2.1, 20.1, 29.4, and 33 cm H_2O in placebo and 50 U, 100 U, and 200 U onaBoNTA groups, respectively
Denys *et al.*[189]	Placebo 15 or 30 injections and aboBoNTA 750 U 15 or 30 injections	Increased by **53.3% in 15-injection** aboBoNTA and **71.8% in 30-injection** aboBoNTA (increases of 150 mL and 206.8 mL, respectively) compared with 4% and 9.3% increase in comparable placebo groups	Reduced by **43.9% in 15-injection** aboBoNTA and **51.9% in 30-injection** aboBoNTA (decreases of 26.1 cm H_2O and 23.8 cm H_2O, respectively) compared with 11.8% and 30.9% increase in placebo groups	N/A

aboBoNTA: abobotulinumtoxinA; MCC: maximum cystometric capacity; MDP: maximum detrusor pressure; N/A: not available; onaBoNTA: onabotulinumtoxinA; $P_{detmaxIDC}$: maximum detrusor pressure during first involuntary detrusor contraction; U: units.

Quality of life improvements following BoNT injection in **LOE 1** studies are summarized in **Table 4-9**.[172,185,187,189,192,193] The most commonly used measure was the validated Incontinence Quality of Life (I-QOL) instrument. Both onaBoNTA and aboBoNTA studies showed significant improvements in total I-QOL scores compared with placebo groups. Approximately two-thirds of patients treated with FDA-labelled 200 U dose of onaBoNTA had a significant improvement in I-QOL scores compared with an estimated 40% of placebo patients. One study evaluated the goals of onaBoNTA treatment for patients with NDO.[193] The top two goals of treatment were: 1) no incontinence and 2) reduction in other urinary symptoms. Investigators found that over 3 times as many patients reached at least one of their treatment goals following onaBoNTA injection compared with placebo. There were no differences in goal achievement between onaBoNTA doses or upon whether patients had to initiate *de novo* clean intermittent catheterization or not. Significant improvement in I-QOL was also demonstrated following aboBoNTA injection compared with placebo but in only the 15-injection paradigm.[189] (**Table 4-9**).

TABLE 4-9 Quality of Life Changes Following Botulinum Toxin Bladder Injection

Reference	Treatment	Quality of life
Schurch *et al.*[172]	Placebo, 200 U onaBoNTA, 300 U onaBoNTA	I-QOL scores significantly greater in both onaBoNTA groups compared with placebo at all time points (2, 6, 12, 18, and 24 weeks); MID higher in one or both onaBoNTA groups compared with placebo at all time points except 18 weeks; MID in total I-QOL scores was achieved in 65%–76% of 200 U onaBoNTA and 68%–89% of 300 U onaBoNTA vs 30%–45% of placebo patients
Herschorn *et al.*[185]	Placebo, 200 U onaBoNTA	Significantly greater improvement in total I-QOL scores in onaBoNTA than placebo at weeks 6, 24, and 36
Sussman *et al.*[192]	Placebo, 200 U onaBoNTA, 300 U onaBoNTA	Significant improvements in mean total I-QOL scores in both onaBoNTA groups compared with placebo at weeks 6 and 12; 58.9%–69.4% of 200 U and 62.8%–65.4% of 300 U onaBoNTA achieved MID vs 36.9%–43% of placebo; Significant improvements in OAB-PSTQ scores and PGA scores in both onaBoNTA groups compared with placebo, although PGA not validated in NDO patients; No difference in QOL scores between onaBoNTA groups
Chartier-Kastler *et al.*[193]	Placebo, 200 U onaBoNTA, 300 U onaBoNTA	62% of 200 U onaBoNTA and 63.9% of 300 U onaBoNTA achieved at least one of goals of treatment compared with 17% of placebo; Initiation of CIC did not impact patients' overall goal achievement: 46.4% of patients who initiated *de novo* CIC vs 54.2% for patients who did not
Ginsberg *et al.*[187]	Placebo, 200 U onaBoNTA, 300 U onaBoNTA	Significant change in total I-QOL score in 200 U and 300 U onaBoNTA groups compared with placebo; I-QOL score improvement similar whether patients were performing CIC at baseline or not
Denys *et al.*[189]	Placebo 15 or 30 injections and aboBoNTA 750 U 15 or 30 injections	Statistically significant improvement in I-QOL scores in aboBoNTA 15-injection group vs placebo 15 injections on days 14 and 84; No significant difference between aboBoNTA 30-injection group and 30-injection group placebo; PGA significantly improved in both aboBoNTA injection groups compared with placebo

aboBoNTA: abobotulinumtoxinA; CIC: clean intermittent catheterization; I-QOL: Incontinence Quality of Life questionnaire; MID: minimal important difference; NDO: neurogenic detrusor overactivity; OAB-PSTQ: Overactive Bladder Patient Satisfaction with Treatment Questionnaire; onaBoNTA: onabotulinumtoxinA; PGA: Patient Global Assessment; U: units.

One small, randomized study evaluated the effect of rimaBoNTB compared with placebo in a mixed population of 20 patients with either neurogenic or non-neurogenic detrusor overactivity.[194] The study found significant improvements in voided volume, urinary frequency, incontinence episodes, and QOL parameters in the rimaBoNTB group compared with placebo. Unfortunately, subjects were followed for only 6 weeks and then crossed over to the other treatment paradigm, making it hard to clearly define the durability of effect.

4.7.1.5 Conclusions

- Botulinum toxin A bladder injections are effective in the treatment of SCI neurogenic bladder dysfunction–related neurogenic detrusor overactivity and incontinence. Botulinum toxin A also improves urodynamic detrusor storage pressure, compliance, and cystometric capacity as well as patient quality of life. **[LOE 1]**
- In NBD patients, 200 U of BoNTA has excellent clinical effectiveness, with only slightly better results with 300 U; however, both doses are safe. **[LOE 1]**
- The most efficacious injection paradigm (number and location of injections) of BoNTA has not been determined. **[LOE 4]**

4.7.1.6 Recommendations

- Clinicians must consider BoNTA bladder injection for people with SCI and neurogenic detrusor overactivity if anticholinergic medications are ineffective or not tolerated. **[LOE 1; GOR A]**
- Surgeons should use a dosage of 200 U when performing cystoscopic injection of onaBoNTA in patients who perform IC. **[LOE 1; GOR A]**
- Surgeons may increase the dosage of onaBoNTA bladder injection to 300 U when 200 U has failed to provide sufficient relief of neurogenic detrusor overactivity in patients who perform IC. **[LOE 1; GOR A]**

4.7.2 Botulinum toxin for external urethral sphincter injections

The use of BoNT to treat detrusor external sphincter dyssynergia (DESD) was the first documented use of BoNT in the urologic literature back in 1988.[195] It would be ideal if the outlet could be weakened with this less invasive therapy rather than sphincterotomy to allow for spontaneous voiding or at least urinary collection in a condom catheter. Unfortunately, thus far, very little literature has supported its use, and clinically it rarely leads to these results in patients who are in retention. One poorly studied but potentially useful application of this therapy would be sphincter injection to assist with IC in those patients who have frustrating sphincter spasms associated with the passage of the IC, or in improving voiding in those patients who are voiding but with elevated residuals. A meta-analysis by Mehta and colleagues determined that BoNTA could effectively reduce postvoid residuals as well as detrusor and urethral pressures, at least in the short term.[196]

Injection of BoNTA into the urethra is a minimally invasive procedure with a low morbidity. It can be performed in an outpatient setting using a variety of techniques—this allows not only urologists but also physiatrists and neurologists opportunities to engage in this therapy. The author prefers transurethral injections—the external sphincter in men is easily visible. One just has to make sure injections are made deep to the target skeletal muscle. Complications of injection are minor and self-limiting.

Another advantage of BoNT injection is that its effect is reversible. This is a significant advantage for patients who are not sure about whether condom catheter drainage will work in the real world, outside of the hospital setting. It can offer the treating physician insight into the effect that a more permanent procedure would have on detrusor function, as well as allow him or her the flexibility through dosage adjustment to partially decrease urethral outlet resistance with milder degrees of DESD or incomplete urethral relaxation in men and women with neurological diseases. Botulinum toxin A can be injected into different muscles (for example, the smooth muscle of the bladder neck or the striated muscle of the external sphincter, or perhaps both) and used as a tool to differentiate the source of obstruction in unclear cases. Finally, it offers for the patient with the hope of neuro-recovery after SCI the potential to walk again without a sphincter that is permanently damaged.

Disadvantages of using BoNT for detrusor external sphincter dyssynergia begin with the fact that it is off-label and so may incur significant out-of-pocket costs for the patient. Secondly, although the meta-analysis suggested short-term benefit from BoNT for reducing PVR, detrusor pressure, and urethral pressure, this benefit is based on a paucity of **LOE 1** studies. Only one **LOE 1** study is available in the literature and this was an RCT in MS patients.[197] Interestingly, only detrusor pressure decreased, while no significant effect on MUP, maximal urinary flow rate (qmax), and PVR was observed. The only double-blinded, controlled study of botulinum toxin in SCI patients with DESD involved 5 patients and used higher formulations of BoNTA with booster injections, so it is hard to extrapolate meaningful results.[198] The most prominent effect of the other studies that provide **LOE 3** is a reduction in PVR and a decrease in maximal intravesical pressure; although only one study demonstrated detrusor pressures below 40 cm H_20. Unfortunately, most studies fail to examine the most important marker predictive of upper tract damage: detrusor leak point pressure (DLPP). The few studies that did measure DLPP found a variable effect (5–37% reduction), although no post-injection DLPPs were below 60 cm H_20, much less the target of 40 cm H_20. In addition, only two studies addressed the effect of botulinum toxin on QOL in patients with DESD, and the results were mixed.

Botulinum toxin A injections that target skeletal muscle generally only last 3 to 4 months compared with much longer durations in the bladder of 6 to12 months. This has financial and social implications for patients. Moreover, only targeting the external sphincter does not address bladder neck dyssynergia, which may be hampering the ability of BoNTA to be an effective treatment. In fact, Soler and colleagues in their retrospective study of 72 patients injected with BoNTA found that bladder neck dyssynergia was a strong predictor of a poor response; only 24% of patients with bladder neck dyssynergia improved compared with 73% without.[199] The authors also found that patients with type 3 DESD responded poorly as well.

4.7.2.1 Conclusions

- Limited data suggests that BoNTA injections into the external urethral sphincter offer a reversible option at relieving outlet obstruction in select male patients with SCI. **[LOE 3]**

- Botulinum toxin A has been used to ease catheter passage through a spastic external urethral sphincter in men on IC. **[LOE 4]**

4.7.2.2 Recommendations

- Clinicians may consider BoNTA external urethral sphincter injection for men with SCI and DESD who are currently voiding with an elevated PVR. **[LOE 3; GOR C]**

- Clinicians may consider BoNTA external urethral sphincter injection for people with SCI and difficulty performing CIC due to sphincter spams. **[LOE 4; GOR C]**

4.7.3 Effects of repeat injections

Kennelly and colleagues demonstrated persistent long-term efficacy of onaBoNTA in an extension trial of patients with NDO receiving up to 6 (68 patients) injections of 200 U of onaBoNTA.[191] The proportion of patients reporting more than 50% reduction in incontinence episodes per week ranged from between 83% and 91%, and the proportion of patients who were completely dry ranged from between 43% and 56%. Between 71% and 81% of patients demonstrated significant improvements in total I-QOL scores.[191] Two other studies that followed a total of 44 SCI patients through 6 onaBoNTA injections demonstrated sustained improvements in MCC (73–187 mL) and sustained reductions in MDP (23.5 cm H_2O) and $P_{detmaxIDC}$ (64 cm H_2O).[200,201]

The largest experience detailing the effect of aboBoNTA preparation on patients with NDO was described by Del Popolo and colleagues.[202] A total of 199 patients with NDO were treated over a 6-year period with 500, 750, or 1,000 international units (IU) of aboBoNTA. Significant improvements in urodynamic parameters (i.e. maximal bladder capacity, reflex volume) as well as significant reductions in incontinence episodes and pad usage were observed.[202] Interestingly, median duration of effect did not differ between the three doses (12–13 months). Approximately 20% of patients responded for more than 12 months. In addition, improvements in key urodynamic parameters were reproducible for up to 7 injections.

4.7.3.1 Side effects

The most common adverse events of intravesical BoNT injection are incomplete bladder emptying and UTIs. In two large, phase 3, randomized, double-blind, placebo-controlled trials, between 28% and 29.5% of patients treated with 200 U of onaBoNTA had to initiate IC for elevated PVR.[186,187] In addition, UTI was more common following onaBoNTA injection compared with placebo (i.e. ~28% vs 20%, respectively). In a follow-up extension trial of patients receiving up to 6 onaBoNT-200 U injections, 29.5% of 200 U patients initiated *de novo* IC following the first treatment.[191] However, *de novo* IC rates declined precipitously following treatment cycles 2 and 3 (3.4% and 6%, respectively) and did not occur from treatment cycle 4 onward. There were no treatment-related deaths.

Interestingly, in one series of 30 patients, investigators found that 300 U-onaBoNTA treatment reduced the incidence of symptomatic UTI over a 6-month period in NDO patients by 88%.[203] A second series in 41 male SCI patients corroborated the earlier results.[204] These investigators found that 300 U BoNTA reduced the 6-month incidence of UTI by 44%. In both cases, it was felt that the reduction in detrusor pressure and improved bladder capacity induced by BoNTA was responsible for the decrease in symptomatic UTIs. No direct antimicrobial effect of BoNTA was observed in a recent prospective study evaluating the inhibitory effect of onaBoNTA and aboBoNTA against various clinical urinary tract bacteria.[205]

American FDA-mandated "black box warnings" are required on all BoNT product inserts discussing the potential risk of systemic side effects, such as botulism (generalized weakness, respiratory depression/failure) following injection. Most cases of serious side effects have resulted in children treated with relatively large doses of BoNT injected into large skeletal muscles of the neck. Systemic side effects, such as generalized weakness, have been reported after bladder injection; however, the incidence is rare and appears to be related to the dose of toxin, or, perhaps, the formulation used.[206] For example, Grosse and colleagues documented 4 patients suffering from transient muscle weakness, all after being injected with aboBoNTA, with symptoms lasting between 2 weeks and 2 months.[207] In addition, Del Popolo and associates noted hyposthenia in 5 patients following injection with 1,000 U of aboBoNTA, but the effects were transient, disappearing after 2 to 4 weeks.[202] Wyndaele and Van Dromme documented two cases of generalized muscle weakness following aboBoNTA (1,000 U) and onaBoNTA (300 U) that lasted 3 months.[208] Only one study has prospectively evaluated for distant spread of BoNTA bladder injections using single-fibre electromyogram (EMG) of striated muscles.[209] Following 300 U-onaBoNTA injection in 21 SCI patients, the authors found the presence of neuromuscular jitter in 7 of 21 patients, suggesting distant spread of onaBoNTA, but no neuromuscular blocking effect was observed, and the effects were determined to be subclinical in nature.

Recent articles have examined the histological and ultrastructural effects of BoNTA injection into the detrusor. While prior work in skeletal muscle demonstrated significant axonal sprouting following BoNTA injection that eventually regressed,[210] Haferkamp and colleagues found little evidence of axonal sprouting in bladder biopsies obtained from 24 patients with neurogenic detrusor overactivity following detrusor BoNTA injection.[211,212] Understanding the differences in recovery of bladder parasympathetic versus somatic nerves may also provide better insight into the mechanisms behind clinical differences in BoNTA's duration of action. Not only does BoNTA appear to have little effect on neuronal architecture within the bladder, but also investigators have shown that onaBoNTA does not induce bladder inflammation or edema.[212] Surprisingly, these same investigators found that patients treated with onaBoNTA displayed significantly less bladder wall fibrosis than non-treated patients. These findings should alleviate concerns from urologists that repeated detrusor injections with BoNTA will induce bladder wall fibrosis and lead patients more rapidly to surgical options. It should also be of reassurance to patients who want BoNTA to be a durable but reversible fix.

4.7.3.2 **Risk of antibody formation**

Failure to respond to BoNT injection might result from the presence of preexisting BoNT antibodies (BoNT-AB; primary failure) or to the production of BoNT-ABs in response to BoNT injection (secondary failure). Neurologic literature has documented a sharp reduction in the incidence of BoNTA-AB formation from 9.5% to 0.5% in cervical dystonia patients with the introduction of a newer formulation of Botox® in 1998 (i.e. reduced protein load from 25 ng/100 U to 5 ng/100 U).[213,214] However, although BoNT use in urologic conditions has increased, little data exists on the risk for BoNT-AB formation in this patient population. A recent extension trial of repeated treatment with onaBoNTA in patients with NDO documented the presence of neutralizing antibodies in only 2.1% of patients treated (8/381) with onaBoNTA and in 1.5% of patients treated with 200 U onaBoNTA.[191] All patients had SCI, and half the patients continued to demonstrate clinical benefit from onaBoNTA injection following seroconversion (50% reduction from baseline in urinary incontinence episodes).

Schulte-Baukloh and colleagues determined the presence of BoNTA-ABs in patients treated multiple times with BoNTA and correlated the presence of BoNT-ABs with clinical response.[214] Eight of 25 patients had either elevated (4 patients) or borderline elevated (4 patients) BoNTA-AB serum titers. Interestingly, the authors found no correlation between the detection of BoNTA-ABs and the number of injections, time between injections, or total dose given. Three of five complete-treatment failure patients had definitively elevated BoNTA-ABs and no other obvious reason for lack of response to repeated injection with BoNTA. The other two complete-treatment failure patients without elevated BoNTA-ABs had obvious reasons for not responding to BoNTA treatment (poor compliance in one and tethered cord in the other). The authors concluded that BoNTA-AB formation appears to be more prevalent after BoNTA application to the bladder compared with skeletal muscle. They recommended a “drug holiday” in clinical nonresponders with elevated BoNTA-AB titers, as BoNTA-ABs disappeared in 2 patients with borderline levels after 6 months in one and 12 months in the other.

Investigators have examined whether NDO patients could be “rescued” with onaBoNTA after failure to respond to aboBoNTA (750 U).[215] Twenty-six patients treated unsuccessfully with aboBoNTA received onaBoNTA (300 U). Fifty-eight percent of patients were successfully treated (i.e. resolution of detrusor overactivity), 65% of patients were completely continent, and the frequency of clean intermittent catheterization decreased by 43%.

4.7.3.3 **Cost-effectiveness**

A recent study evaluated the cost-effectiveness of onaBoNTA for NDO over a 3-year period using a Markov state transition model in the United States.[216] Patients with NDO refractory to anticholinergics could be treated with onaBoNTA or continue to receive best supportive care (incontinence pads, anticholinergics, etc.). Nonresponding patients could undergo sacral neuromodulation or bladder augmentation surgery. Although onaBoNTA increased costs by $1,466 over best supportive care (BSC), its incremental cost-effectiveness ratio was $24,720/ quality-adjusted life years (QALY). Given the conventional threshold cost-effectiveness ratio of $50,000/QALY, onaBoNTA is projected to having a 97% chance of being cost-effective.[216] OnaBoNTA was cost-effective in both MS and SCI subpopulations. However, its cost-effectiveness in SCI patients was dominant by reducing costs and increasing QALY. A similar cost-effective analysis was performed evaluating onaBoNTA in patients with NDO in the United Kingdom.[217] At a threshold cost-effectiveness ratio of 20,000 pounds/QALY, onaBoNTA had a 100% probability of being cost-effective compared with BSC, and was more pronounced in SCI than in MS patients.

4.7.3.4 Multidisciplinary treatment

As more patients become exposed to BoNT injections from multiple clinicians for different indications, questions arise as to the best approach to minimize toxicity and reduce the risk for antibody formation. Although no guidelines have been established, from discussions with fellow BoNT practitioners, we are guided by the following principles: 1) use the same BoNT formulation and 2) inject within 24 hours for each indication, or, if not possible, space injection treatments at least 3 months apart. A total safe dose among differing injectors has not been clarified and is specific for each BoNT formulation.

4.7.3.5 Conclusions

- Repeat bladder injections of BoNTA are safe and the effects sustainable. **[LOE 3]**
- Urinary retention can occur with bladder injection of BoNT, particularly in patients with neurogenic bladder who are voiding. **[LOE 1]**
- BoNTA antibodies can occur due to prior exposure to the drug, but can resolve over time. **[LOE 3]**

4.7.3.6 Recommendations

- Patients with NBD who are voiding must be counselled that urinary retention can occur after BoNTA injections; they should be prepared to initiate IC should this occur. **[LOE 1; GOR A]**
- Patients who respond to BoNTA bladder injections should be offered repeat injections to sustain the benefits. **[LOE 1; GOR A]**
- Patients receiving BoNT for different indications should receive the same formulation and have injections either on the same day or spaced out by 3 months. The total dose injected must not exceed the safe dosage for the formulation. **[LOE 3; GOR B]**

4.7.3.7 Acknowledgment

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C5

Surgical Management of the Neurogenic Bladder After Spinal Cord Injury

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CONTENTS

Surgical Management of the Neurogenic Bladder After Spinal Cord Injury

5.1 Introduction

Neurogenic bladder dysfunction (NBD) is highly prevalent in individuals with spinal cord injury (SCI). Although treatment is usually non-surgical, this treatment modality does not have a good outcome in some: urinary incontinence and elevated bladder pressures can necessitate more aggressive treatment, including surgery.

It is mandatory to evaluate the function of the bladder, bladder neck, and urethral sphincter before a decision is made about which surgery should be proposed. Surgery does not have to be a standalone option; it can be paired with drug treatment and catheterization as necessary. The level and completeness of the lesion, a urological history, and informed consent of the patient are important.

Urinary incontinence can occur as the result of sphincter incompetence, involuntary detrusor contraction, or poor compliance. Elevated bladder pressure can be caused by loss of compliance, neurogenic detrusor overactivity (NDO), and/or detrusor sphincter dyssynergia (DSD). Herein we describe the surgical techniques developed for correction of pathological bladder, bladder neck, and sphincter function. In each section, we will present the evidence regarding the procedure and recommendations for or against its use. Some general conclusions and recommendations applicable to all the surgical procedures deserve mention at the outset:

5.2 Bladder Neck Procedures

Herein we discuss procedures to (1) tighten the bladder neck in order to aid in continence as well as procedures to (2) open the bladder neck in order to cause incontinence and protect the kidneys from elevated bladder pressure.

5.2.1 Bladder neck injection (bulking agents)

Dextranomer/hyaluronic acid copolymer, polytetrafluoroethylene, and collagen have all been used for management of urinary incontinence mainly for children with spina bifida.[1-5]

Polytetrafluoroethylene use as a bulking agent was first reported in children in 1985 by Vorstman *et al.*[6] Of note, there is evidence of regional and distant migration of polytetrafluoroethylene particles in animal and human studies.[7,8] In 1995, Bennett *et al.* reported collagen injections for stress urinary incontinence in 11 NBD patients, including 5 SCI patients.[9] Seven of the 11 were cured or improved after the treatment; this was confirmed by showing improvement in urodynamic leak point pressure, and no significant complications were observed during the follow-up period (mean: 24 months). In 1996, Pérez *et al.* reported the usefulness of submucosal bladder neck injection of bovine dermal collagen for stress urinary incontinence (SUI) in 32 children, including 1 SCI patient (sacral trauma).[7] Only 20% of the children became dry after the treatment. Moreover, Cole *et al.* reported a long-term (almost 10-year), single, institutional experience of continence procedures for pediatric patients in 2003; 49 continence procedures were done for 43 patients, including 3 patients with SCI.[8] Among the continence procedures, such as Young-Dees-Leadbetter (YDL), sling, and bladder neck closure (BNC), only collagen injection (done in 5 patients) achieved poor outcome (1 success in 5 cases). Moreover, Lightner *et al.* investigated the efficacy and adverse events of dextranomer–hyaluronic acid injection into the proximal urethra for urethral incompetence in 56 patients, including 2 SCI patients;[10] outcome was poor. Efficacy was low, and there were high rates of complications including pseudoabscess and *de novo* urge incontinence. Therefore, bladder neck injection cannot be recommended strongly for management of urinary incontinence in SCI patients in the aspect of long-term follow-up.

5.2.2 Bladder neck reconstruction and closure

For management of urinary incontinence due to sphincter incompetence in SCI patients, anticholinergic agents, intermittent catheterization, and surgical approaches can all be done to try to minimize the leakage; however, none of these treatments directly addresses the sphincter incompetence. There is a limited amount of quality scientific evidence, such as randomized controlled trials (RCTs) and prospective trials, to adequately direct management of incontinence due to sphincter incompetence in SCI. Herein, we review the surgical approach for sphincter incompetence in SCI patients, divided into bladder neck reconstruction and bladder neck closure.

5.2.3 Bladder neck reconstruction

Bladder neck incompetence can be addressed by different surgeries: urethral sling, artificial urinary sphincter (AUS), injection of urethral or bladder neck bulking agent, various bladder neck reconstruction techniques including the Young-Dees-Leadbetter (YDL) procedure, the Kropp procedure, and the Pippi Salle procedure, and finally by bladder neck closure. The procedures have been primarily described in children with spina bifida; evidence in SCI patients is inadequate for establishing specific recommendations for a unique treatment approach in this group.

5.2.3.1 The Young-Dees-Leadbetter procedure and its modification

The YDL bladder neck reconstruction is the culmination of many years of effort to design an operation for urinary incontinence using native tissue of the bladder neck. The Young procedure, later modified by Dees *et al.* and Leadbetter *et al.*, has been applied only in a pediatric non-SCI population.[11–17]

5.2.3.2 The Kropp procedure

In 1986 Kropp and Angwafo described a technique of urethral lengthening for achieving urinary continence in children with myelomeningocoele,[18] which involves a rolled bladder tube that acts as a 1-way valve to prevent urine leakage, but allows a catheter to be passed for urine drainage. Intermittent catheterization is essential for managing this procedure. After the first report by Kropp and Angwafo, many reports were published. However, like the YDL reports, application of this procedure has been focused in children.[19–21] There is no large series of the Kropp procedure reported in SCI patients.

5.2.3.3 The Pippi Salle procedure

The Pippi Salle procedure, first described in 1994,[22] involves an anterior bladder wall flap sutured to the posterior wall in an onlay fashion to create a flap valve mechanism. It was devised to mimic the flap valve mechanism of the Kropp procedure but with fewer catheterization problems. Like the other bladder neck reconstruction procedures, the Pippi Salle procedure has not been commonly used for SCI patients, but mostly in children with NBD secondary to congenital problems.[23,24] Nakamura *et al.* reported the long-term follow-up after the Pippi Salle procedure in patients with severe intrinsic urethral sphincter deficiency including 1 SCI female patient.[25] Complete dryness was achieved in 58% of patients including the SCI patient in this report (mean follow-up: 75 months). Complications included continued urinary incontinence (41%), difficulty of catheterizing through the urethra (25%), and urinary calculi (8%).

Although several procedures for bladder neck reconstruction were reported as described above, adequate timing of bladder neck reconstruction is still controversial. Lee *et al.* investigated 35 patients (30% of whom had SCI) who underwent augmentation cystoplasty (AC), and evaluated whether concomitant bladder neck reconstruction is necessary when performing AC.[26] Urodynamic parameters showed that maximum urethral closure pressure was increased after AC without bladder neck reconstruction. Thus, the investigators recommended that anti-incontinence bladder outlet procedures be considered as a staged operation, rather than simultaneously with the AC.[27,28] Therefore, simultaneous bladder neck reconstruction and AC should be done judiciously for management of urinary incontinence in SCI patients.[29]

Conclusion

- There is insufficient evidence to draw conclusions about outcomes of bladder neck reconstruction in SCI patients.

Recommendation

- Surgeons should limit bladder neck reconstruction to children with myelomeningocoele, and should not use it in adults with SCI except in a research setting. **[GOR C]**

5.2.4 Bladder neck closure

When multiple bladder neck reconstruction surgeries fail or seem unlikely to succeed, BNC has been performed as the final intervention to achieve dryness.[30] Bladder neck closure is an irreversible procedure requiring patient compliance with catheterization of a cutaneous stoma. Indications for BNC include intractable urinary incontinence, urethral erosion due to long-term indwelling catheters, scarring from previous trans-urethral procedures, and urethra-cutaneous fistula. In this subset of patients, BNC excludes the irreparable native urethra and provides urethral continence. Surgical BNC is challenging due a high rate of failure (persistent urethral leakage). The recommended technique is that described by Reid *et al.*, in which a transvesical resection of the bladder neck and prostatic urethra is performed. Then, the defect is closed with three overlapping purse-string sutures of 3-0 polyglycolic acid with watertight suture of the bladder mucosa on top.[31] This procedure must be combined with some form of urinary diversion, such as ileo-vesicostomy or continent catheterizable stoma, with or without augmentation enterocystoplasty.[32] Another simple option in patients with adequate bladder capacity is combining BNC with permanent suprapubic catheter diversion.[33] Colli and Lloyd reported good outcomes with this technique in NBD patients, 71% of whom had SCI.[34] In this study, all but 1 patient became continent (97%). Although this report is based on short-term follow-up, no patients showed evidence of upper urinary tract deterioration. The investigators also concluded that BNC with suprapubic catheter placement provides an excellent outcome of urethral continence with a reasonable complication rate. A clinician also must keep in mind that an indwelling catheter can increase the risk for infections, bladder calculi, and bladder malignancy.

On the other hand, Kavanagh *et al.* reported long-term follow-up for patients receiving BNC with enterocystoplasty and Mitrofanoff diversion, including 2 SCI patients (7%).[35] Only 2% of the patients remained wet after surgery. The total surgical re-intervention rate was 39.3%, mainly for bladder calculi. Bergman *et al.* investigated a large series of patients who underwent BNC with modified abdominal stoma creation, including 4 SCI patients (5.7%).[36] Contrary to the Kavanagh study, in the Bergman study 44 patients (85%) were completely incontinent postoperatively, and 7 patients were dry for less than 2 hours during the day and 4 hours at night (13%). The important difference between these two studies may be the lack of an AC in the Bergman study.

Complications after BNC were not uncommon in the various above-listed reports. Nguyen and Baskin reported that although 8 patients (40%) achieved complete continence, complications were frequent and included leakage via stoma in 20% and urethral fistula in 40%.[30] Bergman *et al.* also reported a high rate of complications, including vesicourethral fistula in 12%, stomal incontinence in 10%, and stomal complications in 24% (including 6 with stomal stenosis leading to catheterization difficulty).[36] In the other reports, stomal complications (stomal stenosis and stomal prolapse) were also a problem with long-term follow-up of BNC patients.[37,38] In Colli and Lloyd's report showing BNC with suprapubic catheter placement, the overall complication rate was 16.7%.[34] Besides an intra-operative complication, 6 postoperative complications, such as superficial wound infection, were observed in 5 patients. To reduce the complication rate to a reasonable level, suprapubic catheterization without any additional bladder reconstruction is one of the possibilities.

Conclusion

- Bladder neck closure offers an irreversible option for managing sphincteric incompetence in the SCI patient. It has a high rate of failure, manifest as vesicourethral fistula and persistent urinary incontinence. **[LOE 3]**

Recommendations

- Surgeons may perform BNC in the SCI patient as a final intervention for refractory sphincteric deficiency-related urinary incontinence, after failing other management options. **[GOR C]**

- Surgeons should combine BNC with a procedure to ensure low bladder pressures postoperatively in order to minimize the risk for failure. Such procedures should be tailored to the specific needs of the patient and may include (1) augmentation cystoplasty, (2) continent channel, (3) a combination of augmentation cystoplasty and continent catheterizable channel, or (4) placement of a suprapubic cystostomy tube. **[GOR B]**

5.3 Peri-urethral Autologous Sling and Synthetic Tapes

Spinal cord injury may cause SUI by intrinsic sphincter deficiency (ISD), and sometimes there is coexisting contributory urethral hypermobility. Correction should be directed to the major cause or to both. Autologous fascial sling surgery has long been a recommended surgical approach, as it can restore urethral support and counteract ISD by compressing the urethra. In SCI, additional procedures may be needed, such as treatment of detrusor overactivity (DO), or application of clean intermittent catheterization (CIC). Midurethral synthetic tape operations, such as the transvaginal tape (TVT) or transobturator tape (TOT) procedures, have not been undertaken in many patients with SCI. This partly reflects perceived concerns, firstly about efficacy (as ISD is a significant contributor in many people with SCI), and secondly about possible complications, notably tape exposure (erosion).

Outcomes of autologous fascial sling surgery have generally been reported in case series, and no reported study has had a study population comprising entirely individuals with SCI. Likewise, there is sparse data published on the efficacy of midurethral tape operations in SCI. A recent systematic review of stress incontinence management in NBD including studies of Level of Evidence (LOE) **[LOE 3]** or better found results for synthetic tape in only 20 individuals and for autologous fascial sling in 177.[39]

One study **[LOE 3]** did a retrospective analysis of prospectively collected data in a cohort of 27 women with SCI undergoing TOT placement.[40] Mean age was 56 years (range: 30–82). Twenty-two patients (81.5%) reported full continence from SUI post-surgery. Two of five patients (40%) who voided by straining prior to surgery required CIC postoperatively. No bladder or vaginal injuries, tape erosions, or urethral obstruction was seen. Three patients (11.1%) had transient thigh pain.

In a retrospective series **[LOE 3]** of 12 women with neurogenic lower urinary tract dysfunction treated by TVT[41] with a mean follow-up of 10 years, 9 patients were available for assessment, of which 7 were dry and 2 were improved. No urethral erosions were identified. A retrospective study looking at the full scope of urological surgery in one centre reported use of TVT in 4 patients with SCI (2 infrasacral, 2 suprasacral), stating that a substantial reduction in episodes of SUI was seen after 5 years.[42] No serious complications were reported.

In a case series of 9 women undergoing TOT placement, only 2 patients did not use any pads (continent) and 1 had reduced pad use (improved), indicating that incontinence was not improved in 6 of 9.[43] Vaginal examination and cystoscopy demonstrated erosion and a fistula associated with one tape. The study concluded that implantation of transobturator sub-urethral tapes in women with SUI due to intrinsic sphincter deficiency and a low leak point pressure led to unfavourable results.

El-Azab and El-Nashar compared TVT (*n*=20) with autologous sling (*n*=20) in a series of non-randomized women with neurogenic stress incontinence of whom 30 had sacral SCI.[44] At baseline, women in the TVT group had a higher parity, worse incontinence-related quality of life (QOL), and lower postvoid residual (PVR), all of which may have led to study bias. Outcome measures included objective success defined by no leak on standardized cough stress test, reduction in Incontinence Impact Questionnaire 7-item (IIQ-7) scores, PVR urine volume, and urinary urgency rates. Although short-term sling failure rates were similar, at 4 years, the cumulative failure rate was 41.8% after TVT, compared with 25.4% after autologous sling. Reduction in the total modified IIQ-7 score was greater in the TVT group. The median post-TVT PVR was 200 mL (range: 70–450 mL), significantly less than after autologous sling (300 mL, range: 180–600 mL). Urgency urinary incontinence was seen in 30% (*n*=6) after TVT and 10% (*n*=2) after autologous sling. The comparative findings between TVT and autologous sling need to be interpreted with some caution due to the small series with uneven preoperative conditions: the level of evidence is low.[302]

Conclusions

- Autologous sling results in a higher likelihood of being dry and lower likelihood of urinary urgency than synthetic tapes. **[LOE 3]**

- Autologous sling results in a higher PVR and lower subjective improvement than synthetic tapes. **[LOE 3]**

Recommendations

- Surgeons should consider autologous sling placement for management of urinary incontinence due to sphincteric deficiency in women with SCI. This is usually combined with a plan for intermittent catheterization postoperatively. **[GOR B]**

- Surgeons should not use synthetic sling for management of urinary incontinence due to sphincteric deficiency in women with SCI, except in the context of clinical trials. **[GOR B]**

5.4 Artificial Urinary Sphincter (AUS)

The artificial urinary sphincter (AUS), usually AMS 800™ (American Medical Systems (AMS)/ Boston Scientific, Boston, MA, USA), is considered the gold standard for ISD in male patients with NBD[45] ([**LOE 3; GOR A**]; European Association of Urology [EAU] guidelines 2015, International Consultation on Incontinence 2012). The AUS has been mainly used in men with post-prostatectomy incontinence, and little data is available in the literature for AUS implantation in patients with NBD in general or SCI in particular.[46]

The last International Consultation on Incontinence (ICI 2013)[47] reported briefly on the indications and results of AUS in neurogenic patients, underlying key questions on the risk for infection/erosion, manual dexterity, cuff placement, and ejaculatory dysfunction in men.

5.4.1 Challenges arising from the literature on AUS in NBDs

The literature available on AUS implantation in patients with NBD is limited and based mainly on pediatric neurogenic population data. Levesque *et al.* published the pediatric study with the longest follow-up; they reported a continence rate of 85% with a functioning AUS at 10 years.[48] Many patients had gotten AC pre- or post-implant of the AUS.

A recent review of mechanical devices concluded that there was insufficient evidence to support the use of AUS in women.[49] The current EAU guidelines recommend the use of an autologous urethral sling in women with neurogenic SUI who are able to perform intermittent self-catherization (ISC) (EAU guidelines 2015; [**LOE 4; GOR B**]).

5.4.2 Primary outcome definitions and results

As observed in non-neurogenic AUS studies, there is a lack of standardization with regard to outcome criteria and re-operation rates. Some authors make no distinction between "perfect continence" and "moderate continence" as primary outcome criteria, or they define "moderate continence" as "social continence". Moreover, male versus female results in the neurogenic population should not be mixed. This result accounts for the great disparity in outcomes seen in the literature. Reported continence rates with a functioning AUS range from between 57% and 92%.[50–53] These results must also be interpreted by considering the global bladder or sphincter balance of each individual. This is not always clearly reported.

5.4.3 Impact of bulbar urethra implantation in men with neurogenic stress urinary incontinence (NSUI) versus bladder neck placement

The difference in AUS survival between men and women[54,55] can be explained by several factors. The first is the anatomic location of the cuff in women—the cuff is placed around the bladder neck in women,[54] while in men the cuff is usually placed around the bulbar urethra,[55] a more superficial structure that is prone to injuries and a thinner structure that is prone to erosion. Another factor is the cuff size: larger cuffs of 5.5 cm to 6 cm are inserted in women while in men 4–4.5 cm cuffs are used.[55]

Farag *et al.*'s systematic review of 20 studies of AUS in NSUI[39] showed an overall AUS success rate of 77% ± 16% at 72 ± 18 months of follow-up. In contrast to the studies cited above, there was neither a correlation between gender and AUS success, nor a correlation between success and neurogenic deficit subtypes or AC prior or simultaneous to AUS surgery. The authors also demonstrated a higher postoperative surgical complication rate in male (20%) compared with female patients (10%). The 77% success rate seen with AUS was higher than with urethral bulking agent injections (27 ± 20%) but not significantly different from that with slings (58% ± 25%).

However, AUS shows higher re-operation rates (51% ± 25%) compared with slings (7% ± 9%). A 51% re-operation rate is higher than the 27% rate reported for the non-neurogenic population.[56] Finally, in the Farag *et al.* systematic review,[39] AUS or sling implantation at the bulbar urethra shows a statistically higher complication rate (45% ± 14%) compared with bladder neck implantation (16% ± 21%); $p = 0.04$.

5.4.4 **Mechanical failure**

The AMS 800™ artificial urinary sphincter can suffer from mechanical failure, requiring replacement of some of the device components or the whole device. There is, again, a disparity observed in the manner of reporting re-interventions depending on the team and how closely the follow-up is conducted. Some teams use the "rate of total procedures per year per patient" while others prefer using the "rate of patients needing at least a new procedure" instead. Reported post-prostatectomy AUS insertions revision rates are of 50% at 5 years due to erosions, mechanical failure, infection, or urethral atrophy.[57,58] However, there is an even higher revision rate in patients with NBD. Murphy *et al.* compared the functional durability of AMS 800™ in non-neurogenic versus neurogenic ISD: 85% of the neurogenic group underwent surgical revision compared with 59% in the non-neurogenic group after 6 years of follow-up.[59] Reported overall refitting rates range from 10% to 57% depending on the series, with the majority occurring in the first 2 years following implantation of the device.

Definitive AUS removal rates in both adults and pediatric neurogenic populations range from 18% to 40%.[54,55,58,59]

It is unclear which factors are associated with lower AUS life span. Some pediatric surgeons mentioned previous bladder neck surgery and enterocystoplasty as a factor for lower AUS life span.[60,61] However, such a correlation with enterocystoplasty was not found in adults with NBD, probably because pediatric neurogenic cases are often mixed with anatomical malformations such as bladder extrophy. High revision rates can also be explained by the fact that neurogenic patients are younger (20–30 years) than the non-neurogenic group (70–75 years), with a device known for a limited life span of 10 years. Secondly, neurogenic patients are more fragile, with comorbidities (such as hydrocephalus and recurrent urinary tract infections [UTIs]), and they have often undergone prior urethral or bladder neck surgery.

5.4.5 The question of simultaneous AC

It is often necessary to perform procedures to lower the detrusor pressure at the time of AUS implantation in SCI patients with NBD,[62,63] and AC is performed in 33% to 75% of neurogenic patients fitted with an AUS.[51,53,59,60,62] There is debate about whether simultaneous AC with AUS implantation increases the risk for infection and erosion. Two studies report high rates of these complications: 18% to 50%.[62,63] These studies involved a limited number of patients and had a short follow-up. Other studies[64–67] are strongly in favour of concomitant AUS and AC procedures, as most patients carry on performing IC postoperatively. Chartier-Kastler *et al.* with a follow-up of 20 years, reported that 39% of their patients with NDO underwent AC, of which 21.6% had simultaneous AUS insertion.[45] Their good results advocate for performing simultaneous AUS placement and enterocystoplasty.

5.4.6 AUS implantation around the bladder neck: men and women

Bladder neck AUS is a more invasive technique contraindicated after radical prostatectomy, which can be offered to men with sphincter UI secondary to extrophy or epispadias, myelomeningocoele, and other neuropathic disorders, and whose prostates are intact.[68] Some high-volume centres have initiated robotically assisted bladder neck AUS implantation, and long-term results are necessary.[69] Pressure-regulating balloons (PRBs) of 61–70 cm H_2O are implanted in most bulbar AUS, while those of 71–80 cm H_2O may be reserved for bladder neck cuff placements in neurogenic patients.[70]

The objective of bladder neck placement of the AUS is to decrease erosion rates. There is another anatomical reason for this placement, as the bladder neck is much larger and would cause less damage to the AUS when performing a rigid cystoscopy, which is often required for cystolitholapaxy, a common procedure for bladder stones in neurogenic patients or when patients perform ISC. Furthermore, there is minimal pressure applied in the perineal area, and thus less erosion secondary to decubitus ulcers during extended sitting position in a wheelchair compared with bulbar urethral placement.

Chartier-Kastler *et al.*[45] had a 48% surgical revision rate for removal and/or replacement of the AUS. Mean device survival amounted to 6 years, illustrating the average limited life span of the AUS.

AUS implantation in women is less performed compared with men, and it is limited to 19 centres worldwide.[71] Implanting an AUS in women is rarely used as a first treatment intention and is reserved for severe SUI refractory to previous less-invasive surgical management. As a result, these patients often present with anatomical changes rendering AUS surgery even more challenging and decreasing its success rate.[71] Furthermore, the technique requires a minimum of 20 implantations per year in order to maintain surgical skills, which is why this procedure should be reserved for highly trained centres.[72] Interestingly Farag *et al.*[39] report higher complication rates in men (20%) compared with women with an AUS (10%), a trend previously reported in earlier studies in non-neurogenic series. This should in fact encourage further AUS placement in women with neurogenic NSUI.

The current literature provides very little guidance about the precise indications and the ideal timing for AUS insertion in women. There is even less written on AUS implantation in women with neurogenic SUI. This area is still dominated by surgical expertise rather than evidence-based medicine.

The few studies available are focused largely on non-neurogenic cases. All studies analyzing AUS implantation in neurological bladder dysfunction in both genders include only a limited number of women between 1 and 42 years of age. Costa *et al.* report the largest number of 52 of 344 female patients with neurogenic SUI.[54]

5.4.7 Novel modifications for AUS placements

The main aim of developing modifications is to decrease erosion rate in this particularly vulnerable patient group. Bersch *et al.*[73] analyzed retrospectively 51 patients with NBD mainly secondary to SCI who had undergone a bladder neck placement of a tissue expander port (instead of a pump) under the abdominal wall, connecting the reservoir to the AUS cuff with a static pressure. Both cuff and reservoir were filled through the tissue expander port until the minimum pressure required to prevent urine leakage under fluoroscopic control was reached (theoretically lower pressures than 71–80 cm H_20 usually used in neurogenic patients). The authors reported an overall revision rate of 35%. Twenty percent of the cuffs needed revision, removal, or replacement at a mean of 96 months of follow-up, which is better than the 48% to 85% revision rates reported in previous studies. Social continence was reported in 90.2%. Replacing the pump with an implantable chamber reduces the costs by 60%.

Knight *et al.*[74] developed a single-piece AUS composed of a cuff, a pump, a pressure-regulating balloon, and a stress-relief balloon, allowing the cuff pressure to adapt to high intra-abdominal pressures. This system showed an 85% reduction in stress incontinence.

Ludwig *et al.* are developing a novel AUS device for men and women, where the activation of the cuff is achieved via a small implant located at the inguinal level.[75] The opening of the AUS is triggered through a remote control, allowing patients to urinate easily. The advantage is applying only on-demand pressure increase. A surgical interface enables the medical staff to adjust postoperatively over time. Results in SCI patients are not available as yet.

Recently, the robotically assisted laparoscopic AUS insertion has been introduced in men with SCI. The 3D, high-definition vision, endowrist instrumentation and clear suturing in narrow male pelvis have a positive effect. Chartier-Kastler *et al.*[72] performed bladder neck placement in 6 male SCI patients. They saw no early erosion, device infection, or malfunction. Two patients developed epididymitis. A 7.5-cm or 8-cm cuff was positioned around the bladder neck. The main technical difficulty was the dissection of the Retzius space in patients with previous urine incontinence surgery.

Further experience is needed with standardization of the technique, more patients, and evaluation of cost.

5.4.8 Quality of life

Despite the high AUS revision rates in patients with NBD, patient satisfaction rates are often higher than complete continence rates. Incompletely continent patients express satisfaction with their continence improvement.[72]

Conclusions

- AUS implantation in SCI patients is feasible, safe, and has acceptable success rates; however, it is associated with high re-operation rates. **[LOE 3]**
- Complication rates of AUS insertion are lower in women compared with men with N/SUI. **[LOE 3]**
- Complications of AUS implantation in men with SCI are lower with insertion of the cuff around the bladder neck than around the bulbar urethra. **[LOE 3]**

Recommendations

- Surgeons should consider AUS insertion in the management of urinary incontinence due to sphincteric deficiency in male **[GOR B]** and female patients after SCI. **[GOR B]**
- When inserting an AUS in SCI patients, surgeons should place the cuff at the bladder neck in men and women. **[GOR B]**
- Surgeons should perform autologous urethral sling plus intermittent catheterization rather than AUS insertion in women with neurogenic SUI due to SCI. **[GOR B]**
- Surgeons may perform simultaneous bladder augmentation and AUS insertion. **[GOR B]**

5.5 Sphincterotomy and Urethral Stents

In patients with NBD, two mechanisms can cause deficient bladder emptying and retention: DSD and bladder hypocontractility. It is important to help patients evacuate the urine in order to avoid vesicoureteral reflux, hydronephrosis with subsequent renal insufficiency, and symptomatic urinary tract infections.[76,77] Detrusor sphincter dyssynergia is a characteristic feature of suprasacral and infrapontine lesions. The first-line treatment is conservative, with a combination of antimuscarinic agents and clean ISC.[78] However, there are special situations that require a more invasive management: bladder pressure keeps pathologically elevated with antimuscarinics, severe side effects of antimuscarinic agents develop, or patients are unable to perform clean ISC (e.g. quadriplegia). In these cases, the aim of sphincterotomy or urethral stent insertion is to produce reflex micturition into a condom catheter, thus protecting the upper urinary tract. Clearly, these procedures are best used in men who can successfully wear a condom catheter. In women, or in obese men with a hidden penis, a sphincterotomy or urethral stent merely results in uncontrollable incontinence. These procedures are invasive and irreversible, and the patient has no adaptation period **[LOE 3]**.[79,81]

In patients with DSD, the incidence of autonomic dysreflexia (AD) can be decreased in more than half of the patients when sphincterotomy or sphincter stenting is performed, even for a mean of 5 years after the procedure.[82] Furthermore, resolution of vesicoureteral reflux (VUR) and hydronephrosis has been demonstrated in patients after sphincterotomy or sphincter stent insertion.[82]

5.5.1 Sphincterotomy

The efficacy of the sphincterotomy has been well documented since Emmett and Dunn in 1946 described the trans-urethral resection of the bladder neck and prostate in SCI patients with outlet obstruction.[83] Ten years later, Ross introduced the resection of the external urinary sphincter.[84] Large series have shown that sphincterotomy and bladder neck incision are successful in the treatment of vesical outlet obstruction after SCI. PubMed was used for the search using the MESH terms "neurogenic bladder," "spinal cord injury," "medullar trauma," and "sphincterotomy." Since the last update of the EAU-ICUD "Incontinence" book in 2013, only two new manuscripts have been published reporting long-term efficacy of the technique in patients with SCI.

In **Table 5-1**, we summarize the findings of the level 2 **[LOE 2]** studies included in that book and 5 additional papers not included in the previous report. The most recent studies are all retrospective and do not have a control group, but sphincterotomy is shown to be an efficient technique for the resolution of AD, hydronephrosis, and recurrent urinary tract infections, and for decreasing detrusor pressures and PVR urine.[78,79,81,85,86] The redo rate ranges from 4.3% to 47.4%, but the criteria are not uniform in the different studies. For example, in the manuscript by Perkash,[82] laser sphincterotomy was used also in non-naïve patients, and no differentiation has been made in postoperative results. In an experience in 471 SCI patients, O'Flynn reported that only 6 of 139 patients required a urinary diversion after this procedure.[87]

TABLE 5-1 Literature Data for Bladder Neck Incision and Sphincterotomy

Sphincterotomy	Reference	SCI/ Total number of patients	Follow-up period of study	Site of incision	Success criteria	Success rate	Redo rate	LOE
Bladder neck incision ± sphincterotomy	Vainrib *et al.*[89]	97/97	355.4 mo	12 o'clock	Resolution of: AD, elevated detrusor pressures, recurrent UTI, elevated PVR, and hydronephrosis	First procedure: 52.6% Re-do: 50-85.7%	46/97 (47.4%)	3
Sphincterotomy	Adam *et al.*[85]	30/44	30 mo	11 o'clock	PVR <150 cc	First procedure: 56.8% Re-do: 76.9%	13/44 (29.5%), 9 with alternative bladder management	3
Sphincterotomy	Pan *et al.*[90]	84/84	6.35 yr (range: 1–20)	12 o'clock	Absence of recurrent UTI/ sepsis, no DSD on VUD, no hydronephrosis, and eradication of involuntary detrusor contractions	First procedure: 32.1% Re-do: 43.3%	30/84 (35.7%), 27 with alternative bladder management	3
Sphincterotomy	Pannek *et al.*[86]	62/62	12.3 mo (range: 3.3–26.8)	12 o'clock	DLPP <40 cm H_2O or PVR <100 cc	First procedure: 85.4% Re-do: 100%	9/62 (14.5%), 13 with alternative bladder management	3
Sphincterotomy	Perkash[92]	46/46	5.4 yr (range: 1–12)	Laser	Resolution of AD	91.3%	2/46 (4.3%)	3
Sphincterotomy	Chancellor *et al.*[81]	26/26	24 mo	Not specified	Resolution of: AD, elevated PVR, hydronephrosis and VR reflux, and micturition discomfort	69.2%	2/26 (8%)	2
Sphincterotomy	Rivas *et al.*[104]	22/22	14 mo (range: 3–20)	Laser 12 o'clock	Decrease in voiding pressure, PVR, and hydronephrosis, and improved AD	86.4%	13.6%	2

Abbreviations: AD: autonomic dysreflexia; DSD: detrusor sphincter dyssynergia; LOE: Level of Evidence; mo: months; PVR: postvoid residual; TURP: trans-urethral resection of the prostate; UTI: urinary tract infection; VUD: videourodynamics; yr: years.

Sphincterotomy can also be indicated as adjunctive therapy when patients use Credé and/or Valsalva to empty their bladders, but patients should be informed that the procedure can induce or increase SUI. Before offering this option, surgeons must have assessed that the lower urinary tract is urodynamically safe and that the upper urinary tract is not damaged.[88]

Persistent hydronephrosis or VUR, recurrent UTIs, or autonomic dysreflexia has to be considered as a failure of external sphincterotomy. Patients commonly need repeated sphincterotomies to optimize lower urinary tract management, with success rates ranging from 50% to 85.7%.[89,90] These figures may vary in accordance with the criteria considered for failure and with the experience of the surgeons.

Sphincterotomy is not free of complications, and taking into account the first records, we found re-operation due to hematuria in 12% to 26% of cases, hemorrhage requiring blood transfusion in 5% to 23%, and erectile dysfunction (complete and partial loss of erection) in 2.8% to 64%.[91–97] It has been described that the site of incision can influence the appearance of these complications,[98] and it is accepted that the procedure of choice is the 12 o'clock sphincterotomy, first described by Madersbacher, and O'Flynn.[99,100] The main bulk of the striated sphincter is located anteromedially with a gradual thinning laterally, and also hemorrhage can be minimized when avoiding the lateral walls of the urethra, where there is more vascular supply.[101,102] Besides the conventional trans-urethral electrocautery sphincterotomy, Perkash, and Rivas *et al.* published the first reports using the contact neodymium-doped yttrium aluminium garnet (Nd:YAG) laser with similar results.[103,104]

5.5.2 Urethral stenting

In 1994, Chancellor and colleagues reported in two different studies a prospective comparison of the use of a urethral stent (UroLume®) as an alternative to conventional endoscopic sphincterotomy.[105,106] Functional results with both techniques were similar, and the prosthesis placement showed a shorter operation and admission time, a lower hospitalization cost, and less bleeding than external sphincterotomy. Afterwards, many groups reported their experience with different permanent and temporary stents with good short- and medium-term results, while sphincterotomy was left behind for some years.[107] However, long-term results were not as satisfactory as initially thought, and when followed more than 20 months, nearly all patients required stent removal.[108–111] Gajewski *et al.*, on behalf of the North American UroLume Multicenter Study Group, described the technique of stent removal with minimal trauma (stricture or damage to the external sphincter).[112]

Common complications of urethral stents are device migration, bladder neck obstruction, intravesical stone formation, encrustation, granulation tissue ingrowth, and obstruction.[113,114] Also, an increase in the appearance of AD has been noticed with the use of the stents.[115] The high complication rate led to withdrawal of several devices from the market in some countries.[116] Other groups have reported a similar re-operation rate to the one presented with conventional sphincterotomy, although the number of patients is low.[117]

The greatest advantage of temporary urethral stents lies in the fact that, after stent removal, the patient recovers his previous status. Temporary stents can be used in those patients willing to father children and who are candidates for vibro-ejaculation and sperm collection for an artificial insemination program (with sphincterotomy, patients would have irreversible retrograde ejaculation).[100]

They can also be indicated before sphincterotomy for patients who are not sure about the effect of the procedure on their QOL and for the practitioner who wants to ensure that the patient will get used to the condom catheter. Tamarelle *et al.* reported that ejaculation may be possible with the stent *in situ*.[118]

PubMed was used for the search using the MESH terms "memokath", "diabolo", "urolume", "memotherm", "ultraflex", "spinal cord injury", "medullar trauma", and "urethral stent" in order to identify publications on stenting that were missing in the previous search. In **Table 5-2** we summarize the findings of two papers not included in the last update in 2013, and the papers with Level of Evidence 1 and 2 [**LOE 1** and **2**] included in that report.

Utomo *et al.*[119] performed a systematic Cochrane Review in 2014 studying which can be the best surgical management of functional bladder outlet obstruction in adults with NBD. Patients with SCI were included. The investigators selected 5 of 51 papers analyzing the role of sphincterotomy, implantable urethral stents, urethral balloon dilatation, intraurethral botulinum A toxin (BTX-A) injection, intrathecal baclofen, pudendal nerve block, and suprapubic catheterization. Only one randomized clinical trial by Chancellor *et al.* with 57 patients was included in this review.[106] All participants in this study were men who had traumatic SCI (tSCI) with urodynamic-verified DSD, and the authors compared implantation of the UroLume sphincter stent prosthesis with conventional external sphincterotomy (31 and 26 patients, respectively).

Although a significant decrease in maximum detrusor pressure (P_{detmax}) was shown, there were no statistically significant differences between the sphincterotomy and stent groups. Changes in other urodynamic parameters (bladder capacity and PVR urine volume) were equivalent in both groups. Vesicoureteral reflux resolved after 2 years in both groups. The investigators also reported that results for renal function at 12 and 24 months, and urologic complications related to DSD at 3, 6, 12, and 24 months were inconclusive and consistent with benefit of either procedure. Finally, they concluded that they cannot provide robust evidence in favour of any of the surgical treatment options.

TABLE 5-2 Literature Data on Urethral Stents

Reference	SCI/Total number of patients	Follow-up period of study	Urethral stent, n*	Efficacy, %	Migration, %	Other complications, %	LOE
Polguer *et al.*[116]	18/22	56 mo (range: 24–98)	Memotherm® (11) Ultraflex® (11)	59.1	22.7	86.4	3
van der Merwe *et al.*[113]	28/28	18 mo (range: 1–40)	Memokath® (33)	55	20	12.1	3
Chancellor *et al.*[81]	31	24 mo	UroLume® vs. sphincterotomy	81	9	0	1
Chancellor *et al.*[106]	160	60 mo	UroLume®	84	28	20	2

*n: where indicated refers to the number of patients.
Abbreviations: LOE: Level of Evidence; mo: months.

Conclusions

- Sphincterotomy failure is common, and presents as elevated bladder residual volume, persistent hydronephrosis or VUR, recurrent UTIs, or autonomic dysreflexia. **[LOE 3]**
- Sphincterotomy complications are common and include hemorrhage and erectile dysfunction. **[LOE 3]**
- Temporary urethral stents offer short-term relief of obstruction due to DSD. **[LOE 3]**
- Complications of permanent urethral stents include device migration, bladder neck obstruction, intravesical stone formation, encrustation, granulation tissue ingrowth, and obstruction. **[LOE 3]**

Recommendations

- Surgeons should consider trans-urethral sphincterotomy for treatment of patients with DSD who are unable to perform CIC and are under risk for upper urinary tract damage. **[LOE 2; GOR B]**
- Clinicians should closely monitor patients after sphincterotomy to detect failure or complications of treatment, which are common. **[LOE 2; GOR B]**
- Surgeons should do a sphincterotomy at 11, 12, or 1 o'clock from the level of the verumontanum to the proximal bulbar urethra. **[LOE 3; GOR B]**
- Surgeons may use temporary urethral stents as an alternative to sphincterotomy in select patients with DSD who are unable to perform CIC and are under risk for upper urinary tract damage. **[LOE 3; GOR C]**
- Surgeons should not use permanent stents for management of DSD. **[LOE 3; GOR B]**

5.6 Non-continent Urinary Diversion

5.6.1 Introduction

The mainstay of management of the NBD is CIC, combined with medical management of the hyper-reflexic bladder.[120–125] Where conservative treatment fails to control detrusor leak point pressure (DLPP), bladder compliance, and detrusor overactivity, more invasive surgical options can be considered.

In general, continent methods of urinary reconstruction are preferred to incontinent techniques where there is no method of outlet control, necessitating the need for an external appliance to maintain dryness.

This is reflected in patients with spina bifida, where between 1998 and 2005 (Nationwide Inpatient Sample (NIS) database, USA), 3,403 patients underwent bladder augmentation and just 772 underwent ileal conduit diversion.[126] However, in the same time period, 1,132 patients with SCI underwent augmentation, while 1,909 underwent ileal conduit urinary diversion. Thus, ileal conduit remains a relevant means of urinary diversion, especially in certain patient groups. However, surgery remains a last resort. Ileal conduit is rarely used early after SCI, as evidenced by the fact that just 0.08% of SCI patients underwent ileal conduit urinary diversion by the time of discharge from rehabilitation.[127]

The indications for incontinent diversion include the following:

- Compromised renal function (serum creatinine >150–200 µmol/L)
- Hepatic dysfunction
- Compromised intestinal function
- Deficient intrinsic sphincter
- Impaired cognitive ability
- Inability or unwillingness to perform CIC
- Lack of a reliable caregiver
- Patient preference
- Failure of continent diversion
- Requirement for BNC
- Intractable lower urinary tract obstruction
- Urethro-cutaneous fistula

It should be remembered that patients with NBD also have high rates of bowel dysfunction.[128] This is moderate in 24.8% and severe in 35.2% of patients, and it is worse in patients with spinal dysraphism compared with other causes of NBD such as multiple sclerosis (MS). The risk of bowel dysfunction will influence the type of urinary diversion performed, as less bowel is required for incontinent diversion.

Consistent with the above are the findings reported by Somani *et al.*,[129] who evaluated bowel symptoms in patients undergoing transposition of intestinal segments into the urinary tract. The investigators showed that such patients have high rates of bowel dysfunction postoperatively, which restrict everyday activities such that patients undergoing bladder augmentation for NBD had fecal incontinence (FI) rates of 56%. In contrast, in patients undergoing ileal conduit urinary diversion following cystectomy for cancer, FI was seen in just 17% of cases. Given these findings, patients need to be counselled appropriately when surgeons are discussing options for urinary diversion or reconstruction.

Despite the above, there is no good evidence that precautionary measures, such as nasogastric tube drainage, are required after surgery for NBD,[130] and enhanced recovery protocols may be applied in the immediate postoperative period, such as those applied in cystectomy for bladder cancer.

5.6.2 Ileal conduit

The ileal conduit is the most familiar and most common form of incontinent urinary diversion used for the management of NBD.

5.6.2.1 Contemporary outcomes

Early reports on the procedure showed high complication rates, especially in children with longer follow-up. These complications related to renal deterioration, and so the use of the procedure was abandoned, especially as simpler techniques of bladder management, such as CIC, were developed.[131] However, many of these patients had significant renal deterioration preoperatively and further deterioration judged radiologically, and may have been destined to develop progressive renal failure regardless of management.[132]

Table 5-3 shows outcomes in a contemporary series of patients with NBD (mostly) managed by ileal conduit urinary diversion with or without concomitant cystectomy.[133–143]

TABLE 5-3 Ileal Conduit Urinary Diversion in NBD

Reference	Number	Age, yr	Follow-up, mo	Re-intervention	Upper tract deterioration	Stomal problems or revision	Stone disease	Ureterointestinal stricture	Parastomal hernia	Pyocystis	Secondary cystectomy	LOE
Singh *et al.*[133]	93 (NBD: 37)	50	60	25	28/83* 1/4†	4	ns	1	10	48/93	8	3
Kato *et al.*[135]	16	45.6	104	ns	0	ns	5	ns	ns	8/13	2/13	3
Chartier-Kastler *et al.*[134]	33	40.6	48	4	0	0	1	0	0	4/19	3/19	3
Madersbacher *et al.*[136]	131 (NBD: 24)	62	98	ns	35	8	12	13	18	n/a	n/a	3
Guillotreau *et al.*[137]	48	50.6	≥6	ns	ns	ns	ns	ns	ns	n/a	n/a	3
Legrand *et al.*[138]	53	51	73	11	0	1	4	6	1	2/4	2/4	3
Guillotreau *et al.*[139]	44	53.4	44.5	ns	0	0	0	6	ns	n/a	n/a	3
Abdelhalim *et al.*[140]	29‡ (NBD: 21)	10	91	6	13	1	3	ns	ns	ns	ns	3
Schultz *et al.*[141]	52 (NBD: 38)	51	12	2	2	0	ns	1	ns	ns	ns	2

* Of those with normal UT preoperative.
† Of those with hydronephrosis preoperative.
‡ 16 with CKD ≥stage 3.
Abbreviations: CKD: chronic kidney disease; Lap: laparoscopic; mo: months; n/a: not applicable; NBD: neurogenic bladder disease; ns: not stated; yr: years.

Reference	Number	Age, yr	Follow-up, mo	Re-intervention	Upper tract deterioration	Stomal problems or revision	Stone disease	Uretero-intestinal stricture	Parastomal hernia	Pyocystis	Secondary cystectomy	LOE
Kose *et al.*[142]	75 (NBD: 37)	56	64	17/37	ns	10	ns	6	12	9/53	9/53	3
Deboudt *et al.*[143]	Open: 11	48	30.6	1	ns	ns				n/a	n/a	
	Lap: 14	51.9	48.6	4	ns	ns	6	4	2	n/a	n/a	3
	Robotic: 40	58.6	21.9	2	ns	ns				n/a	n/a	

* Of those with normal UT preoperative.
† Of those with hydronephrosis preoperative.
‡ 16 with CKD ≥stage 3.
Abbreviations: CKD: chronic kidney disease; Lap: laparoscopic; mo: months; n/a: not applicable; NBD: neurogenic bladder disease; ns: not stated; yr: years.

Upper tract deterioration (as judged radiologically or by estimated glomerular filtration rate [eGFR]) is seen in 0% to 33% of adult patients and 45% of children with an ileal conduit. In general, renal dysfunction is seen to increase with increasing length of follow-up, although the studies with the longest follow-up—Kato *et al.*[135] follow-up of 8.7 years and Madersbacher *et al.*[136] follow-up of 8.2 years—show different rates of deterioration (0% and 27%, respectively), which most likely reflects the underlying populations studied, the timing of surgery, and upper tract management both pre- and postoperatively.

Overall, pyocystis was seen in 71 of 182 patients (39%) with a secondary cystectomy rate of 15% (n=28). Stoma problems requiring intervention were seen in 1 of 29 children (3.4%) and 23 of 467 adults (5%), which compares very favourably with other forms of continent diversion (see section 5.4 of this chapter).

5.6.2.2 Quality of life studies

Quality of life studies in adults[136,139] are generally favourable. Guillotreau *et al.*[137] using the SF36v2 and Qualiveen questionnaires showed a significant reduction in limitation scores and the specific impact of urinary problems (SIUP) index. At the same time, there was no adverse effect in SF36v2 scores. Likewise, Chartier-Kastler *et al.*[134] showed overall patient satisfaction to be 9.1 of 10 on a visual analogue scale, and no patient regretted his or her choice of surgery.

In children, the situation is different. Abdelhalim *et al.*[140] using the Mansoura QOL questionnaire show that 17 patients (85%) reported poor QOL and 19 (95%) expressed a desire to undergo another method of diversion.

Schultz *et al.*[141] examined QOL before and 6 and 12 months after diversion in 26 patients managed with either an ileal conduit (n=26) or continent diversion (n=26) in a prospective, non-randomized fashion. The questionnaires used were the WHO Quality of Life-BREF—(WHOQOL-BREF, 26 items, is briefer than the entire WHO-QOL [World Health Organization Quality of Life])—and a urinary problem-specific QOL instrument. Patients improved in all domains of the WHOQOL-BREF, except for social functioning. All dimensions of the urinary problem-specific QOL questionnaire were also improved. Notably, patients showed clinically significant improvement in future perspective. Thus, both general QOL and disease-specific QOL scores were improved. There was no significant difference seen between patients undergoing ileal conduit or continent diversion.

Such findings have been a disappointment to many urologists who feel intuitively that continent diversion (orthotopic or continent cutaneous) should provide a better QOL than conduit diversion. This reflects the fact that what surgeons feel to be important considerations for their patients with NBD and what patients feel to be important to themselves are often not one and the same. Indeed, there is growing support for the view that the existential and dynamic experiences that would seem to fall under the rubric of QOL are unsuited to measurement, and the relatively small role that health status appears to play in QOL makes it a problematic concept for physicians.[144]

5.6.2.3 Technical aspects

The operation of ileal conduit urinary diversion is well described, but principles relating to which intestinal segments to use in conduits, whether ureteral anastomoses should be refluxing, and if continent options should be preferred to incontinent ones are still debated.

A Cochrane Review[145] showed (with the limited data available) that in benign disease, there was no evidence to suggest that bladder reconstruction was better than conduit diversion. Likewise, there was no reported difference between ileal and colonic conduits with respect to upper UTI and uretero-intestinal anastomotic strictures. Similar results were seen with continent versus conduit diversion and, importantly, there was no difference in the rate of upper tract deterioration, and in conduits this was not related to the type of anastomosis performed (refluxing vs. anti-refluxing).

In performing an ileal conduit urinary diversion, the following points should be borne in mind:

- The ileal segment should be as short as is appropriate for the patient in question (8–10 cm where possible).
- In the obese patient with a short mesentery, the stoma may be made flush with the skin, or a loop urostomy used instead.
- The distal (rostral) mesenteric incision should be long while the proximal (oral) mesenteric incision can be shorter. Dividing the mesenteric vessels with a Ligasure Impact™ (Covidien, a division of Medtronic; Minneapolis, USA) instrument saves time.
- To reduce the incidence of para-stomal hernia, the conduit should be anchored to the rectus sheath and brought through the rectus muscle. Alternatively, consideration can be given to the use of a sublay mesh,[146] or to positioning the stoma above the arcuate line of Douglas at the lateral edge of the rectus sheath.[147]
- Technically it has been found helpful to form the ileal spout within the abdomen prior to bringing the spout through the abdominal wall to the skin.
- An adequate trephination should be made in the abdominal wall so as not to compromise blood supply to the distal end of the ileal segment.
- Abdominal wall closure should be with non-absorbable sutures, especially in areas where the skin has reduced sensation. The skin should be closed with interrupted sutures or surgical staples.
- Spinal anesthesia and opiate use should be minimized to allow for a quicker return of bowel function, which may already be impaired in patients with NBD.
- The stoma should be put at a site previously marked as suitable for the patient by a trained stoma care nurse.

Laparoscopic and robotic approaches to surgery have been described, but any advantages over open surgery with respect to time, costs, and length of hospital stay remain to be determined.[148] Deboudt *et al.*[143] have compared the morbidity and mortality of cystectomy and ileal conduit urinary diversion for neurogenic lower urinary tract dysfunction according to the surgical approach—open, laparoscopic, or robotic. They show that a robotic approach to surgery in this patient group is safe and feasible, with complication rates that compare well with the open and laparoscopic techniques.

5.6.2.4 Should the bladder be removed at the time of diversion?

The fate of the residual bladder in patients undergoing conduit diversion without cystectomy has been debated, with some surgeons suggesting that the bladder should always be removed and others stating that this is not always necessary.[149]

Tables 5-3 and **5-4** present the incidence of problems with pyocystis and malignant change within the retained bladder. **Table 5-4**[149–151] shows the incidence of pyocystis to be 13% (12 of 93), with carcinoma seen in 2 patients (<2%). Combining these results with those in **Table 5-3** gives an overall incidence for pyocystis of 30% (83 of 275 patients) and a secondary cystectomy rate of 19% (35 of 183 patients). These figures suggest that the decision as to whether to perform cystectomy at the time of diversion is a nuanced one. This is particularly important, as cystoprostatectomy in men will have a significant negative effect on sexual function, and the same is likely for cystectomy in women even when the vagina is preserved. These are important considerations for some patients.

In general, it is recommended that a discussion be had with the patient so that a considered decision concerning cystectomy can be made. Where there is no evidence of bladder outflow obstruction or cancer on cystoscopy or cytology and there is a desire to preserve sexual function, then the bladder need not be removed, as long as the bladder has unobstructed urethral drainage.

Where cystectomy is desirable, then it can be achieved simply and with minimal blood loss as described by Rowley *et al.*[152] The technique involves bi-valving the bladder in a sagittal plane, amputating the lateral pedicles, and removing the urothelium on the residual trigone. The prostate may be left *in situ*.

TABLE 5-4 Follow-up of the Retained Bladder in NBD

Reference	Number	Age, yr	Follow-up, mo	NBD	Cancer	Pyocystis	Secondary cystectomy	LOE
Fazili *et al.*[150]	24	59	48	8	0	8	6	3
von Rundstedt *et al.*[151]	9	40	120	ns	2	2	1	3
Lawrence *et al.*[149]	60	54	45	28	0	2	0	3

Abbreviations: mo: months; NBD: neurogenic bladder disease; ns: not stated; yr: years.

5.6.2.5 Summary

The ileal conduit is a tried and tested means of urinary diversion in adult patients with NBD. It has an acceptable rate of complications and is associated with significant improvements in QOL. In children, concerns remain about long-term effects on renal function, and while conduit diversion may be considered in this population, alternative methods of bladder management may be preferable.

5.7 Ileo-vesicostomy

Ileo-vesicostomy involves anastomosis of the rostral end of an isolated segment of ileum to the bladder while the caudal end is matured to the abdominal wall as an incontinent stoma.

5.7.1 Contemporary outcomes

Contemporary case series of ileo-vesicostomy in patients with NBD show good results, with mostly excellent protection of upper tract function (**Table 5-5**).

The results are good, with mostly excellent protection of upper tract function. Stomal stenosis was relatively uncommon (0%–38%) as was stone disease (0%–50%). However, Burgess *et al.*[158] set a note of caution because their long-term follow-up of 15 patients over 11 years found significant rates of stomal stenosis (73%; 11 patients), upper tract deterioration (47%; 7 patients), and conversion to ileal conduit urinary diversion (27%; 4 patients). These results were in a population with both NBD and morbid obesity. The latter is a problem that can affect many patients transitioning from childhood and adolescence, especially patients with limited mobility and wheelchair dependence. In this setting, obesity predisposes to stoma stenosis and mechanical loop obstruction with subsequent upper tract deterioration.[160]

TABLE 5-5 Ileo-vesicostomy in NBD

Reference	Number	Age, yr	Follow-up, mo	Re-intervention	Upper tract deterioration	Continent	Stomal problems or revision	Stone disease	Conversion to a different diversion
Gauthier and Winters[153]	7	33.7	37.4	1	0	6	1	1	ns
Tan *et al.*[154]	50 (NBD: 45)	45	26.3	27	0	36	19	1	ns
Hellenthal *et al.*[155]	12	51	66	6	0	11	1	3	ns
Zimmerman and Santucci[156]	8 (NBD: 7)	33	25.8	2/6	ns	ns	ns	ns	ns
Burgess *et al.*[158]	15	ns	132	8	7	ns	1	11	4 (converted to ileal conduit)

Abbreviations: mo: months; NBD: neurogenic bladder disease; ns: not stated; yr: years.

continued on **page 231**

TABLE 5-5 Ileo-vesicostomy in NBD, *Cont'd*

Reference	Number	Age, yr	Follow-up, mo	Re-intervention	Upper tract deterioration	Continent	Stomal problems or revision	Stone disease	Conversion to a different diversion
Vanni and Stoffel[157]	7 (Open)	42	13	1	0	3	1	ns	ns
	8 (Robotic)	53	15	1	0	6	1	ns	ns
Ching *et al.*[159]	9	10.3	11.5	1	0	9	1	0	ns

Abbreviations: mo: months; NBD: neurogenic bladder disease; ns: not stated; yr: years.

5.7.2 Quality of life studies

Quality of life following ileo-vesicostomy has been addressed by Gauthier and Winters.[153] At 6-month follow-up, patient satisfaction was assessed, and 6 of 7 patients (86%) regarded their QOL as improved. However, there were no reports using formal, validated QOL questionnaires.

5.7.3 Technical aspects

Minimally invasive surgery is now used for many urological operations, and ileo-vesicostomy is no exception. Laparoscopic approaches performed with or without an extra-corporeal component have both been described by Hsu *et al.*[161] and Abrahams *et al.*,[162] respectively. Robotic assisted laparoscopy has been reported by Vanni and Stoffel,[157] with associated outcomes in a follow-up of 15 months (see **Table 5-5**).

Where ISD exists prior to surgery, this needs to be managed by urethral or bladder neck closure, a pubo-vaginal sling, or AUS implantation.[131,156,163] Zimmerman and Santucci[156] do not normally perform urethral or bladder neck closure unless there is objective evidence that this is required, e.g. videourodynamics showing a poor proximal urethral function and/or a DLPP <10 cm H_2O.[164]

Initial poor outcomes with ileo-vesicostomy were associated with high outlet resistance due to the end-on positioning of the ileal segment and an inadequate vesicostomy.[163]

Current surgical concepts[165] are based on:

- A wide-mouthed vesical anastomosis
- Avoidance of limb redundancy
- An adequate fascial window
- A stoma conducive to appliance fit

Advantages over ileal conduit urinary diversion include:

- Avoidance of uretero-intestinal stricture
- No risk for pyocystis if the bladder is retained
- No disturbance of the native upper tract anti-reflux mechanism
- Maintenance of sexual function

5.7.4 Summary

Ileo-vesicostomy remains an option for the management of patients with NBD and complex urinary issues especially where

- Patients are unable or unwilling to use CIC
- There is intractable lower urinary tract obstruction
- The lower urinary tract is hostile (stricture, fistula, small capacity, bladder fibrosis)
- Alternatives such as ileal conduit urinary diversion are not feasible

The reported complication rates associated with ileo-vesicostomy are not dissimilar to those of other techniques of urinary diversion, and thus ileo-vesicostomy remains a useful weapon in the urologists' armamentarium.

5.8 Cutaneous Vesicostomy

Cutaneous vesicostomy is a procedure commonly performed in infants but rarely in adults. The bladder dome is opened broadly and sutured directly to the skin as an incontinent stoma. Vesicostomy is a safe, simple, and effective way of managing upper tract deterioration in infants with posterior urethral valves or spina bifida, but it is not an effective management method in older children, or in adults with SCI.

5.9 Cutaneous Ureterostomy

Cutaneous ureterostomy involves directly anastomosing the ureters to the skin as a non-continent form of diversion. Stenosis rates are high; as such, this procedure is rarely used in the modern era. Its use is limited to a temporary form of diversion in pediatric patients with megaureter or as a permanent form of diversion in adults with terminal cancer. It is rarely indicated for permanent diversion in the SCI patient.

Conclusion

- Quality of life is similar with ileal conduit urinary diversion and continent diversion. **[LOE 3]**

Recommendations

- Surgeons should offer non-continent urinary diversion to SCI patients when other more conservative methods of bladder management have failed or are not an option. **[GOR B]**

- Surgeons may leave the bladder *in situ* during ileal conduit urinary diversion if there is unobstructed urethral drainage and no cancer, and if the patient prefers to leave the bladder *in situ* for reasons such as preserving sexual function. **[GOR C]**

- Surgeons may perform a supratrigonal simple cystectomy to minimize the morbidity of cystectomy at the time of urinary diversion. **[GOR C]**

- Surgeons should avoid ileal conduit in children due to the risk for upper tract deterioration over time. **[GOR B]**

- Surgeons may use ileo-vesicostomy in SCI patients when other forms of urinary diversion are not feasible. **[GOR C]**

- Surgeons should avoid vesicostomy and cutaneous ureterostomy in SCI patients. **[GOR B]**

5.10 Conclusions

The main goals of management of NBD are protection of the upper tracts, with low-pressure continent drainage where possible. Still, we must accept that continence is not a realistic option for some patients. In this setting, non-continent diversion techniques need to be considered. Which technique is chosen will depend on a myriad factors, not least of which are the preferences of the patient or their caregivers.

5.11 Continent Urinary Diversion

5.11.1 Methods

We conducted an electronic search of PubMed, BIOSIS, EMBASE, and Cochrane Reviews from articles published from January 1980 to April 2016 with an emphasis on continent urinary diversion. After abstracts were reviewed and overlapping articles were excluded, 87 full-text articles were thoroughly investigated. Finally, 78 articles are cited in this chapter. In addition, the chapter on "Neurogenic urinary and faecal incontinence" in Incontinence 5th. edition[47] was referenced.

5.11.2 Indications

5.11.2.1 AC indications

Indications for AC are unmanageable detrusor overactivity and/or low bladder compliance, both of which lead to the development or progression of upper urinary tract (UUT) deterioration and/or intractable urinary incontinence under maximum conservative treatment or minimally invasive treatment such as botulinum neurotoxin type A intra-detrusor injection therapy (BoNTA).[47] In the cases with severe ISD and/or devastated urethra, bladder outlet procedures as additional procedures become an option; however, precise indications for bladder outlet procedures at AC remain to be determined.[166]

5.11.2.2 Continent catheterizable channel indications

Some patients with spinal cord injury have difficulty or are unable to perform ISC through a native urethra; this is due to severe upper-limb disability in tetraplegic patients, difficulty in transferring, undressing, or positioning, spinal deformity, obesity, or refractory perineal ulcers.[47,167] In such cases, creation of an abdominal stoma using a continent catheterizable channel (CCC), with or without AC depending on the bladder function, should be considered. A CCC is particularly helpful in women with SCI because their ability to access their urethra is more difficult than in men.[168–171] Moreover, when urethral dysfunction and/or destruction is so severe that ordinary anti-incontinence surgeries, for example, bladder neck (BN) sling, BN reconstruction, or implantation of an AUS would not achieve acceptable continence, a concomitant BN closure with a CCC becomes an option. In patients with refractory perineal ulcers, the possibility of an unrecognized urinary fistula should be thoroughly investigated, and a continent urinary reservoir (CUR), that is, a supravesical diversion, should be considered if the lower urinary tract is not suitable for urinary reconstruction.[172] Cooperation between urologic surgeons and plastic surgeons is important in such cases.[173]

5.11.2.3 CUR Indications

Continent urinary reservoir is indicated when the native bladder and urethra are severely devastated functionally or anatomically, especially if BNC and ureteral re-implantation are not avoidable.[47,167,171]

5.11.3 General comments on preoperative selection for continent diversion

A multidisciplinary team approach is of paramount importance for selecting eligible patients and deciding appropriate surgical procedures—that is, evaluations by urologists of the function and anatomy of the upper and lower urinary tract, as well as evaluations by occupational and physical therapists of upper-limb dexterity and the patient's ability to transfer, undress, or position himself to perform ISC.[167,169,174–180] It should be confirmed that after SCI, the patient demonstrates excellent compliance to medical care in general.[179]

When a CCC is indicated, an appropriate stoma site should be carefully selected by the patient and the multidisciplinary team, including an enterostomal therapy nurse.[170,179] The stoma should generally be located in the umbilicus; this is both cosmetically acceptable and facilitates catheterization by making the stoma easy to find. In some tetraplegic patients, surgery for upper-limb reanimation (ULR, tendon transfers, tenodesis, and arthrodesis) and specific rehabilitation procedures (tasked motor training, biofeedback, and new muscle-function integration) are needed to manipulate the catheter.[181] Bernuz *et al.*[181] reported that 15 of 20 patients with C5 to C7 injury (75%) could perform ISC after ULR and rehabilitation. The positive predictive value of key-grip strength ≥0.5 kg for enabling ISC was 86% in that study. In addition, most of the patients who were enabled to perform ISC had undergone bilateral ULR.

If planned intermittent catheterization is dependent on caregivers, the reliability of caregivers and the personal relationships between patients and caregivers should be thoroughly assessed.[179]

5.11.4 Contraindications

An inability to perform intermittent catheterization is usually considered as an absolute contraindication for AC, CCC, and CUR surgeries.[174,182–184] In the past, intermittent catheterization after AC was considered to be a complication, but now intermittent catheterization has become a standard method for lower urinary tract management after AC. The presence of inflammatory bowel diseases is another absolute contraindication. Renal insufficiency is a relative contraindication for urinary tract reconstruction using an intestinal segment except the stomach.[185,186] An upper limit of serum creatinine of approximately 2.0 mg/dL and a lower limit of creatinine clearance of approximately 50 mL/min have been proposed, although the definitive cutoff values remain to be determined.[187]

5.12 Surgical Technique and Outcomes

5.12.1 Augmentation cystoplasty

5.12.1.1 Basic procedure

The bladder is augmented by a detubularized intestinal segment. The goal of AC is to produce a continent, low-pressure, high-capacity reservoir.[188] The native bladder is incised like a clam shell, and the detubularized augment sewn to it. In the cases of a severely fibrotic bladder, some surgeons will resect the thick-walled bladder by a supra- or subtrigonal cystectomy,[170, 189-191] but the benefit is unclear. If a supra- or subtrigonal cystectomy is performed, a longer bowel segment is necessary to augment the bladder.[170, 189-191]

5.12.1.2 Less invasive AC with or without a continent catheterizable channel

Although AC is usually performed as open surgery, several reports of less-invasive AC techniques, namely laparoscopic or robot-assisted laparoscopic AC, have recently been published. It should be noted that evidence to support these procedures is scarce, especially in SCI patients.

Gill *et al.* reported that laparoscopic AC, in which bowel re-anastomosis was performed by exteriorizing the bowel loop outside the abdomen through a 2-cm extension of the umbilical port site, was feasible in 3 patients including 1 with a cervical cord injury.[192] Meng *et al.* first reported pure laparoscopic AC on a woman with cervical cord injury, and concluded that pure laparoscopic AC might become an important tool in the future, although this procedure is technically challenging and requires practice, patience, and longer operative times at present.[193] Rackley and Abdelmalak reported the outcomes of 12 NBD patients who underwent laparoscopic ileal AC (n=2), sigmoid AC (n=2), colonic AC (n=1), and cecal AC with a catheterizable channel (n=7).[194] They concluded that laparoscopic AC was technically feasible and successfully emulated the established principles of open AC while minimizing operative morbidity. Chung *et al.* investigated outcomes of laparoscopic reconstructive surgery in 31 patients including 1 SCI patient (mean age: 14 years) and concluded that at almost 3 years of mean follow-up, laparoscopic-assisted reconstructive surgery offered functional outcomes at least equivalent to conventional open surgery in complicated cases, with excellent cosmetics.[195] El-Feel *et al.* performed laparoscopic AC on 23 patients including 5 SCI patients and showed that mean maximum cystometric capacity (MCC) increased from 90 mL to 700 mL at 12 months and mean P_{detmax} decreased from 93 cm H_2O to 14 cm H_2O at 12 months during a mean follow-up of 39 months.[196] All patients became continent, and VUR (n=3) was improved or resolved. Reported complications were minor bowel disturbances (n=6), bladder stones (n=1), and perforation of the augmented bladder (n=1).

Laparoscopic AC is a safe and technically feasible procedure, with a urodynamic outcome that is comparable to that reported for open augmentation AC. However, the increased costs have been a significant disadvantage.[194]

Cohen *et al.* described a detailed procedure for performing robot-assisted laparoscopic AC and asserted its feasibility.[197] Another retrospective study on robot-assisted laparoscopic AC and Mitrofanoff appendicovesicostomy demonstrated safety and efficacy, with outcomes and complication rates that compare favourably with those of open techniques.[198] Flum *et al.* first performed completely intra-corporeal robot-assisted laparoscopic AC with (n=7) or without (n=15) a continent catheterizable channel (median age: 30 years, SCI: 17).[199] During a mean follow-up of 38.9 months, mean MCC increased from 355 mL to 488 mL and mean P_{detmax} decreased from 71 cm H_2O to 37 cm H_2O. There were 5 minor complications (Clavien ≤2) and 4 major complications (Clavien ≥3), including 1 bladder perforation.

Although the benefits of robot-assisted laparoscopic AC include decreased incisional pain, potentially decreased length of hospital stay, improved cosmetics, and decreased bowel and wound complications, these benefits must be weighed against the steep learning curve, increased cost, and extended operative time.[197,199]

5.12.1.3 Intraperitoneal AC vs. extraperitoneal AC

In one non-randomized series, Reyblat *et al.* compared extraperitoneal AC (n=49) with intraperitoneal AC (n=24) (mean age: 34 years; mean follow-up: 2.5 years).[200] During extraperitoneal AC through a small peritoneal incision of approximately 4 cm to 6 cm, an intestinal segment was isolated for AC and intestinal continuity was reconstructed. A peritoneal incision was loosely approximated around the mesentery of the isolated segment. Patients treated with extraperitoneal AC had a significantly shorter operative time (3.9 vs. 5.6 hours), shorter hospital stay (8.0 vs. 10.5 days), and earlier recovery of bowel function (3.5 vs. 4.9 days). There were no significant differences in continence rate (85% vs. 65%) and complication rate (37 vs. 42%). In conclusion, extraperitoneal AC provides an equally effective method of AC as the standard technique with earlier postoperative recovery.

5.12.1.4 Intestinal segments used for AC

Table 5-6 shows the advantages and disadvantages of each intestinal segment used for AC.[47,186,201] Of the intestinal segments, the ileum has been the most frequently used for AC because of the ease and convenience of using it, its proximity to the bladder, and its tolerable or manageable electrolyte imbalance profile.[47,188] The next most frequently selected intestinal segment is the colon, especially the sigmoid colon.[47] To create a low pressure–large capacity reservoir, the isolated segment is detubularized and then reconfigured to dampen the peristalsis. An ileocecal segment is selected for AC in the same way that an Indiana pouch is selected for a planned continent catheterizable channel.[185]

In patients with renal insufficiency or short bowel syndrome who require AC, the stomach is an option for the isolated segment.[185,186] As the following text focuses on outcomes with ileal or colonic AC, we review outcomes with stomach AC here. The stomach does not result in metabolic acidosis, secretes less mucus than the ileum and colon, and is less prone to UTI due to its acid environment.[201]

Chancellor *et al.* reported outcomes of gastrocystoplasty in 2 SCI patients with renal insufficiency.[202] Capacity increased from 98 mL to 540 mL, end-filling detrusor pressure (P_{detmax}) decreased from 32.5 cm H_2O to 19 cm H_2O, and continence was regained in both patients, while significant complications including renal deterioration did not occur.

TABLE 5-6 Advantages and Disadvantages of Intestinal Segments for Augmentation Cystoplasty

Bowel segment	Advantages	Disadvantages
Ileum	Abundant availability Able to reach the pelvis without tension Well vascularized	Metabolic acidosis Fat and VB12 malabsorption if distal 20 cm not spared
Sigmoid	Thick wall, large lumen guarantees adequate bladder capacity Abundant mesentery ensures good manoeuvrability Already in pelvis and easy to manoeuvre onto the bladder Teniae coli can be useful for ureteral reimplantation Decreased risk for bowel obstruction	Higher risk for UTI due to colonic bacteria Higher theoretical risk for malignancy Increased mucus production
Ileocecum	Constant blood supply Cecal tenia can be used for non-refluxing ureteral anastomosis Can be used as a continent stoma	Fat and VB12 malabsorption Intractable diarrhea Increased mucus production
Stomach	May be used in patients with chronic renal impairment and patients with short bowel Decreased mucus production, therefore lesser incidence of UTI Reduced electrolyte absorption Acid secretion beneficial in acidosis	Hematuria-dysuria syndrome Metabolic alkalosis Risk for gastric segment perforation Higher risk for malignancy Sequelae of partial gastrectomy: Quick satiety, poor feeding, dumping syndrome, exacerbation of preexisting peptic ulcer or gastroesophageal reflux disease

Abbreviations: UTI: urinary tract infection; VB12: vitamin B12.

Abdel-Azim *et al.* investigated the results of gastrocystoplasty in 30 patients including 4 SCI patients.[203] During a mean follow-up of 2.9 years, urodynamic parameters improved (MCC: 116 mL to 375 mL, P_{detmax}: 71 cm H_2O to 37 cm H_2O, vesical compliance [V_{comp}]: 1.5 mL/cm H_2O to 10.2 mL/cm H_2O), and the continence rate was 96.2% in AC alone and 100% in AC with AUS. Renal deterioration did not occur in 96.7% of the patients. Complications were transient hematuria and dysuria (*n*=5), significant mucus production (*n*=3), and VUR (*n*=2).

When using stomach tissue for AC, it is necessary to keep in mind that complications including hematuria-dysuria syndrome, metabolic alkalosis, and malnutrition do occur, and that the risk of developing a malignant tumour would be much higher: 14 to 15 times with stomach versus 7 to 8 times with ileum and colon.[185,201]

5.12.1.5 Management of the ureter during AC

Whether patients with VUR should be treated with ureteral re-implantation at AC has been investigated mostly in pediatric patients with NBD resulting from spina bifida. Vesicoureteral reflux arises from high intravesical pressure in NBD patients, so it is conceivable that VUR would spontaneously disappear or improve when low intravesical pressure is attained by AC.[204] Actually, VUR was resolved in approximately 75% to 80% of patients after AC alone.[175,205] Ureteric re-implantation into the hypertrophied bladder is so difficult, that it puts the upper urinary tract at risk for obstruction or residual VUR.[205]

Simforoosh *et al.* examined the effects of AC alone on VUR in 130 patients including 102 SCI patients (mean age: 21.6 years; mean follow-up: 44.5 months), and found that VUR was resolved in 111 patients (85.4%) and improved in 14 patients (10.8%).[206] All grade I to III VUR, 87.5% of grade IV VUR, and 61.5% of grade V VUR disappeared, and hydronephrosis improved in 97.7% of the renal units. Postoperatively, febrile UTI occurred in only 8 patients whose VUR was resolved.

Zhang *et al.* compared AC alone and AC concomitant with ureteral re-implantation in 31 patients including 4 SCI patients (mean age: 19.6 years; mean follow-up: 57 months).[207] The indication for ureteral re-implantation was a VUR with greater than 20 cm H_2O of intravesical pressure that was seen on the preoperative videourodynamic study. VUR remained in 3 of 16 patients undergoing sigmoid AC alone (18.8%; preoperative intravesical pressure at VUR: 35.8 cm H_2O) and 8 of 15 patients undergoing sigmoid AC with ureteral re-implantation (53.3%; preoperative intravesical pressure at VUR: 18.7 cm H_2O). The grade of all residual VUR was I or II, and hydronephrosis (HN) and renal function were improved. Recurrent UTI due to residual VUR occurred in only 4 patients. The investigators concluded that a preoperative intravesical pressure at VUR of 20 cm H_2O was not an effective cutoff point for determining whether ureteral re-implantation should be performed simultaneously during AC. Augmentation appears to be more important than re-implantation for protecting kidneys from damage resulting from febrile UTI after AC. Therefore, it is suggested that the addition of ureteral re-implantation to AC is not always needed for improving symptomatic UTI and preserving renal function.

5.12.1.6 **Efficacy of AC**

Table 5-7 shows the efficacy of ileal AC and colonic AC from a major case series. In the following summary, the studies in which all patients underwent the creation of an abdominal stoma were excluded. There have been few studies of AC specific to SCI, and most of the studies comprised a heterogeneous population of patients with NBD, including SCI patients.

According to these reports (mean follow-up of 10.1 months to 8.0 years[166,208]), urodynamic parameters significantly improved; that is, MCC and V_{comp} significantly increased, and P_{detend} and P_{detmax} significantly decreased with AC. [175–178,182,183,187,189,205,209-214] Nearly all the augmented bladders safely accommodated a sufficient urine volume at P_{det} less than 30 cm H_2O to 40 cm H_2O.[182,191,208] The incidence of NDO decreased from 55%–59% to 10%–21%,[170,190] and the incidence of low bladder compliance decreased from 17%–88% to 0%–24%.[166,170,191] Upper urinary tract function was preserved or improved in almost all patients.[174,177,182,189,191,205,209-212,215,216] The continence rate ranged from 57% to 100%.[185,205,210] The incidence of symptomatic UTI was reduced in 71% to 88% of patients[178,205,208] and in one report 67% of patients did not have symptomatic UTI anymore.[177] Autonomic dysreflexia improved or disappeared in 67% to 100% of patients.[182,183,208,211]

In the interpretation of the results, it should be noted that concomitant bladder outlet procedures (BN sling in up to 100%,[183] BN tapering in up to 41%,[216] BN closure in up to 11%,[175] and AUS in up to 57%[174]) were performed in many studies and that a CCC was created in up to 49% of the patients.[217] Moreover, an important point to emphasize is the fact that these favourable results were produced by specialized centres in which the multidisciplinary team selected patients very carefully and expert urologists performed AC for those complicated patients.

TABLE 5-7 Surgical Procedures and Efficacy for Ileocystoplasty and Colocystoplasty

Reference	n (% SCI)	Age, (mean, years)	M:F	Intestinal segment	Bladder outlet procedure	Abdominal stoma	
Steinberg *et al.*[206]	33 (18%)	25	6:27	AC :28 (Ileocecal)	BN sling: 24%	BN closure + abdominal stoma: 33%	
Ishizuka *et al.*[207]	7 (29%)	13-22	6:1	Ileum: 7	BN sling: 29%	0	
Sidi *et al.*[182]	12 (100%)	33.5	11:1	Sigmoid: 11 Cecum: 1	AUS: 25%	0	
Noll and Schreiter[174]	46 (43%)	SCI: 14-65	11:35	AC: 41 (Ileum: 39, Sigmoid: 2) Total replacement: 5 (Ileum)	AUS: 57%	0	
Chao *et al.*[32]	24 (42%)	NR	11:13	AC: 7 (Hemi-Indiana)	BN closure + SPC: 71% BN closure + AC: 29%	Hemi-Indiana: 29%	
Herschorn *et al.*[168]	18 (44%)	37	4:14	Hemi-Kock: 15 Stoma alone: 3	BN sling: 50% BN tapering: 6% BN closure: 17%	100%	
Mast *et al.*[175]	28 (21%)	26	14:14	Ileum: 26 Stomach: 1 (borderline renal function)	BN closure: 11% BN sling: 4% Burch: 4% AUS: 4%	Mitrofanoff: 7% Cystostomy: 4%	
Flood *et al.*[176]	122 (26%)	37	40:82	Ileum: 82 Ileocecal: 36 Sigmoid: 4	BN sling: 13% Burch: 0.8% Urethral closure: 4% Supratrigonal resection: 0.8%	17%	
Watanabe *et al.*[208]	18 (72%)	36.7	0:18	CIC + BN sling alone: 3 Ileocystostomy: 8 Ileocystoplasty: 7	BN sling: 89%	22%	

Abbreviations: AC: augmentation cystoplasty; AD: autonomic dysreflexia; AM: antimuscarinic medication; AUS: artificial urinary sphincter; BN: bladder neck; IC: clean intermittent catheterization; F: female; HN: hydronephrosis; ICIQ: International Consultation on Incontinence Questionnaire; LOE: Level of Evidence; M: male; n: number of patients; MCC: maximum cystometric capacity; NDO: neurogenic detrusor overactivity; NR: not reported; P_{det}: detrusor pressure; P_{detend}: end-filling detrusor pressure; P_{detmax}: maximal detrusor pressure; QOL: quality of life; S-Cre: serum creatinine; SCI: spinal cord injury; SPC: suprapubic catheter; UUT: upper urinary tract; V_{comp}: vesical compliance; VUR: vesicoureteral reflux.

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TABLE 5-7 Surgical Procedures and Efficacy for Ileocystoplasty and Colocystoplasty, *Cont'd*

	Anti-VUR, %	Follow-up (mean, months)	Continence rate, %	UUT: stable/ improve, %	Urodynamic outcomes, mean	AM use, %	QOL	LOE
	0	21	97	100	MCC: 60→440 mL	NR	NR	4
	57	Median: 20	57	100	MCC: 129→200 mL	NR	NR	4
	0	15	100	100	MCC: 562 mL (400%↑) P_{detmax} <30 cm H_2O: 100%	NR	NR	4
	13	NR	91	100	MCC: 620 mL P_{detend}: 18 cm H_2O	NR	Satisfaction: 88%	4
	0	SPC: 21 AC: 23	100	100	NR	0	NR	4
	0	26	94.4	100	MCC: 67%↑ P_{detend}: 78%↓	17	NR	4
	25	31	70	VUR: 86	MCC: 235→511 mL V_{comp}: 7.4→27.1 mL/cm H_2O	NA	NR	4
	6	37	80	96	MCC: 108→438 mL	NR	Excellent: 75% Improved: 20%	4
	0	18	NR	100	NR	NR	9-part questionnaire: Self-esteem: 1→4 Sexual desire: 2→4 Ability to cope with disability: 1→4	4

Abbreviations: AC: augmentation cystoplasty; AD: autonomic dysreflexia; AM: antimuscarinic medication; AUS: artificial urinary sphincter; BN: bladder neck; IC: clean intermittent catheterization; F: female; HN: hydronephrosis; ICIQ: International Consultation on Incontinence Questionnaire; LOE: Level of Evidence; M: male; n: number of patients; MCC: maximum cystometric capacity; NDO: neurogenic detrusor overactivity; NR: not reported; P_{det}: detrusor pressure; P_{detend}: end-filling detrusor pressure; P_{detmax}: maximal detrusor pressure; QOL: quality of life; S-Cre: serum creatinine; SCI: spinal cord injury; SPC: suprapubic catheter; UUT: upper urinary tract; V_{comp}: vesical compliance; VUR: vesicoureteral reflux.

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TABLE 5-7 Surgical Procedures and Efficacy for Ileocystoplasty and Colocystoplasty, *Cont'd*

Reference	n (% SCI)	Age, (mean, years)	M:F	Intestinal segment	Bladder outlet procedure	Abdominal stoma
Fontaine *et al.*[183]	21 (29%)	27	0:21	Ileum: 21	BN sling: 100%	0
Kuo[177]	21 (88%)	36	18:3	Ileum	0	0
Herschorn[210]	59 (31%)	30.6	22:37	Ileum: 49 Ileocecal: 8 Sigmoid: 1 Transverse colon: 1 Hemi-Kock: 21	AUS: 3% Trigonal tuburization: 2% BN tapering: 41% BN sling: 32%	Hemi-Kock: 36%
Kuo[178]	251 (100%)	33.8 at SCI	212:39	Ileocystoplasty: 28 Auto-augmentation: 6 Kock: 7	Periurethral Teflon injection: 1	Kock pouch: 7
Sutton *et al.*[180]	23 (70%)	42.2	15:8	AC: 19 (Hemi-Indiana)	BN closure: 30% BN sling: 13% Collagen injection: 4%	AC + continent stoma; 83% continent stoma alone: 17%
Chartier-Kastler *et al.*[213]	17 (100%)	36.5	11:6	Subtrigonal cystectomy + Hautmann cystoplasty: 15 Clam cystoplasty: 2	AUS: 6% Burch: 6%	0
Van Savage *et al.*[239]	5	8 (50%)	29	2:6	AC: 2 (Ileum)	BN sling: 38%
Husmann and Cain[236]	5	63 (67%)	NR	NR	Hemi-Indiana: 63	BN sling: 67% BN closure: 33%

Abbreviations: AC: augmentation cystoplasty; AD: autonomic dysreflexia; AM: antimuscarinic medication; AUS: artificial urinary sphincter; BN: bladder neck; IC: clean intermittent catheterization; F: female; HN: hydronephrosis; ICIQ: International Consultation on Incontinence Questionnaire; LOE: Level of Evidence; M: male; n: number of patients; MCC: maximum cystometric capacity; NDO: neurogenic detrusor overactivity; NR: not reported; P_{det}: detrusor pressure; P_{detend}: end-filling detrusor pressure; P_{detmax}: maximal detrusor pressure; QOL: quality of life; S-Cre: serum creatinine; SCI: spinal cord injury; SPC: suprapubic catheter; UUT: upper urinary tract; V_{comp}: vesical compliance; VUR: vesicoureteral reflux.

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TABLE 5-7 Surgical Procedures and Efficacy for Ileocystoplasty and Colocystoplasty, *Cont'd*

Anti-VUR, %	Follow-up (mean, months)	Continence rate, %	UUT: stable/ improve, %	Urodynamic outcomes, mean	AM use, %	QOL	LOE
0	28.6	Day: 95.2 Night: 85.7	HN: 60 VUR: 100 S-Cre: 100	MCC: 142→535 mL V_{comp}: 14.9→39.8 mL/cm H_2O	10	NR	4
14	36	90.5	HN: 100 VUR: 100 S-Cre (improved): 87.5	MCC: 165→760 mL P_{detend}: 50→13 cm H_2O	NR	Satisfaction: 95% QOL improved: 100%	4
31	72.6	67	100	MCC: 220→531 mL P_{detend}: 48.9→15.8 cm H_2O	NR	Satisfaction: 72%	4
NR	28 (AC or Kock)	AC: 93 Kock: 100	100	AC MCC: 165→760 mL P_{detend}: 50→13 cm H_2O Auto-augmentation MMC↑: 33%	NR	Satisfaction AC: 93% Kock: 100%	4
0	26.9	AC: 94.5 Stoma alone: 100	NR	Total MCC: 247→524 mL AC MCC: 179→495 mL	NR	NR	4
0	6.3 years	88.5	S-Cre (unchanged): 100	MCC: 174→508 mL P_{detend}: 65.5→18.3 cm H_2O	29	NR	4
8 (100%, Transverse retubularized ileovesicostomy	0	3 years	75	NR	NR	NR	4
Hemi-Indiana: 100%	8	Median: 6 years	87	93 VUR: 100	NR	NR	4

Abbreviations: AC: augmentation cystoplasty; AD: autonomic dysreflexia; AM: antimuscarinic medication; AUS: artificial urinary sphincter; BN: bladder neck; IC: clean intermittent catheterization; F: female; HN: hydronephrosis; ICIQ: International Consultation on Incontinence Questionnaire; LOE: Level of Evidence; M: male; n: number of patients; MCC: maximum cystometric capacity; NDO: neurogenic detrusor overactivity; NR: not reported; P_{det}: detrusor pressure; P_{detend}: end-filling detrusor pressure; P_{detmax}: maximal detrusor pressure; QOL: quality of life; S-Cre: serum creatinine; SCI: spinal cord injury; SPC: suprapubic catheter; UUT: upper urinary tract; V_{comp}: vesical compliance; VUR: vesicoureteral reflux.

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TABLE 5-7 Surgical Procedures and Efficacy for Ileocystoplasty and Colocystoplasty, *Cont'd*

Reference	n (% SCI)	Age, (mean, years)	M:F	Intestinal segment	Bladder outlet procedure	Abdominal stoma
Kochakarn and Muangman[237]	5	12 (100%)	35	12:0	AC: 12 (Ileum)	0
Hakenberg *et al.*[169]	5	5 (60%)	31	1:4	AC: 1 (ileum)	0
Nomura *et al.*[209]	5	11 (100%)	29	10:1	Ileum: 21	0
Quek and Ginsberg[28]	5	26 (69%)	29	18:8	Ileum: 24	BN closure: 8% BN sling: 8%
Khastgir *et al.*[203]	5	32 (100%)	36.2	25:7	Ileum	Colposuspension: 3% AUS: 3%
Zommick *et al.*[179]	5	21 (100%)	34.6	12:9	AC: 11 (Ileum) Kock: 9 Hemi-Kock: 2 Indiana: 2	0
Chulamorkodt *et al.*[238]	5	54 (43%)	15.3	17:37	AC: 39	BN sling: 46%
Chen and Kuo[187]	5	40 (100%)	36.3	36:4	AC: 27 (Ileum) Hemi-Kock: 4 Kock: 2	0

Abbreviations: AC: augmentation cystoplasty; AD: autonomic dysreflexia; AM: antimuscarinic medication; AUS: artificial urinary sphincter; BN: bladder neck; IC: clean intermittent catheterization; F: female; HN: hydronephrosis; ICIQ: International Consultation on Incontinence Questionnaire; LOE: Level of Evidence; M: male; n: number of patients; MCC: maximum cystometric capacity; NDO: neurogenic detrusor overactivity; NR: not reported; P_{det}: detrusor pressure; P_{detend}: end-filling detrusor pressure; P_{detmax}: maximal detrusor pressure; QOL: quality of life; S-Cre: serum creatinine; SCI: spinal cord injury; SPC: suprapubic catheter; UUT: upper urinary tract; V_{comp}: vesical compliance; VUR: vesicoureteral reflux.

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TABLE 5-7 Surgical Procedures and Efficacy for Ileocystoplasty and Colocystoplasty, *Cont'd*

Anti-VUR, %	Follow-up (mean, months)	Continence rate, %	UUT: stable/ improve, %	Urodynamic outcomes, mean	AM use, %	QOL	LOE
Appendix: 83% Monti: 17%	0	~1 year	100	100	MCC: 180→800 mL	NR	4
Mitrofanoff: 100%	0	21–40	100	NR	Continence up to 500 mL V_{comp}: 22–44 mL/cm H_2O	100	4
0	91	66	95.2	VUR: 100	MCC: 151→396 mL	NR	4
Hemi-Kock: 4% Mitrofanoff: 19%	23	8.0 years	69	NR	MCC: 201→615 mL P_{detmax}: 81→20 cm H_2O P_{detmax} <40 cm H_2O: 96%	8	4
Mitrofanoff: 9%	3	6.0 years	100	100	MCC: 143→589 mL P_{detend}: 108→19 cm H_2O	NR	4
Mitrofanoff: 33% Kock: 43% Hemi-Kock: 5% Indiana: 10%	5	59.5	60	NR	NR	10	4
Mitrofanoff: 85% Monti: 15%	0	2.5 years	Stomal: 91% Urethral: 94%	NR	NR	NR	4
Hemi-Kock: 10% Kock: 5%	18	7.8 years	90	S-Cre: 97.5	MCC: 115→513 mL V_{comp}: 6.08→33.5 mL/cm H_2O	NR	4

Abbreviations: AC: augmentation cystoplasty; AD: autonomic dysreflexia; AM: antimuscarinic medication; AUS: artificial urinary sphincter; BN: bladder neck; IC: clean intermittent catheterization; F: female; HN: hydronephrosis; ICIQ: International Consultation on Incontinence Questionnaire; LOE: Level of Evidence; M: male; n: number of patients; MCC: maximum cystometric capacity; NDO: neurogenic detrusor overactivity; NR: not reported; P_{det}: detrusor pressure; P_{detend}: end-filling detrusor pressure; P_{detmax}: maximal detrusor pressure; QOL: quality of life; S-Cre: serum creatinine; SCI: spinal cord injury; SPC: suprapubic catheter; UUT: upper urinary tract; V_{comp}: vesical compliance; VUR: vesicoureteral reflux.

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TABLE 5-7 Surgical Procedures and Efficacy for Ileocystoplasty and Colocystoplasty, *Cont'd*

Reference	n (% SCI)	Age, (mean, years)	M:F	Intestinal segment	Bladder outlet procedure	Abdominal stoma
Gurung *et al.*[202]	5	19 (100%)	28.9	12:7	Ileum	AUS: 5%
Gobeaux *et al.*[212]	5	61 (100%)	34.7	30:31	Supratrigonal cystectomy + Hautmann: 61	AUS: 11% BN sling/tape: 16%
Khavari *et al.*[217]	34 (38%)	39.8	10:24	Hemi-Indiana: 34	BN closure: 9% BN sling: 12% AUS: 3%	Hemi-Indiana: 34 (100%)
Herschorn *et al.*[215]	145 (32%)	32	56:89	Ileum: 128 Colon: 17	female/male BN sling: 53%/11% BN tapering: 25%/63% BN closure: 7%/4%	49%
Lee *et al.*[26]	5	17 (35%)	34.3	9:8	Ileum: 15 Sigmoid: 2	0
Ramos *et al.*[218]	5	48 (84%)	34	81%:19%	Ileocystoplasty: 30 Ileovesicostomy: 8 Urinary conduit: 6 Continent stoma: 4	BN sling: 10% BN closure: 10%
Zhang *et al.*[205]	52 (4%)	21.7	29:23	Sigmoid	0	0

Abbreviations: AC: augmentation cystoplasty; AD: autonomic dysreflexia; AM: antimuscarinic medication; AUS: artificial urinary sphincter; BN: bladder neck; IC: clean intermittent catheterization; F: female; HN: hydronephrosis; ICIQ: International Consultation on Incontinence Questionnaire; LOE: Level of Evidence; M: male; n: number of patients; MCC: maximum cystometric capacity; NDO: neurogenic detrusor overactivity; NR: not reported; P_{det}: detrusor pressure; P_{detend}: end-filling detrusor pressure; P_{detmax}: maximal detrusor pressure; QOL: quality of life; S-Cre: serum creatinine; SCI: spinal cord injury; SPC: suprapubic catheter; UUT: upper urinary tract; V_{comp}: vesical compliance; VUR: vesicoureteral reflux.

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TABLE 5-7 Surgical Procedures and Efficacy for Ileocystoplasty and Colocystoplasty, *Cont'd*

Anti-VUR, %	Follow-up (mean, months)	Continence rate, %	UUT: stable/ improve, %	Urodynamic outcomes, mean	AM use, %	QOL	LOE
0	5	14.7 years	88.2	HN & S-Cre: 100	MCC: 229→ 494 mL at last follow-up P_{detmax}: 81→ 28 cm H_2O at last follow-up	21	4
0	6	5.84 years	74.1	VUR: 80	MCC: 305→509 mL V_{comp}: 15→42.7 mL/ cm H_2O P_{detend}: 54.1→19.1 cm H_2O NDO: 59%→21%	16	4
0	31	100	NR	MCC: 240→444 mL	NR	NR	4
NR	7.9 years	83	NR	MCC: 206→522 mL P_{detend}: 42→14 cm H_2O	NR	NR	4
0	0	10.1	ICIQ score: 16.7→1.1 Pads (/day): 2.2→0.9	VUR: 53	MCC: 246→467 mL NDO: 65%→18% Low compliance: 88%→24%	NR	4
8%	NR	17	86	Mean S-Cre: 0.64 mg/dL	NR	NR	4
29	49	NR	HN: 100 Bilateral VUR: 71 Unilateral VUR: 57	Safe MCC (<40 cm H_2O): 114→373 mL V_{comp}: 2.96→14.07 mL/ cm H_2O			4

Abbreviations: AC: augmentation cystoplasty; AD: autonomic dysreflexia; AM: antimuscarinic medication; AUS: artificial urinary sphincter; BN: bladder neck; IC: clean intermittent catheterization; F: female; HN: hydronephrosis; ICIQ: International Consultation on Incontinence Questionnaire; LOE: Level of Evidence; M: male; n: number of patients; MCC: maximum cystometric capacity; NDO: neurogenic detrusor overactivity; NR: not reported; P_{det}: detrusor pressure; P_{detend}: end-filling detrusor pressure; P_{detmax}: maximal detrusor pressure; QOL: quality of life; S-Cre: serum creatinine; SCI: spinal cord injury; SPC: suprapubic catheter; UUT: upper urinary tract; V_{comp}: vesical compliance; VUR: vesicoureteral reflux.

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TABLE 5-7 Surgical Procedures and Efficacy for Ileocystoplasty and Colocystoplasty, *Cont'd*

Reference	n (% SCI)	Age, (mean, years)	M:F	Intestinal segment	Bladder outlet procedure	Abdominal stoma
Deboudt *et al.*[143]	29 (100%)	Median: 35	7:12	Supratrigonal cystectomy + Hautmann: 29	0	Mitrofanoff: 52% Monti: 38% Casale: 10%
Gonzalez *et al.*[240]	16 (38%)	37	NR	AC + continent ileal conduit	NR	16 (100%)
Krebs *et al.*[211]	29 (41%)	31	17:12	Supratrigonal cystectomy + ileocystoplasty: 29	0	0

Abbreviations: AC: augmentation cystoplasty; AD: autonomic dysreflexia; AM: antimuscarinic medication; AUS: artificial urinary sphincter; BN: bladder neck; IC: clean intermittent catheterization; F: female; HN: hydronephrosis; ICIQ: International Consultation on Incontinence Questionnaire; LOE: Level of Evidence; M: male; n: number of patients; MCC: maximum cystometric capacity; NDO: neurogenic detrusor overactivity; NR: not reported; P_{det}: detrusor pressure; P_{detend}: end-filling detrusor pressure; P_{detmax}: maximal detrusor pressure; QOL: quality of life; S-Cre: serum creatinine; SCI: spinal cord injury; SPC: suprapubic catheter; UUT: upper urinary tract; V_{comp}: vesical compliance; VUR: vesicoureteral reflux.

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In appropriately selected patients, AC alone achieved a 69% to 95.2% continence rate,[177,191,204] decreased the International Consultation on Incontinence Questionnaire (ICIQ) score from 16.7 to 1.1, and reduced pad usage from 2.2/day to 0.6/day.[166] Lee *et al.* claimed that a staged bladder outlet procedure would be appropriate because AC alone obtained acceptable continence in the majority of patients.[166] Krebs *et al.* reported that after AC (*n*=29), detrusor relaxation therapy can be reduced or withdrawn in 80% of patients.[191]

Using a 9-part questionnaire, Watanabe *et al.* reported significant improvements in self-esteem, sexual desire, and ability to cope with disability.[211] The satisfaction rate with AC was 72% to 100%,[174,177,178,214,216] and the proportion of patients who reported "excellent results" or "subjective improvement" was approximately 95%.[176,205] Thus, AC demonstrated a high satisfaction rate if adequate surgical procedures were done for carefully selected patients.

TABLE 5-7 Surgical Procedures and Efficacy for Ileocystoplasty and Colocystoplasty, *Cont'd*

Anti-VUR, %	Follow-up (mean, months)	Conti-nence rate, %	UUT: stable/ improve, %	Urodynamic outcomes, mean	AM use, %	QOL	LOE
0	Median: 66	Stomal: 100 Urethral: 96	Ccr: 85→105 mL/min HN: 100	Median MCC: 375→552 mL Median P_{detmax}: 35→25 cm H_2O NDO: 55%→10% Low compliance: 17%→0%			4
NR	30.2	75	NR	MCC: 113→426 mL P_{detmax}: 87→17 cm H_2O			4
NR	Median: 2.4 years	69	Cystatin C: 100%	Median MCC: 240→500 mL Median V_{comp}: 13→50 mL/cm H_2O P_{detmax}: 38→15 cm H_2O P_{det} >40 cm H_2O: 52%→3% V_{comp} <20: 41%→3%			4

Abbreviations: AC: augmentation cystoplasty; AD: autonomic dysreflexia; AM: antimuscarinic medication; AUS: artificial urinary sphincter; BN: bladder neck; IC: clean intermittent catheterization; F: female; HN: hydronephrosis; ICIQ: International Consultation on Incontinence Questionnaire; LOE: Level of Evidence; M: male; n: number of patients; MCC: maximum cystometric capacity; NDO: neurogenic detrusor overactivity; NR: not reported; P_{det}: detrusor pressure; P_{detend}: end-filling detrusor pressure; P_{detmax}: maximal detrusor pressure; QOL: quality of life; S-Cre: serum creatinine; SCI: spinal cord injury; SPC: suprapubic catheter; UUT: upper urinary tract; V_{comp}: vesical compliance; VUR: vesicoureteral reflux.

5.12.1.7 Complications

Table 5-8 shows representative complications of ileal AC and colonic AC. In the following summary, the studies in which all patients underwent creation of a CCC were excluded. Perioperative mortality ranged from 0% to 4% (mainly due to pulmonary embolism).[175,218] Complications occurred in 30% to 41% of the patients, and 38% to 83% of complications corresponded to Clavien ≤2. [190,191,216,218]

Early postoperative complications were anastomotic leakage (7%–36%),[174,175,206,208,212] prolonged paralytic ileus (4%–12%),[170,174,189] symptomatic UTI (4%–11%),[174,175] wound infection (2%–9%),[176,212,216] AUS infection (2%),[174] and AUS cuff erosion (2%). [174]

Late postoperative complications were bowel obstruction (3%–10%),[176,190,204,205] bowel dysfunctions, for example, chronic diarrhea or loose stool (0%–28%),[177,178,187,189,190,205,208] bladder stone (0%–33%),[174-178,183,187,190,204,205,211,216] renal stone (2%–23%),[175,176,187,204,216] symptomatic UTI (3%–65%),[187,189,190,204,205,209,211] bowel-to-bladder anastomotic stenosis (3%–6%),[176,190,211] mucus secretion (2%–77%),[176-178] metabolic acidosis (0%–11%),[177,208,209,214] AUS infection (4%–6%),[174,189,204] perforation (0%–7%),[176,177,183,189,205,214] and malignant neoplasms (0%–5%).[177,187,190,204]

Although vitamin B12 (VB12) deficiency could be encountered in the case of ileocecal AC, a deficiency that required VB12 supplementation was not found in the literature.[187] In addition, malabsorption of a vitamin other than VB12 was not reported.[187,190,204,215]

TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty

Reference	n (% SCI)	Mean age, years	M:F	Intestinal segment
Steinberg *et al.*[206]	33 (18%)	25	6:27	AC: 28 (Ileocecal)
Sidi *et al.*[182]	12 (100%)	33.5	11:1	Sigmoid: 11 Cecum: 1
Noll and Schreiter[174]	46 (43%)	SCI: 14–65	11:35	AC: 41 (Ileum: 39, Sigmoid: 2) Total replacement: 5 (Ileum)
Chao *et al.*[32]	24 (42%)	NA	11:13	AC: 7 (Hemi-Indiana)
Herschorn *et al.*[168]	18 (44%)	37	4:14	Hemi-Kock: 15 Stoma alone: 3

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

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TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty, *Cont'd*

Bladder outlet procedure	Abdominal stoma	Mean follow-up (months)	Complications	LOE
BN sling: 24%	BN closure + abdominal stoma: 33%	21	Leakage from anastomotic site: 9% Late complications requiring surgery: 27% BN closure: 12% Valve repair: 9% Another BN sling: 6% Difficulty in catheterization: 3% Transient metabolic acidosis: 6%	4
AUS: 25%	0	15	UTI: 33% Change in bowel function: 0%	4
AUS: 57%	0	NA	Early Anastomotic leakage: 7% Prolonged ileus: 4% Febrile UTI: 4% AUS infection: 2% AUS cuff erosion: 2% Late Bladder stone: 7% Distal ureteral stenosis: 4% Tissue shrinkage underneath the cuff: 9% AUS infection: 4%	4
BN closure + SPC: 71% BN closure + AC: 29%	Hemi-Indiana: 29%	BN closure + SPC: 21 BN closure + AC: 23	Metabolic acidosis: 0% Unmanageable diarrhea: 0% Malabsorption: 0%	4
BN sling: 50% BN tapering: 6% BN closure: 17%	100%	26	Occasional diarrhea: 6% UTI: 28% Early Vesicourethral fistula: 17% Late Stomal revision: 22% Bladder stone: 11%	4

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

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TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty, *Cont'd*

Reference	n (% SCI)	Mean age, years	M:F	Intestinal segment
Mast *et al.*[175]	28 (21%)	26	14:14	Ileum: 26 Stomach: 1 (borderline renal function)
Flood *et al.*[176]	122 (26%)	37	40:82	Ileum: 82 Ileocecal: 36 Sigmoid: 4
Watanabe *et al.*[208]	18 (72%)	36.7	0:18	CIC + BN sling alone: 3 Ileocystostomy: 8 Ileocystoplasty: 7
Fontaine *et al.*[183]	21 (29%)	27	0:21	Ileum: 21

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

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TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty, *Cont'd*

Bladder outlet procedure	Abdominal stoma	Mean follow-up (months)	Complications	LOE
BN closure: 11% BN sling: 4% Burch: 4% AUS: 4%	Mitrofanoff: 7% Cystostomy: 4%	31	Early Urosepsis: 11% Peritonitis: 4% Perivesical abscess: 4% Pulmonary embolism: 4% (death) Late Clam adhesions: 4% Renal dysfunction: 4% Urethral fistula: 4% Chronic augmented bladder infection: 57% Bladder stones: 11% Renal stones: 7% Re-intervention: 59%	4
BN sling: 13% Burch: 0.8% Urethral closure: 4% Supratrigonal resection: 0.8%	17%	37	Early Anastomotic leakage: 14% Urethral fistula: 10% Suprapubic fistula: 0.8% Ileus: 10% Wound infection: 2% Late Bladder stones: 16% Renal stones: 7% Perforation: 7% Pyelonephritis: 3% Anastomotic stenosis: 3% Small bowel obstruction: 3% Mucus retention: 2% Revisional surgery: 15%	4
BN sling: 89%	22%	18	No significant early postoperative complications Late Bladder stones: 6% Pyelonephritis: 11% Anastomotic stenosis: 6% Metabolic disturbances: 0%	4
BN sling: 100%	0	28.6	Asymptomatic bacteriuria: 62% Bladder stones: 0% Alkalization therapy: 0% Difficulty in catheterization: 0% Perforation: 5%	4

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

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TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty, *Cont'd*

Reference	n (% SCI)	Mean age, years	M:F	Intestinal segment
Kuo[178]	21 (88%)	36	18:3	Ileum
Herschorn[210]	59 (31%)	30.6	22:37	Ileum: 49 Ileocecal: 8 Sigmoid: 1 Transverse colon: 1 Hemi-Kock: 21
Kuo[177]	251 (100%)	33.8 at SCI	212:39	Ileocystoplasty: 28 Auto-augmentation: 6 Kock: 7
Sutton *et al.*[180]	23 (70%)	42.2	15:8	AC: 19 (Hemi-Indiana)
Chartier-Kastler *et al.*[213]	17 (100%)	36.5	11:6	Subtrigonal cystectomy + Hautmann cystoplasty: 15 Clam cystoplasty: 2

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

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TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty, *Cont'd*

Bladder outlet procedure	Abdominal stoma	Mean follow-up (months)	Complications	LOE
0	0	36	Early Acute tubular necrosis: 5% Late Ileus: 5% Metabolic acidosis: 14% Bladder stones: 24% Chronic diarrhea: 10% Mucus secretion: 52% Bladder cancer: 5%	4
AUS: 3% Trigonal tubularization: 2% BN tapering: 41% BN sling: 32%	Hemi-Kock: 36%	72.6	Complications: 41% Re-interventions: 36% (Median time to re-intervention: 116 months) Early Small bowel obstruction: 2% Fascial sling erosion: 2% Deep vein thrombosis: 2% Wound dehiscence: 2% Late Bladder stones: 11% Renal stones: 2% Perforation: 2% Bowel problems: 19%	4
Periurethral Teflon injection: 1	Kock pouch: 7	28 (AC or Kock)	Symptomatic UTI: AC, 25%; Kock, 29% Mucus secretion: 77% Occasional abdominal pain: 21% Loose stools: 24% Bladder stones: 12%	4
BN closure: 30% BN sling: 13% Collagen injection: 4%	AC + continent stoma: 83% Continent stoma alone: 17%	26.9	Febrile UTI: 17% Re-intervention: 9% Metabolic problems: 0%	4
AUS: 6% Burch: 6%	0	6.3 years	Early Prolonged ileus: 12% Acute pyelonephritis: 6% Late Recurrent pyelonephritis: 6% AUS infection: 6% Bladder stones: 0% Bowel dysfunctions: 0% Perforation: 0%	4

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

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TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty, *Cont'd*

Reference	n (% SCI)	Mean age, years	M:F	Intestinal segment
Van Savage *et al.*[239]	8 (50%)	29	2:6	AC: 2 (Ileum)
Husmann and Cain[236]	63 (67%)	NA	NA	Hemi-Indiana: 63
Kochakarn *et al.*[237]	12 (100%)	35	12:0	AC: 12 (Ileum)
Hakenberg *et al.*[169]	5 (60%)	31	1:4	AC: 1 (ileum)
Nomura *et al.*[209]	11 (100%)	29	10:1	Ileum: 21
Quek and Ginsberg[28]	26 (69%)	29	18:8	Ileum: 24

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

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TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty, *Cont'd*

Bladder outlet procedure	Abdominal stoma	Mean follow-up (months)	Complications	LOE
BN sling: 38%	8 (100%, Transverse retubularized ileovesicostomy	3 years	Bladder stones: 13%	4
BN sling: 67% BN closure: 33%	Hemi-Indiana: 100%	Median: 6 years	Febrile UTI: 24% Perioperative death: 2% (PE) Worsening of fecal incontinence: 3% Re-intervention: 47% Bladder stones: 29% Stomal incontinence: 12% Stomal stenosis: 6% Perforation: 6% Small bowel obstruction: 3% Ureteral obstruction: 2% Metabolic acidosis: 9% Abnormal VB12: 0%	4
0	Appendix: 83% Monti: 17%	~1 year	Orchitis: 8% Diarrhea: 0% Metabolic complications: 0% Upper tract UTI: 0%	4
0	Mitrofanoff: 100%	21-40	UTI: 40% Stomal stenosis: 0%	4
0	0	66	Early Paralytic ileus: 36% Transient VUR: 36% Wound infection: 9% Late Urethral stricture: 9% Overdistension: 9%	4
BN closure: 8% BN sling: 8%	Hemi-Kock: 4% Mitrofanoff: 19%	8.0 years	Subsequent urological procedure: 46% Bladder stones: 19% Renal stones: 8% Nephrectomy: 4% Revision afferent nipple: 4% BN closure: 4% Epididymectomy: 4% Puboprostaic sling: 4% No significant change in bowel function: 88% Metabolic disturbances: 0%	4

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

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TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty, *Cont'd*

Reference	n (% SCI)	Mean age, years	M:F	Intestinal segment
Khastgir *et al.*[203]	32 (100%)	36.2	25:7	Ileum
Zommick *et al.*[179]	21 (100%)	34.6	12:9	AC: 11 (Ileum) Kock: 9 Hemi-Kock: 2 Indiana: 2
Chulamorkodt *et al.*[238]	54 (43%)	15.3	17:37	AC: 39
Chen and Kuo[187]	40 (100%)	36.3	36:4	AC: 27 (Ileum) Hemi-Kock: 4 Kock: 2
Gurung *et al.*[202]	19 (100%)	28.9	12:7	Ileum

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

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TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty, *Cont'd*

Bladder outlet procedure	Abdominal stoma	Mean follow-up (months)	Complications	LOE
Colposuspension: 3% AUS: 3%	Mitrofanoff: 9%	6.0 years	Recurrent UTI: 6% Transient Increased mucus: 28% Bladder stones: 6% Perforation: 3% Bowel obstruction: 3% Minor bowel dysfunction: 19%	4
0	Mitrofanoff: 33% Kock: 43% Hemi-Kock: 5% Indiana: 10%	59.5	Stomal revision: 10% UTI: 10%	4
BN sling: 46%	Mitrofanoff: 85% Monti: 15%	2.5 years	Bladder stones: 15% Stomal stenosis: 9% Stomal bleeding: 5% False passage: 3% Bowel obstruction: 2% Stomal revision: 9% Urethral closure: 5% Removal of Mitrofanoff: 2%	4
0	Hemi-Kock: 10% Kock: 5%	7.8 years	Bladder stones: 33% Renal stones: 23% UTI: 65% Recurrent epididymitis: 6% *de novo* diarrhea: 8% VB12 deficiency: 0% Malabsorption: 0%	4
AUS: 5%	0	14.7 years	Bladder stones: 21% Renal stones: 5% Urethral stricture: 5% Small bowel obstruction: 5% VUR: 10% Perinephric abscess: 5% Urosepsis: 5% AUS infection: 5% Bladder cancer: 0% Change in bowel function: 0% Metabolic disturbances: 0%	4

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

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TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty, *Cont'd*

Reference	n (% SCI)	Mean age, years	M:F	Intestinal segment
Gobeaux *et al.*[212]	61 (100%)	34.7	30:31	Supratrigonal cystectomy + Hautmann: 61
Khavari *et al.*[217]	34 (38%)	39.8	10:24	Hemi-Indiana: 34
Herschorn[210]	145 (32%)	32	56:89	Ileum: 128 Colon: 17
Lee *et al.*[166]	17 (35%)	34.3	9:8	Ileum: 15 Sigmoid: 2
Ramos *et al.*[218]	48 (84%)	34	81%:19%	Ileocystoplasty: 30 Ileovesicostomy: 8 Urinary conduit: 6 Continent stoma: 4
Zhang *et al.*[205]	52 (4%)	21.7	29:23	Sigmoid

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

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TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty, *Cont'd*

Bladder outlet procedure	Abdominal stoma	Mean follow-up (months)	Complications	LOE
AUS: 11% BN sling/tape: 16%	NA	5.84 years	Overall complications: 37.7% (Clavien ≤G2: 82.6%) Ileus: 10% AUS removal: 3% Pelvic abscess: 2% Pouch leak: 3% Pouch obstruction: 5% Perforation: 2% *de novo* diarrhea: 28% Bladder stones: 2% Bladder cancer: 0% Metabolic disturbances: 0%	4
BN closure: 9% BN sling: 12% AUS: 3%	Hemi-Indiana: 34 (100%)	31	Overall early complication: 17.6% Prolonged ileus: 7% Wound infection: 3% Transfusion: 3% Overall late complication: 44.1% Recurrent UTI: 19% Pyelonephritis: 3% Bladder stones: 6% Stomal revision: 12% AUS removal: 3% Chronic diarrhea: 0%	4
Female BN sling: 53% BN tapering: 25% BN closure: 7% Male BN sling: 11% BN tapering: 63% BN closure: 4%	49%	7.9 years	Re-operation: 45% Bladder stone: 21% BN revisions or closure: 6% Valve revisions: 6% Stomal revisions: 6% Bladder cancers: 1% (at 4 and 18 years, Dead of disease)	4
0	0	10.1	NA	4
BN sling: 10% BN closure: 10%	8%	17	Overall complications: 40% (Clavien ≤2: 63%) Re-operation: 12% Perioperative death: 2% UTI: 21% Stones: 4%	4
0	0	49	Recurrent UTI: 21% Re-intervention: 4% Metabolic acidosis: 0% Perforation: 0%	4

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

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TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty, *Cont'd*

Reference	n (% SCI)	Mean age, years	M:F	Intestinal segment
Deboudt *et al.*[143]	29 (100%)	Median: 35	7:12	Supratrigonal cystectomy + Hautmann: 29
Gonzalez *et al.*[240]	16 (38%)	37	NA	AC + continent ileal conduit
Krebs *et al.*[211]	29 (41%)	31	17:12	Supratrigonal cystectomy + ileocystoplasty: 29

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

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Cheng *et al.* investigated the long-term metabolic outcomes in 40 patients including 23 NBD patients undergoing AC (mean age: 43 years; mean follow-up: 13 years).[219] Nine patients (22.5%) developed metabolic acidosis, and 6 patients (15%) required bicarbonate supplementation. Subgroup analysis showed that the use of neither the ileum or colon nor the most recent eGFR was associated with an increase in risks for metabolic acidosis.

The rate of bladder stone, a bothersome complication after AC, seems significant. Bladder stone probably is caused by chronic infection in the augmented bladder, which exists in 57% of the patients, as well as mucus.[175,220] While some studies suggested the usefulness of prophylactic periodic bladder irrigation for pediatric NBD patients after AC, there was no firm evidence of its benefit in SCI patients after AC.[221,222]

Hensle *et al.*[221] assessed the incidence of bladder stone in mostly pediatric NBD patients who underwent AC before (Group I, *n*=91, at follow-up: at least 8 years) and after starting a periodic bladder irrigation protocol (Group II, *n*=42, at follow-up: at least 3 years). Normal saline twice a week (240 mL)

TABLE 5-8 Surgical Procedures for and Complications of Ileocystoplasty and Colocystoplasty, *Cont'd*

Bladder outlet procedure	Abdominal stoma	Mean follow-up (months)	Complications	LOE
0	Mitrofanoff: 52% Monti: 38% Casale: 10%	Median: 66	Overall complications: 44.8% Re-operation: 24.1% Early Hemoperitoneum: 3% Sepsis: 3% Initial false passage: 3% Fistula: 7% Late Fistula: 7% Stomal/Channel stenosis: 7% Bowel obstruction: 3% Bladder stone: 10%	4
NA	16 (100%)	30.2	Early Urinary fistula: 6% Paralytic ileus: 13% Urosepsis: 13% Late UTI: 25% Bladder stone: 13%	4
0	0	Median: 2.4 years	Overall complications: 38% (Clavien G2: 38%; G3b: 38%) Re-intervention for complications: 21% Later additional bladder outlet procedure: 28%	4

Abbreviations: AC: augmentation cystoplasty; AUS: artificial urinary sphincter; BN: bladder neck; CIC: clean intermittent catheterization; F: female; LOE: Level of Evidence; M: male; n: number of patients; NA: not available; PE: pulmonary embolus; SCI: spinal cord injury; SPC: suprapubic catheter; UTI: urinary tract infection; VB12: vitamin B12; VUR: vesicoureteral reflux.

and gentamicin sulphate solution once a week were used for bladder irrigation. The incidences of bladder stone were 43% and 7% in Group I and II, respectively. Furthermore, in Group I the incidence was significantly higher in patients with an abdominal stoma (66%) than without a stoma (15%).

Van den Heijkant *et al.*[222] performed 50 mL saline flushes in 29 pediatric NBD patients after AC, and they also used acetylcysteine for children with severe mucous-related problems and catheter blockage. Irrigation was done 1 to 3 times a day for 3 months after AC, but after that once a day to rarely. During a median follow-up of 49 months, bladder stone occurred in 2 patients (7%), which was lower than the incidence (10%–50%) in the previous reports.

Taking these results into consideration, periodic bladder irrigation after AC, particularly for those patients who underwent construction of a CCC, is an option for preventing the formation of bladder stone.

Perforation of the augmented bladder is a severe complication that is caused by non-compliance with IC, overdistension due to difficult catheterization, UTI, and traction due to adhesion.[184] Patients with SCI often do not manifest typical symptoms and signs of peritonitis, so that suspicion of perforation is of paramount importance to prevent a delay in diagnosis.[184]

As shown in **Table 5-8**, malignant neoplasms arose in 3 NBD patients including SCI patients after AC. One patient developed muscle invasive bladder cancer at 70 months after AC, and he died of the disease 10 months later.[177] The other 2 patients developed bladder cancer at 4 years and 18 years after AC, and both ultimately died of the disease.[213] Biardeau *et al.* reported a systematic review of malignant neoplasms after AC.[223] According to the review, the follow-up time probability of developing a malignant neoplasm after AC was 0% ± 5.5%, and the estimated incidence ranged from 0 to 272.3 per 100,000 patients/year. Adenocarcinoma was the most common histological type (51.6%). Malignant lesions predominantly occurred at the entero-urinary anastomosis (50%). The mean latency period was 19 years, and most malignant lesions were diagnosed more than 10 years after surgery (90%).

Malignant neoplasms arising from the augmented bladder often have an aggressive nature and are found at an advanced stage due to delayed diagnosis, which results in poor prognosis.[170] Although from this standpoint, surveillance would be very important for earlier diagnosis, long-term surveillance by cystoscopy is still controversial because of its lack of efficiency. In spite of its limitations, annual cystoscopic surveillance is now the only validated tool available (also discussed in Chapter 3). Biardeau *et al.* asserted that it should be started 10 years after surgery and completed by a regular clinical examination associated with surveillance imaging.[213]

Others assert that an annual clinical examination searching for symptoms or signs suggestive of tumour occurrence followed by selective cystoscopy is sufficient. Signs and symptoms may include the occurrence of recurrent UTI, bladder or pelvic pain, gross hematuria, persistent microscopic hematuria, or abnormalities found in imaging studies.[170,201,302]

The re-intervention rate for late complications was 4% to 59%[175,176,191,208,209,213,214,216,218] and the median time to re-intervention was 116 months.[216] Bladder outlet procedures, such as BN closure or BN sling, and surgery for bladder or renal stone accounted for the majority of re-interventions. The rate of late additional bladder outlet procedures was 28%.[191]

5.12.1.8 **Cost**

Detailed cost-effective analysis using a Markov model for AC has not been reported yet. Padmanabhan *et al.* analyzed the 5-year costs of AC and BoNTA. If the complication rate of AC was 50%, BoNTA was less expensive than AC over 5 years.[224] Because this analysis was sensitive to the durability of the effects of BoNTA, the cost of AC was favourable if the effects of BoNTA were maintained for less than 5.1 months. In addition, if the AC complication rate changed and was less than 14%, AC was less expensive than BoNTA.

Watanabe *et al.* used a US payer perspective and analyzed 3-year costs of AC and BoNTA.[225] AC was more expensive ($12,315–$16,830) than BoNTA ($4,586–$11,476). The cost of AC was affected by the intra-operative complication rate and the incidence of bladder stone.

Data from the United States National Inpatient Sample (ileal conduit [n=1,919] and AC [n=1,132]) showed that patients with AC were significantly younger (34 years vs. 46 years), while patients with ileal conduit included significantly more Medicare recipients (55% vs. 30.8%) and used significantly more health care resources.[226] In addition, patients at teaching institutions were significantly more likely to undergo AC (42%) than those at nonteaching institutions (23%), a finding that might indicate an opportunity for quality improvement.

5.12.2 Auto-augmentation

5.12.2.1 Indications and procedure

There are very few studies about auto-augmentation for SCI patients, as most of the studies investigated outcomes of this procedure in pediatric NBD patients.[47] Generally speaking, the best outcomes can be expected in patients with good bladder capacity but poor bladder compliance.[201] In this procedure, detrusor myotomy or myectomy is done, resulting in diverticulum-like expansion of the urothelial mucosa.

5.12.2.2 Efficacy and complications

As mentioned above, there is no data available on auto-augmentation in SCI patients, and there were no randomized comparisons between auto-augmentation and AC in this patient population. The improvement of MCC and bladder compliance sometimes takes approximately 6 months.[227]

Stöhrer *et al.* investigated outcomes of auto-augmentation in 29 patients, including 9 SCI patients.[228] During a follow-up of 2 months to 52 months, MCC improved, and maximum detrusor pressure and bladder compliance were normalized. Vesicoureteral reflux was resolved in 40% of the patients, and was reduced to one side in another 40% of the patients. In terms of subjective evaluations, 16 patients reported “excellent” and 8 reported “good” results. No complications occurred in this series except for intra-operative mucosal perforation (n=12).

Oge *et al.* reported outcomes in 13 patients, including 4 SCI patients.[229] During a mean follow-up of 15 months, MCC increased by 18.6%, bladder compliance increased from 3.4 mL/cm H_2O to 5.8 mL/cm H_2O, the continence rate was 46.1%, vesicoureteral reflux was resolved in 40% of the patients, and antimuscarinics were needed in 40% of the patients. No significant complications occurred.

The long-term efficacy of auto-augmentation was not so good, in that up to 50% of the patients required additional procedures.[227] Auto-augmentation is not the standard of care for AC in adults with SCI. Physicians should use standard techniques of enterocystoplasty instead.

5.12.3 Small intestinal submucosa augmentation cystoplasty

Zhang *et al.* anastomosed small intestinal submucosa (SIS) to the bladder after a clam-shell cystotomy in 6 patients with spina bifida and 2 patients with SCI.[230] During a mean follow-up of 12 months, MCC increased from 170 mL at baseline to 366 mL at 3 months and 386 mL at 12 months, bladder compliance increased from 5.9 mL/cm H_2O at baseline to 20.0 mL/cm H_2O at 3 months and 36.3 mL/cm H_2O at 12 months, and maximum detrusor pressure decreased from 43.6 cm H_2O at baseline to 21.1 cm H_2O at 3 months and 15.1 cm H_2O at 12 months. Hydronephrosis was resolved or improved in 71% of the patients. No significant complications occurred. The investigators concluded that functional bladder augmentation using SIS as a scaffold is a potentially viable option for genitourinary reconstruction. However, based on the current state of data, bladder augmentation using SIS cannot be recommended as a substitute for AC; it should be considered experimental.

5.12.4 Continent catheterizable channel

5.12.4.1 Procedure

A CCC is constructed using the appendix (Mitrofanoff procedure),[231] a retubularized short intestinal segment (Yang-Monti method),[232] or a similar method using the efferent limb of a Kock pouch or Indiana pouch.[233] The abdominal stoma is often located at the umbilicus or in the right lower quadrant. If the length of a single Yang-Monti tube is insufficient, a double Yang-Monti tube or a Casale[234] procedure ("spiral Monti") is an alternative, but that increases the complication rate.[47]

As mentioned above (see "Indications"), the degree of upper-limb disability in tetraplegic patients should be thoroughly evaluated, and, if indicated, ULR and specific rehabilitation procedures are needed before the construction of the catheterizable channel.[181]

There have been many controversies about whether concomitant BNC closure should be performed at the creation of a CCC or the native urethra should be preserved after anti-incontinence surgeries such as a BN sling. Some authors prefer to preserve the native urethra as a safety valve for trans-urethral manipulation in the case of cystolithotripsy and/or difficulty in catheterization via the stoma.[168]

5.12.4.2 Efficacy

As shown in **Table 5-8**, there is a paucity of data about the CCCs specific to SCI patients. In the following summary, studies in which all patients underwent the creation of the abdominal stoma were included. Concomitant AC was performed in the majority of the cases, and BN procedures were combined in significant cases (BN closure: up to 100%,[215] BN sling: up to 67%,[235] BN tapering: up to 63%,[213] and AUS: up to 3%[213]). During a follow-up of less than 1 year to a median of 8.0 years,[235,236] the overall continence rate ranged from 60% to 100%,[168,169,179,217,236] while the stoma continence rate ranged from 91% to 100%[170,237] and the urethral continence rate ranged from 94% to 96%.[170,237] Deboudt *et al.* reported that 18 of 22 patients taking antimuscarinics prior to AC no longer needed antimuscarinics after AC.[170]

In terms of QOL, 80% of patients judged their postoperative condition to be more independent and 53% thought it to be more social after CCC.[237] Satisfaction ranged from 60% to 100%.[169,179,237,238]

5.12.4.3 Complications

Perioperative mortality was 2%, resulting from a pulmonary embolism in 1 patient undergoing a hemi-Indiana pouch construction, otherwise known as an ileal channel cecocystoplasty.[235] Reservoir-related complications were the same as those in AC, and the rate of bladder stone was also similar to the rate in AC: 6% to 29%.[168,170,217,235,237,238] In other words, the addition of a CCC does not increase complications that are inherent to AC, such as bladder stones or UTI. Complications vary by the type of channel but, in general, stomal incontinence occurs in approximately 12% of patients,[235] stoma stenosis occurs in 0% to 9%,[169,170,235,237] and the stoma revision rate is 9% to 22%.[168,179,217,237,239] Much of the data is in pediatric cases but stomal stenosis rates can be as high as 33% in adult NBD patients.[240] It should be noted that the stoma-related complication rate and subsequent re-intervention rate seem to be high, even if experienced surgeons construct the CCC at a specialized centre.

5.12.5 Continent urinary reservoir

5.12.5.1 Procedure

A large case series of CUR in SCI patients has not yet been reported.[167] If ureteral re-implantation is not indicated, the use of the native bladder avoids ureteral anastomosis. In addition, if the native urethra can be preserved with or without a BN sling or BN reconstruction and IC can be performed via the native urethra, it is better than the construction of a catheterizable channel because significant stoma and channel-related complications could occur. Therefore, the indications for CUR would be very limited, and patients who have markedly poor compliance with a severely trabeculated and fibrotic bladder and a nonfunctional urethral sphincter mechanism that cannot be used for urinary reconstruction are considered to be subjects for CUR construction.[167] Although various CURs that have been constructed in patients with bladder cancer could be used for SCI patients, the Indiana pouch and its modification have been selected in the majority of the small case series.

Whether cystectomy should be done at the construction of CUR is controversial; this has been covered earlier in the chapter in the section on ileal conduit.

5.12.5.2 Efficacy and complications

Riksen *et al.* reported a successful case of a woman with a thoracic cord injury who underwent the construction of Indiana pouch and whose reservoir capacity reached 600 mL.[241]

Moreno *et al.* constructed a modified Indiana pouch with a simple cystectomy in 3 women with a cervical cord injury, and showed that during a follow-up of 18 months to 30 months, pouch capacity increased up to 500 mL to 800 mL, the frequency of symptomatic UTI and AD decreased, QOL as well as sexual life and body image improved, and no patients had stoma incontinence.[242]

Plancke *et al.* constructed an Indiana pouch without cystectomy (n=5) or BN closure (n=2) in 7 female patients, and showed that during a mean follow-up of 28 months, mean pouch capacity reached 600 mL, the stomal continence rate was 100%, and no patients developed UUT deterioration. Complications were bladder stone (n=1) and stoma stenosis (n=2).[171]

5.12.6 Conclusions

Augmentation enterocystoplasty:

- AC provides urodynamic and QOL improvements, acceptable continence, UUT preservation, and reduced detrusor relaxation therapy over the long term. **[LOE 3]**
- Vesicoureteral reflux in NBD often resolves with AC alone. **[LOE 3]**
- In the limited case series, laparoscopic or robot-assisted laparoscopic AC is a safe and technically feasible procedure with a urodynamic outcome that is comparable to that reported for open AC. **[LOE 3]** However, the increased cost is a significant disadvantage. **[LOE 3]**

- Upper-limb reanimation surgery can help patients with cervical SCI to perform self-IC. **[LOE 3]**

Auto-augmentation and SIS:

- Ileal or sigmoid AC has more evidence in adult SCI patients and yields better long-term results than auto-augmentation or SIS augmentation. **[LOE 3]**

Continent catheterizable channel:

- The construction of a CCC should be considered if the patient is unable to perform IC via the native urethra but would be able to perform IC through an abdominal stoma. **[LOE 4]**
- The catheterizable channel provides independence in toileting and improvements in QOL. **[LOE 3]**
- Catheterizable channels have a high rate of re-operation for stenosis or incontinence. **[LOE 3]**
- Compliance with IC prevents stomal stenosis and helps lower the incidence of complications. **[LOE 4]**

Continent urinary reservoir:

- The construction of a CUR may be considered if the patient desires a continent reconstruction but the lower urinary tract cannot be used. **[LOE 3]**

Recommendations

- Surgeons should offer augmentation enterocystoplasty to SCI patients who have NDO or reduced bladder compliance refractory to medical therapy. **[GOR B]**
- Surgeons should offer CCC to SCI patients who would benefit from IC but are unable or unwilling to perform IC through the native urethra. **[GOR B]**
- Surgeons should offer CUR to SCI patients who desire a continent urinary diversion but have lower urinary tract pathology that prevents orthotopic reconstruction with bladder augmentation and CCC. **[GOR B]**
- Clinicians should confirm that the patient or reliable caregivers can perform IC before offering the patient a continent diversion, including augmentation cystoplasty. **[GOR B]**
- Surgeons must recommend long-term follow-up after continent diversion, due to the high risk for complications. **[GOR A]**
- Enterocystoplasty should be performed rather than auto-augmentation or SIS, except in research settings. **[GOR B]**

5.13 Sacral Anterior Root Stimulation, Posterior Sacral Root Rhizotomy (SARS)

The combination of sacral anterior root stimulation and posterior sacral root rhizotomy, also referred to as the "Brindley procedure", has been used as an alternative treatment with relative success for the restoration of bladder function after suprasacral SCI.[243–246]

We reviewed the literature, searching for the level of evidence of different studies reporting clinical results of the Brindley procedure in individuals with SCI. A PubMed search (including all references up to date) was performed using the terms "sacral anterior root (electrical) stimulation/stimulator" OR "Brindley procedure/stimulator" OR "posterior rhizotomy" AND "bladder" AND "spinal cord injury" OR "paraplegia". Human and English filters were applied. After reading the abstracts and full texts, where relevant, a total of 18 publications were selected. **Table 5-9** presents all 18 resulting papers.[247]

TABLE 5-9 Publications on Clinical Results of the Brindley Procedure with Level of Evidence

Reference	Year	Country	Surgical technique	Rhizotomy, %	Patients (included), n	Female	Use for micturition, %	Continence, %	Follow-up	Level of Evidence
Brindley *et al.*[269]	1982	UK	Intradural	NR	11	2	100	59	2–50 mo	3
Arnold *et al.*[270]	1986	New Zealand	Intradural	NR	6	1	83	83	5–30 mo	3
Brindley *et al.*[271]	1986	UK	Intradural	34	50	12	86	62	1–9 yr	3
Robinson *et al.*[272]	1988	UK	NR	NR	22	2	73	68	NR	3
Madersbacher *et al.*[260]	1988	Austria	Intradural	100	7	6	100	100	NR	3
Tanagho *et al.*[250]	1989	USA	Extradural	84	22 (19)	9	42	82	6 yr	3
Sauerwein *et al.*[273]	1990	Germany/Austria/UK/France	Extradural	100	12	6	75	64	3–29 mo	3
Madersbacher and Fischer[274]	1993	Austria	Intradural	100	30	22	90	93	0–8 yr	3
Sarrias *et al.*[275]	1993	Spain	Barcelona	100	7	6	100	100	NR	3

Abbreviations: mo: months; NR: Not reported; yr: years.

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TABLE 5-9 Publications on Clinical Results of the Brindley Procedure with Level of Evidence, *Cont'd*

Reference	Year	Country	Surgical technique	Rhizotomy, %	Patients (included), n	Female	Use for micturition, %	Continence, %	Follow-up	Level of Evidence
Brindley[244]	1994	UK, New Zealand, France, Austria, Denmark, Australia, Germany, The Netherlands, Spain	Intradural/ Extradural	70	500	229	86	NR	0–16 yr	3
Van Kerrebroeck *et al.*[257]	1996	The Netherlands	Intradural	100	47	18	96	91	3.5 yr	3
Schurch *et al.*[261]	1997	Switzerland	Intradural	100	10	7	70	80	3.4 yr	3
Egon *et al.*[255]	1998	France	Intradural/ Extradural	100	96	28	89	89	5.4–5.8 yr	3
Van der Aa *et al.*[276]	1999	The Netherlands	Intradural	100	38	4	100	84	0–12 yr	3
Creasey *et al.*[258]	2001	USA	Barcelona	100	23	7	78	87	1 yr	3
Vastenholt *et al.*[256]	2003	The Netherlands	Intradural	100	42 (37)	5	87	57	1–13 yr	3
Kutzenberger *et al.*[259]	2005	Germany	Intradural	94	464 (440)	220	95	83	6.6 yr	3
Krasmik *et al.*[254]	2014	Switzerland	Intradural	100	137	56	78	62	0–24 yr	3

Abbreviations: mo: months; NR: Not reported; yr: years.

The first studies on electrical stimulation of the sacral roots date back to the 1970s, when Brindley in England[248] and Tanagho *et al.* in the USA[249] carried out the first experiments in baboons and dogs, respectively.

From these studies in baboons, Brindley developed the sacral anterior root stimulator (SARS) for individuals with severe bladder disorders. The first implant in humans was achieved in 1976.[250]

The stimulator, an implantable device (Finetech–Brindley SARS, Finetech Medical Limited, UK; Vocare® Bladder System, USA) works by stimulating motor pathways of sacral roots (S2-S4), which produces an effective contraction that can empty the bladder. The stimulator can also be used to support defecation and to restore penile erection. The stimulator is composed of two parts: first, an implanted part (without batteries) that consists of electrodes, cables, and a receiver that is placed subcutaneously; and second, an external part that controls the stimulation and has a transmitter block. When the transmitter block is positioned over the receiver, the external part sends radiofrequency signals that induce an electrical current in the implanted part.

In addition to the implant, the Brindley procedure also entails a sacral deafferentation, or dorsal sacral root rhizotomy, which is required to treat NDO.

Three different surgical techniques have been used: intradural, extradural, and Barcelona, the latter being a combination of the other two. The intradural, or classical technique, consists of implanting the tripolar electrode cuffs inside the dura and performing a posterior rhizotomy at the level of the cauda (L3-L5). This was the technique proposed initially by Brindley; however, compared with the extradural technique, the intradural technique entails a higher risk for cerebrospinal fluid leakage because of the opening of the dura.

With the extradural technique, both implantation of the electrodes and the rhizotomy are performed extradurally at the sacrum level (S1-S3). The main disadvantage is that it is slightly more difficult to divide posterior roots, and therefore rhizotomy may not be complete.[251]

The Barcelona technique combines both techniques (i.e. extradural implantation of electrodes and intradural rhizotomy); however, it proposes an additional laminectomy at the conus level (T12-L1) to perform the rhizotomy, which may produce destabilization of the column if there are fixations or fractures at that level,[252] besides adding time to the surgery. Of the 18 publications, only 2 used the Barcelona technique and 3 the extradural technique. The rest of the works were reported using the intradural technique.

Over the past 40 years, more than 2,000 patients have undergone the Brindley procedure worldwide.[250] The publications selected in this document report the clinical results of only some of these patients, and several of them present overlapped results. In general, the acceptance of the Brindley procedure by implanted individuals is positive, as the Brindley stimulator is used for micturition in 70% to 100% of patients at follow-up. Only Tanagho *et al.* in 1989[249] reported low use rates (42%). Many of the 19 patients in this study did not undergo a complete posterior rhizotomy, which, according to the authors, could lead to an inefficient electrical stimulation for micturition. With respect to NDO, it seems that the effect of posterior rhizotomy was good, as the majority of the subjects in all studies were dry at follow-up. Continence rates among the different publications were between 57% and 100%.

Other benefits of the Brindley procedure reported by different authors are: reduction of UTIs,[249,253–256] reduction of AD episodes,[256–258] and increase of bladder capacity.[250,259,260]

The effects of the Brindley procedure on QOL have been assessed in several papers. In 2003, Vastenholt *et al.* administered the Qualiveen questionnaire to assess urinary QOL in a group of 42 patients with complete SCI that had received the Brindley stimulator. Results were compared with a reference group of 400 subjects with SCI not using the stimulator. In general, patients using the stimulator obtained better outcomes in all Qualiveen domains.[255]

Then Borau in 2004 compared general QOL using the SF-36 in a group of 60 patients that had received the Brindley stimulator with a population of 2,250 patients with SCI without the implant. The QOL levels were higher in subjects with the Brindley stimulator.[261]

Martens *et al.* in 2011[262] also compared effects on QOL of the Brindley procedure with a matched control group using both the Qualiveen and the SF-36 questionnaires. These authors reported data from 93 patients who had received the implant and 70 individuals with complete SCI who had not received an implant. Results were divided in three groups: Brindley group, rhizotomy group (patients with the implant but not using it), and control group. Results showed that only the Brindley group showed significantly better scores both in the Qualiveen and the SF-36 questionnaires. In general, the rhizotomy and control groups did not statistically differ from each other. Only in Qualiveen scores, the rhizotomy group showed better scores, although the difference was not statistically significant.

Finally, the Brindley procedure has not been widely adopted, if we consider the low number of implants worldwide.[263] This low adoption occurs despite the Brindley procedure being the only available method that is able to restore bladder management in a "physiological" manner, having better QOL outcomes compared with controls,[254,261,262] and having economic advantages compared with other treatments.[264–267] Reasons for the low adoption of the procedure may include a lack of knowledge of the procedure, fear of surgery, uncertainty of the effects of the surgery and, above all, the irreversibility of the posterior rhizotomy.[248]

Unfortunately, none of the publications selected in this document showed Level of Evidence superior to "studies of 'case series' without a comparison control group". Although it will be almost impossible to run an RCT with the Brindley procedure because of ethical implications, studies with concurrent controls ("prospective case-control or cohort studies") would be, in principle, possible and therefore warranted in the future.

Conclusions

- SARS enables spontaneous voiding and reduces the incidence of UTI in select patients with suprasacral SCI. **[LOE 3]**
- SARS improves QOL in individuals with neurogenic bladder due to SCI. **[LOE 2]**

Recommendations

- Surgeons may use the combination of sacral anterior root stimulation and posterior sacral root rhizotomy as an effective alternative treatment for neurogenic bladder in select patients with suprasacral spinal cord injuries and NDO/DSD. **[GOR C]**
- Surgeons must clearly explain to the patients the effects of SARS on bladder, bowel, and sexual function. **[GOR A]**

5.14 Sacral Neuromodulation

5.14.1 Introduction

Voiding and bowel dysfunction secondary to underlying neurologic disorders is very common. Etiologies include tSCI, central nervous system (CNS) insults such as infections, stroke, MS, Parkinson's disease, and congenital disorders such as spina bifida and caudal regression syndrome. NBD has a profound impact on voiding function, and treatment is typically directed toward the underlying clinical presentation. We review the current literature with regard to electrical stimulation for NBD and the clinical outcomes associated with sacral neuromodulation (SNM), pudendal neuromodulation, and tibial neuromodulation. Neuromodulation plays a key role in the management of non-neurogenic voiding dysfunction; its role in NBD varies greatly with the type of underlying neurologic condition. We focus on its potential in NBD due to SCI.

5.14.2 The physiology of neuromodulation

Neuromodulation is the electrical, chemical, or physical modulation of a nerve to influence the physiologic behaviour of an organ. Tanagho *et al.* in 1989 pioneered the initial investigations into electrical stimulation for neuromodulation.[249] Since this early work, neuromodulation has become an important tool in the treatment of bladder dysfunction.

The exact neural mechanisms responsible for the effects of electrical neuromodulation on the lower urinary tract are unknown. A significant amount of research has focused on the effect of SNM on afferent sensory nerve fibres, with the dominant theory being that electrical stimulation of these somatic afferent fibres modulates voiding and continence reflex pathways in the CNS.[276] The control of sensory input to the CNS is thought to work through a gate-control mechanism.[277] The gate-control theory states that perception of noxious stimuli does not entirely depend on the A-delta and C-fibre sensory nerves transmitting information to the CNS, but on the pattern of peripheral nerve activity.[278] A-delta bladder afferent nerve fibres project to the pontine nuclei to provide inhibitory and excitatory input to reflexes controlling bladder and sphincter function. Afferent C-fibres within the bladder are normally thought to be mechano-insensitive and unresponsive, and thus referred to as "silent" C-fibres. These normally inactive C-fibres may be sensitized by inflammation or infection, thus causing activation of involuntary micturition reflexes and detrusor overactivity.[279] Sensory input from large myelinated pudendal nerve fibres may modulate erroneous bladder input conveyed by A-delta or C-fibre afferents at the gate-control level of the spinal cord.

NDO may then be attributed to a deficiency of the inhibitory control systems involving pudendal afferent nerves. The success of electrical neuromodulation for NDO may result from the restoration of the balance between bladder inhibitory and excitatory control systems.[280] Stimulation of urethral afferents to facilitate the micturition reflex and stimulation of the dorsal nerve of the clitoris to inhibit bladder activity have been demonstrated in animal models for SNM.[281]

Another theory behind the effectiveness of SNM for NDO is that electrical neuromodulation may alter cortical sensory areas of the brain. Blok *et al.*[282] used positron emission tomography (PET) to evaluate regional cerebral blood flow in patients with chronic SNM and those patients with recently activated SNM. The authors' findings demonstrated activation of different areas of the cerebral cortex among patients with chronic and acute SNM. This finding also implies that the brain undergoes neuroplasticity during periods of long-term SNM in the areas of NDO, awareness of bladder filling, the urge to void, and the timing of micturition. Other studies have used changes in somatosensory evoked potentials before and after SNM to illustrate the cortical effects of SNM.[283]

SNM has also been used effectively for the treatment of non-obstructive urinary retention, and while the mechanism of action is not entirely clear, experimental data does shed some light in this area. One such study by Schultz-Lampel *et al.*[284] investigated the effects of direct sacral nerve stimulation on detrusor contractility in cats. The authors' data suggested that sacral nerve stimulation at low frequencies resulted in detrusor contractions with an associated "rebound" effect, with increasing amplitude of detrusor contractions with cessation of the sacral stimulus. The authors suggest that this rebound effect may be attributed to the sacral stimulus enabling previously inhibited bladder efferent activity and thus allowing a bladder contraction.

Neuromodulation may also remedy DSD and the inability to void by mediating the alteration of afferent signals delivered to the spinal cord that affect activity and basal tone of the pelvic floor.[285]

5.14.3 Sacral nerve stimulation after SCI

5.14.3.1 Efficacy

Sacral nerve stimulation has long been a reliable form of neuromodulation for various types of lower urinary tract dysfunction including overactive bladder (OAB) and non-obstructive urinary retention. These two therapeutic indications make sacral nerve stimulation an attractive option for the treatment of patients with NBD.

In 2001, Chartier-Kastler and colleagues evaluated urodynamic changes with acute stimulation of the sacral nerve.[286] Fourteen patients with NDO and DSD related to SCI underwent baseline urodynamic testing. These patients then had a temporary electrode placed at the S3 foramen and stimulated for 10 minutes. Urodynamics were repeated and improvement in maximum bladder capacity and resolution of NDO were documented, suggesting the SNM may have an acute effect on these parameters in the SCI NBD patient.

Lombardi *et al.* described their experience with SNM in patients with an incomplete SCI and NBD with a mean follow-up of 61 months.[287] The authors divided their study population into two groups, with one group consisting of patients with urinary retention (n=13) and the other group consisting of patients with OAB symptoms (n=11). In the urinary-retention group, 9 of 13 (69%) patients reported a 50% improvement in baseline voiding parameters with a significant decrease in the number of catheterizations and a significant increase in the frequency of void and volume voided. At the conclusion of the study, 38% of patients no longer required catheterization for bladder emptying. Among the patients with OAB symptoms, an 80% reduction in daytime frequency was observed, with 3 of

7 subjects with previous urge incontinence remaining completely dry during the study period. This study illustrates the dual efficacy of SNM for the spectrum of voiding dysfunction found in SCI patients.

In 2014 Lombardi *et al.* published another series of patients with partial SCI with non-obstructive urinary retention treated with SNM.[288] This was a retrospective review of 87 patients who underwent first-stage SNM from 2003 to 2012. In the study, 49 subjects (57.5%) did not respond to first-stage SNM while 36 (42.5%) had a positive response and underwent a permanent implant. Those with a positive response had a significant reduction in PVR and reduced intermittent catheterization.

Patients having a first sensation of bladder filling during urodynamics at baseline were more likely to respond to SNM. At 50 months (range: 6–95 months), 23 patients maintained a clinical response to SNM and 11 patients were deemed "inconstant responders", as they had a least one failure during the post-implant follow-up. These 11 patients underwent a new implant at the contralateral S3 nerve root, and all recovered a positive clinical response. Two of these patients failed again, and both underwent an S4 lead placement and responded again to SNM. As all subjects who failed over time to SNM had restored voiding by the placement of an electrode at a "virgin" sacral nerve root, the authors suggest that nerve fatigue may be the root cause of the failure.

A recent study by Chen and Liao included 9 SCI patients with neurogenic bowel and bladder tested with SNM.[289] Two patients had complete cord injury and neither had a clinical response, suggesting that afferent transmission is important in the success of SNM. Of the 7 patients with partial SCI, 5 went on to permanent implant, and at 17.5 months of follow-up, 4 of the 5 maintained at least a 50% improvement in voiding or bowel symptoms.

Other trials of SNM for NBD have been less promising. Hohenfellner *et al.* described their experience with SNM among patients with NBD.[290] Their patient population consisted of patients with bladder storage failure due to detrusor hyperreflexia (n=15), failure to empty due to detrusor areflexia (n=11), and combined bladder hypersensitivity and detrusor areflexia (n=1) with a mean follow-up of 89 months. In 8 patients (30%), symptoms of lower urinary tract dysfunction were attenuated by 50% for 54 months (range: 11–96 months). After this time period, all implants became ineffective, except in 1 patient. This study illustrates that while SNM may be effective for NBD, the results may be temporary.

A fascinating study by Sievert *et al.* aimed to investigate the effect of early bilateral SNM in SCI patients during the atonic "spinal shock" phase on final bladder function after resolution of spinal shock.[291] Ten patients with acute SCI were implanted with bilateral sacral nerve stimulators at 2.9 months (range: 0.8–4.5 months) from the initial injury. Compared with a similar SCI group not treated with SNM, the early-stimulation group did not develop incontinence or DSD, suggesting that early SNM during areflexia and "spinal shock" might preserve nerve plasticity and avoid NDO.

5.14.4 Complications of SNM

Complications from SNM have been well described and are usually minor adverse events. The rate of complication ranges from 12% to 53% depending on the examined series.[292,293] A recent article by White and colleagues[293] followed patients receiving SNM for urinary urge or frequency, urge incontinence, and urinary retention to record the incidence of adverse events and determine whether there are predictive factors predisposing patients to adverse events. At a mean follow-up of 37 months, 30% of patients had experienced adverse events. Lead migration, lack of efficacy, and trauma were the most common adverse events. Significant predictors of adverse events included a history of trauma, a change in body mass index class, enrollment in a pain clinic, the duration of follow-up, and a history of adverse events.

5.15 Pudendal Neuromodulation for Neurogenic Bladder

The pudendal nerve is a peripheral nerve that is composed mainly of afferent sensory fibres from sacral nerve roots S1, S2, and S3. The bulk of afferent sensory fibres are contributed by S2 (60%) and S3 (35%) according to afferent activity mapping procedures.[294] Consequently, the pudendal nerve is a major contributor to bladder afferent regulation and bladder function. Pudendal nerve entrapment often leads to significant voiding dysfunction including urinary incontinence and NDO.[295] Because the pudendal nerve carries such a large percentage of afferent fibres, neuromodulation of the pudendal nerve is an attractive option for refractory NDO.

Opisso and colleagues compared patient-controlled pudendal nerve stimulation with automatic stimulation as treatment for NDO.[296] A total of 17 patients with NDO underwent 3 cystometric filling trials. The first filling cystometry was used to determine bladder capacity. The second filling cystometry was done with automatic electrical stimulation of the pudendal nerve when the bladder reached a threshold pressure of 10 cm H_20 above the mean detrusor pressure. The third filling cystometry was done with patients controlling the pudendal stimulation who were asked to begin stimulation when they could sense the onset of an uninhibited bladder contraction. Automatic and patient-controlled pudendal nerve stimulation resulted in greater bladder capacity in all subjects and inhibited more than an average of 2 detrusor contractions per filling. The authors suggest that based on their findings patients with neurogenic detrusor overactivity may be able to use patient-controlled stimulation of the pudendal nerve to increase bladder capacity and prevent uninhibited detrusor contractions.

Spinelli *et al.* described their experience with pudendal nerve stimulation using the InterStim™ device (Medtronic, Minneapolis, Minnesota, USA) with a quadrapolar tined lead placed at Alcock's canal in 15 patients with NBD.[297] In this study, the average number of incontinent episodes among this group of patients decreased from 7 to 3 episodes per day. Eight patients became continent during the screening phase of the study and 4 patients had a greater than 50% improvement in the number of incontinent episodes experienced per day. Urodynamic evaluation in 7 patients revealed a significant increase in detrusor capacity and a decrease in maximal detrusor pressure. Constipation improved in the majority of patients, and the one patient with FI became dry.

The authors suggest that based on this preliminary data, pudendal nerve stimulation is an effective therapeutic alternative for neurogenic OAB patients who are non-responders to antimuscarinic drugs and for whom traditional sacral neuromodulation has had poor results. The authors also point out that the minimally invasive nature of pudendal nerve stimulation using the quadrapolar tined lead is an attractive alternative to more invasive procedures such as bladder augmentation.

5.16 Neuromodulation of the Posterior Tibial Nerve for Neurogenic Bladder

The posterior tibial nerve is a peripheral mixed sensory-motor nerve that originates from spinal roots L4 through S3, which also contribute directly to sensory and motor control of the urinary bladder and pelvic floor. Stimulation of the posterior tibial nerve was pioneered by Stoller and colleagues with the introduction of the Stoller Afferent Nerve Stimulator (SANS), which delivers electrical stimulation to the posterior tibial nerve via a 34-gauge needle just cephalad to the medial malleolus.[298] Randomized controlled trials have shown posterior tibial nerve stimulation (PTNS) to be effective in the management of OAB.[299]

Unfortunately, there is sparse data on PTNS for the treatment of bladder or bowel dysfunction after SCI. A single article by Mentes *et al.*[300] on 2 patients with partial SCI looked at the impact of PTNS on FI. The subjects were treated with 30 minutes of PTNS every other day for 4 weeks, and maintenance treatments were performed every 2 months. Rectal sensory thresholds, resting and maximum squeeze pressures, Wexner FI score, and the FI severity index were all improved in both patients after treatment. Additional data is needed on the impact of PTNS in the management of SCI.

Conclusion

- Sacral neuromodulation has been used extensively in non-neurogenic bladder dysfunction and in select etiologies of NBD such as MS, but there is little evidence in SCI NBD. **[LOE 2]**

Recommendations

- Urologists may safely use neuromodulation in well-selected NBD patients, but use in SCI should be considered experimental and limited to the research setting. **[GOR C]**

- Researchers should pursue robust, randomized, controlled clinical trials to provide better level of evidence for the role of neuromodulation in SCI. **[GOR A]**

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C6

Neurogenic Bowel, Fertility, and Sexuality in the Spinal Cord Injured Patient

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Committee 6

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6.1 Introduction

A spinal cord injury (SCI) impacts many other body systems in addition to the urinary tract. In this chapter, we review neurogenic bowel management of the SCI patient, female and male fertility potential after injury, pregnancy after injury, and sexual rehabilitation.

6.2 Methods

A comprehensive literature search regarding neurogenic bowel management, sexual function, sexual rehabilitation, fertility, and pregnancy in SCI patients was performed. Articles were compiled, and recommendations in the chapter are based on group discussion and follow the Oxford Centre for Evidence-based Medicine system for Levels of Evidence (LOEs) and Grades of Recommendation (GORs).

6.3 Management of Neurogenic Bowel

6.3.1 Physiology

Neurogenic bowel in SCI patients manifests as changes in colon motility and/or loss of anorectal sphincter function. Patients with injuries above the conus medullaris (above approximately L1–L2) generally have symptoms of increased bowel motility and poor anorectal sphincter relaxation. Patients with injuries below the conus medullaris (below approximately L2) are more likely to have an areflexic colon and low anal sphincter tone. Trivedi *et al.* demonstrated this physiological difference in anorectal manometry in 24 suprasacral injury, 13 intrasacral injury, and 20 normal control patients.[1] Retrospective studies also suggest that complete SCI lesions result in slower colon transit time compared to incomplete injuries.[2]

6.3.2 Symptoms

Neurogenic bowel symptoms are highly prevalent in the SCI population and can have a significant impact on quality of life (QOL). Liu *et al.* surveyed 128 SCI patients and demonstrated a negative relationship between severity of neurological bowel symptoms and physical functioning.[3] In a different study, Stone *et al.* prospectively studied 127 consecutive SCI patients and noted that 34% reported chronic bowel problems. The symptoms that most impacted QOL included poorly localized abdominal pain (14%) and difficulty with bowel evacuation (20%).[4]

Other survey studies demonstrate that constipation, fecal incontinence, and fecal urgency are the most common bothersome symptoms for SCI patients. Ng *et al.* surveyed 110 people with longstanding SCIs (mean time with injury: 17 years) using validated instruments, and found that the most common gastrointestinal symptoms were constipation and fecal incontinence (46% and 41%, respectively).[5] Similarly, Tate *et al.* reported on bowel QOL in 291 SCI patients managed in an SCI Model System unit, and found that constipation and bowel incontinence were reported by 38.5% and 74.2% of the patients, respectively, with 14% noting that the symptoms were severe.[6] In a different cross-sectional analysis of the same institution, Cameron *et al.* found that neurogenic QOL scores were also reported to be worse in patients with SCIs than in those with other neurogenic conditions (excluding spina bifida). QOL scores were particularly severe in SCI patients with higher-level injuries.[7] Lynch *et al.* also found that fecal urgency and fecal incontinence were significantly more prevalent in SCI patients than in uninjured controls.[8]

Autonomy in regulating bowel function may also be predictive of future morbidity from neurogenic bowel. Pagliacci *et al.* prospectively studied 511 SCI patients from 7 SCI units and 17 rehabilitation centres across Italy between 1997 and 1999, and found that patients without bowel/bladder autonomy had greater odds of experiencing a significant complication or of requiring a hospital readmission (odds ratio [OR]: 2.2; p<0.001). Some of the more common complications included urological and spinal hardware complications.[9]

6.3.3 Assessment tools

There are several different assessment tools and QOL questionnaires for measuring bowel function in the SCI patient, but none are universally accepted. Krogh *et al.* have worked to develop a standardized data set to compare bowel function across SCI populations. The data set includes 26 different items describing symptoms, a clinical assessment of the anal sphincter, and a description of colorectal transit times. Although the data set has shown reliability among providers, it has not been validated across SCI populations.[10,11] More recently, Tulsky *et al.* created a combined bladder and bowel QOL questionnaire (the Spinal Cord Injury – Quality of Life [SCI-QOL]) that evaluates 38 bladder items and 52 bowel items. When used as a computer adaptive questionnaire, the instrument proved to be robust in differentiating severity of symptoms.[12] Patel *et al.* performed a systemic review of existing neurogenic bladder and bowel questionnaires, and found that current patient-reported outcome measures and QOL assessments are heterogeneous among neurogenic bladder studies. Therefore, this may lead to different conclusions, depending on which questionnaire is used.[13]

6.3.4 Treatment

Treatment plans for SCI-related neurogenic bowel focus on timely, predictable evacuation of the bowels.

6.3.4.1 Diet modification

The effect of diet modification on treating neurogenic bowel symptoms in SCI patients is poorly understood. Cameron *et al.* studied the relationship between fibre intake and colon transit time in SCI patients. They found that a high-fibre diet increased colon transit time in 11 SCI patients, and prolonged constipation from 28.2 to 42.2 hours.[14] Tate *et al.* also noted that elevated neurogenic bowel symptom scores, indicating a lower bowel-specific QOL, correlated with increased fibre intake.[6] Similarly, Badiali *et al.* found that transit time improved in 10 SCI patients after 4 weeks of a low-residue diet, a planned fluid intake schedule, and a bowel regimen.[15] Ozisler *et al.* created a comprehensive bowel-monitoring program for both upper and lower motor neuron SCI patients that included diet regulation and fluid management. After implementation in 55 patients, the patients' use of oral medications, enemas, and manual evacuation applications to manage bowel symptoms decreased. The patients also had less constipation and abdominal pain.[16]

6.3.4.2 Bowel stimulation and irrigation

Many SCI patients who experience constipation perform anorectal stimulation. There is some single-study observational evidence to suggest that digital stimulation increases colonic motility. Korsten *et al.* studied colonic motility with a manometric catheter in six SCI patients undergoing digital rectal stimulation (DRS). They noted that the mean number of peristaltic waves per minute increased from 0 at baseline to 1.9 during stimulation ($p<0.05$), and this increased colonic activity continued during the period immediately after cessation of DRS.[17] However, there are sparse data supporting the clinical efficacy of suppository use or digital stimulation for neurogenic bowel management. A 2014 Cochrane review examining the management of fecal incontinence and constipation in central neurological diseases commented that with the exception of a small trial comparing two bisacodyl suppositories, one polyethylene glycol-based and one hydrogenated vegetable oil-based, there are surprisingly little outcome data on these therapies. **[LOE 2]**[18]

More robust data support the efficacy of transanal irrigation to treat constipation in SCI patients. Christensen *et al.* performed a prospective, randomized, multicentre study comparing transanal irrigation (42 patients) with conservative bowel therapy (45 patients). Over a 10-week period, transanal irrigation improved constipation, fecal incontinence, and symptom-related QOL compared with conservative treatment (all $p<0.05$). When followed over time, only two bowel injuries were observed in over 110,000 irrigation procedures in the study population.[19] Examined through a Markov decision process model to determine long-term cost-effectiveness, initiating transanal irrigation could result in a 36% reduction in fecal incontinence episodes, a 29% reduction in urinary tract infections, a 35% reduction in the likelihood of stoma surgery, and a 0.4% improvement in quality-adjusted life-years compared with continuing conservative therapy.[20]

6.3.4.3 Pharmacologic

Few medications are available that improve bowel transit time after SCI. Although cisapride has been shown in three randomized controlled trials to significantly reduce colon transit time,[21] the medication has since been withdrawn in the United States and several other countries due to risk of cardiac arrhythmia. In a small double-blind, crossover study, Rosman *et al.* examined the efficacy of intramuscular neostigmine/glycopyrrolate injections in seven SCI patients, and found that neostigmine/glycopyrrolate reduced total bowel evacuation time from 98.1 ± 7.2 min to 74.8 ± 5.8 min ($p<0.05$). Heart rate and blood pressure were not significantly affected by the injections.[22]

6.3.4.4 Neurostimulation and neuromodulation

Neurostimulation and neuromodulation have been investigated for the treatment of neurogenic bowel. However, since many studies are limited by small sample sizes and/or follow-ups, there is little definitive evidence on the safety and efficacy of neurostimulation and neuromodulation in the SCI population.

One of the most studied neurostimulation interventions is the Brindley procedure, which combines a sacral dorsal root rhizotomy with sacral anterior root stimulation to treat neurogenic bladder and bowel symptoms. Van Kerrebroeck *et al.* reported on the treatment of 52 patients. After undergoing the Brindley procedure, 43 of 47 patients noted improvements in bladder symptoms, and 17 of these patients used stimulation alone to defecate over a minimum 6-month follow-up period.[23]

Lombardi *et al.* retrospectively examined sacral neuromodulation treatment in 23 patients with neurogenic bowel from incomplete SCI. In 12 of the subjects with constipation, the median number of evacuations shifted from 1.65 to 4.98 per week ($p<0.05$). In 11 subjects with fecal incontinence, the median number of episodes per week shifted from 4.55 (prior to neuromodulation) to 1.32 ($p<0.05$).[24]

6.3.4.5 **Surgery**

SCI patients may change bowel management strategies over time. Hwang *et al.* longitudinally studied 131 SCI adults who had sustained an injury prior to the age of 19 years. The group found that over time, the odds of an SCI patient selecting a colostomy for bowel management increased (OR: 1.071; $p=0.047$). Longer evacuation time was a risk factor for prompting a change in bowel habits.[25] Ostomy has been compared with conservative management bowel programs, and has been found to have equivalent or superior QOL outcomes in symptomatic patients. Branagan *et al.* reported that time spent on bowel care decreased from 10.3 to 1.9 hours/week after ostomy in 28 surveyed SCI patients.[26] Munck *et al.* reported similar improvements in time spent on bowel management in 23 SCI patients treated with colostomy.[27] Satisfaction appears to be high among SCI patients treated with an intestinal ostomy. Coggrave *et al.* performed a multicentre, retrospective, cross-sectional survey of 92 SCI patients across five UK SCI centres, and found that 89% of those with an intestinal stoma would definitely or probably undergo surgery again.[28] Although there is no consensus on the best surgical technique, solid stool is generally considered easier to manage than more liquid stool.[29] In addition, high patient satisfaction has been reported for both left- and right-sided colostomy.[30] Small series note a higher dissatisfaction among SCI patients with ileostomy compared to colostomy.[28]

Malone antegrade continent enema (MACE) surgery can also be offered to facilitate bowel emptying. In this procedure, the appendix is imbricated along the taenia right colon to create a flap valve, and the tip of the appendix is brought out through the abdominal wall as a continent catheterizable stoma for bowel irrigation. In some patients with severely impacted stool, enemas may be more effective if they can get "upstream" of the stool. Although primarily used in the pediatric neurogenic bowel population, there are data to suggest the efficacy of MACE in adults with neurological or congenital bowel conditions.[31,32]

6.3.5 Conclusions

- Patients with injuries above the spinal cord conus medullaris will most likely have symptoms of increased bowel motility and poor sphincter relaxation. Patients with injuries below the conus medullaris are more likely to have an areflexic colon and low anal sphincter tone. **[LOE 2]**

- Severity of neurogenic bowel symptoms affects overall physical functioning and QOL in SCI patients. **[LOE 2]**

- QOL survey data demonstrate that constipation, fecal incontinence, and fecal urgency are the most common bothersome bowel symptoms in SCI patients. **[LOE 1]**

- High-fibre diet may increase colon transit time, resulting in more constipation in SCI patients. **[LOE 3]**

- Transanal irrigation is an effective, low-morbidity intervention for refractory neurogenic bowel in SCI patients. **[LOE 1]**

- Colostomy may significantly reduce stool transit time in SCI patients compared to conservative bowel management plans. **[LOE 2]**

- Colostomy may offer a better QOL compared to ileostomy. **[LOE 3]**

6.3.6 Recommendations

- Clinicians should follow bowel symptoms in SCI patients using validated questionnaires (e.g., the SCI-QOL or the International Bowel Function Basic SCI Data Set) to determine the impact of symptoms and the effectiveness of treatment plans. **[GOR B]**

- Clinicians may recommend a low-fibre diet to reduce colon transit time for SCI patients. **[GOR C]**

- Clinicians should discuss transanal irrigation as a treatment option for appropriate SCI patients with refractory constipation. **[GOR B]**

- Clinicians should discuss colostomy with SCI patients who have a low QOL when using conservative bowel management plans. **[GOR B]**

6.4 Sexual Function

6.4.1 Neurophysiology

The physiology of sexual function in able-bodied men and women is well described in the literature and is beyond the scope of this chapter. Sexual responses (sexual interest, genital arousal in men and women, ejaculation in men, and orgasm in men and women) depend on minute-to-minute feedback. This feedback is influenced by emotional contexts, physical reactions, and reinforcing triggers and/or negative distracters, as outlined in the biopsychosocial sexual response model.[33] SCI alters sensation and motor ability. In addition, SCI can be associated with pain and incontinence (both negative distractors) and even concomitant brain injury, which can alter central processing.

Genital arousal consists of vasocongestion to the pelvis and the development of neuromuscular tension, resulting in penile erection in men, and vaginal lubrication and accommodation in women, accompanied by various cardiovascular responses, such as increased heart rate, blood pressure, and respiratory rate. Genital arousal, which can be can be objectively measured, is also usually accompanied by subjective or psychogenic arousal in the brain. Able-bodied persons describe a fullness and awareness of tingling, pleasant sensations in their pelvis and sexual arousal in the brain. The mind-body interplay of sensations, especially genital sensations, and ability to move to accommodate sexual stimulation is a given for able-bodied persons. After SCI, significant adaptation to altered signaling and feedback must occur.

Arousal is triggered by many inputs to the cerebral cortex, including inputs from all the five senses to the brain. All afferent sensory and hormonal influences are assessed to generate neuronal signals coordinated in the limbic system, the hypothalamus, and other midbrain structures. The sensorimotor, emotional, and cognitive aspects of sexual behaviour stem from several cortical areas, particularly the temporal lobes, and the coordinated activity of the autonomic nervous system comes from the insula, the anterior cingulate cortex, and the hypothalamus.[34] Subjective sexual arousal is a complex phenomenon made up of multiple interoceptive and attentional processes (recently documented by functional magnetic resonance imaging [MRI]),[35] whereas objective sexual arousal is made up of the genital arousal responses discussed below. After SCI and loss of sensory feedback, subjective sexual arousal takes on a new importance.

Neurological signals from the brain descend the spinal cord to the specific spinal cord centres responsible for genital arousal (penile erection and vaginal lubrication and accommodation) and ejaculation. Since descending brain pathways are both excitatory and inhibitory, in nonsexual situations (i.e., the majority of the time), inhibitory tone dominates (supratentorial inhibition). When the balance of central excitatory and inhibitory neurotransmitters shifts to primarily excitatory, supratentorial inhibition is removed, and descending signals allow for spinal cord activation, as long as the spinal cord is intact. After SCI, the descending neurological signals are variously interrupted, depending on the level and completeness of the injury. Incomplete injuries may allow for some volitional or supratentorial control over the reflexes, whereas high complete injuries do not, accentuating the sexual reflexes (i.e., sensitive reflex erections).

The sexual response involves the coordinated participation of the nervous system, comprising the sacral parasympathetic (pelvic nerve), thoracolumbar sympathetic (hypogastric and lumbar sympathetic chain), and somatic (pudendal) nerves.[36] After leaving the spinal cord, these nerves travel jointly through the pelvic plexus and cavernous nerves to the genitalia, creating vasocongestion and neuromuscular tension. Nitric oxide (NO) is the primary neurotransmitter responsible for smooth muscle relaxation, resulting in tumescence of the erectile tissue in both sexes (filling of the corpora cavernosal bodies results in penile erection in men and vulvar swelling, clitoral engorgement, and vaginal lubrication and accommodation in women). NO is primarily released from intact nerve endings (neuronal nitric oxide [nNO]), but is also generated from healthy endothelium nitric oxide (eNO). In men, a stocking-like fibroelastic structure (tunica albuginea) surrounds the expanding erectile corporeal bodies, increasing the intracavernosal pressure. The tunica is pierced by veins, and with the expansion of the corporal bodies, the veins are compressed against the tunica, creating a veno-occlusive mechanism. Erectile rigidity occurs when arterial inflow exceeds outflow, and is accentuated by pelvic floor contraction. Women have a thinner tunical structure around the clitoral body, and the clitoris becomes tumescent rather than rigid.

The ejaculation reflex is controlled by both sympathetic (arising from T10–L2 through the sympathetic chain and the hypogastric plexus) and somatosensory neural inputs (from the S2–S4 spinal segments).[37] The spinal sympathetic and parasympathetic centres appear to have crucial roles in emission, while the somatic centre appears to have a crucial role in expulsion. In addition, there is likely a spinal generator of ejaculation in the L3, L4, and L5 segments.[38] Erection, seminal emission, and propulsatile ejaculation are separate phenomena and have different innervations.

The neurology of orgasm is not clearly understood, nor is there a universally agreed upon definition. However, rhythmic pelvic floor contraction, smooth muscle contraction, and internal genital and/or viscus distension are interpreted by the cerebral cortex as pleasurable, especially in the pelvic area (genital orgasm) if sensation is intact.[39] For genitally induced orgasm to be recognized, the lateral spinothalamic tract and corticospinal tract need to be at least partially intact. Non–genitally induced orgasm can be provoked by high mental arousal from fantasy, or from other somatic inputs from outside the genital area (level of lesion, nipple stimulation, head and neck stimulation), or visceral inputs secondary to cardiovascular excitation.[39]

6.4.1.1 Genital arousal

Genital arousal signals travel in the spinal cord via two distinct pathways: the *psychogenic* pathway, which originates in the brain and communicates through the T10–L2 region of the spinal cord, and the *reflex* pathway, which is located in the sacral (S2–S4) cord. Studies have shown the neurological ability to achieve psychogenic arousal after SCI can be predicted in both men and women by the combined degree of preservation of surface sensation to pinprick and light touch in the T11–L2 dermatomes.[40] Genital arousal occurs with parasympathetic stimulation, promoting the tumescence or erectile process. Genital sympathetic stimulation will cause the detumescence of genital structures. Without the use of medications or assisted devices, the natural erectile ability of men with SCI, from either psychogenic or reflexogenic sources, will depend on the level and completeness of the lesion. Although erectile ability has been reported to be 62% to 75%,[41] about two-thirds of men with SCI find their erections to be unreliable or short in duration, necessitating the use of some form of erection enhancement in 60% of them.[41]

The vast majority of men and women with SCI find it difficult to become physically aroused, and more women (74.7%) than men (48.7%) have difficulty becoming psychologically aroused.[42,43] Tingling sensations (35.3%) and spasms (35%) were the most reported physical sensations noted by men and women with SCI.[43] Of the women with SCI (*n*=87), 58.6% could feel the buildup of sexual tension in their body during sexual stimulation (this was positively correlated with the presence of genital sensation), and 64.4% stated that they could feel this buildup in their head.[42] Of the men (*n*=199), roughly half reported no difficulty becoming mentally aroused (48.7%), but difficulty becoming physically aroused was reported by the vast majority (84.9%). Only about half the men could feel a buildup of sexual tension in their head and their body,[41] and 61.8% were able to achieve erection without medication or assistance (albeit not reliable and of short duration).[41] As with women, having genital sensation assisted men with genital arousal. However, the presence of spasm also assisted with erection.[41] For both men and women, head, neck, and torso areas were arousing, as were the genitals, if they had sensation. With the reduction or elimination of genital sensation after SCI, paying attention to sexual or pleasant signals from areas that do have sensation becomes paramount. These areas can be regarded as uncovered potential or "new" areas. In the study by Anderson *et al.*, both men and women with SCI noted new areas of arousal, especially at the level of their lesion (mainly men), with just under 50% experiencing new areas of arousal above the level of their lesion.[41,42] Furthermore, there is also a focus on cerebrally initiated sexual response, illumining the power of "brain sex," which is often suggested for SCI through Tantric practices.[44]

6.4.1.2 Ejaculation

The ejaculation reflex, which is primarily a sympathetic phenomenon, consists of two phases (seminal emission and propulsatile ejaculation), and results in the propulsion of sperm and seminal fluid (semen) distally out the urethral opening. While ejaculation potential depends, like erection, on the level and completeness of the lesion, ejaculation is more likely in men who have preserved bladder and bowel control, spasticity, the ability to achieve a psychogenic erection, the ability to retain an erection, and through direct penile manipulation versus vaginal intercourse.[45,46] Ejaculation is more predictable when there is a significant increase in blood pressure with sexual stimulation.[46] With unassisted masturbation alone, only about 10% to 15% of men with SCI can ejaculate. With the use of penile vibrostimulation (PVS), this number increases, especially if the injury is at or rostral to T10.[37] Having an intact dorsal penile nerve when the injury is rostral to T10 (indicating an intact ejaculatory reflex) is predictive of ejaculatory capacity to vibrostimulation, as is the level of the lesion (ejaculatory capacity is 86% when the injury is T10 or rostral, and is 15% when the injury is T11 or caudal).[37]

6.4.1.3 Orgasm

Orgasm is the release of vasocongestion and neuromuscular tension or the peak of sexual excitement. It is usually accompanied by pleasant genital and physical sensations, and is associated with mental euphoria. Orgasmic release (often accompanied by ejaculation in men) occurs physiologically once the neurological orgasmic threshold is crossed.[47] Varying orgasmic thresholds are inherent in each person. These thresholds can be altered by neurological changes, medications (e.g., selective serotonin reuptake inhibitor [SSRI] antidepressants increase the threshold, making orgasm more difficult to achieve), or hormone alterations (e.g., lowered testosterone makes orgasm more difficult to achieve in men). While orgasmic release is often generated by genital stimulation, it can also be accomplished by nongenital stimulation and by the brain alone (fantasy-induced orgasm or orgasm during sleep). Although orgasm most likely has a reflexogenic component, since it can be trained and reinforced with practice, the actual neurology of orgasm has not been accurately identified. The physiological correlates of orgasm include rhythmic contraction of the lower pelvic muscles (women may also experience uterine contractions), and other involuntary spasms or vocalizations.[48] However, a satisfying sexual experience is not dependent on orgasmic ability.

Approximately 40% to 50% of men and women with SCI are able to reach either self-defined or laboratory-recorded orgasmic release, although the length and intensity of stimulation required to reach orgasm may be longer than it was before injury.[40] After SCI, having a complete versus incomplete injury (regardless of level of injury), having an intact sacral reflex arc, and having genital sensation are more predictive of orgasm in both sexes.[40,45] Although orgasm and ejaculation are likely to occur together in men with SCI, the presence of orgasm is not necessarily connected with the presence of ejaculation.[49] Chéhensse *et al.*[38] published a review of articles from 1955 to 2012, and found that ejaculation after complete SCI occurred with masturbation or coitus 11.8 % of the time, with the use of PVS followed by masturbation 47.7% of the time, and with the use of acetylcholinesterase inhibitors followed by masturbation 54.7% of the time. In men with incomplete SCI, the percentages were 33.2%, 52.8 %, and 78.1%, respectively. While most men with lower lumbosacral lesions maintain natural ejaculation, in some, the distressing onset of secondary premature ejaculation may occur, likely from simultaneous activation of psychogenic erection and emission.[50]

The likelihood of either reaching ejaculation or experiencing orgasm after SCI may be modestly enhanced by the utilization of oral erection medications, such as phosphodiesterase type 5 (PDE5) inhibitors, which are now commonly used in many men with SCI, either sexually or in fertility clinics. The likelihood of reaching ejaculation and/or experiencing orgasm may also be improved with the use of sympathomimetic drugs, such as midodrine.[51,52]

Pleasurable or orgasmic experience at ejaculation may also be related to the phenomenon of autonomic dysreflexia (AD), which is defined as an increase in systolic blood pressure by 20 mmHg.[53] AD is a potentially dangerous condition of episodic hypertension triggered by noxious and non-noxious afferent stimuli below the level of the SCI lesion and is well known in the SCI population.[45] It can result in severe headache, nausea, and sweating. It can also render sex unenjoyable or lead to active avoidance of sex. In fact, in a recent survey, AD interfered with the motivation to be sexual in 28% of women and 16% of men.[41] However, researchers have found that if AD does not occur, few orgasmic sensations are reported and that with mild-to-moderate AD, pleasurable climactic sensations are reported. In contrast, unpleasant or painful sensations are reported with severe AD.[54] The data for men with SCI encourage sexual rehabilitation, emphasizing self-ejaculation, self-exploration, and cognitive reframing to maximize the perception of sexual sensations and climax. These principles may also apply to women with SCI. Especially for women, compounding psychological issues beyond the sensation changes (e.g., feeling unattractive or less attractive, having less self-confidence, or having fear of incontinence) may also interfere with the ability to reach orgasm.[55]

There are few tools in the literature to describe and assess sexual climax, referred to as orgasm. However, Mah and Binik[56] did develop a questionnaire to assess the subjective experience of orgasm in able-bodied persons, as did Courtois and colleagues for patients with SCI.[51] Functional MRI studies have also attempted to look at cerebral correlates of orgasm after SCI.[57] Functional MRI of the brain during orgasm in women with an injury at T10 or higher using vaginal-cervical mechanical self-stimulation suggested that the vagus nerves provide a spinal cord–bypass pathway for vaginal-cervical sensibility, and activation of this pathway can produce analgesia and orgasm.[58]

6.4.2 Management

6.4.2.1 Sexual drive

6.4.2.1.1 Low sexual drive

Managing biological or medical factors (e.g., replacement of lowered testosterone or estrogen), treating depression (which leads to low libido and poor genital arousal), addressing the method of bladder or bowel management and of incontinence, and managing fatigue or pain can greatly improve sexual motivation and payoff. Iatrogenic medications primarily affect sexual drive, as well as affect sexual function, and secondarily affect sexual interest. Psychological and relationship issues affecting sexual motivation also need to be addressed by the appropriate resources. Testosterone replacement to the eugonadal range can be considered in hypogonadal men with SCI,[59] and has been used in postmenopausal women without SCI with some precautions. Flibanserin, a newly US Food and Drug Administration (FDA)-approved drug for premenopausal woman with hypoactive sexual desire, has not been studied in women with SCI. There are also some concerns around flibanserin lowering blood pressure.[60]

6.4.2.1.2 Hypersexuality

Overt hypersexuality must be managed by ruling out brain injury, other neurological conditions, and medications that may be causing the issue. Treatment of hypersexuality is mainly behavioural, with the rare use of antiandrogens or psychotropic medications.

6.4.2.2 Genital arousal disorders

Treatment for erectile dysfunction (ED) in men includes the use of PDE5 inhibitors, which have been quite successful (>80% response), especially in those with an upper motor lesion. Headache and facial flushing are common side effects and can be misinterpreted as AD. PDE5 inhibitors rely on NO to relax the smooth muscle in erectile tissue and create an erection. NO, while usually released from nerve endings secondary to sexual arousal, can be released by sacral reflex activity in men with higher and/or complete SCI. NO is also produced by healthy endothelium. The main issues with the use of PDE5 inhibitors in men with SCI are that they can cause hypotension and dizziness in an already hypotensive population, and that they cannot be used with nitrates (which are traditionally used for angina, but can be used to treat AD). Starting with lower doses of prn (as needed) sildenafil citrate (Viagra®) and vardenafil (Levitra®), whose maximal effect is from 1 to 4 hours after taking, is prudent due to their hypotensive effects. The use of tadalafil (Cialis®), prn or once daily, can also be beneficial, but has a longer-lasting effect. In addition, daily low-dose use of tadalafil in quadriplegics may cause frequent unwanted erections. The new PDE5 inhibitor avanafil (Stendra®), currently available in the United States, has not been evaluated in the spinal cord population, but can be assumed to be similar in efficacy.

Second-line choices for erection enhancement include the use of vacuum erection devices (VEDs), where a cylinder is placed over the penis and blood is drawn into the tissues, thereby creating an erection. The erection is maintained by a penile ring at the base. However, the ring should not be left on for more than 45 minutes because this can be a potential hazard in men who are genitally insensate. Perineal training for men who retain some innervation to their pelvic floor may assist with penile tumescence and make second-line therapies potentially more viable.[61]

Third-line choices include invasive intracavernosal (penile) injections of single or mixed medications (prostaglandin E1, papaverine, and phentolamine) that directly relax the cavernosal smooth muscle. While these intracavernosal injections are very effective, there is the risk of priapism in the SCI population. Very small doses and appropriate training are required, along with instructions on how to conservatively reduce the erection with the use of over-the-counter sympathomimetic medications, such as pseudoephedrine (with awareness of AD risk); with ejaculation (if possible); or with the application of cold to the penis. Prevention is the best strategy. The intraurethral application of prostaglandin (alprostadil [MUSE®]) has not been very successful in the SCI population.[62] The fourth-line intervention, surgical penile prosthesis, is only utilized when reversible methods are not satisfactory. Highlights of specific considerations for erection enhancement in men with SCI can be found in other readings.[63]

The use of testosterone in hypogonadal men with SCI is safe and effective. It can improve sexual QOL by improving response to PDE5 inhibitors and potentially assisting with the ejaculation threshold. It can also potentially improve lean body mass and reduce fat tissue mass, which can affect sexual self-image. Proper dosing and monitoring are required. Since an association between low vitamin D and hypogonadism exists in men with SCI,[64] and is associated with ED,[65] vitamin D supplementation may be required.

There are fewer options to assist women with genital lubrication and accommodation. Options include external lubricants (preferably water-soluble and with minimal chemicals). Furthermore, studies are sparse. However, small but significant improvements in subjective arousal in women with SCI have been seen with sildenafil, especially when accompanied by manual and visual stimulation. Sildenafil citrate may be considered for off-label use in women with complaints of sexual dysfunction, especially if the injury is incomplete. EROS Therapy (clitoral therapy device [CTD]; UroMetrics, Inc.) is a small, battery-powered vacuum device designed to enhance clitoral engorgement by increasing blood flow to the clitoris, and is the only FDA cleared-to-market device available by prescription to treat female sexual dysfunction. Theoretically, for some women with SCI, there may be some benefit, and there may be an additional training effect from EROS Therapy on the pelvic floor in women who have retained the bulbocavernosus reflex. This, in turn, may reinforce the remaining sacral reflexes.

6.4.2.3 **Ejaculatory disorders**

Ejaculation can often be provoked in men with SCI through the use of step-by-step masturbatory training[66] or the use of PVS. Caution should be taken with PVS because of the likelihood that it will provoke AD, and silent AD can be clinically misleading and lead to false reassurance during home practices.[67] Electroejaculation (EEJ), which involves the use of an anal probe to deliver an electric current to produce seminal emission within a clinically monitored setting, is reserved for fertility purposes only.

6.4.2.4 Orgasmic difficulties

Orgasmic potential in men and women with SCI can be improved by several factors. That is, interventions that increase genital stimulation, improve awareness of sensate areas (e.g., through body mapping), and allow for cerebral inputs to be appreciated at a higher level (and assist with neuroplasticity) may improve this potential. Allowing the freedom to focus by removing interferences (i.e., pain, spasticity, AD, and incontinence) through medical treatments can also help. The practice of mindfulness with sexual stimulation and the use of relaxation, meditation, fantasy, recalling positive sexual experiences, breathing, and "going with the flow" can also help improve orgasmic potential. Being with a trusted and long-term partner is the most predictive factor in orgasmic attainment after SCI.[68]

Focusing on cerebrally initiated sexual response can, despite lost abilities, result in an adapted but very satisfying sexual experience. The principles of neuroplasticity that were learned in motor rehabilitation after SCI can also apply to the sexual experience. Areas that remain sensate take on a sexually arousing role (i.e., neck and ear stimulation can lead to "eargasms" in quadriplegics), even if such areas were not in the sexual repertoire prior to injury. One small study on sensory substitution following SCI highlights the potential with these areas and the need for further study.[69]

6.4.3 Conclusions

- The vast majority of men and women with SCI find it difficult to become physically aroused, and more women than men have difficulty becoming psychologically aroused. **[LOE 2]**
- Compared with placebo, PDE5 inhibitors are associated with a significant improvement in erectile quality and tolerable side effects in men with SCI. **[LOE 1]**
- Intracavernosal injections are effective in treating erectile dysfunction in men with SCI. **[LOE 2]**
- Intraurethral agents (i.e., alprostadil [MUSE®]) are not effective for the treatment of ED in men with SCI. **[LOE 4]**
- PVS can help improve forceful ejaculation in men with SCI, particularly those with a higher-level injury. **[LOE 1]**
- Vaginal moisturizers and lubricants assist with genital arousal in women with SCI. **[LOE 2]**
- Clitoral or cervical (intravaginal) vibrators may increase orgasmic capacity in some women with SCI. **[LOE 2]**
- Hormone replacement therapy may be required in some women with SCI to maintain the elasticity and lubrication abilities of the vagina. **[LOE 3]**

6.4.4 Recommendations

- Clinicians should offer men with SCI who have ED a PDE5 inhibitor as first-line therapy, and intracavernosal injections and VEDs as second-line therapies. **[GOR A]** Intraurethral agents should be avoided. **[GOR B]**

- Clinicians should offer vibrator therapy to men with SCI wishing to ejaculate or reach orgasm. **[GOR A]**

- Men with SCI are at higher risk for, and should be tested for, low testosterone and should be treated if necessary. **[GOR B]**

- Women with SCI should be offered vaginal moisturizers and lubricants, vibrators, and topical hormone replacement therapy. **[GOR B]**

6.5 Male Fertility

Men with SCI may have concerns about fertility (conception) potential. They should be reassured that men with SCI can have realistic expectations of becoming a biological father.[62]

6.5.1 Semen quality

Men with SCI cannot achieve ejaculation during intercourse or with masturbation. Emission of the semen is controlled by sympathetic nerve segments from T10–L3. An injury above the vertebral level of T6–7 can interfere with the process of seminal emission and closure of the bladder neck. Forward propulsion of the semen can also affect the bulbospongiosus and bulbocavernosus muscles, as well as the muscles of the pelvic floor. These muscle group innervations depend on the somatic segments of S2, S3 and S4, which travel through the pudendal nerve.[70] After an SCI, men may experience anejaculation due to ejaculation dyssynergy between the external sphincter and the bladder, which results in loss of forward propulsion of sperm.[71]

Semen analysis studies have also demonstrated that men with SCI have low semen quality.[72] In general, sperm count is normal, but sperm mobility is reduced after SCI. This may be caused by inflammatory changes in the seminal fluid. Seminal plasma in SCI patients shows a large number of activated T cells that secrete cytokines such as interleukin-1, interleukin-6, and tumour necrosis factor-alpha, which researchers have linked to impaired sperm motility.[73] Furthermore, it has also been shown that neutralization of these factors results in improved sperm motility.[74]

6.5.2 Assisted male reproductive techniques

Men with SCI may benefit from assisted reproductive techniques to achieve pregnancy. If semen cannot be retrieved through masturbation, it may be possible to retrieve semen through PVS. First described by Brindley in the 1980s,[75] PVS is performed by placing a vibratory device on the dorsum of the penis, thus activating the penile dorsal nerve. With continued stimulation, the ejaculatory reflex arc is activated at the level of the spinal cord and ejaculation occurs.[76] Pregnancy outcomes for this technique have been reported to be as high as 43% when combined with vaginal self-insemination.[77]

EEJ is an alternative method for sperm retrieval. It is reserved for men who do not respond to PVS. During EEJ, a stimulator is placed by a physician inside the rectum, and the seminal vesicles/prostate/pelvic floor peripheral nerves are directly stimulated. Consequently, EEJ does not need stimulation of the spinal reflex to elicit ejaculation.[38] Studies have shown that EEJ sperm have a lower motility rate than PVS sperm, but EEJ can be successful after PVS has failed.[78] Clinicians should be aware that sedation is frequently required for this procedure, and AD is common during EEJ in men with lesions above T6.[68]

6.5.3 Conclusions

- Fertility is impacted in men with SCI because of ED, ejaculatory dysfunction, and poor semen quality. **[LOE 2]**
- Most men with SCI have normal sperm concentrations, but have low sperm viability and motility. **[LOE 2]**
- Surgical retrieval of sperm in men with SCI can be successful with PVS or EEJ. **[LOE 2]**

6.5.4 Recommendations

- Clinicians should refer men with SCI with ED and/or fertility concerns for multidisciplinary care to help maximize sexual potential and increase the likelihood of pregnancy. **[GOR B]**
- In SCI men desiring fertility, clinicians should discuss the potential of reduced fertility because of ejaculatory dysfunction and low sperm quality. Clinicians should also discuss infertility treatment options. **[GOR B]**

6.6 Female Fertility

6.6.1 Resumption of menses

In general, women have normal reproductive function after SCI. Neither the level of injury nor the completeness of the lesion seems to have an influence on the menstrual cycle over time.[79]

However, the event of an SCI does induce a transient episode of acute amenorrhea immediately after the injury. Menses usually resumes after approximately 6 months (50% at 6 months and 90% at 1 year) and normalizes into a predictable cycle. By this time, most women with SCI have already left the rehabilitation centre. It is, therefore, important that these women are adequately informed on this topic prior to discharge.[80,81] Depending on the level of injury, additional education on the use and application of hygiene products might be required (hand splinting or use of mirror).[82] Patients with SCI may experience increased premenstrual and menstrual symptoms, and some additional symptoms not present in able-bodied women, such as AD and bladder and muscle spasms. Patients should be counseled to expect these changes.[81]

Similar to menses, menarche also follows a predictable pattern in SCI females.[83] Although the injury can elicit menopause in a small number of premenopausal women (reported in 14% of subjects), this is relatively uncommon. Except for an increase in mood disorders, menopausal symptoms do not seem to differ greatly between SCI women and able-bodied women.[82]

Experts have commented on a generalized low utilization of reproductive and gynecological health care for women with SCI.[81] This deficit is likely multifactorial and stems from a lack of knowledge regarding reproductive potential among both patients and providers, and the presence of physical barriers (e.g., wheelchair access) that reduce access. These factors can lead to unwanted pregnancies, and potentially delayed diagnoses of gynecological cancers and sexually transmitted diseases in SCI women.[84]

6.6.2 Contraception

After the transient period of amenorrhea, most women with SCI will return to their preinjury fertile status. Similar to the general population, they should be counseled on contraception, taking into account the benefits and risks of different methods. Basal body temperature methods of birth control are not recommended[85] due to changes in temperature regulation after SCI.

Although hormonal birth control can be prescribed to women with SCI, some specific points of attention should be made. Due to increased thromboembolic risk, hormonal contraceptives should be avoided in the first year after SCI in women who continue to smoke and in women with a history of cardiovascular circulatory problems.[81] Some authors have counseled against hormonal contraceptives in SCI-injured women older than 35 years due to a general concern over reduced mobility increasing the risk of a hypercoagulable state.[86] Care should also be taken when prescribing depot medroxyprogesterone acetate (MPA) for birth control. Although MPA can comfortably diminish the amount of menstrual blood loss, it may also place SCI females at risk for increased bone loss, which is already a potential problem in this population.[83]

Barrier methods can be used for SCI women, but information should be given regarding the risk of pelvic inflammatory disease (PID). In SCI women, this risk may be higher compared with the general population due to a higher prevalence of urinary tract infections among SCI females. Furthermore, PID-related pain symptoms might not be detected in SCI females due to sensory changes.[81] Barrier methods, such as diaphragms, cervical caps, and vaginal sponges require dexterity by the user, which may their limit utilization. When discussing barrier methods of contraception, caregivers should also discuss with SCI women the risk of erosion. Condoms can be used without restrictions and have the additional benefit of protection against sexually transmitted diseases.[87] However, caregivers should discuss the risk of latex allergy, especially in SCI patients with a young onset of injury.[84]

6.6.3 **Pregnancy complications**

Although women with SCI can normally reproduce, the presence of an SCI does have important implications for pregnancy that may not always be communicated to this population. In a retrospective survey of 114 women with SCI, only 23 of 114 women reported that they had received information on this subject during rehabilitation, and only 12 found this information adequate.[88] This lack of information may result in a misunderstanding regarding the possibility of a healthy pregnancy in SCI women. In a questionnaire survey of SCI women of childbearing potential, results showed that the pregnancy rate is lower after SCI than before SCI. However, pregnancy rates were higher when SCI was acquired at a younger age. There were no other predictive variables (e.g., no influence of level of injury). This age-related difference is probably not fertility related, but is determined by many other factors, including the probability of receiving more education over time.[82,89]

As in the general population, experts recommend that pregnancy counseling should start from the moment a woman considers having a child. Preconception counseling should include a visit to the obstetrician to talk about nutritional needs (which included speaking about smoking, substance use, and alcohol) and to screen the current (and future) medications.[89] Specific attention needs to be given to the teratogenic effects of specific medications on the fetus. In general, gynecological and primary care training do not address pregnancy concerns among SCI patients. Indeed, a past survey noted that gynecological and internal medicine residents were not comfortable managing pregnancy in SCI women.[90]

During pregnancy, providers should be aware of the possibility of AD in women with SCI at the T6 level or higher, as AD has been reported to occur in 48% to 85% of women. In some cases, AD has even been reported in patients with a lesion at the T8 level.[87] It is important for clinicians to also remember that labour can similarly cause AD. After ruling out pre-eclampsia as an underlying cause of hypertension and decompressing the bladder and bowels, clinicians should proceed with further treatment of AD, with specific attention to the fetus since overtreatment and hypotension cause fetal distress.[84]

Urinary tract infections can also create potential problems in SCI women during pregnancy. In a review of published series by Pannek and Bertschy in 2011, 64% of pregnant SCI women experienced at least one symptomatic urinary tract infection during pregnancy. This led to eight hospitalizations, with one case of septicemia leading to preterm labour.[91] Postvoid residual urine should be monitored and addressed if related to urinary tract infections. If necessary, this can include a change in the bladder management strategy. Indwelling catheters should be avoided, as these can increase the risk of urinary tract infections. If necessary, intermittent catheterization can be started. Pyelonephritis should be avoided since it may induce preterm labour and delivery. In a prospective observational study, six women with SCI were given a weekly oral cyclic antibiotic schedule. This led to a significant reduction in urinary tract infections, without obstetric complications and with good infant outcomes.[92]

Caregivers should also address the mobility and the reseating needs of pregnant SCI patients. In high-level (thoracic and cervical) lesions, pregnancy can induce changes in respiratory function, which might mandate adapted respiratory rehabilitation.[93-95] Throughout pregnancy, an upright-seated position has to be strived for, and if necessary, repetitive adaptations have to be made by the seating specialist.[83] Particular attention should be given to a changed cushion-skin interface, as the risk of decubitus ulcers also increases in this population due to a combination of weight gain, change of body habitus, and increased spasms, pain, immobility, and even anemia.[96] In the lower limbs, water retention and edema can also aggravate this problem. Additionally, pregnant women with SCI might require extra help or technical instructions, and aids for transfers and for several activities of daily life, such as dressing/undressing, bathing/showering (need for tub bench/roll-in shower chair), and driving. For these reasons, physical and occupational therapists should be involved.[83,95] Lack of mobility may lead to an increased thrombosis risk.[89] Therefore, compressing stockings and low-molecular-weight heparins from the fourth month onwards until the end of the postpartum period are advised.[84]

Providers should also be aware that bladder and bowel symptoms may change during pregnancy in SCI women. In particular, SCI women may have increased constipation problems during pregnancy. Adequate fluid intake and, if necessary, mild laxatives can prevent this problem.[84]

Last, but not least, the psychological aspects of pregnancy should be considered. Very importantly, postpartum depression occurs more frequently in women with SCI.[89] Caregivers should reinforce that pregnancy and childbearing can be important issues in regard to QOL, despite all the other problems that can arise.[80] Tebbet *et al.* described this interaction between biomedical problems and psychosocial strain in SCI patients during pregnancy, counseling caregivers to address both simultaneously.[96]

6.6.4 Labour and delivery risks

Clinicians should discuss labour and delivery plans with SCI women early in pregnancy. Since the uterus is innervated by T10–L1, women with higher spinal cord lesions may not sense the onset of labour. Furthermore, women with lesions at T10–L1 may experience insufficient labour contractions. With lower lesions, uterine sensibility is preserved.

Labour in the setting of an SCI can be indicated by very different signs and symptoms.[81,82,84,89] Atypical signs include pain above the level of the injury, abnormal pain, ruptured membranes (which can easily be confused with urinary incontinence), increased spasticity in the legs/abdomen, respiratory changes, bladder spasms, or AD. Occasionally, no symptoms at all are present. Uterine palpation techniques or home uterine monitoring could be an aid.[89,94]

Moreover, SCI women tend to have more preterm deliveries. In a small series of 37 pregnant SCI women, 33% had a preterm delivery.[89] Cervical effacement and dilatation should be checked routinely from week 28 onwards, and SCI women should be hospitalized from week 36 onwards, or earlier if labour begins or if the cervix is dilated or effaced.[81,87,89,97] After delivery, there is a higher rate of low birth weight and a higher rate of admission to the neonatal intensive care unit. To prevent the consequences of AD, patients at risk should undergo general or epidural (preferable) anesthesia with continuous blood pressure monitoring.

Due to the presence of contractures, heterotopic ossification, and severe spasticity, there is an increased rate of complications during delivery. This leads to more forceps deliveries, more vacuum extractions, and more caesarian sections.[81] Nevertheless, women with SCI can still have a normal vaginal delivery. Different series report that between 37% and 53% of SCI women will have spontaneous vaginal deliveries.[82,94] Cross *et al.* report that 53% of SCI women will deliver via caesarean section.[86] Women with SCI should have discussions with obstetric physicians specializing in high-risk pregnancies to better understand the individual risks associated with a spontaneous vaginal delivery versus a planned caesarian delivery.

6.6.5 Postpartum and breastfeeding

Even after delivery, the risk of thromboembolic disease remains high. Additionally, there is still the need for extra attention to bowel and bladder management. An occupational therapist can deliver aid when upper limb function or balance is impaired. If necessary, extra help should be sought to take care of the mother and/or the child. With lesions above T6, milk production might pose a problem due to diminished nipple sensation. According to SCI women who have undergone pregnancy, a peer-mentor system (i.e., presenting the positive experiences of other women with SCI that have gone through childbirth and being able to speak with these women) can improve self-efficacy and prepare women with SCI for the experience of childbirth and motherhood.[98]

6.6.6 Parenting issues

According to the literature, mothers with SCI, in general, perform quite well.[90] Indeed, it has been suggested that having child can even be a motivation for SCI parents to stay healthy. In a small survey, being a parent was noted to have increased the QOL of 23 of 24 women who had given birth.[80] Alexander *et al.* investigated a matched-pair cohort study of 88 mothers, 46 of their partners, and 31 of their children. Parents with an SCI did not negatively affect their children in terms of self-esteem, attitudes towards parents, gender roles, and family functioning. Furthermore, SCI mothers did not show more stress, and they saw their children as being more comfortable and less rigid. The study concluded that having a parent with SCI did not predict psychological difficulties, diminish parenting satisfaction, increase parenting stress, affect family functioning or engender marital adjustment.[98]

6.6.7 Conclusions

- Women with SCI will likely resume normal menses more than 6 months after injury. **[LOE 2]**
- Fertility usually returns to its preinjury fertility status after SCI. **[LOE 3]**
- Systemic hormonal contraceptives in SCI females can potentially increase the risk of thromboembolic events in the first year after SCI and may increase bone loss over time. **[LOE 4]**
- Pregnancy in SCI patients is associated with higher rates of urinary tract infections and thromboembolic events for all injury levels, and is associated with AD for injury levels above T7. **[LOE 2]**
- Pregnant women with SCI can have atypical symptoms of labour and are at increased risk for preterm labour. **[LOE 3]**

6.6.8 Recommendations

- Women with SCI must undergo routine gynecological checkups and receive routine gynecological advice. **[GOR A]**
- Clinicians must inform women with SCI that fertility usually returns to its preinjury fertility status. **[GOR A]**
- Birth control must be offered to women of reproductive age after SCI. Different forms of contraception, and their advantages and disadvantages, should be discussed with patients. **[GOR A]**
- Clinicians must monitor pregnant SCI patients for urinary tract infections and thrombotic vascular events. **[GOR A]**
- Women with SCI should be counseled by a multidisciplinary team about the risks of pregnancy and followed regularly by a multidisciplinary team once pregnant. **[GOR B]**
- Women with SCI should have discussions with obstetric physicians specializing in high-risk pregnancies to better understand the individual risks associated with a spontaneous vaginal delivery versus a planned caesarian delivery. **[GOR A]**
- Cervical effacement and dilatation should be checked routinely from week 28 onwards, and SCI women should be hospitalized from week 36 onwards, or earlier if labour begins or if the cervix is dilated or effaced. **[GOR B]**

6.7 Sexual Rehabilitation

People are and remain sexual beings after SCI. There is evidence, described by Biering-Sørensen and colleagues,[99] that persons with SCI continue to be sexually active 10 to 45 years after their injury. These researchers surveyed 279 participants to learn about their sexual satisfaction, and found that 69% of women and 54% of men with SCI reported being satisfied with their sex lives. Additionally, 90% of women had no difficulty with vaginal lubrication, and 22% gave birth after injury. Of the men, 70% were able to achieve erection, but 94% used vibrostimulation and other aids for erection and ejaculation. Furthermore, 19% of men impregnated a partner, and this was associated with greater sexual satisfaction for them. Younger age was associated with greater sex life satisfaction for both women and men; this has also been confirmed by other research in this area.[100] While it is encouraging that both men and women continue to be sexually active after SCI, and that many have adapted to their new sexual bodies and sexual lives, it is clear that many others are neither active nor satisfied with their sex lives.

6.7.1 The importance of sexuality

After SCI, sex matters. Researchers who have documented the physiological sexual problems of the SCI population suggest that sexuality is a highly important area of postinjury life that requires attention and rehabilitation.[47,67] In a recent multicentre, prospective cohort study, where the objective was to describe and compare the impact of health problems secondary to SCI on functioning at home and on social activities at 1 year and 5 years after discharge from first inpatient rehabilitation, sexuality was one of the most frequently mentioned health problems.[101] Several studies have attempted to understand the perspective of persons with SCI in regard to their views of the importance of sexual health. One large-scale, cross-sectional questionnaire including 350 respondents over four European countries identified sexual activity as the greatest unmet need in persons with SCI.[102]

Sexuality is prominent when examining the rehabilitation priorities of persons with SCI. Anderson and colleagues asked people with SCI which "gain of function would dramatically improve their life." Choices included hand/arm function, upper body/truck strength and balance, bladder/bowel function and elimination of AD, sexual function, elimination of chronic pain, normal sensation, and walking movement. Among the 681 men and women, 51% were quadriplegics and 49% were paraplegics. Additionally, of the patients, 25% were female, 65% were male, and 10% did not endorse a gender. The researchers found that of the seven functions proposed, regaining sexual function was the first or second highest priority for 28.3% of quadriplegics and 45.5% of paraplegics. Regaining sexual function was equally important to men and women with quadriplegia (second priority for both), but slightly more important to women (30.4%) with paraplegia than men (23.1%) with paraplegia.[103]

Similarly, Kreuter *et al.*[55] surveyed women with SCI and matched controls in Sweden, Denmark, Iceland, Norway, and Finland to ascertain their experiences and attitudes towards many aspects of sexuality after SCI. Of the women, 82% were sexually active after injury. Of those, 51% continued to think of sexual activity as important after injury, with 8% considering it to be more important after

SCI than prior to injury. In a systematic review of 24 studies, Simpson and colleagues found that both paraplegic and quadriplegic participants endorsed sexuality as one of the key health priorities, along with mobility and urinary and bowel control.[104]

New and colleagues, in an Australian mixed methods, exploratory study, sought to understand the sexual health education experience and the preferences of individuals with spinal cord issues.[105] They surveyed 115 participants with trauma-related SCI and 39 participants with nontraumatic spinal cord dysfunction (SCDy). They also interviewed 21 participants with SCDy. They found that individuals with SCDy received less sexual health education than those with trauma-related SCI. Overall, only 18% of participants were satisfied with the education that they received, while 36% were dissatisfied. Women received less education than men. One of the dissatisfactions expressed by the men in the study was the narrow focus on discussions regarding erectile function without attention to the way that other bothersome symptoms, such as urinary and bladder incontinence and bladder infection due to catheterization, affected their ability to be sexually active.

6.7.2 Changes in sexuality following SCI

The general able-bodied population is not without sexual problems. Sexual dysfunctions are highly prevalent in the general population, affecting about 43% of women and 31% of men, and significantly impact interpersonal functioning and overall QOL in both men and women.[106] It is, therefore, important to remember that a person with SCI may have had sexual concerns, sexual dysfunctions, or relationship problems prior to their SCI, and this needs to be recognized and accounted for in regard to expectations and prospects of their sexual future post injury.

SCI not only affects the motor, sensory, and autonomic components of sexual function, but also can significantly impair other body functions. These altered functions then secondarily affect the sexual ability, enjoyment, and opportunities for persons with SCI. In one study, participants cited being single or having spasticity, pain, pressure ulcers, or bowel and bladder incontinence as barriers to sexual satisfaction.[102] However, the primary reason for men and women to pursue sexual activity after SCI was intimacy need (57.7%). This was followed by sexual need (18.9%), self-esteem (9.8%), and keeping a partner (8.4%). Fertility was the least important reason (1%).[43] Furthermore, the psychosocial impact of SCI on sexuality is finally being appreciated and researched. Since sexuality is much more than the performance of sexual acts, sexual rehabilitation after SCI must recognize and appreciate the additional complexity SCI adds to an already complex subject.

SCI, as with any physical or mental illness, contributes to sexual problems through four etiological mechanisms:[107] direct, indirect, iatrogenic, and contextual. Direct effects include neurological, vascular, hormonal, or anatomical damage to an area functionally connected to sexual response (brain, erogenous zones, and internal and external genitalia). Indirect effects include mental and physical alterations following SCI to perception, judgment, behaviour, mood, and other bodily functions, such as bladder and bowel, sensory and motor, and thermoregulation, that significantly affect sexuality. Iatrogenic effects include medications, medical or surgical procedures, or other treatments that can affect sexuality. Even the awareness, openness, and professionalism of the health care provider about sexual issues can iatrogenically influence the patient's motivation and comfort in being sexual after an injury, which, in effect, created a new sexual body. Last, contextual effects include relationship, environmental, social, religious, and cultural influences related to sexuality on the person with SCI. An SCI can cause necessary changes in the living environment and accessibility to social venues, and increase dependence on others, which can interfere with sexual expression.

6.7.3 Psychosocial aspects of sexual rehabilitation in SCI

There is now an awareness that the wishes and priorities of SCI survivors need to be taken into account and that sexual health education needs to comprise information about the impact of SCI on sexual function and options for functional rehabilitation. However, despite this awareness, the psychosocial aspects of sexuality, such as the individual's sexual confidence, emotional health, and relationship with a partner, are only beginning to be recognized as influential factors in an SCI survivors' ability to maintain or re-create satisfying sexual lives.[67] It is thought that, for most SCI survivors, the primary reason for staying sexually active is their desire to remain intimate with their partner. Biering-Sørensen and colleagues[99] hypothesize that men's lower level of sexual satisfaction, compared to women's (54% vs. 69%), may be due to their greater emphasis on sexual function (erectile and orgasmic) per se.

6.7.4 Biopsychosocial model of sexuality

With the expansion of the conceptualization of the SCI survivor's experience of sexuality from mere function to the importance of the relationship, it is also important to recognize that sexuality is a complex experience with physiological, psychological, and social components. It should be understood as an essential aspect of the well-being and QOL of individuals and families.

In 2002, the World Health Organization (WHO) provided a definition for the biopsychosocial model of sexuality that has been used to underpin research on sexual health in chronic illness:

A state of physical, emotional, mental, and social well-being in relation to sexuality; it is not merely the absence of disease, dysfunction or infirmity. Sexual health requires a positive and respectful approach to sexuality and sexual relationships, as well as the possibility of having pleasurable and safe sexual experiences, free of coercion, discrimination and violence. For sexual health to be attained and maintained, the sexual rights of all persons must be respected, protected, and fulfilled.[134]

In a more recent commentary on sexual health in America, former Surgeon General David Satcher promoted an emphasis on sexual wellness as a means to move away from silence and stigmatization and acknowledging that sexual health is a part of general health.[108]

The biopsychosocial model of sexuality has been used extensively in cancer research and cancer literature, acting as a theoretical underpinning for interventions.[109] According to the model, which can be viewed as reasonably applicable to spinal cord trauma, physiological function is altered by cancer or its treatment, usually in an irreversible manner. The loss of function brings about grief and mourning, anxiety (about coping), and uncertainty (about the level of function that can be recovered).[110] Sexual confidence diminishes as the individual is unable to perform sexually and/or achieve a familiar level of pleasure. As the affected individual struggles with the functional changes, and the emotions triggered by these changes, their partner cannot help but react emotionally to their inability to have familiar sexual interactions. The partner's grief and anxiety are paralleled in the patient. How a couple works through their grief and mourning and the development of a new, flexible sexual paradigm are challenges that must be faced and overcome if a sexual connection is to remain.[111] Positive sexual interactions require mutuality, which means that the patient and their partner must learn about each other's sexual needs in the SCI context and support each other.

6.7.5 The sexual rehabilitation framework

Sexuality should be addressed through a biopsychosocial lens. Therefore, the multidisciplinary utilization of a sexual rehabilitation framework (SRF) is very helpful when looking at the apparently overwhelming medical and/or psychosocial factors that impede or improve sexual and reproductive functioning.[112] To assess and manage sexual issues, single or multiple disciplines can be recruited to suit the needs of any patient.

Health care providers involved in the sexual rehabilitation of persons with SCI can include physicians, nurses, occupational therapists, physiotherapists, recreational therapists, psychologists, vocational rehabilitation specialists, social workers, and trained peer counselors.

The SRF consists of eight sexual areas. While all areas may not be applicable, depending on the level and completeness of injury, they are there to remind the health care provider to assess the areas for abnormalities. The SRF can also delineate the factors contributing to sexual concerns, allowing for proactive solutions. The SRF is not a substitute for a full sexual history, but rather an adjunct tool to utilize within the current context and the past psychosocial history of the client. It is important to know that as early as 1986, sexuality was recognized as an activity of daily living (ADL) by the American Occupational Therapy Association, thereby rendering it an important aspect for rehabilitation.

The SRF is best utilized to identify sexual areas that need more immediate attention (and by which discipline), to categorize the severity of the sexual issues (according to the priorities of the SCI patient), and to outline further investigations or referral.

The SRF can be used in both inpatient and outpatient settings. It can be attached to a patient chart or used as a tool to ensure sexual and fertility rehabilitation has been established and followed up. For example, the SRF could be used for a patient with SCI having difficulty with sexual positioning due to loss of motor function and spasticity. Having a physician assess the potential use of an antispasmodic medication; a physical therapist assess for stretch, transfer, and spasm reduction; and an occupational therapist assist with adaptive positioning aids or cushions is more effective than having only one discipline involved.

6.7.6 Sexual function measures for SCI populations

The Female Sexual Function Index (FSFI), the measurement of vaginal pulse amplitude (VPA), the International Index of Erectile Function (IIEF), and the measurement of ejaculatory function and semen quality are considered appropriate measures to assess sexual response and reproductive function after SCI. However, no measure has been identified to assess female reproductive function. For clinical trials aiming to improve sexual function after SCI, the FSFI or the IIEF is currently preferred. Although VPA is an appropriate means to assess female sexual response, it is only useful in laboratory studies and is too invasive for use in clinical trials. For male fertility potential, assessment of ejaculatory capacity and semen analysis are recommended.[49]

There are new data sets for documenting residual function after SCI, including the inter-rater validated International Standards to Document Remaining Autonomic Function after Spinal Cord Injury (ISAFSCI),[113] the International SCI Male Sexual Function Basic Data Set, and the International SCI Female Sexual and Reproductive Function Basic Data, which should be used for research purposes in the future.

6.7.7 Psychosocial treatments for sexual issues following SCI

Whenever possible, the partner, if there is one, should be included in the psychosocial interventions. There may be issues that the patient may want or need to address individually, at least at first, such as anxiety about incontinence during sexual activity. However, it is important to realize that the partner is usually affected by the same difficulties and will have similar concerns. The ability to share and cope with these concerns can enhance the sexual recovery of both the individual and the couple.

6.7.7.1 Psychoeducation

Unfortunately, survivors of SCI cannot prepare for the challenges of living with the consequences of their injury. However, preparation for postinjury life is essential. Early after the injury, information can be provided to alert the patient that sexual rehabilitation will be available when they are ready for it. Research for other health conditions has shown that psychoeducation can have an effect on patients' and partners' knowledge about sexual side effects, rehabilitation, and suboptimal functioning.[114-116] Patients need to be educated on the relationship between their injury and their sexual problems. Understanding the biology will reduce any tendency to misinterpret cause and effect, and with it, the psychological pressure to perform sexually beyond what is possible. Realistic expectations not only help the patient cope with sexual changes, but also facilitate the onset of the grieving process. Patients can learn to anticipate the grieving process, which will make its intensity less frightening and more manageable. Learning early on about sexual functioning aids will help patients consider options as they move forward in their sexual recovery.

6.7.7.2 Grief work

As with any loss, the onset and process of grief are inevitable for most individuals with SCI and their partners. Grief about sexual changes may be embedded in grief about the injury and its aftermath. Grief can be intense, with strong feelings of anger, sadness, and hopelessness. It is important, in the course of assessment, to distinguish grief from depression because intense grief, unlike untreated depression, requires that the grieving person feels and tolerates their feelings. Supportive counseling can be helpful, but medical treatment is usually not required. Grief tends to lessen over time. If it becomes chronic—intense feelings and longing for the past do not diminish after 6 months to 1 year—assessment for complicated grief and/or depression is warranted.[117] Complicated grief and/or depression may warrant medical treatment in addition to counseling.

6.7.7.3 **Cognitive behavioural therapy**

During the process of coping with sexual changes, which may include the need to use sexual aids, it is possible that dislike or aversion to nonspontaneous sex and to assisted sexuality may develop. In addition, coping with urinary or bowel leakage and AD may prove to be barriers to sexual activity. Cognitive behavioural therapy (CBT) has been useful in sexual health interventions in prostate cancer.[118] One hundred and eighty-nine couples were randomized to one of three groups: nurse intervention, peer intervention, or usual care. Of the participants, 74% completed the study. In addition to education on sexual changes and options for rehabilitation, participants' negative beliefs were challenged and opportunities were provided for sexual health–related goal setting. At 12 months post intervention, participants in the nurse and peer interventions reported using sexual aids more than three times more frequently than those in usual care. Vandyken and Hilton proposed using a biopsychosocial approach to the management of pelvic pain in women.[119] Based on evidence from other health conditions, CBT techniques can be used to develop interventions for SCI survivors (and their partners) as they navigate their postinjury sexuality. CBT can be a method to successfully address intrusive negative thoughts about sexual aids, and potentially unpleasant or painful experiences.

6.7.7.4 **Mindfulness**

The ability to be aware of one's emotions and physical sensations is a critical aspect of re-engaging in sexual activity after SCI. Changes in or loss of sensation can be upsetting. Sexual desire and sexual arousal signals may be weaker or different after SCI. Mindfulness is a technique that has been employed to manage distress and to achieve emotional self-regulation.[120-122] It has also been used as a tool to increase awareness of sexual desire and arousal.

6.7.7.5 **Sexual communication**

According to the research literature, health care providers experience discomfort when addressing sexual issues with patients. However, it is important to recognize that patients and their partners may have similar difficulties. Coaching patients with SCI and their partners to describe their sexual experiences after injury and to express their sexual needs is critical to the development of a positive sexual relationship.

6.7.7.6 **Individual or couple therapy**

The impact of the SCI may not be the only challenge to an individual's or couple's sexuality. Some individuals and couples will have pre-existing mental health or relationship problems that may need to be addressed before sexual health can be addressed. A sexual health assessment that evaluates mental health and relationship problems is needed to determine how an individual or couple will navigate sexual recovery. Referral to an appropriate mental health and/or sexual health professional will provide the individual or couple with the support they need when mental health or relationship problems interfere with addressing their sexual concerns. Currently, there are no sexual health interventions for couples coping with SCI. There are interventions for couples coping with other chronic conditions. These interventions have been tested in pilot randomized controlled studies, and have included psychoeducation, psychological counseling, CBT techniques, and sexual aids.[123] The studies focused on increasing knowledge, increasing emotional disclosure, reducing negative feelings about sexual aids, and setting sexual health goals. Furthermore, the studies have had small-to-moderate effects, and can be considered as a reference for future research and development of interventions for couples who are recovering sexual intimacy after one member had a traumatic spinal injury.

6.7.8 Sexual health psychological measures

Measuring sexual health is challenging, as generally no measure addresses all components of sexuality. New and Currie developed a comprehensive sexuality survey with a patient-reported outcome measure of sexual function.[124] A common feature of sexual health measures is their focus on sexual interest, function, and satisfaction. Influential issues, such as sexual self-esteem, patient's relationship with their partner, and effects of urinary and fecal incontinence and AD, are not included.

6.7.9 LOE for treatments for psychosexual problems after SCI

The research on sexual dysfunction in SCI has been established in large cohort studies across several countries, showing that both men and women continue to be sexually active after SCI. There are measures that are able to capture specific functional deficits. At the same time, beyond functional losses, individuals with SCI experience multiple psychosocial problems that make continued sexual activity challenging and potentially unsatisfying.

Studies on the psychosocial aspects of sexuality after SCI are emerging. However, more research is needed to understand fully the experiences and needs of this population. More descriptive research will put investigators in a better position to build and test meaningful interventions. As there are currently no measures to effectively assess the psychosocial issues of SCI patients and their partners, mixed methods research is needed. Mixed methods research can leverage currently available sexual function measures and learn from the experiences of SCI survivors and their partners to conceptualize the important impacts of SCI on sexual concerns and relationships. Relevant measures of psychosocial issues can then be developed to assess these impacts and concerns. Even the limited amount of research points to the need to recognize that the approach must avoid adopting heteronormative standards. Applying a cultural lens is important, as patients with disabilities are perceived both similarly and uniquely by different cultures.

6.7.10 The necessity for a multidisciplinary approach to sexuality after SCI

A biopsychosocial approach to sexuality requires multidisciplinary expertise. Physicians specializing in SCI are most qualified to educate and provide care for physiological issues that affect sexuality, such as neurological dysfunction, fecal and urinary incontinence, pressure ulcers, AD, and related cardiovascular issues. Other specialists must become familiar with SCI issues before they can become effective in their roles. Urologists trained in sexual medicine and gynecologists educated in sexual dysfunction and sexual health are best qualified to assist patients with rehabilitation of sexual function. They are also best qualified to advise on pro-erectile and vibrostimulation methods for men, and lubricants and vibrostimulation methods for women. Physical therapy experts in pelvic floor rehabilitation can provide patients with exercises that address urinary and fecal incontinence, erectile function, and pelvic pain. They can also assist in vibrostimulation training and help develop strategies for comfortable sexual positioning. Trained sexuality counselors, often nurses, physician assistants, and physicians certified by the American Association of Sexuality Educators, Counselors and Therapists (AASECT), can assist in providing education on the impact of SCI on sexuality, path to rehabilitation, and sexual aids. AASECT-certified sex therapists are mental health providers who are trained to guide individuals and couples through the grieving process, which can sometimes manifest as a barrier to sexual recovery. They also work with individuals to re-eroticize their bodies[112] and with couples to work towards a new sexuality. Where necessary, sex therapists can address pre-existing individual or couple problems that interfere with sexual rehabilitation.

6.7.11 Talking to patients with SCI and their partners about sexual health

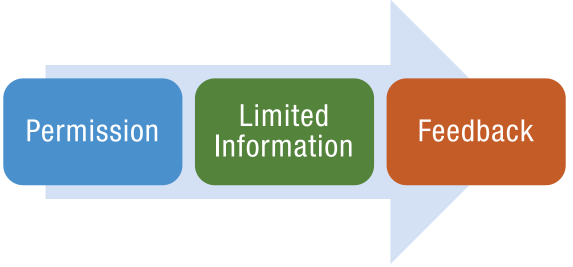
The effectiveness of the multidisciplinary providers depends on their ability to communicate with patients about sexual issues. Discomfort with sexual health conversations and feeling unprepared for such conversations have been topics in the health care literature for many years.[125-128] The lack of preparation for sexual health discussions by SCI health care providers and the unavailability of providers with sexual training have been noted by several authors.[47,67,109,129]

Providers may not address sexuality at all, viewing SCI survivors as "sexually invisible" or asexual, and thus stigmatizing them as incapable of this essential adult method of seeking and experiencing pleasure and couple intimacy.[109,130] In a focus group study, Esmail and colleagues explored the attitudes to sexuality with disability of health care providers and of individuals with visible and invisible disabilities.[131] They found that individuals with disabilities perceived themselves to be seen as "not equivalent" to those living without disabilities and that their self-esteem was negatively affected by a heteronormative approach to sexuality in health care, which emphasizes vaginal penetration as a standard. The lack of sensitivity in health care to the fact that sexuality can be diverse has been expressed in research with nondisabled patients as well.[132] Training is needed to enable health care providers to discuss sexual concerns with individuals with SCI and their partners with confidence and with respect to their unique needs. Providers must be able to offer flexible alternatives to pursuing sexual intimacy and pleasure, based on the body altered by injury.

The field of sexual health uses a model that delineates a hierarchical program of interventions for sexual health concerns, called the Permission, Limited Information, Specific Suggestions, and Intensive Therapy (PLISSIT) model.[133] Physicians and nurses are in the best position to engage in *permission and limited information*. By enquiring whether patients and their partners have any sexual concerns, physicians normalize and legitimize the concerns. Providing limited information usually means explaining the relationship between the injury and sexual problems. If patients and their partners are interested in help with sexual concerns, the physician can refer them to other professionals whose expertise is best suited to sexual rehabilitation. The professionals who guide sexual rehabilitation can provide *specific suggestions*. For example, nurses with relevant training can provide education on sexual aids, while coordinating with the physician to ensure patients' safety, or physical therapists can guide pelvic floor rehabilitation to help patients cope with fecal and urinary incontinence and pain. Referral to a sex therapist is warranted when *intensive therapy* is needed for individuals who are unable to cope with grief over sexual losses, who need basic sex education, or who are unable to work towards their sexual health goals due to mental health, relationship, or pre-existing sexual problems.

6.7.12 Utilizing the PLISSIT model: a quick, biopsychosocial assessment during a health visit

As a starting point, it is important that the health care provider for patients with SCI has a library or resources, including a list of multidisciplinary providers who can assist with sexual health issues and who are familiar with SCI conditions. In addition, a list of websites and existing handbooks on SCI sexual health care should be available. Equipped with an armamentarium of resources, the clinician can confidently start the conversation:



6.7.12.1 Permission

- Since SCI affects how people function sexually, do you have any concerns or worries in this area?
  - Can you fill me in on the context of your sexual life—are you attracted to men, to women, or to both?
  - Some of our patients are transgender, and I do not want to overlook transgenderism if it is relevant to you. Do you identify as male, female, transgender, or in transition?
  - Do you have concerns about how your body works?
  - Do you understand how your injury created the changes in your sexual response?
  - Would you like me to explain how it happened?

6.7.12.2 Limited information

- Let me sketch out for you what has happened to your body sexually after the injury. Do you have any questions?
- Here are some of the emotional responses that people with SCI have had to changes in their sexuality.
- Here is the way rehabilitation can help.
- Many people wish to be sexual after their SCI. Are you sexually active, either with yourself or with a partner?
- Sometimes patients feel less confident in their ability to enjoy sex and to be a good lover after the injury. They also feel sad and angry about losing their usual way of being sexual.
  - Is this true for you?
  - Which aspect troubles you the most?
- Has your relationship with your partner been affected by the way your body now reacts sexually?
  - What have you noticed?
  - Do you and your partner talk about this?

6.7.12.3 Feedback

- I have noticed in our conversation that you have the following concerns: [specify concerns]. Do you agree?
- If you agree, would you like me to help you find the right person or people to help with these concerns?
- Here is the specialist (are the specialists) who can help you and your partner get back to being sexually connected.

More extensive assessment can be pursued if time is available and if the health care provider plans to assume responsibility for guiding one or more aspects of rehabilitation. However, the most important function of the first conversation about sexuality is to make the patient comfortable with sexual health discussions. By giving permission, providing limited information early, and inquiring periodically, a physician or a mid-level provider can alert patients and their partners to the fact that help is available any time that they wish to pursue it.

6.7.13 Conclusions

- Both men and women continue to be sexually active after SCI. **[LOE 2]**
- Successful SCI rehabilitation requires a multidisciplinary approach that addresses all aspects of sexuality (physiological, psychological, and relational). **[LOE 2]**
- Despite the high priority placed on sexuality by patients with SCI, most health care providers have inadequate sexual health rehabilitation knowledge, and thus are unable to deliver the required sexual health education and care to persons with SCI. **[LOE 3]**
- It is important to acknowledge/normalize patients' feelings of sexual loss and resultant mourning while encouraging a positive and optimistic outlook towards a "new sexual normal" to help create an optimal setting for the recovery of sexual QOL. **[LOE 4]**
- Maximizing the remaining capacities of the total body before relying on medications or aids will support patients' sexual self-efficacy:
  - Learning new sexual body maps **[LOE 4]**
  - Nurturing the cognitive aspects of sexuality **[LOE 4]**
  - Mindfulness to enhance sensory experiences **[LOE 4]**
- Fostering adaptation to residual limitations by utilizing specialized therapies and sexual aids will lead to greater sexual satisfaction. **[LOE 2]**
- Assistance with positioning and spasm, incontinence, AD and pain associated with sexual positioning aids, and medical therapies may provide a more conducive sexual environment and improve sexual satisfaction. **[LOE 3]**
- Providing access to sexual health counseling or sex therapy will enable single or coupled men and women with SCI to develop a new sexual paradigm for reaching satisfaction in their sex lives. **[LOE 3]**

6.7.14 Recommendations

- Clinicians should acquire competency in sexual rehabilitation following SCI through accredited sexual health training in order to deliver optimal care. **[GOR B]**

- Clinicians should refer patients with SCI seeking sexual or fertility rehabilitation to a multidisciplinary team to address all biopsychosocial factors (physiological injury, psychological distress, consequential relationship issues). **[GOR B]**

- The perspective that improvement in sexual QOL will lead to improvement in overall QOL should be discussed with men and women with SCI. **[GOR C]**

- Clinicians must assess (alone or collaboratively with a sexual health specialist) pre- and postinjury sexual history to determine the type and severity of sexual issues, the patient's psychological response to these issues, and the impact of these issues on the patient's relationship with their partner. **[GOR A]**

- Men and women with SCI must maximize their own physiology by first reducing interfering factors (spasm, pain, incontinence, AD, etc.), and then utilize medical or psychological therapies to adapt to residual limitations. **[GOR A]**

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C7

Special Considerations in the Urologic Management of Children with Spinal Cord Injury

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Committee 7

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Special Considerations in the Urologic Management of Children with Spinal Cord Injury

Committee 7

7.1 Introduction

The urologic management of children with spinal cord injury (SCI) differs from that of the adult patient insofar as the care will involve a developing organ system and will be ongoing for many years. Preservation of renal function as well as prevention of urinary tract infection (UTI) in concert with achievement of both bladder and bowel continence are the essential guiding principles. The epidemiology of SCI in children indicates that it is less frequent than in adults and affects mainly older children and teenagers. The etiology of SCI in children is usually associated with motor vehicle accident (MVA) injuries. The cervical spine is often the site of injury and therefore neurologic side effects will more than likely affect bladder and bowel function. The urologic evaluation is similar to that used for the adult population but may involve more frequent radiologic and urodynamic assessment so as to monitor the upper urinary tract and renal function as the child grows. Treatment may be divided into medical versus surgical and mirrors the approach to children who have a neurogenic bladder due to spina bifida. Bladder management should be associated with bowel management so as to achieve the optimal goals of continence and social acceptability.

7.2 How Epidemiology of Spinal Cord Injury in Children Differs from Adults

Evidence Acquisition

An exhaustive computerized search for articles and book chapters as well as peer-reviewed publications relating to SCI in children and adults was carried out. The search was then narrowed to information limited to a population of ages 0 to 21 and to articles published in the last 15 years. The articles were then reviewed, selected, and graded. Given that most of the articles are either retrospective, large cohort studies, or meta-analyses, the Levels of Evidence are 2a or 3a–b. It should also be noted that the majority of the articles come from high-income countries and may not reflect the global reality.

Spinal cord injury in children can be divided into either traumatic spinal cord injury (tSCI) or nontraumatic spinal cord injury (ntSCI). Evaluation and management are similar but the focus will be on tSCI as it is much more common in children.

7.2.1 SCI prevalence in children

Data on the prevalence of SCI in children (an important factor in assessing social and health care needs) is, unfortunately, sparse, as the search did not yield any reliable global or regional data. A single study carried out recently in Canada, looking at age-specific prevalence of SCI, shows that tSCI affects mostly the age group 25 to 50 years and is uncommon under age 20 years.[1]

7.2.2 SCI incidence in children

The annual incidence of SCI in children is low (4 to 8 per million) compared to adults (40 to 80 per million) and seems to be most frequently due to trauma but cause may vary greatly depending on the country. In the United States, one study shows an incidence of 20 per million, but most cases seem to affect young men aged 20 to 29 years and aged 15 to 19 years.[2] A more recent study (also from the United States) reports an age-adjusted incidence rate of 26.9 per million with a trend toward a decreasing incidence over the 15-year study period.[3]

7.2.3 Etiology of SCI in children

With regard to etiology of SCI in children, there is little to no data available. Conclusions can therefore be extrapolated from only the general population. Three main causes are reported: transportation accidents (mostly MVAs), falls, and violence in decreasing order of frequency. Regional variations are again noted. In industrialized countries, MVAs and sports-related activities seem to be the leading cause of SCI in the pediatric population. In fact, up to 65% of all tSCI cases from 0 to 5 years of age are due to MVAs.[4] In the United States, MVAs are also the most common etiology of tSCI in children and young adults, especially in girls. Violence is a more common cause of tSCI in boys over age 5 years; after age 13 years, sports-related injuries affect boys far more frequently than girls.[5]

7.2.4 Nature of injuries causing SCI in children

The epidemiology of SCI in children differs from adults in the nature of the injuries themselves. Cervical spine injuries appear to be more common in children, comprising 60% to 80% of all pediatric SCI compared to 30% to 40% in adults.[6] This is felt to be due to differences in the anatomy (weaker neck muscles, hypermobility of the pediatric spine, incomplete ossification, ligamentous laxity, and the fulcrum effect at the neck caused by the relative increased weight difference between the cranium and the body). In a more recent study from the United States, of the 4,418 patients evaluated, most were in the 15- to 18-year-old age group with 31.4% experiencing an upper cervical injury. In the younger patients (under age 8 years), the incidence of upper cervical injury was much higher (73.6%).[7]

In another study of children under 5 years of age, 34% of patients having sustained a SCI ultimately suffered from tetraplegia and 66% from paraplegia.[4] Of those children with an injury level at or above T6, 34% will experience symptoms of autonomic dysreflexia (AD) associated with a full bladder while in adults the range is 48% to 85%.[8,9]

7.2.5 Long-term consequences of SCI

Abnormalities in bladder and/or bowel function are present in 82% of young patients with SCI; these problems are more common in those with tetraplegia. The types of bladder dysfunctions affecting children with SCI have not been studied in any detail but are assumed to be similar to those affected with neurogenic bladder due to spina bifida. Other consequences include urinary tract infection, urolithiasis, upper urinary tract deterioration, and renal failure.[2]

Of note is that urinary tract dysfunction was historically a major cause of morbidity and mortality in patients with SCI, especially in younger patients. However, due to major improvement in neurogenic bladder management, the last 40 years have seen a reduction in annual mortality to about 2.3%.[10] Septicemia due to urinary tract infection remains a major source of morbidity.[11,12]

Finally, ntSCI is quite rare in the pediatric age group and is usually caused by neoplastic tumours, infections, and degenerative conditions. No data is available, as congenital and genetic conditions such a spina bifida are usually not considered in studies on SCI.

7.2.6 Conclusions

1. SCI in children is rare and affects mostly older children. **[Level of Evidence (LOE) 2]**
2. Motor vehicle accidents are the main cause of pediatric SCI. **[LOE 2]**
3. Younger children are more prone to cervical injuries due to the anatomy of the neck. At least a third of young children with SCI will have autonomic dysreflexia. **[LOE 2]**

7.2.7 Recommendations

5. Clinicians and community leaders should educate the public about the risks and causes of SCI in children. **[Grade of Recommendation (GOR) B]**
6. Clinicians should work with leaders of children's sports organizations to improve safety standards for contact sports in order to prevent SCI. **[GOR B]**
7. Further studies on the nature of pediatric SCI should be undertaken in countries across the world to better determine the demographics and extent of this health issue. **[GOR B]**
8. Encourage the tracking and monitoring of the morbidity and mortality factors associated with SCI neurogenic bladder.

7.3 Interpreting Urodynamic Studies (UDS) in Children with Neurogenic Bladder Secondary to Spinal Cord Injury

Life expectancy and quality of life in children with SCI are closely linked to the management of the lower urinary tract. The goal of urodynamic studies (UDS) in children with SCI is to evaluate bladder function after injury in order to optimize treatment and long-term management. Outcome measures are adequate bladder storage at low pressure and complete bladder emptying, also at low pressure. UDS are aimed at monitoring these outcomes and the effects of therapy.[13] UDS are carried out in a similar manner as for any patient with neurogenic bladder (NGB) but the methodology must be tailored to children. Interpretation of the study should be done by an experienced pediatric urologist.[14] The role of follow-up UDS is essential as children with SCI will need long-term evaluation as they grow and bladder function may change over time. To our knowledge no guidelines have been published on this subject.

A review of the literature reveals that, regarding UDS in children, the evidence is based either on case series (Level of Evidence **[LOE] 3**) or expert opinion **[LOE 4]** with grades of recommendations **[GOR] B** or **C**. Most recommendations are based on a consensus opinion for evaluating NGB in children. There is a lack of level 1 or 2 studies and thus the recommendations are a compilation of best practices.

7.3.1 Indications for urodynamic studies in children with SCI

A urodynamics study (UDS) evaluation is recommended for any child who has experienced an SCI in order to assess the impact of the neurologic lesion on bladder function. The initial UDS evaluation should be performed at least 3 months after the injury so as to allow resolution of spinal shock. There is variability in the duration of spinal shock, with recovery of some neurologic function after a month.[15] Spinal shock has been reported to be of shorter duration in children.[16] Therefore, urodynamic evaluation in children may be performed earlier than in adults.

A full UDS should include uroflowmetry if the child is able to void voluntarily, cystometry (measurement of bladder pressures and volume as the bladder is filled and then allowed to empty), and electromyography (EMG) of the urinary sphincter. Adjunct radiologic studies such as a renal and bladder ultrasound and voiding cystourethrogram (VCUG) are essential in obtaining an anatomic survey of the urinary tract. A video UDS (carried out under fluoroscopic guidance) will combine UDS study with VCUG and may be more efficient.

7.3.2 Methodology for performing UDS in children with SCI

Performing a reliably reproducible UDS study in a child may be difficult but can be done provided the environment is calm and comfortable. The smallest dual-lumen catheter should be used. Latex-free equipment is essential, as many patients will have a history of severe latex allergy.[4] Alternatively, placement of a supra-pubic tube may facilitate the procedure in sensate children. A rectal probe is necessary to evaluate intra-abdominal pressures. Warmed saline solution (37 degrees Celsius) should be used and instilled slowly so as not to cause artifacts (rate of 10 cc/min or less).[17,18] Needle electrodes are more reliable than patch electrodes.

Timing of the first UDS has yet to be determined. During the acute phase following the injury, the bladder may not contract (spinal shock). Once spinal cord edema has resolved, bladder and sphincter activity will return, and UDS may be performed when the child can be safely transported to the urodynamic suite.

Anxiolytic medications can be administered but are usually not recommended, as they may affect bladder dynamics.

7.3.3 Interpretation of UDS

Evaluation of the amount of residual urine in the bladder by ultrasound or by catheterization after the child has voided may help ascertain how well the bladder empties. In children, the essential criteria that must be sought are:

7.3.3.1 Bladder capacity

Bladder capacity will determine if the storage capability of the bladder has been retained and will allow for possible continence. Alternatively, reduced bladder capacity may impact continence and may be indicative of high bladder pressures and loss of compliance. Bladder capacity in children is calculated in mL as follows:[19]

Age under 2 years:

$$\left[\frac{\text{Age (years)}}{2} + 6\right] \times 30 = \text{volume (mL)}$$

Age over 2 years:

$$(\text{Age (years)} + 2) \times 30 = \text{volume (mL)}$$

7.3.3.2 Intravesical pressures

A pressure measurement at the time of catheter insertion should be made. Intra-abdominal and intravesical pressures should be recorded throughout filling in a standard manner. Interpretation of the tracing should look for:

1. abrupt elevation in pressure indicative of neurogenic detrusor overactivity (NDO);
2. pressure measurement at estimated capacity;
3. pressure measurement at first leak;
4. pressure measurement during voiding and after voiding. Measurement of post-void residual will indicate how well the bladder empties. In children, a residual of 10 to 30 cc, depending on age, is reasonable.

7.3.3.3 Bladder compliance

Good bladder compliance is the ability to maintain a constant low intravesical pressure with increasing volume. Bladder compliance can be calculated using a standardized formula, but most of the data applies to adults and has not been evaluated in the pediatric population.[20]

7.3.3.4 Detrusor leak point pressure (the resting bladder pressure at which the child starts to leak)

Data from the pediatric spina bifida literature has been adapted to the pediatric SCI population regarding safe bladder leak point pressure, considered to be below 40 cm H_2O. Above that threshold pressure, changes in the upper urinary tract may ensue.[21,22]

7.3.3.5 Presence of abnormal elevations in pressure or detrusor overactivity

Urodynamic tracings should be correlated with fluoroscopic imaging of the lower urinary tract in order to observe that bladder contraction (changes in vesical pressure) is coordinated with bladder neck opening (seen on fluoroscopy) and relaxation of the voluntary urinary sphincter (lack or silencing of the motor action potentials as seen on EMG). Elevated bladder pressures associated with closure of the bladder neck and/or evidence of persistent contraction of the urinary sphincter may indicate a pathologic situation such as detrusor sphincter dyssynergia (DSD), which will negatively affect bladder function and will require prompt treatment to prevent upper urinary tract damage. In children with thoracic-level SCI, the most common urodynamic pattern is that of NDO with DSD and high voiding pressures, with or without complete emptying.[23]

7.3.4 Long-term role of UDS

Over time, UDS has two specific roles: one, to monitor the effects of treatment, and two, to provide long-term monitoring of lower urinary tract function. Lower urinary tract function in children with SCI may evolve as they grow. Changes in bladder dynamics may occur and are poorly correlated with symptoms.[24] Timing of the UDS has not been studied in SCI patients but the common practice is that, based on experience in the pediatric spina bifida population, they should be carried out 2 to 3 months after the initial injury, then every 6 to 12 months until bladder function is deemed stable and treatment has been felt to be effective.

7.3.5 Adjunct studies to UDS in children with neurogenic bladder

Recommendations are for pediatric patients with SCI to undergo an ultrasonographic survey of the urinary tract in conjunction with the urodynamic study so as to rule out upper urinary tract dilation and kidney or bladder stones. Initial evaluation should also include a VCUG to evaluate the lower urinary tract anatomy and to search for vesicoureteral reflux. Ultrasounds should be repeated yearly.

7.3.6 Conclusions

1. Normal bladder volume changes with growth of the child and is measured by formulas based on age. **[LOE 2]**

2. Spinal shock may resolve more quickly in children than in adults, and upper tract damage may occur more rapidly in children than in adults; this may warrant performing UDS earlier after injury. **[LOE 3]**

3. Detrusor leak point pressures above 40 cm H_2O may be associated with renal damage, based on findings in children with spina bifida. **[LOE 3]**

7.3.7 Recommendations

1. Children diagnosed with SCI should undergo UDS 2 to 3 months after the initial injury, irrespective of whether they empty their bladder when voiding. **[LOE 2; GOR B]**

2. Clinicians should repeat UDS in children with SCI every 6 to 12 months until bladder function has stabilized. **[GOR B]**

3. Clinicians should carry out urodynamic studies in children with SCI using a latex-free, dual-lumen urethral or suprapubic catheter and by instilling warm fluid at a slow rate. **[LOE 2; GOR B]**

4. Important parameters to measure during UDS include: bladder capacity, bladder pressure, bladder compliance, detrusor leak point pressure, and the presence of DSD. **[LOE 2; GOR B]**

5. Adjunct studies to UDS should include a renal and bladder ultrasound and a VCUG if a video UDS has not been performed so as to provide anatomic imaging of the entire urinary tract. **[LOE 2; GOR B]**

6. Once bladder function has stabilized and UDS is no longer performed on a regular basis, UDS may be repeated in children with SCI if there are changes in the neurological examination, new hydronephrosis, changes in voiding behavior, new incontinence, or frequent UTIs. **[LOE 4; GOR C]**

7.4 Long-term Urologic Follow-up of Children with SCI

Fewer than 5% of spinal cord injuries (SCI) occur in children under 16 years of age, with the majority occurring in those between 18 and 25 years of age.[25] Depending on the nature of the injury, these individuals may require significant neurological, gastrointestinal, and urological care in addition to orthopedic and neurosurgical care.

7.4.1 Renal function/upper urinary tracts

Chao and Mayo reported on a series of 40 patients who sustained SCI under 18 years old, of whom 28 underwent close surveillance with annual physical examination, and upper urinary tract evaluation and video urodynamics every 1 to 2 years.[25] They found only one patient developed vesicoureteral reflux during the follow-up period, and this was effectively managed with intermittent catheterization (IC) and anticholinergics. None of the others had upper tract deterioration.

In 1988, Fanciullacci *et al.* published a study on 18 children with SCI (16 boys and 2 girls).[23] All underwent evaluation of the upper urinary tract for UTIs and urodynamics, although the timing varied. Fourteen had long-term follow-up (mean time since the trauma was 7.7 years), with normal kidney tracts in 8, slight dilation in 1, and vesicoureteral reflux with a normal intravenous pyelogram in 2.

Generao *et al.* followed 42 children who sustained SCI, with a mean age at injury of 5.3 years and mean follow-up of 5.5 years.[26] Of the 42, 40 required clean intermittent catheterization (CIC), and 37 required anticholinergics. None had vesicoureteral reflux, hydronephrosis, or renal scarring on Technetium-99m dimercaptosuccinic acid (DMSA).

The question of optimal lower urinary tract management with regard to long-term renal function was addressed by Sekar *et al.* in 1997.[27] A total of 1,114 patients with SCI were identified in their cohort, including 496 cervical injuries, and 618 thoracic or lumbosacral injuries. Age at the time of injury ranged from 1 to 87 years, with a mean age of 31.25 years. Renal scans were performed annually, and patients were managed with either indwelling urethral catheter, suprapubic tube, condom catheter, CIC, Credé manoeuvre, or were voiding normally. In their analysis, the authors found that no single management regimen was superior to the others with regard to renal function. The study concluded, however, that the lower the neurological level of spinal cord injury, the better the long-term renal function outcome.

7.4.2 Urinary stones

Due to prolonged periods of immobility following the injury and because of an abnormal susceptibility to UTIs, patients with SCI are at increased risk for stone disease, varying from 1.9% of patients after 5 years to 9.4% of patients after 20 years.[28] There is no information on stone disease in the pediatric population. Surgical treatment of the neurogenic bladder, specifically the use of certain bowel segments to augment the bladder, may further increase the risk for urolithiasis. The occurrence of bladder calculi after augmentation cystoplasty is about 50% and recurrence rates are also quite high, with 50% of patients experiencing a recurrent stone within 5 years.[29]

7.4.3 Urinary continence

Among their cohort, Fanciullacci *et al.* reported a return of bladder function early in the post-traumatic period, typically less than the 4 to 6 weeks seen in adults with upper motor neuronal spinal shock.[23] Among their series of 18 patients, 12 had lesions resulting in NDO (6 with DSD) managed with anticholinergics, 3 had detrusor areflexia and were managed by IC, and 3 were not evaluated.

A study by Perrouin-Verbe *et al.* reported on genital and urethral tolerance to IC among a mixed cohort of children and adults followed annually, of whom 90% had sustained SCI.[30] Of these 21 male patients, the mean age was 37 years (ranging from 16 to 65), and the indications were detrusor areflexia (10 patients) and DSD (11 patients). One patient had continuous incontinence, 2 had occasional incontinence at night or during activities, 7 had occasional leakage, and 11 had complete continence.

In the series of 42 patients by Generao, where 40 required IC, and 37 required anticholinergics,[26] 80% of those with cervical injuries, 58% with thoracic injuries, and 50% with lumbar injuries had bladder pressures greater than 40 cm H_2O at capacity.

Gurung *et al.* followed 21 patients with SCI who underwent ileocystoplasty, 3 of whom were children 18 years or younger (two 18-year-olds and one 12-year-old).[31] Of the 17 patients with 10-year follow-up or greater, 15 were completely dry compared to none prior to surgery. Only 4 patients required anticholinergic therapy after surgery compared to all of them prior to surgery.

The long-term goal of maintaining urinary continence can be achieved by both medical and surgical means. Strategies to attain urinary continence should be based on a careful assessment of the lower urinary tract and must be tailored to the patient's particular clinical circumstances.

7.4.4 Urinary tract infections

Because of abnormal drainage of the urinary tract, patients with neurogenic bladder are more prone to developing UTIs. In the series by Fanciullaci *et al.*, UTIs were present in 50% of patients.[23] In a cohort of 21 patients, Perrouin-Verbe *et al.* showed symptomatic infections occurred less than once every 2 years in 11 patients (52%), less than once a year in 1 patient (5%), once or twice a year in 5 patients (24%), and twice to four times per year in 4 patients (19%).[30] As in the adult population, it is important to distinguish symptomatic bacterial infection, which may not be clinically relevant, from symptomatic UTIs, which may lead to pyelonephritis and sepsis. Prompt recognition and efficient treatment of UTIs in children with SCI will allow for a much less morbid long-term outcome.

7.4.5 Cancer surveillance

There is a lack of data regarding patients who underwent surveillance cystoscopy for augmentation cystoplasty after spinal cord injury. Husmann showed that, in a small group of patients who had undergone augmentation as children, the incidence of developing cancer per decade following surgery was 1.5% for ileal/colonic and 2.8% for gastric bladder augmentations.[32] Whether or not this applies to the SCI population is unclear. One of the few studies to address the topic was the study by Gurung *et al.* from 2012.[31] There was a mean 14.7-year follow-up among all patients (including the 18 adults and 3 children), and annual cystoscopies were performed starting 5 years after surgery. None of the patients in this series had malignancy identified on surveillance cystoscopy. Cystoscopic surveillance is not felt to be necessary.

7.4.6 Conclusions

1. Renal function outcomes are better with lower levels of SCI. **[LOE 2]**
2. No single bladder management method produces superior renal function outcomes compared to other methods. **[LOE 2]**
3. The risk of bladder cancer is low after pediatric bladder augmentation. **[LOE 2]**

While there is little data to support any routine surveillance regimen among pediatric patients who have suffered an SCI, there are reasonable recommendations that can, nonetheless, be made. Routine screening for renal function/upper tract deterioration and infections seems logical, while frequent testing of lower urinary tract function by UDS and cancer surveillance by cystoscopy may be unwarranted unless there is a clinical indication. Given the heterogeneity in this population, the vigilance and discretion of the physician is critical.

There is a paucity of data regarding children as they age. As such, the optimal long-term follow up for adults who had SCI as children is unknown, but recommendations may be gleaned from the existing data regarding renal function and upper urinary tracts, continence, infections, and cancer surveillance.

7.4.7 Recommendations

1. Clinicians should monitor children with neurogenic bladder secondary to SCI with annual evaluation of the upper urinary tracts by ultrasound. **[LOE 3; GOR B]**

2. Clinicians should evaluate the lower urinary tract using UDS annually for the first several years, and at the discretion of the clinician thereafter. Stabilization of the urodynamic parameters should allow spacing out of the studies. New onset symptoms should prompt an evaluation. **[LOE 3; GOR C]**

3. Clinicians should monitor children with SCI and intestinal bladder augmentation for stone formation by performing a yearly bladder ultrasound. **[LOE 3; GOR C]**

4. Urologists should not screen for bladder malignancy using urine cytology or cystoscopy. **[LOE 3; GOR B]**

7.5 Considerations in the Nonsurgical Management of the Neurogenic Bladder in Children with Spinal Cord Injury

The nonsurgical management of neurogenic bladder dysfunction (NBD) in children with SCI is a crucial and initial component of any rehabilitation program. The aims are to protect the upper urinary tract, improve urinary continence, and ultimately ensure a satisfactory quality of life.[33,34] Other considerations, when planning treatment of NBD in children with SCI, should include the patient's condition, potential complications, technical aspects, and cost effectiveness. The patient's quality of life is a very important consideration when making any treatment decision. Medical management of neurogenic bladder can be divided into: therapy to facilitate bladder emptying and therapy to facilitate bladder filling, or storage of urine.[35] Special consideration should also be given to patients with SCI above the thoracic level, as they are prone to autonomic dysreflexia (AD), which could be a source of significant morbidity and possible mortality.

Evidence acquisition

A detailed literature search for high-quality data published in pediatric and adult patients with NBD and/or SCI was done using Medline and other source documents (e.g. textbooks and medical and scientific websites). Sixty-nine articles were found, from which 35 seemed more relevant for this review. Finally, 16 articles were available and contained useful information about the medical management of neurogenic bladder in SCI in children.

7.5.1 Facilitate bladder emptying

7.5.1.1 Indwelling catheter: urethral catheter or suprapubic catheter

Urethral catheterization is useful in the acute phase, but the catheter should be left in the bladder for as short a time as possible. In the immediate management (first few days), a urethral catheter is almost always necessary to assess urinary output and fluid management.[36–38]

When the patient´s condition is considered stable, intermittent catheterization (IC) can be started on a regular basis. Empirical evidence and expert opinion suggest that silicone catheters have advantages over latex catheters. They are less prone to encrustation, and also, patients with NBD have a higher incidence of latex allergy. Complications, such as epididymitis and UTIs, tend to be higher in patients with an indwelling catheter as compared to patients on IC.

A small group of patients may require ongoing management by an indwelling catheter such as patients with tetraplegia, poor hand skills, or limited assistance from a caregiver, or patients who are clinically unstable. In cases of associated urethral injury or abnormality, suprapubic catheterization is clinically indicated to prevent further urethral trauma.

The complication rate is higher using indwelling catheters than other methods of bladder management. Bladder capacity and compliance tend to decrease over time. The possible mechanism for this outcome is the constant decompression of the bladder and infections related to the catheter, causing, over time, bladder wall fibrosis.

7.5.1.2 Intermittent catheterization (IC)

IC provides a method of emptying the bladder at regular intervals (every 4–5 hours), and maintaining a low level of intravesical pressure, thus improving urinary incontinence, preventing ureteral reflux, with subsequent upper urinary tract dilatation, and decreasing the risk for urinary tract infection.[35]

After the acute phase post-injury, IC is the preferred treatment modality to facilitate bladder drainage.[37,38] It has become the standard procedure for managing neurogenic bladder in patients with SCI. It is performed by parents, caregivers, or by the patients themselves if they have sufficient hand skills and maturity. IC teaching and training for individuals prior to discharge from the acute phase of rehabilitation is mandatory. IC is indicated for chronic management of neurogenic patients who are unable to void or who have high voiding pressures. In children, catheter size depends on patient age and varies from 6 Fr to 14 Fr. Bladder volumes in each catheterization should be less than the expected bladder capacity for patient age [(age + 2) x 30] in children under 18 years old.[39]

IC should be avoided if the patient is unable to catheterize themselves and when there is no caregiver willing or available to perform catherization. IC should also be avoided if the patient has little motivation or has difficulties adhering to the catheterization time schedule, and in patients with a small bladder capacity (high filling and voiding pressure). It should also be avoided in patients with a tendency to develop AD with bladder filling (patients with injuries at T6 and above) unless the AD can be prevented with medical therapy.[40] IC per urethra should be avoided in patients with urethral or bladder neck abnormalities. Although IC has many advantages, some patients experience IC as a traumatic procedure and may develop periodic or permanent aversion to IC.

In pediatric patients, the use of small catheters and assisted catheterization are risk factors for complications (urethral injury, false passage, strictures, epididymitis). Routine follow-up is mandatory in patients with neurogenic bladder doing IC to avoid complications.[37,38,41]

Patients who will potentially benefit from a continent stoma are those with an abnormal urethral anatomy (urethral strictures, false passages, and/or bladder neck obstruction), obese patients, sensate patients who experience urethral pain with IC, or wheelchair-bound patients. Catheterization can be performed easily through a continent stoma with a 12 to 14 Fr catheter. The risks of channel complications include stomal stenosis at the skin level, channel stricture, kinking of the channel, false passage, or urinary incontinence. Risk of complications continues over the lifetime of the channel.[42]

Bacteriuria is present in as high as 70% to 76% of children with NBD who perform IC.[43] Based on the current literature, it is unclear whether antibiotic prophylaxis is helpful or harmful in preventing UTIs: some studies reported an increased incidence (with more resistant organisms), whereas others reported a decreased rate of symptomatic UTI. In the British Association of Pediatric Urology consensus on the management of neurogenic bladder, conclusions were that, in the absence of vesicoureteral reflux, asymptomatic bacteriuria does not appear to be a significant risk for renal scarring, and a patient doing CIC does not require antibiotic therapy.[44] These findings are supported by the Cochrane Review on the use of long-term antibiotic prophylaxis.[45] In this report, the authors noted that the small benefit of the antibiotic prophylaxis should be balanced against the risk for antibiotic resistance and allergic reactions. Antibiotic therapy is only indicated in symptomatic bacteriuria or in symptomatic exacerbations of chronic UTIs.[46–48]

7.5.2 Assisted bladder emptying

Bladder compression techniques (Credé) and voiding by abdominal straining (Valsalva) produce an increase in bladder pressure but do not empty the bladder effectively, and can lead to complications from both high intravesical and abdominal pressure.[49] Silent complications involving the upper urinary tract are not uncommon with the Credé technique and should be avoided, or, if it has been regularly used in a patient, it should be routinely monitored. The effectiveness of Credé is limited by sphincter pressure. It should be especially avoided in patients with DSD, bladder outlet obstruction, vesicoureteral reflux, or hydronephrosis. However, Credé may be indicated when the external urinary sphincter is completely paralyzed (in cases of low SCI) and will not close with suprapubic pressure. Credé may be more effective in babies than adults, as the bladder is an abdominal organ in young children while it is a pelvic organ later in life.

Stimulation of the sacral or lumbar dermatomes in patients with suprasacral SCI can elicit reflex contraction of the detrusor. Such triggered reflex voiding depends on an intact sacral micturition reflex. It can lead to upper urinary tract deterioration due to high voiding pressures from a reactive external urethral sphincter. Thus, trigger reflex voiding is not recommended, and, when used, the patients should be closely monitored, as strict urodynamic control is required.

7.5.3 Autonomic dysreflexia

Autonomic dysreflexia (AD) can occur in children who have a SCI at the thoracic level 6 (T6) or above. AD is a sustained sympathetic response caused by a noxious stimulus occurring below the level of injury. The most common causes are bladder distention (which provokes NDO and DSD) and bowel problems such as constipation and impaction. The most dramatic reaction associated with AD is a sudden severe elevation in blood pressure often associated with bradycardia.[1] Of note, children and adolescents with cervical and upper-level SCI have lower baseline blood pressure compared with the general population. AD is frequently defined as systolic blood pressure elevations more than 15 to 20 mm Hg above baseline in adolescents with SCI or more than 15 mm Hg above baseline in children. Another definition is a systolic blood pressure 20 to 40 mm Hg above baseline.[50] Other common problems that can occur in AD include severe headaches, sweating, flushing, goose bumps, chills, feelings of anxiety, and a slower pulse rate. However, about 30% to 40% of people with AD have elevated blood pressures, with few if any other symptoms (silent dysreflexia).[51–53]

7.5.4 Drug treatment to decrease bladder outlet resistance

There are very few reports on the use of alpha-blockers in children with neurogenic bladder dysfunction. Selective and nonselective alpha-blockers have been used to treat DSD and to lower bladder pressure during voiding with variable degrees of efficacy reported when using selective alpha-blockers in children with NBD. In most series, alpha-blockers have been used as an addition to intermittent catheterization and oxybutynin. It has been reported to be partially successful for decreasing bladder outlet resistance, residual urine, and AD in only a small percentage of pediatric patients.[54,55] As in adults, alpha-blockers should be avoided in patients with symptomatic hypotension. Patients should take medication at night, when supine.

7.5.5 Drugs that facilitate bladder filling or storage of urine

Several randomized controlled studies revealed no significant evidence for differential efficacy across different antimuscarinic medications.[56–58] Oxybutynin is the only licensed (FDA approved, United States) anticholinergic for pediatric patients. It can be given orally, transdermally, or intravesically. It binds to muscarinic receptors and stabilizes the detrusor muscle, reducing its overactivity and improving bladder compliance. It is useful in the management of neurogenic detrusor overactivity, reducing symptoms and helping to prevent renal and bladder damage. Oxybutynin can cause anticholinergic adverse effects, however, including oral (dry mouth, dysphagia), visual (dry eyes, blurred vision), and gastrointestinal (diarrhea, constipation, distention) symptoms in up to 76% of patients. The majority of available studies evaluated oxybutynin and tolterodine.

Tolterodine tartrate is an M2 and M3 antimuscarinic drug. Oral and extended-release capsules have been found both to be effective and well tolerated by children with neuropathic bladder.[59] Solefenacin is an M3 selective antimuscarinic. This agent has been reported to be well tolerated and safe, even during long-term treatment. It has been reported to be effective in the treatment of neurogenic detrusor overactivity in children.[58] Other anticholinergic medications that have been used include fesoterodine, darifenacin, and trospium chloride.

As mentioned previously, anticholinergic medications can cause adverse effects, including oral (dry mouth, dysphagia), visual (dry eyes, blurred vision), gastrointestinal (diarrhea, constipation, dyspepsia, abdominal distention) and impaired cognitive function symptoms in up to 76% of patients.[59]

Mirabegron is a beta-3-adrenoceptor agonist not yet approved for use in children. It has been approved for the treatment of overactive bladder (OAB) symptoms in adults. In adults, the recommended starting dose of mirabegron is 25 mg, which can be increased to 50 mg, based on individual efficacy and tolerability. Mirabegron is reported to have similar efficacy to antimuscarinic agents and has lower rates of side effects than antimuscarinic medications. Several phase 2 and 3 studies have shown significant improvement in clinical OAB symptoms in adults treated with mirabegron with a favourable tolerability profile. Mirabegron has not been studied yet in children with SCI and no recommendation with regard to its use has been issued by the manufacturer or medical regulatory bodies. Only one study has been published in pediatric patients with idiopathic OAB, and the authors reported that it was a safe and effective alternative for children with OAB refractory to antimuscarinics.[60]

7.5.6 Conclusions

1. Early IC will allow easier bladder emptying and may reduce the incidence of clinical UTIs. **[LOE 3]**

2. Prophylactic antibiotic administration in children with SCI on IC is associated with increased bacterial antibiotic resistance. **[LOE 2]**

3. The Credé manoeuvre may be more effective in babies than in adults because the bladder is an abdominal organ in babies. **[LOE 3]**

4. Autonomic dysreflexia in children with SCI may be associated with a smaller elevation in blood pressure, compared to adults. **[LOE 3]**

5. Alpha-blocker medications are not effective at decreasing bladder outlet resistance, residual urine, and autonomic dysreflexia in children. **[LOE 3]**

6. Anticholinergic medication is the first-line treatment for detrusor overactivity in children with SCI.

7. Oxybutynin is the only FDA-approved anticholinergic medication for use in children.

8. Anticholinergic medications can cause non-life-threatening but potentially severe side effects. **[LOE 2]**

7.5.7 Recommendations

1. Clinicians should use IC in the initial acute phase after SCI. **[LOE 2; GOR B]**
2. Clinicians should consider placing a suprapubic catheter in those patients who require long-term bladder drainage and are unable to do IC. **[LOE 3; GOR C]**
3. Clinicians should perform routine follow-up in SCI children on IC in order to ensure early detection of complications such as UTIs and bladder stones. **[LOE 2; GOR B]**
4. Surgeons should offer a continent stoma to pediatric SCI patients who are good candidates for IC yet cannot perform IC through the urethra. **[LOE 3; GOR B]**
5. Clinicians should not administer antibiotic prophylaxis routinely to pediatrics patients with neurogenic bladder doing IC. **[LOE 2; GOR B]**
6. Clinicians should not recommend the Credé and Valsalva manoeuvres in children with suprasacral SCI. **[LOE 3; GOR C]**
7. Clinicians should not recommend triggered reflex voiding in pediatric patients with SCI. **[LOE 3; GOR C]**
8. Clinicians should recognize and treat autonomic dysreflexia as an emergency, in order to avoid complications. **[LOE 2; GOR B]**
9. Clinicians should not use alpha-blockers to manage voiding dysfunction in children with SCI. **[LOE 3; GOR C]**
10. Clinicians should use antimuscarinic agents as the first choice in treating neurogenic detrusor overactivity and lower intravesical pressures. **[LOE 2; GOR B]**
11. Clinicians should discuss the side-effect profile of anticholinergic medications with parents or caregivers when prescribing these in children with SCI. **[LOE 2; GOR B]**

7.6 Special Considerations in the Surgical Management of Neurogenic Bladder in Children with Spinal Cord Injury

Surgical procedures involving the urinary tract in children with SCI may be needed to support or augment nonoperative measures. As with nonoperative measures, the goals of surgical procedures include preservation of renal function, allowance of urine storage, controlled drainage of urine, and, as much as possible, aiding the patient in achieving social acceptability and some degree of independence from caregivers. In children, surgical procedures have two goals: first, to maintain low bladder pressures and adequate volume to protect the kidneys, and second, to help patients achieve continence. Broadly the types of procedures that can be performed can be grouped into two categories: procedures that achieve the first goal in that they will ensure low bladder pressures through constant (incontinent) drainage of urine; and procedures that achieve both goals by ensuring low bladder pressure such that continence can be preserved. In children with SCI, the choice of a surgical procedure to manage a neurogenic bladder must be made very carefully in light of the complex nature of the surgery, the lifelong considerations, and the social environment in which the child lives.

A thorough search of the literature reveals very few articles solely dedicated to the surgical management of the neurogenic bladder in children with SCI. Most of the information is derived from the published information related to NBD management, mostly in children with NBD secondary to spina bifida. The principles of surgical management are similar.

7.6.1 Incontinent procedures aimed simply at preservation of renal function

7.6.1.1 Vesicostomy

A cutaneous vesicostomy using the technique advocated by Duckett and attributed to Blocksom[61] provides an effective means of protecting the kidneys in infants and young children with hostile neurogenic bladders when CIC and anticholinergics are ineffective or cannot be implemented.[62,63] Although some authors have recommended its use as a permanent diversion in children with myelomeningocele,[64] it is an incontinent form of diversion, with its accompanying disadvantages, such as the need for diapers, skin irritation, and negative social implications, and thus it can only be recommended as a temporary measure for infants and young children.

7.6.1.2 Suprapubic cystostomy

Since the popularization of CIC in the 1970s, the use of permanent indwelling catheters in children has been almost abandoned.[65] In the rare cases in which a long-term indwelling bladder catheter is considered necessary, a suprapubic cystostomy is an alternative to a urethral catheter. The theoretical advantages are the avoidance of genital lesions caused by the prolonged presence of the urethral catheter,[66] but published evidence of the superiority of suprapubic cystostomy over urethral catheterization is lacking.[67] Long-term use of indwelling bladder catheters has an adverse effect on the bladder epithelium and an increased risk of bladder cancer.[68–72] In one study, including more than 500 adults, the incidence of UTIs was higher with indwelling urethral catheters, less with suprapubic cystostomy, and about equal between CIC and no catheter.[73] The incidence of epididymitis in men is lower with suprapubic cystostomy. Nevertheless, from the point of view of preservation of renal function, there seems to be little difference between patients managed with CIC or indwelling catheters.

7.6.1.3 Cystostomy buttons

Gastrostomy buttons in the urinary bladder with CIC and no indwelling catheter have been used as an alternative to the suprapubic cystostomy tube for the last 20 years,[74] but in most cases this is only a temporary measure for patients in whom CIC has not been possible.[75]

7.6.1.4 Procedures to decrease outlet resistance: external sphincterotomy and Botulinum toxin to the sphincter

External sphincterotomy or botulinum toxin injection at the level of the urinary sphincter can be combined with a condom catheter in adult men. However, these techniques are of no use in boys given the difficulty of applying penile collection devices and the long-term complications associated with external devices such as skin breakdown and erosion.

7.6.1.5 Ileovesicostomy

Ileovesicostomy represents a form of incontinent diversion, which has been used mostly in adults with NBD.[76] It consists of the interposition of a segment of ileum between the bladder and the skin. The advantage over a simple cutaneous vesicostomy is that the stoma can be placed in a location in the lower abdomen where it can be fitted with a collection bag. It has the advantage over an ileal or colonic conduit of avoiding a uretero-intestinal anastomosis with its accompanying risk for stenosis (see next section). The main disadvantage is that in most cases there is considerable residual urine and the potential for UTIs. The experience with ileovesicostomy in children is very limited. The indication for this procedure in the patients described by Ching *et al.* included patients felt to be incapable of performing CIC in a reliable manner due to family unwillingness, poor social support, or patient refusal. The median follow-up was 48.2 months. Postoperative complications included ileus and a wound infection in 1 patient. Long-term complications included urinary tract infection in 2 patients, stomal issues in 2 patients and temporary urethral leakage in 1 patient. The authors concluded that incontinent ileovesicostomy is a viable approach in children with few other options, "particularly those who are noncompliant or physically/socially unable to handle catheterization. This operation can help keep such patients out of diapers" but requires use of a stoma bag.[77]

7.6.1.6 **Incontinent intestinal diversions**

After the description of the ileal conduit (cutaneous uretero-ileostomy) by Bricker in 1950 as a means of urinary drainage after pelvic exenteration, pediatric surgeons and urologists adopted the use of incontinent ileal or colonic conduits for children with neurogenic bladder, mostly secondary to myelomeningocele, as a means to protect the upper urinary tracts and to provide controlled urinary drainage. Stevens and Eckstein described their experience with 113 children followed for a mean of 5 years and considered this method as "very effective in preventing infection and loss of renal function. The incidence of early and late complications can be minimized by proper patient selection, attention to surgical details and diligent postoperative follow-up."[78] However, in a series of 96 children with a mean follow-up of 4.5 years, Schwarz and Jeffs reported a concerning rate of renal deterioration caused by ureteroileal stenosis, stoma stenosis, and excessive conduit length.[79] Shapiro *et al.* reported on 90 patients, 75 of whom were still living after 10 to 16 years. Seventy-five percent of the renal units improved or remained normal, and 69% of those that were initially normal at the onset remained so. In the absence of obstruction, creatinine clearance remained normal.[80]

In a recent study, Stein *et al.* reviewed a cohort which dated back to 1983 and included 88 patients under 20 years of age (mean age at operation 10.1 years).[81] The indications to perform an incontinent colonic conduit included patients with either chronic renal failure and dilated upper urinary tracts with deterioration of the renal function or those unable to catheterize. Of the 88 children, 11 were later converted to continent diversion and not included in the follow-up. Of the remaining 77 patients, 21 patients were not available for follow-up: 11 were deceased and 10 were lost to follow-up. Fifty-six patients had a mean follow-up of 21 years. Of these, 21 patients (37.5%) developed complications requiring reoperation in 18 patients (32%). It can therefore be concluded that, for pediatric patients requiring an incontinent diversion, a colonic conduit is a reasonable option, but close scrutiny of the data may suggest otherwise.

7.6.2 **Continent procedures that achieve continence and low bladder pressure**

7.6.2.1 **Injection of botulin toxin**

Children with NGB and NDO or poor compliance who are on IC and exhibit poor response to anticholinergic agents have been treated with intravesical injection of botulinum A toxin in hopes to reduce intravesical pressures and augment dry periods between catheterization.

Initial results were encouraging, with significant improvement in capacity and compliance and reduction of detrusor pressure for a duration of up to 10 months.[81] Repeated injections appear to be equally effective.[82] However, another report evaluating 11 children with myelomeningocele showed only a 17% decrease in detrusor pressure associated with an increase in bladder capacity of 33%, rather insignificant values when the capacity and compliance are already severely compromised. In addition, in 10 patients, bladder compliance remained poor.[83] A recent study reported a 45% increase in bladder capacity with a similar decrease in detrusor pressure, again insufficient to ensure upper tract protection in patients with significant bladder dysfunction.[84] With regard to quality of life, patients with spinal cord injury and high intravesical pressure seem to do better after augmentation cystoplasty rather than with repeated botulin toxin injections.[85] It must be noted that these studies are retrospective and include only small cohorts of patients.

7.6.2.2 **Bladder augmentation**

The application of enterocystoplasty in patients with neurogenic bladder became possible only after the use of CIC became widely accepted. The use of ileal segments to increase bladder capacity and compliance in SCI individuals is well documented.[31] Preconditions for this operation are the acceptance and ability to perform CIC by patients and parents. Although the use of a reconfigured ileal segment for augmentation cystoplasty has been the preferred method for many urologists, there is evidence to support the use of a reconfigured segment of the sigmoid colon over an ileal segment.[86] With the use of the colon, the incidence of long-term metabolic complications such as vitamin B12 deficiency is nil, the intestinal transit is not altered, the incidence of postoperative bowel obstruction is reduced, and the thicker wall of the colon allows for easier implantation of the catheterizable conduits.[87,88] Furthermore, when the sigmoid segment is correctly reconfigured, the urodynamic results are excellent.[89]

Although enterocystoplasty is urodynamically effective, the potential development of complications makes long-term follow-up mandatory.[88] Complications of bladder augmentation include development of calculi, metabolic acidosis, bladder perforation, febrile UTIs, nutritional deficiencies, and development of tumours. These will be briefly analyzed in the following paragraphs and are of particular concern in children, as they will require lifelong monitoring.

Lithiasis. Both SCI[90] and CIC[91] are associated with an increased incidence of urinary tract lithiasis, particularly in the bladder. It is not clear if the presence of an augmented bladder increases this risk, *per se*. Nevertheless, routine irrigation of the augmented bladder seems to be associated with a decrease in the incidence of bladder calculi and symptomatic UTIs, and it should be recommended to all patients after augmentation.[92]

Metabolic acidosis. Metabolic acidosis is an unavoidable consequence of enterocystoplasty.[93,94] However, in most patients with normal renal function, acidosis is compensated and no treatment is required. Nevertheless, serum electrolytes, bicarbonate, and when possible venous blood gasses should be checked at regular intervals during follow-up, as chronic acidosis may interfere with normal growth in children.

Bladder perforation. Bladder perforation is a serious consequence of enterocystoplasty. It is particularly problematic because the perforations are usually intraperitoneal and the urine often contains bacteria and may lead to peritonitis, sepsis, and death. Perforation is the result of poor compliance with the catheterization regime. It tends to be seen more frequently in adolescence and in substance abusers.[95] The symptoms and signs of peritonitis may be obscured by the sensory alterations resulting from the SCI. A high index of suspicion is recommended for patients presenting with sepsis, abdominal pain, abdominal distension, vomiting, or hematuria.

Nutritional deficiencies. Vitamin B12 deficiency has been reported in patients in whom a long segment of ileum has been used for bladder reconstruction.[88] It is recommended that B12 levels be checked starting 10 years after ileocystoplasty. This complication may be avoided by using the sigmoid colon.

Bladder tumours. Spinal cord injury and long-term indwelling catheters are associated with an increased risk for bladder cancer.[69,70] Whether or not enterocystoplasty adds to this risk is not clear.[96]

7.6.3 Continent catheterizable channel

Catheterization of the bladder has an indisputable predominant role in the management of neurogenic bladder of all etiologies. Independence from caregivers to perform bladder catheterization every 4 hours is important for quality of life. SCI patients at the cervical level often have impaired hand function and depend on attendants to perform catheterization. In 1993, at the request of a patient with a cervical lesion, the author of this section constructed a continent catheterizable channel in an adult patient who had read about the Mitrofanoff procedure and thought that with an umbilical stoma he could self-catheterize, which would allow him to return to work as an engineer. This was reported along with a small series of other cases in 1997.[97] Although only one other small series has been reported, this procedure has been carried out in many tetraplegic patients who have been very appreciative to gain daytime independence from caregivers.[98]

Many other barriers exist for the implementation of self-catheterization programs in SCI patients, including: "*(1) caregivers or nurses are not available to carry out five or six catheterizations a day; (2) lack of time to perform intermittent catheterizations; (3) unavailability of suitable toilet facilities in public places, including restaurants and offices; (4) redundant prepuce in a male patient, which prevents ready access to urethral meatus; (5) urethral false passage; (6) urethral sphincter spasm requiring the use of flexible-tip catheters and alpha-adrenoceptor-blocking drugs; (7) reluctance to perform intermittent catheterization in patients >60 years by some health professionals; and (8) difficulty in accessing the urethral meatus for catheterization while the patient is sitting up, especially in female patients.*"[99] Many of these barriers could be overcome with the use of umbilical continent catheterizable stomas. Interestingly, as recently as 2015, Sorokin and De suggested sphincterotomy and external collection devices, suprapubic cystostomy, ileal conduit, and ileovesicostomy as methods to provide controlled bladder drainage in patients with high spinal lesions and compromised hand function, but failed to mention the potentially excellent option of a continent catheterizable channel.[100]

Appendicovesicostomy, also known as the creation of a Mitrofanoff channel, plays a uniquely important role in children with SCI. Adult obesity, combined with a relatively short appendix, can limit the application of the appendicovesicostomy, but in the child the anatomy is usually more favourable for application of this technique. Other options include the Monti-Yang procedure or a tapered ileal segment, and are described elsewhere in this text. Unless a low-pressure and large-volume bladder are present, a continent, catheterizable channel is often combined with either anticholinergic treatment, bladder injection of botulinum toxin, or enterocystoplasty in order to ensure a low-pressure urine storage system.

7.6.4 Procedures to increase bladder outlet resistance

Children with lower-level SCI may demonstrate normal bladder volumes but reduced bladder outlet resistance due to an incompetent sphincter. This leads to urinary incontinence, either constant or with elevation of the intra-abdominal pressure (stress) as documented by urodynamic study. Procedures to increase outlet resistance in children include injection of bulking agents at the level of the bladder neck or proximal urethra, periurethral slings, and artificial urinary sphincters. In boys, the prostate is underdeveloped, and thus may provide less bladder outlet resistance. In addition, the anatomy may be more amenable to placement of artificial sphincter at the level of the bladder neck. A recent systematic review of the literature (in adult patients mostly) reported that: *"None of the studies followed a randomized controlled trial (RCT) design. Three primary surgical procedures were used in 29 of 30 studies: artificial urinary sphincter (AUS), urethral slings, and urethral bulking agents. One study used a ProACT device. AUS was considered more successful than urethral bulking agents (77 ± 15% vs. 27 ± 20%, p=0.002). Urethral bulking agents reported higher failures than urethral sling procedures (49 ± 16% vs. 21 ± 19%, p=0.016) and AUS (21 ± 19%* vs. 10 ± 11%, *p<0.002)."*[101]

7.6.5 Conclusions

1. Vesicostomy provides a low-pressure method to drain the bladder and protect the kidneys in young children. **[LOE 3]**
2. Ileovesicostomy in children with SCI is associated with complications of residual urine and recurrent UTIs. **[LOE 4]**
3. Noncontinent ileal or colonic conduits in children are associated with complications of renal deterioration due to ureterointestinal anastomotic strictures and stomal stenosis. **[LOE 2]**
4. Botulinum toxin injection of the bladder is a minimally invasive option that can temporarily improve symptoms of neurogenic bladder dysfunction in children with SCI. **[LOE 3]**
5. Bladder augmentation offers superior bladder-related quality of life compared to botulinum toxin injections of the bladder. **[LOE 3]**

7.6.6 Recommendations

1. Surgical treatment of the bladder in children with SCI should only be considered if medical treatment has failed to provide low bladder pressures and continence. **[LOE 3; GOR C]**

2. Surgeons should recommend vesicostomy as a temporary measure in infants and children with SCI when medical management and CIC are ineffective or cannot be implemented. **[LOE 3; GOR C]**

3. Surgeons should not perform sphincterotomy or botulinum toxin injection in the urinary sphincter in boys with SCI, except in circumstances where a condom catheter can be fitted to the penis and the family is fully aware of the potential complications. **[LOE 3; GOR B]**

4. Surgeons should not recommend ileovesicostomy in children. **[LOE 3; GOR B]**

5. Surgeons should not recommend Ileal or colonic noncontinent diversion in children with SCI because of the severe potential complications. **[LOE 2; GOR B]**

6. Surgeons may offer endoscopic injection of botulinum toxin in the bladder as a temporary treatment of neurogenic bladder dysfunction in children with SCI. **[LOE 3; GOR C]**

7. Bladder augmentation with or without creation of a catheterizable channel may be offered to older children who can be catheterized reliably and who have failed medical management. **[LOE 3; GOR B]**

8. Surgical procedures to increase bladder outlet resistance should be offered in patients with an incompetent urinary sphincter and incontinence. **[LOE 3; GOR C]**

9. Surgeons may recommend bladder neck sling or artificial sphincter insertion over less-effective methods such as bulking agent injection in children with SCI. **[LOE 4; GOR C]**

7.7 Special Considerations in Bowel Management in the Urological Management of Children with Spinal Cord Injury

Urological and gastrointestinal problems have a major impact on the quality of life of children with SCI, negatively impacting daily activities and restricting social development. Even more, bladder and bowel autonomy are predictive factors in the success of discharging a patient home after initial treatment for the injury.[102] Bowel alterations are due to dysfunction on peristaltic movement and on defecation. In addition, patients suffer from partial or complete loss of ability to consciously feel stools in rectum or to initiate or delay defecation with a high prevalence of fecal incontinence and/or constipation.[103] Signs, symptoms, and complications include prolonged intestinal transit, fecal impaction, abdominal distension, colonic dilatation, and megacolon. In the search for improving quality of life of the children, specialized centres have developed bladder-bowel management programs tailored to each patient's needs. The essentials of bowel management in young people with SCI entail complete and regular defecation, continence, expediency, aesthetics, and prevention of constipation and complications.[104,105]

Evidence acquisition

A literature review performed through PubMed using MeSH terms "bowel management," "medullar trauma," and "children" resulted in 39 articles being selected, from which 13 seemed relevant for this review. Finally, 10 articles were available and contained useful information about bowel management in spinal cord injury in children.

Bowel management

Bowel management includes a variety of different approaches. No single method has proven to be satisfactory, and every patient must undergo a "trial and error method" for each approach to find the most suitable scheme for his or her own bladder and bowel regimen. These approaches include addition of dietary regular toileting habit, digital stimulation and manual removal of stool, stool softeners, oral laxatives, suppositories, enemas, oral cathartics, anal plugs, biofeedback, and nerve stimulation.[102,104,105]

Bowel programs should be initiated in children 2 to 4 years of age or earlier if they are experiencing diarrhea or constipation.[103] Therefore, prevention of incontinence must focus on proper technique, hygiene, as well as timing of performance of bladder and bowel management program.[106] Management of upper motor neuron bowel with a spastic external sphincter includes daily to every-other-day suppository use, digital stimulation, and, if needed, oral agents to soften stool or laxative agents.[106,107] Lower motor neuron bowel has an hypotonic external sphincter, also leading to fecal incontinence.[106,107]

7.7.1 Nonpharmacologic measures

Manual removal of stool is recommended in lower motor neuron lesion and areflexic bowel in combination with digital stimulation and spontaneous bowel evacuation, which can reduce the incidence of fecal incontinence, reduce duration of defecation (less than 60 minutes), and increase consistency of stool.[103] Increased suprapubic or abdominal pressure (Credé manoeuvre or Valsalva manoeuvre) can contribute to achieving defecation but may be contraindicated in children with vesicoureteral reflux.[104,105] Patients should take advantage of gastrocolic reflex for defecation timing and adopt a gravity-aided position. Bowel emptying by sitting on a toilet or commode facilitates the process because of the mechanics of the vertical position that enable better intestinal transit.[104]

7.7.2 Pharmacologic measures

Pharmacologic measures are required in 80% of patients. This can be oral, rectal, or a combination of both. Oral laxatives are recommended if there is completeness of sensory function and are related to longer defecation times (longer than 60 minutes).[104] Oral laxatives can increase the occurrence of fecal incontinence, leading to more difficulties in bowel evacuation and increased consumption of it over time.[103] Approximately 34% of patients will require an additional laxative or stool softener or combination thereof.[103]

7.7.3 Rectal irrigations/enemas

Transanal irrigation (TAI) consists of administration of isotonic saline solution at 20 mL/kg for 5 minutes through a rectal catheter with posterior abdominal massage, every 1 to 2 days. In children with SCI, use of TAI has been shown to reduce the use of diapers in 73% of patients with SCI.[106] TAI reduces hard stools in up to 20% of patients.[106] In addition, reduction in fecal incontinence has been reported in up to 29% in patients using this modality.[107] Improvements in bowel continence are seen when treatments are carried out consistently over 30 months.[108]

Potential complications associated with this procedure are allergic reaction to latex, trauma and perforation of rectum and colon, electrolyte imbalance, hyponatremia, bacteremia with posterior endocarditis, infections of rectum and colon, and autonomic dysreflexia.

Bowel evacuation is accomplished by "Malone," a catheterizable conduit with a stoma on the lower abdomen linked to the proximal colon. In general, the appendix can be used, allowing the introduction of an enema directly into the cecum.[109]

7.7.4 Nerve stimulation

The main principle of this approach is to improve bowel motility by causing smooth muscle contraction in the distal colon.[110]

The Praxis multifunctional implantable functional electrical stimulation (FES) system (Cochlear Ltd, Australia) is a 22-channel implant stimulator for bowel and bladder function and epineural electrodes. Bladder and bowel stimulation require extradural pararadicular electrodes on the S2, S3, and S4 mixed nerve roots, with final position determined by the simulated response and guidance from fluoroscopy. Low-frequency electrical stimulation of bilateral S3 can increase anal and sphincter pressure. With daily use, a reduction in time of defecation was reported. Improved satisfaction in bowel management was noted after 2 months of treatment, with an increased frequency of stooling in larger quantities.[110]

7.7.5 Conclusions

1. Bowel management in the child with SCI is an integral part of the treatment plan.
2. A stepwise, individualized approach can achieve the goals of early hospital discharge, prevention of constipation, and stool continence.
3. Bowel programs can provide children and young adults with a good quality of life and social acceptability.
4. Transanal irrigation reduces hard stools and fecal incontinence. **[LOE 3]**

7.7.6 Recommendations

1. A bowel program should be initiated immediately in children with SCI. **[LOE 2; GOR B]**
2. Oral or rectal stool softeners should be offered to prevent constipation in children with SCI. **[LOE 2; GOR B]**
3. Transanal irrigation should be offered for children with hard stools and stool incontinence. **[LOE 2; GOR C]**
4. Creation of a catheterizable channel for antegrade enema administration should be considered in children with SCI. **[LOE 3; GOR C]**

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C8

Special Considerations in the Urologic Management of Older Patients with Spinal Cord Injury

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Committee 8

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Special Considerations in the Urologic Management of Older Patients with Spinal Cord Injury

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8.1 Introduction

By 2050, the proportion of the population over the age of 60 will exceed 30% in many countries around the world.[1]

There is a rising incidence of both traumatic and nontraumatic spinal cord injury (SCI) in the aging population. Furthermore, improvements in health care and nutrition mean patients with SCI are living longer. Patient outcomes after an SCI in the older patient are a sum of the effects of the injury and its management at any age, but compounded by specific effects of aging and the emergence of unrelated comorbidities.

Changes in health, comorbidities, cognition, and dexterity with aging have an impact on function and are important considerations in the management of the older patient with SCI. Treatment decisions for the older patient are increasingly complex, due to the need to take into account comorbidities and polypharmacy.

For the patient living with an SCI, changes in circumstances (social, financial) have an impact on quality of life and influence management and support strategies. In fact, these may be the key drivers in determining realistic goals and expectations.

This chapter will address issues pertaining to the older patient who sustain an SCI and the time-related changes relevant to the urological, gastrointestinal, and functional management of the SCI patient.

8.2 Methodology

A literature search using the PubMed and Ovid search engines was carried out, examining pertinent literature regarding SCI in the older patient. References were screened for relevance, and full text articles obtained. The Committee found a paucity of information in the literature regarding many aspects of SCI in older patients. As such, the literature search was not time-restricted and we have selectively included older seminal articles based on the expert opinion of the reviewers. The studies examined commonly include a heterogeneous mix of ages and conditions. There were also difficulties in interpretation and comparison of data related to historical era, changes in management and rehabilitation of SCI patients, and survivor effects. Most studies have been cross-sectional in nature so that some people might have died for reasons other than their SCI, leaving a cohort of healthier people, and thus distorting the outcomes. Longitudinal studies would be preferable, but are not often practical.

Considering outcomes for men and women separately might be reasonable but, as the ratio of men to women sustaining spinal injuries is approximately 4:1, this is often difficult and there are different management possibilities for lower urinary tract disorders. We did not attempt to analyze these separately, but the results of considering males and females together may be misleading.

Due to the limitations in the available literature, the conclusions and recommendations in this chapter are generally based on a lower level of evidence (LOE).

8.3 Epidemiology of Spinal Cord Injury in Older Adults

According to the World Report on Ageing, both the proportion and absolute number of older people in populations around the world are increasing dramatically. By 2050, over 30% of the population will be aged over 60 years in the following countries and regions: Japan, Europe, North America, Chile, China, the Islamic Republic of Iran, the Republic of Korea, the Russian Federation, Thailand, and Vietnam.[1]

Data on the epidemiology of traumatic spinal cord injury (tSCI) or nontraumatic spinal cord damage (SCD) in elderly patients are essential for government health bureaus to establish policies for prevention, to improve the lives of elderly patients with SCI, and to anticipate their future needs. Unfortunately, only a handful of high-income countries are able to provide national statistics of tSCI on a regular basis.[2,3]

8.3.1 Traumatic spinal cord injury

Worldwide, motor vehicle accidents and accidental falls are the two most common causes of tSCI in all age groups.[3-5] Reports from developed nations (Iceland, France, the United States, South Korea, the Netherlands, Ireland, Portugal, Australia) have shown that the average age of tSCI is increasing and the rate of tSCI due to simple low-velocity falls is also increasing.[5-9]

A recent retrospective cohort study from the Quebec Trauma Registry in Canada has shown that there was a 13-year increase in age in patients suffering from tSCI between 2002 and 2010. This aging population of patients with tSCI is more frequently associated with sustaining injuries with central cord syndrome (50% in patients aged ≥55 years compared to 19% in patients <55 years), incomplete neurological injury, and tetraplegia.[10] The upper limbs are more affected than the lower limbs in central cord syndrome, resulting in hand function impairment with significant long-term disability. Another retrospective Canadian study also revealed an increased incidence of tSCI after 65 years.[11] An earlier Canadian study in 2006 showed an increased incidence of tSCI with age (51.4/1 million >64 years vs. 42.4/1 million for individuals ≥15 years and ≤64 years). In addition, the mortality was significantly related to age (13.8% in ≥55 years vs. 2.5% in <55 years).[12] Studies from Taiwan and Australia also showed similar results.[13,14] In the past 25 years in Australia, the incidence of tSCI in people aged 65 and older has increased from 4% to 12%, reflecting the higher incidence of falls among older adults.[14] A systematic review of 13 studies that included populations from Western Europe, Canada, Australia, Turkey, the United States, and Taiwan confirmed that the incidence rate of tSCI increased steadily with age.[15]

In a retrospective review of 12 years of data from a Canadian nationwide database (1998–2009), the rate of hospitalization for cervical spondylotic myelopathy (CSM) was 4.04 per 100,000 person-years, with higher rates in male elderly patients. During follow-up, SCI was more likely to occur in those CSMs that were treated conservatively than those that were treated surgically.[16]

Results from a cross-sectional analysis of the US National Spinal Cord Injury Database longitudinal data from 1972 to 2014 have also shown similar findings as Canada and other developed countries: an increase in injuries caused by falls, particularly in the ≥46 years age group.[17] During this 40-year period, there has been a particularly marked increase in tSCI in the age group >65 years (3.1%–13.2%) when compared to the general population (9.8%–13.1%).[17]

Another retrospective study that analyzed the US Nationwide Inpatient Sample database (1993–2012) also detected an increased rate of tSCI in elderly patients.[18] The incidence rate in men aged 65 to 74 years suffering from tSCI increased from 84 cases/1 million in 1993 to 131 cases/1 million in 2012. In those aged 65 years or older, tSCI due to fall increased significantly, from 28% of all SCI in this age group from 1997 to 2000 to 66% from 2010 to 2012. Mortality increased with increasing age, although there was an observed decreasing trend of mortality from 24.2% in 1993–1996 to 20.1% among patients aged 85 years or older.

In Tianjin, China, from 1998 to 2000, patients aged 55 to 64 years and ≥65 years accounted for 10.4% and 4.2%, respectively, of all hospitalized tSCI; from 2007 to 2009, this increased to 20.8% and 11.1%, respectively.[19] Fall from a low height accounted for 70% of tSCI in those older than 65 years in this study, and 40.3% of cervical injury was due to such a fall.[19] Another retrospective study analyzing the inpatient data of traumatic cervical SCI in Chongqing, China, also demonstrated that the proportion of those patients aged 61 to 75 years increased from 6.5% from 2001 to 2002 to 12.3% from 2009 to 2010. There was also a corresponding increase in the proportion of injuries due to low fall, from 14.3% to 21.1%.[20] This high level of SCI may cause an increase in the death rate compared to low-level injury.[21]

Another retrospective cross-sectional study from Brazil that analyzed the database of inpatients admitted for SCI from 2005 to 2010 showed that fall from standing was the most prominent mechanism for tSCI in elderly patients.[21]

The increasing trend of elderly tSCI suggests that more geriatric expertise and input will be required for rehabilitation programs for these patients in the coming decades. A multidimensional risk assessment and multifactorial intervention, especially to reduce falls and subsequent SCI in older adults, is necessary to reduce the incidence of tSCI in the elderly population.[17,22]

The research represented herein would suggest that such interventions should be directed at preventing falls that occur in the home due to slipping, tripping, stumbling, and falling on the same level and from stairs, steps, beds, chairs, and toilets, as suggested by previous studies.[17,23]

8.3.2 Nontraumatic spinal cord injury

There are fewer studies of nontraumatic SCD epidemiology, including incidence, than tSCI. This is due to a range of factors, including the wide range of conditions that can cause nontraumatic SCD, making the establishment of central registries very difficult. These patients are typically managed in a variety of acute and rehabilitation hospitals that are neither centralized nor coordinated in the way that they care for tSCI.[166]

There is emerging evidence that the incidence of nontraumatic SCD may be 60% to 70% higher than tSCI.[11,24-26,166] Etiologies of nontraumatic SCD in geriatric patients include vertebral spondylosis (spinal stenosis), tumour compression, vascular ischemia, and infection.[27] For instance, a report from Japan in 1993 showed a high rate of degenerative deformity of the spine (59% of nontraumatic SCD), and this accounted for 76% of tetraplegic cases. The observation is most likely due to the older age profile of Japanese patients.[28]

A study in Australia showed that the frequency of nontraumatic SCD increases with age (38.1/1 million for the age group of 55 to 64 years, 63.4/1 million for 65 to 74 years, 77.9/1 million for 75 to 84 years, and 89.1/1 million for older than 85 years).[26] Elderly men had a significantly higher incidence of nontraumatic SCD than elderly women: 74.1/1 million versus 53.4/1 million in 65 to 74 year olds, 101.9/1 million versus 77.9/1 million in 75 to 84 year olds, and 127.4/1 million versus 71.5/1 million in those older than 85 years, respectively.[26] With the aging of the global population, nontraumatic SCD will most likely increase in future decades.[29]

Conclusions:

1. Falls are a common cause of tSCI in the elderly population [LOE 3]; low level falls are an increasing source of tSCI in elderly people. **[LOE 3]**
2. Nontraumatic SCD accounts for a higher proportion of SCI in older adults than it does in younger age groups. **[LOE 3]**

Recommendations:

1. Clinicians and social scientists should work to adapt our living environments to an aging population so as to prevent falls, which are a frequent case of SCI. **[LOE 3, Grade of Recommendation (GOR) B]**
2. Public education about the risks associated with falls and other traumatic injuries is needed, and research about the effects of this type of education are warranted. **[LOE 3, GOR B]**
3. Future epidemiological studies should take into account comorbid medical conditions, mental health, physical function, and cognition when exploring opportunities for SCI prevention. **[GOR B, LOE 3]**

8.4 Aging With Spinal Cord Injury: The Impact of Comorbidities

One of the great successes of modern medicine and technology is the rapid increase in the proportion of the population surviving into late life. For persons with tSCI or nontraumatic SCD, advances in acute management, specialist spinal cord rehabilitation, and long-term periodic review have led to markedly increased longevity. Additionally, the average age at which SCI or SCD is sustained has also increased. For the general population, this increase in longevity has come at a cost. A greater number of people enter old age with multiple chronic conditions. The rise in multimorbidity or medical complexity (defined as having two or more chronic medical conditions) has increased rapidly over the last 20 years (**Figure 8-1**). Interestingly, people living with long-term disability appear to "age" rapidly. Much like the general population, those with SCI or SCD appear to be at greatest risk for the acquisition of additional medical conditions in midlife. Whether this risk is greater than that for the general population is not well characterized, with a dearth of controlled longitudinal studies. Studies that do exist report considerable attrition and are subject to the "survivor effect," whereby those persons who are better adjusted, more likely to be employed, and better integrated into social supports live longer. This in itself has reinforced the need to actively promote healthy aging behaviours and concentrate on additional social supports in SCI patients.[30]

FIGURE 8-1
Prevalence of multimorbidity (defined as ≥2 diseases) reported in primary care settings.

Note: Data reported in the studies were adjustes to fit into the graph, as described in the Methods section.

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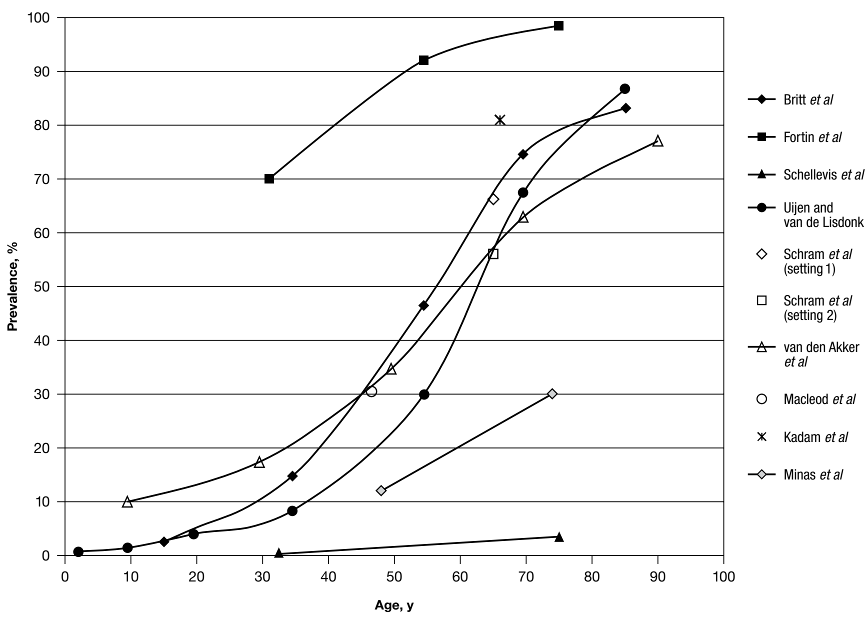

For older people with a new SCI or SCD, there is an increased degree of disability and a greater likelihood of discharge from hospital to an institutional setting. Several cross-sectional studies have examined the association of age at time of injury with various outcomes after SCI. Individuals who are older at injury onset have reported poorer health outcomes, although the lack of quality studies from different countries makes definitive assertions about the influence of age difficult. For example, persons who were at least 61 years old at the time of their injury were more likely to develop pneumonia, gastrointestinal hemorrhage, pulmonary embolus, or renal stones before their initial hospital discharge. Additionally, they were more likely to be rehospitalized during the second year after injury, to require ventilator support, and to be discharged to a nursing home than individuals 16 to 30 years of age at time of injury. A greater number of medical complications were associated with older age and duration of injury.[31,32,167]

Older people with SCI or SCD are as much at risk of the diseases of later life as the general population, but appear to have a greater propensity to develop them and will face additional challenges in dealing with them. For example, over a 3.5-year period, persons with SCI reported new onset of arthritis (percent incidence 14%), followed by hypertension (9%) and cancer (7%). Report of a new condition was greatest in adults aged between 56 and 65 years, and risk factors included greater body mass index (BMI), waist circumference, and the presence of another chronic comorbid condition at baseline.[33] A 2013 scoping review, with no age-related analysis found that individuals with SCI experienced a number of secondary health conditions at a higher rate than the normal population. The most common conditions or symptoms found were pain, bowel and bladder regulation problems, muscle spasms, fatigue, esophageal symptoms, and osteoporosis. A number of conditions, including cardiovascular disease (CVD), diabetes, bone mineral density (BMD) loss, fatigue, and respiratory complications or infections, occurred with a higher frequency in older individuals or those with longer SCI duration relative to younger individuals or those with shorter SCI duration. The lack of longitudinal data was noted.[34] A recent cross-sectional study of people with SCI or SCD living in the community[168] found that the most common troubling secondary conditions reported were sexual problems in 41% of the population studied; chronic pain in 24%; bladder dysfunction in 17%; spasms in 17%; joint and muscle pain in 15%; bowel dysfunction in 14%; circulation problems in 14%; contractures in 9%; urinary tract infections in 9%; pressure ulcers in 7%; and postural hypotension in 5%. There was, however, no influence from gender, age, or years postinjury on the severity and frequency of secondary conditions, but those with tetraplegia and higher disability were more likely to have more severe and frequent secondary conditions.

There is an age-related loss of spinal cord neurons in persons even without injury. This results in reduction of vibration sense, proprioception, muscle mass, and strength; a slower reaction time; decreased fine coordination and agility; decreased deep tendon reflexes, particularly the ankle jerks; and increased postural instability.[35-38] A study of individuals aging with an SCI of more than 20 years' duration showed that 12% reported some sensory loss, and more than 20% reported increasing motor deficits over the years.[39] A Canadian study reported a prevalence of neurological deterioration in 11% of 633 individuals with tSCI.[40]

The adverse effect of sedentary behaviour is also increasingly well documented.[41] The increase in inactivity imposed by SCI leads to an increase in BMI for many and, consequently, an increased incidence of central adiposity and insulin resistance, components of the metabolic syndrome. This, in turn, leads to an increased risk of diabetes, an independent risk factor for mortality in people with SCI.[42] In a study of male veterans with SCI, 22% were found to be diabetic on oral glucose tolerance testing, compared with 6% in nondisabled control subjects. Eighty-two percent of the control subjects had normal glucose tolerance, compared with 50% of those with paraplegia and 38% of those with tetraplegia.[43] BMI is, however, inaccurate in people with SCI and, in some surveys, up to three-quarters of the sample has been classified as either overweight or obese.[44]

Changes in the respiratory system in association with aging are well described.[45,46] In the general population, studies have shown a number of changes that result in reductions in most spirometric variables, including forced vital capacity (FVC), total lung capacity, and forced expiratory volume (FEV). In addition, there is an increase in the prevalence of obstructive sleep apnea. The prevalence of sleep-disordered breathing increases in association with increases in body weight, loss of upper airway muscle tone, and other factors.[47-49] In older persons with SCI, respiratory complications are more common in those who sustain an injury at older age and in those with more severe impairment. Respiratory disorders continue to be the leading causes of rehospitalization and death in people with chronic SCI.[50] In a longitudinal study of 174 men with SCI, there was an age-related acceleration of decline in FEV and FVC. A UK longitudinal study of 834 individuals with at least 20 years' duration of injury found the incidence of pneumonia and atelectasis to increase with age (from 1.6% in those <30 years old to 5.4% in those >60 years old), but there was no association with duration of injury.[51]

Similar findings have been reported from the United States.[52] The prevalence of sleep-disordered breathing in individuals with SCI is higher than in the general aging population (25%–53%).[53-55] However, level of impairment, increased abdominal girth, neck circumference, and duration of injury did not predict those at greatest risk for sleep-disordered breathing. In one large US controlled cohort study, there was, paradoxically, strong association between an increase in chronological age and a reduction in sleep difficulties, which may be related to survivor effect, suggesting an adverse impact of sleep disorders on survival.[56]

Persons with SCI develop painful arthritis, particularly of the upper limbs, earlier than noninjured persons, and develop impaired ability to perform activities of daily living associated with aging.[57,58]

Heart disease is one of the leading causes of mortality in long-term SCI.[31,42] A longitudinal study of long-term SCI survivors showed the risk of developing CVD was associated with both level and completeness of injury.[59] A number of studies have documented abnormalities of glucose, lipid metabolism, and other risk factors for the development of CVD in people with SCI.[43,60,61] Individuals with SCI tend to have a lipid profile characterized by low high-density lipoprotein compared with matched nondisabled controls.[62] Nonetheless, a report from the US Agency for Healthcare Research and Quality concluded that there was insufficient evidence to suggest that adults with SCI are at greater risk of carbohydrate and lipid disorders, nor did it support the use of different thresholds to define or treat lipid abnormalities in this population. In a study comparing the prevalence of cardiovascular and metabolic conditions in male veterans who had SCI for at least 20 years (*n*=794) versus those in noninjured veterans (*n*=13,528) and the general population (*n*=6105), it was found that the prevalence in those with SCI was 20.3% for diabetes, 18.7% for myocardial infarction, 9.8% for stroke, and 15.5% for coronary heart disease (CHD). Compared to those without SCI, the odds of having CHD were lower, but the odds of having a stroke were 1.4 times higher in veterans with SCI than noninjured veterans, and slightly higher than in the general population. The presence of usual cardiovascular risks (diabetes, smoking, hypertension) increased the risks for disease across populations.[63]

Investigators who examined functional changes over time in individuals 20 or more years after injury noted a greater need for physical assistance and a greater need for additional help with activities of daily living as they aged.[64] Other studies found functional decline (especially caused by pain and weakness), and a reduced ability to perform activities of daily living associated with aging .[65] Clearly, SCI is associated with a decline in performance and function of many body systems in excess of those noted with "normal" aging . While there are some controlled studies, there is a lack of carefully controlled, age-matched longitudinal studies describing the additional disease load attributable to the SCI.

Furthermore, the level of support for older patients with SCI varies between countries with different sophistication of health services. Developing countries may not be in a position to provide acute or rehabilitation services. Providing disposables like catheters is often a major difficulty. Nursing care is well intentioned, but rest home facilities are often meagre and sparse, which may increase the risk of pressure ulcers and other complications.

Conclusions:

1. Increasing age at time of SCI is associated with poorer health outcomes, and higher levels of disability and likelihood of discharge to institutional settings. **[LOE 3]**
2. CVD, diabetes, bone loss, fractures, and respiratory complications are more common in older SCI patients or those with longer duration of SCI. **[LOE 3]**
3. There is functional decline with increasing time following SCI, resulting in a greater need for physical assistance and help with activities of daily living. **[LOE 3]**

Recommendations:

1. The healthcare system should provide increased resources to support the aging SCI patient and caregivers. **[GOR B]**
2. Outreach assistance should be provided in health services planning for the older patient with SCI. **[GOR B]**

8.5 Upper Urinary Tract Changes With Aging

8.5.1 Renal function changes

In the older patient with SCI, renal function can deteriorate as a part of the aging process, or may be related to neurogenic bladder dysfunction (NBD). Risk factors for renal impairment include complete versus incomplete SCI, indwelling catheter, neurogenic detrusor overactivity, and a low bladder compliance.[66] Independent risk factors for renal deterioration were detrusor overactivity causing high bladder pressures above 75 cm of water pressure, a cystometric bladder capacity of less than 200 mL, and an absence of anticholinergic medications.[67]

Many papers use the term renal *impairment* or *deterioration* without specifying whether it is due to obstruction, stones, reflux nephropathy, infection, or other conditions. These terms are frequently used without definition, and can refer to renal pelvic dilatation, global parenchymal thinning, or patchy polar scarring as seen in reflux nephropathy. The serum creatinine is frequently used to estimate renal function, but it is an insensitive parameter until the renal impairment is quite marked. As discussed in a previous chapter, after an SCI the muscle mass is reduced due to disuse or denervation, so that the serum creatinine will rise only late in the progression. Renal function assessed from serum cystatin C appears to be more accurate than the serum creatinine, as serum cystatin C is not affected by gender, age, race, or muscle mass.[68,69]

Preservation of renal function is a primary goal of lower urinary tract management. Renal failure after SCI became much less common due to better bladder management in more recent decades. Still, a recent study showed new onset renal dysfunction in 84 of 2,023 (4.2%) tSCI patients, followed for a median of 4.8 years postinjury. This was significantly higher compared to matched controls.[70] Using cystatin C as a measure of renal function in an older SCI population, a Korean group examined 314 patients with a mean age of 58±8.8 years, and found evidence of renal impairment in 8% after a mean of 18.9 years postinjury.[71] Some reduction in renal plasma flow might be expected as a part of the aging process, although evidence is sparse and somewhat conflicting. In one study of aging after an SCI, renal plasma flow diminished by 4.5 mL per year,[72] although another study found no deterioration in a group of 77 consecutive cases.[73] More studies relating the development of renal impairment to time since injury and age are needed.

8.5.2 Renal scarring and time since injury

In a group of 100 males with SCI, renal dilatation became apparent in 63 in the first year after injury, and only 1% experienced any damage after 10 years.[74] A Danish group showed that, in a cohort of 116 SCI patients admitted between 1956 and 1975, the risk of severe renal deterioration (glomerular filtration rate [GFR] <51%) over 45 years of follow-up was 58%; renal deterioration was mainly associated with upper tract dilatation and/or a history of renal stones. The cumulative risk of renal deterioration with relative GFR of 51% or less was 29%. Some of the deterioration may be confounded by the management of renal stones and the effect of renal infections.

A retrospective cohort study of 2,023 patients from Canada found that in a median follow-up period of 4.5 years, 84 (4%) developed new renal impairment. However, the definition of the renal impairment was not stated.

One retrospective study of 27 patients with renal scars indicated that the renal scars developed at a mean of 13 years postinjury. Once a scar had been noted, it did not usually progress with time.[75] However, this does not take into account the occasional patient with reflux nephropathy who goes on to develop glomerulosclerosis and renal failure.

8.5.3 Renal stones

Renal stones are common among those with an SCI, due to calcium mobilization from bones, relatively reduced exercise and mobility, and recurrent urinary infections with urea-splitting organisms. In the non-neuropathic situation, the risk of renal stones differs according to geographic region; this is not always taken into account, which underscores the wide variability of prevalence. The management of urinary stone disease in SCI is discussed in Chapter 3.

8.5.3.1 Risk factors for renal stones: effect of age and time since injury

Patients who were aged 61 years or older at time of injury were 16.8 times more likely to have had renal stones prior to first definitive discharge than their 16- to 30-year-old counterparts. These data were collected in a collaborative study of 866 US patients from the National Spinal Cord Injury Database who were injured between 1973 and 1985.[76,77] In a Korean study of 140 males followed for a mean of 17 years, 39 developed bladder stones and 21 had renal stones. This group also showed that the risk of renal stones was greater in those aged >24 years compared to younger patients, and for those who had bladder stones.[78,79]

In a longitudinal multicentre cohort study of 8,314 SCI patients in the United States, 286 incident renal stone cases were documented. There was a significant increased risk of renal stones in the first year postinjury and in those aged ≥45. Risk was greatest in the first 3 months after injury, and thereafter reduced from 31 to 8 cases per 100 person-years within 10 years of injury.[80] However, patients with SCI remain at risk of developing renal stones over time. In an Australian group of 58 SCI renal stone formers, 53% developed their first renal stone >10 years after the injury, and 49% had indwelling urinary catheters. Of those who had one renal stone and had follow-up for an average of 7 years, 34% developed another renal stone within 5 years. The risk was higher for men than women and higher for white patients than for black patients.[81]

Conclusions:

1. Renal function deterioration can occur early but can also occur at later stages following SCI, and can be related to aging, obstruction, stone disease, or reflux. **[LOE 3]**

2. Incidence of renal injury/deterioration varies due to different definitions, historical periods, and changes in urological management. **[LOE 3]**

Recommendations:

1. Clinicians should perform regular urinary tract imaging surveillance after an SCI to detect stone disease or late scarring, and this should be continued for the long term. **[GOR B]**

2. Better research is needed into the role of age- versus SCI-related factors such as NBD in the development of renal dysfunction over time. **[GOR B]**

8.6 Lower Urinary Tract Changes With Aging

8.6.1 Non-neuropathic lower urinary tract dysfunction

There is little mention in the literature of pre-existing lower urinary tract symptoms and the outcome after an SCI, or the development of non-neuropathic problems after an SCI.

Urological problems may occur independently of the SCI, and may precede the injury and complicate management issues. Age-related changes in the lower urinary tract, such as benign prostatic enlargement resulting in outlet obstruction, reduction in detrusor contractility, pelvic floor changes with aging and/or after menopause can all result in lower urinary tract dysfunction in the older SCI patient. Following an SCI, each patient needs to be assessed and problems dealt with as they arise. These may include symptoms in those with incomplete lesions, evidence of increased residual urine, and incomplete bladder emptying. Urodynamic studies are essential in defining the nature of these issues and guiding management. Pharmacological management may be indicated with alpha-adrenergic blockers, anticholinergics, or beta-adrenergic agonists. However, caution is required, especially with outlet surgery in those with partial SCI, if the patient is continent beforehand.

8.6.2 Bladder pressure changes with time since injury

Patients with SCI using reflex emptying and an external collecting device had high pressures in the first decade after injury, but maximum detrusor pressures were lower in the subsequent 4 decades of surveillance. Whether this is due to long-term effects of reduced detrusor sphincter dyssynergia or to aging remains unclear.[82]

Analysis of changes in urodynamic function among 246 SCI patients who were studied at a mean of 6 years apart, and who were a mean of 17 years postinjury at the second study, showed increased bladder capacity, with improved compliance and reduced detrusor sphincter dyssynergia between the studies.[83] It is unclear how much the changes were due to aging, natural evolution of NBD post-SCI, or medical management of NBD such as with anticholinergics or onabotulinum toxin A injections.

8.6.3 **Urodynamics**

As mentioned in previous chapters, urodynamics has a key role in the assessment and management of NBD following SCI. The methodology, indications, and timing of urodynamic evaluation is covered in Chapters 2 and 3. While multichannel urodynamics is an invasive investigation with risks of sepsis and autonomic dysreflexia (AD), it is a valuable test in the older patient with SCI where NBD can be further complicated by age-related changes of the lower urinary tract. For example, voiding symptoms in an older male with SCI may be due to bladder outlet obstruction secondary to prostatic enlargement, dyssynergic bladder neck obstruction, detrusor-external sphincter dyssynergia, underactive detrusor (from neurogenic or age-related causes), or urethral stricture. Especially in the elderly SCI patient, clinicians should optimize the general condition of the patient prior to the test and take due care of limbs and pressure areas during transfer to the urodynamic table.

8.6.4 **Changes in bladder management with aging**

Intermittent catheterization (IC) is generally preferred to an indwelling catheter (either urethral or, preferably, suprapubic). However, in those who do not wish to or are not able to perform IC independently, an indwelling catheter does help with bladder emptying function and incontinence. This discussion is particularly relevant in this section on aging because, for convenience and for preservation of quality of life, older patients may prefer a suprapubic catheter to IC, and there is some evidence that IC use does increase with age or time since injury.[84] The use of IC in the United States rose to a peak of 56.2% between 1991 and 1995, but fell slightly in the years from 2001 to 2005, to 49.6%. Indwelling catheter use fell from 33.1% in the years from 1973 to 1975 to 16.5% in the years from 1991 to 1995. It rose again to 23.1% in the period from 2001 to 2005. Among those individuals with follow-up data 5 to 30 years postinjury (*n*=12,984), a significant drop in use of IC with increasing time since discharge was observed, particularly in the first 5 years, with only 20% of those initially doing IC continuing to do so at 30 years postinjury.[84,85]

8.6.5 **Barriers to intermittent catheterization in older patients**

While age is not a specific barrier to IC, there are various factors that may preclude this method of bladder management in the older patient with SCI or, alternatively, make the patient reliant on caregiver-performed IC. Upper limb function, including strength and coordination, is essential for older patients performing IC. (Also see the later section on orthopedic issues in this chapter. [Section 8.10]) Motivation and cognitive ability for new learning, planning, and organization, as well as adequate vision are all important considerations for IC. In males, development of prostatic enlargement with aging can make IC difficult. As men age, there is loss in the length of the penis, and this can lead to difficulties in performing IC or applying a condom-drainage system. In some females, postmenopausal changes can make the urethra more difficult to locate. When these anatomic changes are exacerbated by obesity or morbid obesity, it can make IC impossible. Finally, for practical and pragmatic reasons, some people with SCI choose not to perform IC even if they are capable of doing so.

8.6.6 Autonomic dysreflexia and aging

AD can occur either spontaneously during bladder filling or it can be precipitated by bladder or bowel care.[86] The risk may be lower with increased time postinjury.[87] AD occurs mainly in those with tetraplegia or high-level thoracic injuries above T6. Those with complete lesions (ASIA Impairment Scale [AIS] classification A) are more prone to AD than those with incomplete lesions.

The influence of aging remains to be assessed, but one study found the odds ratios (ORs) for cardiac complications, high blood pressure, and respiratory complications increased per year with age, whereas AD, bladder infections, heterotopic ossification, psychological distress, and drug addiction decreased. Following SCI, the ORs for pressure ulcers, AD, and heterotopic ossification increased per year postinjury, whereas high blood pressure, bowel problems, psychological distress, and depression decreased.[87]

8.6.7 Prostate and bladder cancer

Prostate and bladder cancers are more common in the older patient. However, patients with SCI showed a significantly lower risk of developing prostate cancer compared with subjects without SCI (adjusted hazard ratio [HR]=0.73; 95% confidence interval [CI], 0.59–0.90) after accounting for the competing risk of death. No significant difference in the risk of bladder cancer emerged between the 54,401 patients with SCI and matched control groups in this large study from Taiwan.[88]

Conclusions:

1. Bladder pressures may decrease with time following SCI, but the relationship to upper urinary tract damage remains unclear. **[LOE 3]**

2. Decline in trunk stability and upper limb function, cognition, vision, and changes in social circumstances may make bladder management with intermittent catheterization difficult **[LOE 3]**, and some patients may be managed with indwelling catheterization, preferably using a supra-pubic catheter (SPC).

Recommendations:

1. Clinicians should have a lower threshold to perform urodynamics in the aging patient with SCI because age-related changes in lower urinary tract function can complicate the changes due to SCI. **[GOR B]**

2. Clinicians should take into account patient quality of life, cognition, orthopedic issues, and the availability and training of the caregiver when selecting the best bladder management in the older SCI patient. There should be multidisciplinary input where possible. **[GOR B]**

8.7 Bowel Function Changes

8.7.1 Bowel dysfunction

Constipation, a common problem of persons with SCI, becomes more troublesome with age. Although bowel regimen does not change with aging, the effect of impaired mobility, multiple medications, and coexistent disease will have an impact. For example, one longitudinal study that involved people more than 20 years post-SCI in the United Kingdom indicated that 42% had difficulties with constipation; additionally, 27% reported fecal incontinence.[52,89] An even greater prevalence of constipation and fecal incontinence in up to 86% of individuals with SCI has been reported by others.[90]

Although NBD and its symptoms and the urodynamic findings can be broadly characterized by level of SCI and its completeness, this cannot be said of the symptoms of neurogenic bowel dysfunction.[91-93] This relates to the very complex intrinsic and extrinsic nerve supply of the bowel. It is clear that colon transit times can be prolonged.[94] Megacolon was frequently observed radiologically in older patients aged >50 years old and those >10 years postinjury.[95] This study did not evaluate the megacolon against the spinal injury level.

The literature is somewhat conflicting. Studies at 1 year were compared with repeat studies at around 19 years postinjury. Bowel transit times were not delayed with time after a spinal injury, and megacolon was not more prevalent in another study from Denmark.[96]

Constipation was more prominent in paraplegic patients 20 years after injury in a UK study, and fecal incontinence and diarrhea were more common in tetraplegic participants.[97]

None of the urodynamic parameters, including cystometric capacity, presence of detrusor overactivity, poor bladder compliance, nor detrusor sphincter dyssynergia, correlated with any of the bowel symptom scores.[92]

Inserting suppositories is part of bowel routine to achieve controlled fecal continence for many patients with SCI. Satisfactory upper limb function, both strength and coordination, is essential. (Also see Section 8.10 on orthopedic issues) Adequate vision also essential for independent performance, and obesity can make suppository insertion impossible.

8.7.2 Bowel stoma

For some patients, managing bowel incontinence or constipation can be time consuming and require a combination of laxatives and stool-bulking agents, manual evacuation with or without the use of suppositories, and/or enemas, administered per rectum or through an antegrade colonic enema procedure. Bowel dysfunction and its management can have a significant impact on quality of life, as indicated in Chapter 6. It is likely that the bother from bowel dysfunction and its management would be more significant as the person ages. A colostomy can be a very appropriate option to lessen the time needed for bowel care, reducing the need for laxatives, and the occurrence of bowel-related AD. These outcomes are associated with significant improvement in quality of life. For independent stoma management, postural stability and adequate hand function are essential, as discussed in the section on orthopedic issues (see Section 8.10). Many older patients with SCI will still require the aid of a caregiver to manage the stoma.

Spousal support for those with an SCI is important to the patient's quality of life and the impact on depression and community integration.[98] For patients with SCI, the need to have a spouse or caregiver assist with bowel management is much reduced after a colostomy has been performed. This can be especially important in the older patient if the spouse is no longer able or available to assist with intimate cares, and an unrelated caregiver is needed.

8.7.3 Aging with a stoma

Visualizing the stoma may be difficult for older adults, especially if obesity has led to an abdominal fold above the stoma, which can impede the secure positioning of the flange over the stoma. With those appliances that have a separately applied flange, some patients can manage to change the disposable bags, whereas assistance might be required to place the flange itself. Siting of the stoma in the older SCI patient needs careful consideration by the patient and caregivers, stoma nurse, and surgeon, taking into account residual motor function.

Conclusions:

1. Constipation and fecal incontinence are common in older patients, including those with SCI. **[LOE 3]**
2. Impaired mobility, multiple medications, and coexistent disease affect bowel function. The prevalence of constipation and incontinence in SCI patient cohorts is variable. **[LOE 4]**

Recommendations:

1. Surgeons should offer colostomy to select older SCI patients who have unsatisfactory outcomes with medical management of fecal incontinence. **[LOE 3]**

8.8 Skin and Pressure Area Care

As people age, the skin loses collagen and elastin fibres and the risk of pressure ulcers increases. Comorbidities that are more common in older people with SCI can involve treatment with steroids (fecal incontinence, chronic airways disease, asthma, connective tissue diseases, and rheumatologic conditions, as well as cancers), further increasing the risk of pressure ulcers. As a result, older people may need greater vigilance to prevent pressure ulcers, and they may need to perform pressure lifts more frequently. In people who have their SCI at a younger age, it is important to educate them about the increased risk with pressure ulcers due to age-related changes in an appropriate way and at an appropriate time. In older people with SCI who do develop a pressure ulcer, the pressure ulcer can take longer to heal.

8.9 Polypharmacy

Approximately 60% of people over age 65 take at least one prescribed medication, and about one-third take more than five prescribed drugs. In addition, many take over-the-counter and naturopathic or herbal agents, with the rate of use varying across countries and cultures.[99] The likelihood of adverse drug effects (ADEs) and drug interactions rises exponentially as the number of medications increases. This has led to the recommendation in geriatric prescribing to "subtract before adding," to consider whether target symptoms might be due to medications before adding another drug targeting those symptoms. This can help to prevent what has been termed the "prescribing cascade." ADEs are extremely common in older persons,[100] with rates of up to 35% among community-dwelling persons aged >65 years in the United States[101] and up to two-thirds of long-term care residents.[102] In a UK study, 59% of ADEs requiring hospital admission involved patients aged >60 years old.[103]

Factors associated with higher ADEs in elderly patients are female gender, higher drug doses, age-related pharmacological changes (**Table 8-1**), polypharmacy, comorbid conditions, and the interactions between them.[104,105] Given the prevalence of comorbid conditions in a population of SCI patients who are surviving longer, the prevalence of polypharmacy is likewise expected to increase, and this has been consistently reported; however, once again, data regarding older persons are scarce.[106]

TABLE 8-1 Age-Associated Changes in Drug Metabolism

Parameter	Age-associated changes
Absorption	Minimal quantitative change despite decreased gastric motility, yet little is known regarding effect on slow-release agents; effect of SCI not known Decreased skin thickness
Distribution	Decrease in lean body mass leads to increased Vd, decreased T½ for hydrophilic drugs, and increased Vd and T½ for lipophilic agents Decreased protein binding in frail patients with low albumin, leading to higher a concentration of free drug
Hepatic metabolism	Impaired phase 1 reactions (oxidation/reduction) No change in phase 2 reactions (glycosylation) Decreased hepatic blood flow and hepatic mass, leading to reduced clearance of agents with first-pass metabolism Stereoselectivity in metabolism (hypothetical) Cytochrome P450
Clearance	Decrease in renal clearance

Abbreviations: T½: half-life; Vd: volume of distribution.

Persons with SCI are no more likely than those without to be subject to the age-related changes in drug handling. They are perhaps more likely to be taking medications that may elicit unwanted side effects, such as gabapentin, and to be taking more drugs than a noninjured person. In a retrospective case-control study of a commercially available claims dataset including patient cases from 4,800 US hospitals between 2007 and 2009, there was a higher rate of prescribed medications from multiple high-risk classes (e.g. analgesic narcotics, anticonvulsants, antidepressants, and skeletal muscle relaxants), as well as multiple medications within each class (e.g. multiple analgesic narcotics).

Persons with SCI had a higher incidence of drug-related problems than did the noninjured group.[107] In a study of 74 patients presenting to a primary care clinic (19 with SCI) with a mean age of 46.7 years, 74% male, the most common medication-related problems were untreated conditions (41%), ineffective medications (21%), ADEs (18%), and under- and overdosage (each 9%). Patients with SCI most frequently used products to treat pain (68%), constipation (42%), muscle spasm (42%), hypertension (42%), and depression (37%). When including natural health products, vitamins, and minerals, polypharmacy was present in 74% of patients with SCI. When the additional involvement of a pharmacist was included in the analysis, a mean of 3.2 medication-related problems per patient was identified, compared to 1 per patient when no pharmacist was included.[108]

Conclusions:

1. SCI patients have higher rates of prescribed medications from multiple high-risk classes (e.g. analgesic narcotics, anticonvulsants, antidepressants, and skeletal muscle relaxants) and multiple medications within each class (e.g. multiple analgesic narcotics). **[LOE 3]**

2. Persons with SCI had a higher incidence of drug-related problems than noninjured persons **[LOE 3]**

Recommendation:

1. Clinicians should be mindful of the risks of polypharmacy in managing the older patient with SCI and should involve the assistance of other professionals, including pharmacists, as necessary. **[GOR B]**

8.10 Falls, Osteoporosis, and Orthopedic Issues

8.10.1 Falls

Older persons with SCI or SCD are at risk of falls, similar to the older adult without disability. In one study of 759 persons aged 65 years or more who responded to questions about falls and injuries, 19.2% reported one or more injuries over the previous year, and 10.4% reported a fall resulting in an injury. Among those who were injured, 22.8% had at least one hospitalization. Additionally, 47.6% were limited in their normal daily activities for a week or more due to injury. Prescription medication use was associated with injury and falls resulting in injury over the past year.[109] In a cross-sectional study of fall prevalence in a convenience sample of 484 persons with SCI, 193 reported falling in the previous 6 months. The likelihood of sustaining a fall was positively associated with level of mobility, degree of physical activity, and number of coexisting conditions.[110] Again, to what extent the existence of SCI increases this risk above that of the general older population is not well described.

8.10.2 Osteoporosis

The disuse and paralysis associated with SCI results in a rapid loss of bone density in the affected limbs within the first year after injury. Approximately one-third of original bone mass is lost by 16 months postinjury before stability is achieved.[111] Others have reported that as much as 50% of BMD is lost within the first 3 years following injury.

In a recent study of 26 subjects (5 female, 21 male) with SCI (12 paraplegic, 14 tetraplegic, 16 to 76 years old), repeated measures of BMD at three monthly intervals revealed a significant effect of time since injury on key bone parameters at the epiphyses of the tibia and femur. There was no significant effect of gender or age, but there was a tendency for women to experience greater decreases in cortical BMD.[112] After the initial rapid phase of rapid bone loss, demineralization slows to reach a steady state or a much slower rate of demineralization for several years. Bone loss in the legs appears to be partly due to the loss of weight bearing, but that in the spine may be partially preserved due to weight bearing through sitting.[113]

Various interventions have been proposed to limit bone loss and enhance bone growth, including standing, vibratory stimulation, and electrical stimulation. There is some evidence that high-volume functional electrical stimulation (FES) cycling induces bone formation at the distal femur, although other areas of the lower limbs do not appear to benefit.[114] Frotzler and colleagues studied five individuals with motor and sensory complete SCI who had participated in high-volume FES cycling and, after detraining or reduced cycling, found that the bone mass gained was maintained longer term with reduced cycling.[115] Likewise, a cohort study of FES and cycling in 364 consecutive SCI patients reported a prevalence of osteoporosis of 34.9% (*n*=127). Use of FES was associated with 31.2% osteoporosis prevalence compared with 39.5% among those not using FES. FES use was associated with

42% decreased odds of osteoporosis after adjusting for sex, age, BMI, type and duration of injury, Lower Extremity Motor Scores (LEMS), walking, previous bone fractures, and use of calcium and vitamin D.[116]

Trials of pamidronate have shown benefit in reducing bone loss in the acute-phase post-SCI,[117] but more recent evidence suggested limited efficacy in preventing long-term bone loss.[118] Several small studies of varying designs have suggested efficacy of denosumab and zoledronic acid injections given over 12 months and alendronate over 2 years for improving sublesional BMD, a marker of bone turnover, but the number of older persons included in each study was not stated.[119-121]

The effect of physical activity on BMD in those with SCI has been mixed. Standing using frames, braces, or harnesses; treadmill walking with various degrees of weight bearing; neuromuscular electrical stimulation; and vibration activities have been studied. Use has varied in intensity and frequency; there is no consensus regarding the dose of physical activity required, but it is clear that passive exercise appears to be largely ineffective in making a significant difference.[122-124] Where benefit has been reported, the interventions have included standing with braces rather than using a standing frame or a standing wheelchair.[125]

A recent meta-analysis has confirmed the efficacy of early postinjury bisphosphonates and later FES in reducing sublesional limb osteoporosis; however, there are no age-stratified results by which to compare relative efficacy of these interventions for older persons.[126] Intensive exercise does preserve upper limb BMD but, again, the extent to which this is the case in the older person is unclear based upon available evidence.[127]

A lower limb fracture rate of more than 30% for individuals with SCI followed for several decades has been reported. Most fractures occur during normal activities of daily living such as transferring, dressing, and bathing. After SCI, 14% have fractures within 5 years of injury, 28% within 10 years of injury, and 39% within 15 years of injury.[128] Lower limb fracture becomes increasingly common as the time since injury increases. However, this is not true for vertebral fracture, where there is a reduced fracture risk; this may be due to the compression of the vertebrae from sitting.[129,130] The general characteristics associated with higher incidence of fracture after SCI appear to be: motor complete injuries, paraplegia, white race, longer times since injury, and female sex.[131] In a recent Canadian cross-sectional survey, 1,137 people (70.9% male, mean [standard deviation, or SD] age 48.3 [13.3] years) with chronic SCI completed a survey regarding, amongst other factors, fracture and osteoporosis. Eighty-four participants (7.4%) reported a fracture in the previous 12 months and 244 (21.5%) reported having osteoporosis in the same period, with corresponding treatment rates of 84.5% and 64.8%. The variables most strongly associated with fracture were osteoporosis (OR: 4.3; 95% CI, 2.72–6.89) and having a sensory-complete injury (OR: 2.2; 95% CI, 1.38–3.50) or a motor complete injury (OR: 1.7; 95% CI, 1.10–2.72).[132]

8.10.3 Orthopedic issues

With aging, bones and joints can be subject to overuse in all people and, for those with a history of SCI, there are additional stresses. These include lifting movements to relieve pressure while seated, the vigorous movements to propel a wheelchair, and other movements affecting the spine, shoulders, elbows, wrists, and hands. Joint pain or limited movement can impact on bladder and bowel care, as well as whether caregiver assistance is required.

8.10.3.1 Upper limb function and postural trunk stability

To manage intermittent self-catheterization or external collecting devices independently and to cope with bowel care requires not only appropriate hand function, but also balance and stability of the spine to achieve and maintain the desired posture. The person needs to be able to adjust clothing while undertaking these procedures. Otherwise, a caregiver or assistant is required.

Trunk stability can be impacted by impaired function of the muscles involved, but also by the vertebral injury, especially if deformity develops. One study suggested that increasing age and duration of SCI were associated with more extreme pelvic angle and forward head posture. They found that thoracic kyphosis was greater in tetraplegic patients than in able-bodied controls, but did not increase with length of time since injury.[133]

For some tetraplegic C7 patients to achieve a key grip, upper limb tendon transfers and tenodesis can be undertaken using muscles with some preserved function to allow both elbow and wrist extension, and hence thumb apposition.[134] An additional benefit of such surgery is that this may enable the patient to hold a catheter for IC, but the adjusting of posture and balance would remain a major impediment for many.

The extent to which such tendon surgery can increase independence for urological cares awaits further research.

Syringomyelia can occur as a long-term complication of an SCI, and reduce motor function. In an analysis of 138 patients, it was mainly found in those with complete SCI; cervical level injury dominates over other levels and can impact on hand function. Those aged >30 years had an increased risk of syrinx formation within 5 years of injury.[135]

8.10.3.2 Joint pain

Upper extremity musculoskeletal pain occurs more frequently in tetraplegic patients than paraplegic patients in the first year after injury, and appears to improve with time during the latter part of rehabilitation, as well as with improved muscle strength and better functional outcomes.[136] Joint pains can interfere with the ability to perform bladder and bowel cares. Shoulder pain is common after spinal injury and requires careful assessment and diagnosis, as it may arise from the neck, arm, or shoulder. Arthritis can occur from overuse in the shoulders due to lifting to relieve pressure on pressure areas, and from the use of a mechanical wheelchair.

In a study of 71 SCI patients (mainly men, 73% were paraplegic, with an AIS A, and had a mean age of 51.8 years and a mean interval since injury of 23.5 years at the time of diagnosis), shoulder pain due to acromioclavicular arthrosis diagnosed by magnetic resonance imaging was more common in those with an SCI than in able-bodied people, and in the older patient and those with longer time since injury.[137] Pain in the wrist with carpal tunnel syndrome and arthritis in the metacarpophalangeal joint of the thumb, especially of the right hand in paraplegic patients due to overuse from propelling a wheelchair, can be a problem, especially after 25 years or more of using a wheelchair.[138]

Charcot neuropathic arthropathy is a rare, severe, progressive degenerative disease, with the absence of deep sensation. One retrospective study of 28 SCI patients with 39 Charcot joints of the spine analyzed the clinical symptoms, which included spinal deformity, sitting imbalance, and localized back pain. Risk factors included long segment stabilization procedures, laminectomy, scoliosis, and excessive loading of the spine.[139] It has been seen in some patients following sacral root deafferentation (i.e. dorsal rhizotomy) and sacral neurostimulation.[140]

8.10.3.3 Residual motor function and aging

Residual motor function and joint integrity can also decrease with age and indirectly impact on urological management. It might lead to increased dependence on caregiver assistance. The motor Functional Independence Measure (FIM) was used in one study that indicated that the older the age at the time of injury, the greater the influence age has on disability.[141]

The difficulty in research on aging with an SCI is compounded by survivor effects and changes in management.[142]

Conclusions:

1. Older patients, including those with SCI, are at risk of falls/accidents, generally occurring during activities of daily living such as transfers, toileting, and bathing. **[LOE 3]**
2. Osteoporosis and complete sensory or motor injuries are associated with higher risk of fractures. **[LOE 3]**
3. Postural stability, joint pain, and arthritis of shoulder and wrist can affect the ability to perform bladder and bowel management. **[LOE 4]**

Recommendations:

1. Clinicians should consider early prevention and treatment of osteoporosis in the older patient with SCI. **[GOR B]**
2. Clinicians should be aware of orthopedic and joint issues that may impact on bladder and bowel management in the SCI patient. **[GOR B]**

8.11 Cognition

Cognitive ability for new learning, planning, organization, and motivation are important for patients living with SCI. In later life, the proportion of people living with dementia, a group of conditions also associated with an impairment in quality of life and physical function, increases; prevalence estimates suggest that, globally in 2010, 35.6 million people lived with dementia, with numbers expected to almost double every 20 years, to 65.7 million in 2030.[143,144]

Up to 40% of patients with tSCI exhibit varying degrees of cognitive function deficit symptoms such as difficulties in abstract thinking and learning new skills and impairment in concentration and memory.[145,146] In a similar manner to traumatic brain injury, neurodegeneration in the brain after isolated SCI can be associated with sustained neuroinflammation.[147] However, whether SCI poses an additional risk for dementia is unclear.

A recent case-control survey from Taiwan examined the incidence of dementia in SCI in a nationwide cohort. There were 941 SCI patients and 5,060 sex- and age-matched controls. Each participant was followed for 7 years until diagnosis of dementia or December 31, 2010. The incidence of dementia was significantly higher in the SCI cohort (1,106 per 100,000 person-years) than in the non-SCI cohort ($p<0.001$). Patients with SCI had a significantly higher risk of dementia than those without SCI (crude HR=2.14; 95% CI, 1.57–2.92; $p<0.001$ vs. adjusted HR=1.95; 95% CI, 1.43–2.67; $p<0.001$). There was no statistically significant higher risk for Alzheimer's disease among SCI patients, but there was for other dementia types. When the effect of age was compared for SCI patients aged more than 70 years old, the adjusted HR for dementia was 1.59 (95% CI, 1.08–2.39, $p=0.018$) compared to non-SCI cohorts aged more than 70 years old.[148]

Persons with SCI will have a number of vascular risk factors, perhaps in addition to impairments in mental health, and social and intellectual domains, all associated with cognitive dysfunction. Clearly, the development of dementia will have profound implications for an older person with SCI, over and above those for a noninjured person, but there are no data examining the impact of this group of diseases or management for persons with SCI of any age group.

Conclusion:

1. Elderly people with SCI have higher rates of dementia than elderly people without SCI. **[LOE 2]**

Recommendation:

1. Clinicians should develop programs to detect and manage cognitive problems (including, but not limited to, dementia) in the elderly SCI patient. **[GOR B]**

8.12 Nutrition and Obesity

Persons with disabilities have higher rates of obesity than those who are able-bodied. Persons with SCI are less physically active than nondisabled persons and their diet is often of low quality,[149] which may predispose them to weight gain, particularly visceral obesity, observed postinjury. Data on nutrition and obesity in older persons (>65 years) are typically lacking, perhaps reflecting that the research agenda has failed to keep abreast of the rapid changes in life expectancy of people with SCI or SCD. Where older persons were included in studies, their results are usually not reported separately, making it impossible to draw conclusions without considerable extrapolation.

In a Korean study, obesity rates were 43.4% among 92,623 people with SCI versus 34.6% among age-, sex-, and geographic region-matched healthy controls.[150] Persons with SCI tend to have a higher proportion of visceral adiposity than able-bodied persons, perhaps leading to an underestimation of cardiovascular risk, although data on aged adults are lacking.[151-153] A single study of SCI persons up to 79 years of age, but that did not report age-associated results separately, found that in 135 persons, more than 80% had at least one CVD risk factor, including hypertension and diabetes; dyslipidemia appeared to be common and unrelated to BMI in both men and women.[154] These findings have been consistently reported across a number of cross-sectional studies, including in those up to 80 years of age; the number of controlled studies is few.[44,155]

An association with abdominal obesity and serum leptin has also been reported in middle-aged adults with SCI.[156] Likewise, there are multiple cross-sectional studies examining the distribution of diabetes amongst persons with SCI. A single study in 135 US veterans with mean age of 55 years reported that the association between BMI and diabetes was no stronger in the SCI population than in the able-bodied population.[157] The same group also reported a positive association between overweight and hypertension in a large veterans' group. Veterans with SCI who were older and had a higher BMI were more likely to be hypertensive.[158] Although common, obesity in SCI, at least in middle age, does not appear to be associated with significant impairment of quality of life compared to population norms for the Patient Reported Outcomes Measurement Information System (PROMIS®), whereas impairment could be detected for patients with multiple sclerosis, muscular dystrophy, and polio.[159]

In a retrospective review of 100 charts of veterans with SCI, 95.0% male and 68% Caucasian, with an average age of 60.6 years (SD 12.3, range=27.7–93.4), three-quarters (73.0%) of veterans had information indicating a need for weight management. Individuals with paraplegia were more likely to demonstrate a need for weight management than individuals with tetraplegia.[160] Data from a recent randomized controlled trial of a behavioural and educational intervention to reduce weight proved that the strategy was ineffective, suggesting that more intensive measures might be required.[161]

Another study investigating dietary intake matched to the US 2010 dietary intake recommendations for nutrients in SCI (ages 35–55) showed that, compared with able-bodied individuals, those with SCI consumed fewer daily servings of fruit, dairy, and whole grain foods and concluded that nutritional education might be warranted for this group.[162] No data are available for older persons with SCI.

Acutely, under-nutrition may be an additional risk factor for poor clinical outcomes from SCI. In a UK multicentre, prospective, cross-sectional observational study of 150 SCI patients (aged 18–88 years [median: 44 years], ages not reported separately), of which 30.7% were female, with a length of in-patient stay and mortality 12 months after admission to a spinal cord injuries (SCIs) centre showed that those who were initially undernourished or at risk of under-nutrition (44.6%) had a significantly longer length of stay and greater 12-month mortality.[163]

Persons with acute SCI frequently need assistance to feed, limiting the potential for adequate nutrition; a common need for nutritional supplementations is seen, particularly in older patients.[164] In a cross-sectional survey of otherwise healthy individuals with SCI, it was noted that older persons and those with a longer duration of injury tended to have lower calorie, fat, carbohydrate, saturated fat, and cholesterol intakes and higher fibre intakes. Unfortunately, the study only included persons up to the age of 62 years.[165]

Conclusion:

1. People with SCI have less access to nutritious meals but it is unclear whether the elderly SCI patient is specially affected. **[LOE 3]**

Recommendation:

1. Clinicians should screen SCI patients for malnutrition and obesity. **[GOR B]**

Concepts for Future Research:

1. There is a lack of evidence examining the impact and optimal management of cognitive impairment, obesity, and nutrition in older persons with SCI. This information would be of benefit in developing programs supporting the older patient with SCI.
2. Research into the effect of aging SCI patients on caregivers would be of benefit in developing support services for the older SCI patient.

8.13 Conclusions

As reviewed in this chapter, older patients with SCI or SCD face additional challenges, both in the acute setting and with aging. Clinicians should take into account comorbid conditions, mental health, physical function, cognition, and social support in making management decisions. With the global aging population, health services planning will need to allow for increases in the resources required to care for older patients with SCI.

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C9

Current and Future International Patterns of Care of Neurogenic Bladder After Spinal Cord Injury

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Committee 9

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Current and Future International Patterns of Care of Neurogenic Bladder After Spinal Cord Injury

9.1 Introduction

The scope of urologic complications following spinal cord injury (SCI) is significant, as is the cost of caring for individuals with SCI. The lifetime costs for a person injured at 25 years of age has been estimated to be US $4.6 million for high tetraplegia, and US $2.3 million for paraplegia.[1] Each afflicted individual requires a customized bladder management program that takes into consideration factors such as patient sex, bladder function, mobility, sitting balance, hand function, lifestyle, social support structure, and religious and/or cultural beliefs and preferences. Thus, special consideration should be given to the advantages and disadvantages associated with each method of bladder control and their appropriateness and availability in the individual's context.

When the concept of "patterns of care" is considered from the international angle, the discussion is a challenge. First, registries of patients with SCI are quite rare and, if present, are restricted to the most developed countries. Second, while guidelines for the management of SCI patients with neurogenic bladder dysfunction (NBD) do exist (again in the most developed countries), it is not entirely clear if adherence to guideline principles is rigorous. Furthermore, it remains in question if guideline principles are disseminated effectively to remote regions of developing countries. In all, the debate comes down to a fundamental difference between the "haves" and the "have nots," with overarching themes such as basic transportation, physical access to care, and monetary allocation for treatment of SCI patients with NBD being at the forefront of the discussion.

Below, we present our findings and evidence-based recommendations regarding current international patterns of care for patients with NBD following SCI. Our search methods included PubMed database searches, reference checks, communication with professional societies, registry evaluations, and browsing-related websites. Recommendations based on our findings are provided.

9.2 Catheter Management

Evidence suggests that intermittent catheterization (IC) is one of the most effective methods of bladder management in patients with NBD. It is a preferable option, since it is generally associated with fewer complications, particularly compared to in-dwelling catheterization.[2] Research has also shown that IC can be a safe, efficient, and cost-effective method to use in low-resource settings.[3,4] Manual methods such as the Credé manoeuver are generally discouraged, and using them as the only means for bladder emptying in the long term is not considered best practice.[2,5]

In Taiwan, Lin *et al.* investigated long-term outcomes of SCI/NBD patients with bladder management via suprapubic cystostomy or regular exchange of urethral Foley catheter by investigating their 11-year nationwide database.[6] Among the total population of 22.8 million, 34,227 (0.15%) SCI patients were recruited into the study. In SCI patients, 2,923 (8.54%) had the diagnosis of NBD. Of 2,923 patients, the suprapubic catheter group was 381 (13.03%), the urethral catheter group was 64 (2.19%), and the group of those not emptying their bladder with a catheter was 427 (14.61%). Male patients were more likely to receive a suprapubic catheter ($p<0.001$) and, although there was no significant difference in geographic location within Taiwan, suprapubic catheter was more acceptable in more urbanized areas ($p<0.001$). The urethral catheter group had higher risk of acute and chronic renal disease (hazard ratio [HR]=3.20, $p<0.001$) and calculus of the urinary tract (HR=1.89, $p<0.001$). Both the urethral and suprapubic catheter groups had higher rates of iatrogenic trauma and complications than the control group (HR=4.26, $p<0.001$ and HR=6.42, $p=0.031$, respectively). There was no obvious difference among all three groups in the incidence of prostatitis and epididymo-orchitis; however, the duration of infection and the incidence of iatrogenic trauma and renal disease were significantly lower in the suprapubic catheter group ($p<0.001$). In summary, regular urethral catheter exchange has a higher risk of urinary tract calculus and renal disease than suprapubic catheter; however, both urethral or suprapubic catheter have a high risk of iatrogenic trauma or complication.

The literature reveals that IC has been a part of routine SCI patient management in several Asian countries (China, India, Pakistan, Turkey, Malaysia, and Iran), Brazil, and Mexico.[7-14] While the use of IC appears to be widely accepted, several barriers to wide adoption exist. First, education regarding IC use is beneficial. A randomized controlled trial (RCT) carried out in the United States demonstrated that a brief education program (consisting of an experienced nurse observing catheterization techniques, medical counselling on how to improve bladder management and when to access health care, provision of written information on management of urinary tract infections [UTIs], and a follow-up call to discuss questions that arose after the educational session) brought about a reduction in reporting of symptoms, antibiotic treatment episodes, and the number of UTIs.[15]

On the other hand, access to IC teaching and catheter manipulation is very limited in Kenya,[16] Ethiopia,[17] and Thailand.[18] In less-developed nations, IC catheters are typically supplied by international donors or Western health promotion organizations.[16] Owing to cost constraints, disposable silicone catheters have been reused in some countries, including Thailand, India, Kenya, and Brazil.[8,16,18,19] The Thai study reported an average catheter reuse time of 3 years, and this practice was shown to reduce costs significantly, from US $4,722 to US $18 over a 2-year period.[18] Glass and metal catheters are still in use in some countries.[19,20] The use of bleach or other methods of sterilizing catheters may be a reasonable, and less costly, alternative to new IC supplies in developing countries.[21]

Another barrier to widespread implementation is low IC acceptance by patients in many African and other less-developed countries. Proposed reasons for low IC acceptance are low literacy rates and cultural resistance brought on by fear of infertility, inability to practice Muslim prayers, and inability to marry.[16,22] In some African cultures, individuals can be extremely resistant to this technique,[23] and practices that have fallen out of favour in developed nations, such as Credé manoeuver, persist in developing nations such as Pakistan.[24] IC has not been widely accepted in China, mainly because of inconvenience/difficulty in performance and the need for long-term bladder management. Most SCI patients with large-volume bladders prefer the Credé manoeuver to expel urine, while those with small-volume bladders favour condom collection bags in men and diapers in women.[5] In Ethiopia and Malaysia, the reasons cited for stopping IC were predominantly financial (no funds for transportation to medical clinics or for purchasing medical supplies) and social (lack of sustainable access to basic sanitation and difficult entry into hygienic sanitation facilities for IC).[17,25] As a result, the rate of serious complications, including renal failure and related death in NBD patients living in underdeveloped countries, remains high.

Conclusion:

1. Indwelling catheters (urethral or suprapubic) are associated with a high risk of iatrogenic complications.

2. IC remains the most documented method of bladder management in developed and developing countries. Access to supplies may be limited in developing countries, and novel catheter sterilization techniques are welcome methods to reduce costs. **Level of Evidence 3 [LOE 3]**

Recommendation:

1. In these countries, efforts should be made to improve education of both local physicians and patients, in order to minimize cultural and religious barriers to performing IC. **Grade of Recommendation B [GOR B]**

9.3 Pharmacotherapy and Other Treatment Options

Muscarinic receptor antagonists (antimuscarinics) are the primary class of anticholinergic medications for the treatment of NBD in the Western world; however, little is known about their use in in developing countries. Although several anticholinergics (e.g. oxybutynin, propiverine, trospium, tolterodine, and solifenacin) are available in some less-developed countries, they may not necessarily correspond with everyday clinical practice due to financial issues or absence of national recommendations.[26] Furthermore, in many countries where anticholinergics are not yet available, other cheap, nonselective muscarinic receptor inhibitors, such as oxyphencyclimine, have been given as alternatives to anticholinergics.[27]

Additional treatment options, such as acupuncture, transcutaneous tibial nerve stimulation, and intravesical onabotulinumtoxinA injections, are currently being used in China.[7] These NBD treatments may be effective, especially if treatment is introduced in an early stage of the disease. However, in many developing countries, the condition is often diagnosed at a more advanced stage and, thus, requires a more aggressive treatment regimen. Reports on augmentation enterocystoplasty in the management of NBD patients have come from the largest countries of the developing world (China, Iran, Mexico, Pakistan, Brazil, and India).[7,12,14,22,28,29]

Conclusion:

There is little information regarding the use of pharmacotherapy or active treatment options such as neuromodulation or intravesical onabotulinumtoxinA injection in developing countries. **[LOE 3]**

9.4 Urologic Surveillance

The Agency for Clinical Innovation (Australia) has proposed the following regularly scheduled health maintenance measures for adults with SCI/NBD: 1) review bladder management programs regularly; 2) investigate further if there are changes in bladder function (e.g. urinary retention, episodes of incontinence, UTIs, hematuria); 3) test renal function; 4) carry out regular imaging of the urinary tract; and 5) conduct prostate cancer screening for men after appropriate shared decision-making takes place.[1] Limited information is available regarding the international use of these measures.

Serial ultrasonographic evaluation to ascertain bladder wall changes, such as thickening and trabeculations as indirect evidence of high bladder pressures, is commonly performed in many countries, including Malaysia and most parts of Africa.[16,17,25,30] Access to ultrasound or creatinine testing may not be readily available to some patients, as reported in Kenya, Pakistan, and Ethiopia.[16,22,29] Video-urodynamics for the screening of voiding and storage dysfunction in NBD patients are available in developed countries, such as the United States, Canada, and the United Kingdom. Likewise, video-urodynamics may be available in China,[31] but are not available in many developing parts of the world. Hence, both the diagnostic process and subsequent patient treatment are commonly insufficient or unavailable to a majority of the population. As a consequence, many patients still present, or are referred late, for bladder dysfunction management.

Conclusion:

There is little information regarding the use of imaging modalities in the follow-up of patients with NBD after SCI in developing countries. **[LOE 3]**

9.5 Limitations in Access to Care

Cultural and regional differences are likely to influence differences in access to care. In developing countries, untreated or inadequately treated SCI cases with late presentation are more frequently seen, but reports of these cases seldom make it into the literature.[32,33] Mortality rates among people with SCI are strongly affected by the capacity of the health care system, especially emergency care. The first 24 hours after SCI, including transportation and time of admission postinjury, are critical factors affecting survival. As an example, the 6-week mortality rate in a Nigerian study was 16.7%, with higher risk if the patient was in a crouched position during transfer (odds ratio [OR]: 23.52) and presenting 24 hours or more postinjury (OR: 5.48).[34] While overall in-hospital mortality in the high-resources settings of Canada and the United States are 11.6% and 6.1%, respectively,[35,36] Nigeria has an average mortality rate of nearly 35%,[37] and Sierra Leone of 29%, with most people with SCI dying within a few years of injury.[38]

Hence, in high-resource countries, there has been a shift in principal causes of death from urologic complications, such as urosepsis or renal failure, to causes of death similar to the general population, such as respiratory problems.[39-43] Although there are few data because of the extremely high rate of "lost to follow-up" patients (97% in some studies),[38] anecdotal evidence indicates that potentially preventable urologic complications remain a common cause of death in low-resource countries.[44] In a study of Saudi Arabian SCI patients, 80.7% had developed recurrent UTIs, 50.9% developed pressure sores during the course of their lives, and 21.1% began to contract chronic diseases such as diabetes and hypertension.[32,45] Furthermore, the availability of quality assistive devices such as wheelchairs is very limited, medical and rehabilitation services are minimal, and opportunities to participate in all areas of personal and social life are constrained.[46,47]

Conclusion:

In low-resource (developing) countries, patients with SCI and urologic complications have higher mortality rates than in high-resource countries. **[LOE 3]**

9.6 Registries of SCI Patients

Some high-income countries have established a central registry of SCIs that applies scientific criteria for the collection, management, and analysis of SCI information. For example, the Rick Hansen Spinal Cord Injury Registry is a Canada-wide database of patients admitted to 31 major trauma and rehabilitation facilities across all provinces.[48] Additional registries are the Australian Spinal Cord Injury Register and the Spinal Cord Injury Model database administered by the National Spinal Cord Injury Statistical Center in the United States.[49-51] While these registries have varying degrees of representativeness, no low- or middle-income country currently has a national SCI registry.

Recommendation:

1. Groups should collaborate to develop registries of SCI patients in low-resource countries. **[GOR C]**

9.7 Guidelines

Several countries around the world have introduced guidelines for treatment and follow-up of patients with SCI/NBD. However, it is unknown if these guidelines are necessarily followed in day-to-day clinical practice.[16,25] Additionally, few doctors in less-developed countries may be aware of continental and international society guidelines.[7,12,52,53]

9.7.1 North America

At present, the Consortium for Spinal Cord Medicine has a bladder management guideline that is under development, and the Guidelines for the Management of Acute Cervical Spine and Spinal Cord Injuries put out by the American Association of Neurological Surgeons has no section on bladder management.[54,55] Nutrition guidelines for patients with SCI have emerged.[56] The review found one nonrandomized crossover trial that showed that adherence of bacteria to uroepithelial cells was significantly decreased in SCI patients who consumed 250 mL cranberry juice three times per day.[57] Cranberry juice intake resulted in a significant reduction in urinary tract biofilm load compared to baseline (p=0.013) and to water treatment (p=0.028). However, evidence suggests that cranberry extract supplements, ingested in tablet or capsule form, are not effective in prolonging the UTI-free period or decreasing bacteriuria or white blood cells (WBC) count in persons with SCIs, based on one large, positive quality double-blinded RCT,[58] one small, double-blinded RCT,[59] and one small, double-blinded, placebo-controlled crossover trial.[60]

9.7.2 South America

Incidence rates are not available for many countries in Central America, South America, and the Caribbean due to lack of published traumatic SCI data. Subsequently, there are big differences between the regions of the continent, and the costs and quality of medical attention are not known. While regionally specific guidelines for the management of NBD have not been written, the adoption of international guidelines in some Latin American countries where resources are available has been associated with improved patterns of care. A Latin American series emerged regarding the primary care of SCI patients, medication usage (anticholinergics, onabotulinumtoxinA, etc.), surgery, and, more recently, the introduction of sacral neuromodulation and sacral neurostimulation for SCI patients in Colombia and Chile.[61]

9.7.3 Europe

The International Spinal Cord Society (ISCoS) originated in the United Kingdom and serves as a resource for SCI patients.[1,62] Likewise, the National Guideline Clearinghouse of the National Institute of Health and Clinical Excellence (NICE) has come out with a set of guidelines for management of lower urinary tract dysfunction in neurological disease.[63] SwiSCI is a longitudinal, rehabilitation-based cohort study.[64] Finally, the European Association of Urology (EAU) guidelines on neurogenic lower urinary tract dysfunction, while not specific to SCI, provide additional information.

9.7.4 **Asia**

The Chinese Urological Association of (CUA) published the first NBD guidelines, chaired by Liao in 2011, and with updates in 2014 and 2015. Although these guidelines are not specific to patients with SCI, the CUA NBD guidelines provide information for clinical practitioners on the incidence, definition, diagnosis, therapy, and follow-up of NBD. The guidelines represent the current opinion of experts in this field who are from China, and thus represent a state-of-the-art reference for all clinicians in China.[65,66] The Taiwanese Continence Society has published clinical guidelines for the diagnosis and management of neurogenic lower urinary tract dysfunction.[67] Likewise, Chen *et al.* published a review of bladder management and urologic complications in patients with chronic SCI in Taiwan.[68] Recommendations have emerged from Malaysia, as well.[69]

9.7.5 **Africa**

The Continence Advisory Panel (CAP), under the auspices of the Southern African Spinal Cord Association (SASCA), has recently produced a guideline to further evidence-based bladder management (mainly in SCI) that ensures social continence and appropriate and safe bladder drainage.[70] Among other areas, this guideline provides guidance on imaging and diagnostic studies and recommendations regarding optimal bladder emptying methods.

9.7.6 **Australasia**

The Agency for Clinical Innovation (ACI), New South Wales State Spinal Cord Injury Service has released the document *Management of the Neurogenic Bladder for Adults with Spinal Cord Injuries*.[71] Recommendations regarding IC, management of detrusor sphincter dyssynergia (DSD), and cystoscopy for cancer surveillance are similar to US/European recommendations.

9.8 Access to SCI Specialists

The British Association of Spinal Cord Injury Specialists (BASCIS) is an organization and resource for locating specialty referral centres for the treatment of SCI.[72] There is evidence in the United Kingdom that specialized care for SCI patients leads to better outcomes. Smith retrospectively recruited a sample of 800 participants from the database of the Spinal Injuries Association (SIA) in the United Kingdom to complete a postal, self-reporting questionnaire ascertaining perceived outcomes across health, functional, and social perspectives.[73] All participants had received rehabilitation within the UK National Health Service (NHS). Despite having more severe injuries, the spinal injury unit (SIU) cohort demonstrated statistically significant improved outcomes in 10 out of 18 health outcomes, 16 out of 18 functional outcomes, and five out of 10 social outcomes. This was in comparison with the non-SIU cohort, which was made up of those patients not managed at one of the 11 national specialist SIUs, but rather in nonspecialist rehabilitation areas. These results should encourage commissioners of health care and those working in trauma settings to ensure people with SCI are managed in a specialist SIU setting both nationally and internationally.

As in the United Kingdom, the Australasian experience confirms that patients admitted to specialized SCI units derive more improvement. The Australasian Rehabilitation Outcomes Centre national database was queried to compare demographic characteristics and rehabilitation outcomes for both nontraumatic SCI (ntSCI) and traumatic SCI (tSCI) patients admitted into either specialist SCI rehabilitation units (SCIRUs) or nonspecialist rehabilitation units (NSRUs).[74] There were 668 patients with confirmed SCI admitted (ntSCI: n=361, 54.0%; tSCI: n=307, 46.0%). ntSCI patients were much less likely to be admitted into a specialist SCIRU (30.5%) compared with tSCI patients (70.4%). For both ntSCI and tSCI patients, those admitted to a specialist SCIRU tended to be younger (p=0.000), have a longer length of stay in rehabilitation (p=0.000), and lower Functional Independence Measure (FIM) motor subscale score on admission (p=0.000) than those admitted to an NSRU. For ntSCI patients, after adjusting for covariates, those admitted into specialist SCIRU had greater improvement in their FIM motor score during rehabilitation. This finding was not demonstrated in tSCI patients.

Conclusion:

Access to specialized SCI units affords patients quicker and more standardized access to care and improved outcomes. **[LOE 2]**

Recommendations:

1. Efforts should be directed toward establishing specialized centres for the comprehensive management of SCI patients. **[GOR B]**
2. SCI patients should be cared for in a specialized SCI centre, when available. **[GOR B]**

9.9 New Technology and Interventions

ClinicalTrials.gov reports 99 completed, current, or not yet initiated trials identified via the search terms "spinal cord injury and bladder." Forty-two of these are located in the United States, 15 in Canada, and 44 in Europe; the remainder are scattered.[1] A total of 32 studies are still open to recruitment.

Of the open studies, a number of topic areas are common. The early use of onabotulinumtoxinA is being studied at Oslo University Hospital (Norway) in a small, double-blind randomized placebo-controlled trial in patients with acute complete motor SCI to examine whether the development of neurogenic bladder may be modified (NCT01698138). At the Rick Hansen Institute (Canada), 200 U intradetrusor injections of Botox are being examined to reduce the frequency of autonomic dysreflexia (NCT02298660). The University of British Columbia (Canada) is also studying the use of 4 mg fesoterodine for similar purposes (NCT02676154). Ipsen is sponsoring two studies, dubbed CONTENT 1 and CONTENT2, to confirm the safety and efficacy of 600 U and 800 U of onabotulinumtoxinA in adults with neurogenic detrusor overactivity (NDO) due to SCI (NCT02660138 and NCT02660359). OnabotulinumtoxinA is also being compared to oral oxybutynin 10 mg extended release (ER) in SCI patients by the Baylor College of Medicine (United States) (US; NCT01050114).

Nerve stimulation is also being studied. With funding from the Department of Defense (United States), investigators from the Universities of Michigan, Minnesota, and Utah are enrolling 50 patients within 2 months of SCI for either implantation of a bilateral sacral neuromodulator or for usual care. This is an effort to study whether neuromodulation during the spinal shock phase can block the development of overactive signalling in the spinal reflex pathway and resultant NDO. The University of Texas Health Science Center (United States) is studying the use of transcutaneous tibial nerve stimulation (10 sessions of 30 minutes each over 2 weeks) in acute traumatic SCI in regards to changes in urodynamic parameters (NCT02573402). University of California, Los Angeles (United States) is studying the use of transcutaneous electrical stimulation and/or magnetic stimulation to improve bladder function in SCI patients (NCT02331979). The American Society Of Thermalism And Climatology Inc. is sponsoring a phase 1 study applying magnetic therapy in SCI patients, with the hope of stimulating bladder emptying (NCT02333695). The Glostrup University Hospital, Copenhagen (Denmark) is studying the use of pelvic floor muscle training with versus without intravaginal neuromuscular electrical stimulation (NEMS) in reducing urinary incontinence in female SCI patients (NCT02427230). Finally, the University of Zürich (Switzerland) is sponsoring a multicentre, randomized trial assessing the use of sacral neuromodulation in neurogenic lower urinary tract dysfunction (NCT02165774).

Imaging represents another common theme. The Universities of Zürich and Balgrist (Switzerland) are studying the use of functional magnetic resonance imaging (fMRI) in response to retrograde filling of the bladder at different volumes and temperatures in normal patients versus those with multiple sclerosis, SCI, and non-neurogenic overactive bladder (OAB) (NCT01768910). The Swiss Paraplegic Centre Nottwil is studying the use of diffusion tensor imaging with magnetic resonance imaging (MRI) to assess the structural innervation of the bladder following SCI, and comparing it to somatosensory evoked potentials (SEP) in SCI patients (NCT02449512).

Clinical outcomes, as reported by patient-reported questionnaires, are being studied longitudinally by the Universities of Utah, Michigan, and Minnesota (United States) in regards to neurogenic bladder management via IC, indwelling catheter management, and bladder surgery (NCT02616081).

Bladder cancer screening for SCI patients via quantification of urinary cytokeratins represents another topic being studied by the Swiss Paraplegic Centre Nottwil (NCT02538809). The University Hospital Inselspital, Bern (Switzerland) is studying changes in microRNA expression during neurogenic-induced organ remodelling compared to that seen in bladder outlet obstruction (NCT02410876). Rennes University Hospital (France) is sponsoring a study, named ESTIME, that will assess self-esteem and neuro-urologic follow-up in patients with spina bifida or SCI, with the hypothesis that global self-esteem and lower perceived self-efficacy may be a causal predictive factor for reduced access to services and reduced compliance with medical therapy (NCT01606618). Shriners Hospitals for Children (Canada) is studying baseline blood pressure and heart rate measurements in children with SCI during rest and urodynamics testing, with the hypotheses that 1) blood pressures will increase with increasing age and body mass index, 2) heart rate will decrease with increasing age, 3) blood pressures will increase with increase in bladder filling, and 4) blood pressures will increase with increasing duration of injury (NCT01599455). Finally, Balgrist University Hospital is assembling a prospective database of clinical, video-urodynamic, and radiologic data of patients with neurogenic lower urinary tract dysfunction treated at the University of Zürich (NCT01293110).

Clinical therapeutics are also being studied. Uro-Research, LLC (United States) is sponsoring a phase 1 clinical trial in SCI patients examining the use of tissue bonding cystostomy, a "closed access" abdominal drainage antibacterial tube permanently placed in the abdominal muscle to bond with the body's tissue (NCT01771159). The Buckinghamshire Healthcare NHS Trust (United Kingdom) is sponsoring a trial with Uro-Vaxom®, a vaccine containing inactivated traces of the bacteria that normally cause at least 83% of UTIs in neurogenic bladder patients (NCT02591901). The Kessler Foundation (United States) is sponsoring a trial examining the combined use of dalfampridine, a potassium channel blocker, in combination with locomotor training in persons with chronic, motor incomplete SCI; one of the secondary goals is to assess changes in bladder management (NCT01621113). This is similar to the study headed by Stony Brook University (United States), which is examining bladder function in SCI patients enrolled in the NeuroRecovery Network (NRN) (United States) after locomotor training (NCT02201173), as well as the study sponsored by the VA Office of Research and Development (United States), which is assessing bladder-related quality of life with exoskeleton assisted-walking in SCI patients (NCT02658656). Finally, InVivo Therapeutics (United States) is sponsoring a study assessing the use of a neuro-spinal scaffold for patients with complete thoracic SCI (NCT02138110), while the Medstar Health Research Institute aims to develop, validate, and assess a patient-initiated, self-management protocol using probiotics that is initiated at the time of urinary symptoms in SCI patients (NCT02748356).

While new interventions are constantly being assessed for the treatment of neurovesical dysfunction related to SCI, neural rerouting and stem cell treatments are perhaps the most thoroughly studied. A recent meta-analysis of the impact of stem cell–based preclinical studies on bladder dysfunction specifically investigated the urodynamic changes after treatment.[75] Consistent improvements in nonvoiding bladder contractions were noted across the studies, despite a variety of treatment paradigms. Transplanted stem cells are believed to inhibit unmediated C-fibre sprouting from afferent neurons, thereby reducing the development of aberrant bladder-to-bladder spinal micturition reflexes. Additionally, reductions in voiding pressure and postvoid residual volumes have also been shown after stem cell transplantation, indicating an improvement in sphincter dysfunction induced by SCI.

Changes in bladder function following neural reconstruction strategies have also been studied. A variety of techniques have been described, some directly involving the bladder reinnervation, others attempting to improve pudendal nerve function, and still others directed more centrally, utilizing nerve transfers of the sacral roots. The indications for each technique are not yet completely understood, and the potential impact on lower urinary tract function is just beginning to be uncovered. Still, there is great hope that, in the not-too-distant future, nerve transplantation strategies could greatly ameliorate lower urinary tract function in patients with SCI.[76]

Conclusion:

Extensive research efforts are underway to improve the diagnosis and treatment of patients with NBD due to SCI. **[LOE 4]**

9.10 Conclusions

There is an absence of high-level worldwide evidence in the literature regarding patterns of care in patients with SCI/NBD. Developed countries such as the United States, Canada, the United Kingdom, and other European countries typically have established systems of care for patients with SCI. This includes registries, regional specialty centres, and protocols regarding acute and chronic management strategies. As such, access to various levels of care is abundant and, subsequently, outcomes and life expectancies are better in developed countries. On the other hand, SCI patients in developing nations may not have access to specialty care, and socioeconomic barriers may prohibit quality care and follow-up. Furthermore, simple access to wound care supplies and catheterization materials impact both the quality and quantity of life. Finally, cultural and religious beliefs may play a significant role in the integration of practices such as IC in many Asian and African countries.

While the situation may seem disheartening for those individuals sustaining SCI in developing countries, there are reasons to be hopeful. Epidemiological studies are being undertaken that will provide an accurate estimate of the incidence and prevalence of SCI in developing nations. This information, in turn, can be used to focus organizations' efforts, not only to provide supplies, but also to provide education regarding the diagnosis and treatment of urologic complications after SCI. New guidelines should be formulated for developing countries, as some of the existing ones have little applicability in those regions of the world.

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The occurrence of a spinal cord injury (SCI), and its sequela of paraplegia or tetraplegia, is undoubtedly one of the worst catastrophes a human being can suffer. The majority of these injuries are the result of trauma, which generally affects young and previously healthy people. The SCI not only compromises the physical sphere of the patient, but also severely affects the affective, social, economic, and occupational spheres, thus presenting a formidable challenge for rehabilitation.

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