A Multicenter Disease Management Program for Hospitalized Patients With Heart Failure

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ABSTRACT

Background: Despite the availability of proven therapies, outcomes in patients with heart failure (HF) remain poor. In this 2-stage, multicenter trial, we evaluated the effect of a disease management program on clinical and economic outcomes in patients with HF.

Methods and Results: In Stage 1, a pharmacist or nurse assessed each patient and made recommendations to the physician to add or adjust angiotensin-converting enzyme (ACE) inhibitors and other HF medications. Before discharge (Stage 2), patients were randomized to a patient support program (PSP) (education about HF, self-monitoring, adherence aids, newsletters, telephone hotline, and follow-up at 2 weeks, then monthly for 6 months after discharge) or usual care. In Stage 1 (766 patients) ACE inhibitor use increased from 58% on admission to 83% at discharge ($P < .0001$), and the daily dose (in enalapril equivalents) increased from 11.3 ± 8.8 mg to 14.5 ± 8.8 mg ($P < .0001$). In Stage 2 (276 patients) there was no difference in ACE inhibitor adherence, but a reduction in cardiovascular-related emergency room visits (49 versus 20, $P = .030$), hospitalization days (812 versus 341, $P = .003$), and cost of care ($CDN 2,531 less per patient) in favor of the PSP.

Conclusion: Simple interventions can improve ACE inhibitor use and patient outcomes.

Key Words: Congestive heart failure, ACE inhibitors, disease management, health care economics.

Heart failure (HF) affects approximately 1% to 1.5%[1–3] of the North American population and is the only cardiovascular (CV) condition increasing in prevalence.[3–7] It is associated with high morbidity and mortality,[1–3,5] especially hospitalizations,[1,2,5] and is an important public health problem. Indeed, three quarters of the estimated $10 billion spent annually in the United States for management of HF is spent on hospitalizations.[3,4,6] A recent Canadian report has shown that more than 106,000 admissions and 1.3 million hospital days per year are associated with HF.[7]

Treatment of HF includes the use of diuretics, angiotensin-converting enzyme (ACE) inhibitors, β-blockers, spironolactone (in moderate to severely symptomatic patients), and digoxin (in selected cases).[8,9] ACE inhibitors are a mainstay of therapy of HF,[8,9] reducing mortality[10–12] and hospitalizations[11,13] by about 25%, and are highly cost-effective.[14–18] Despite this, a review of the published literature on ACE inhibitor use indicates that only 37% (median) of patients

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were receiving ACE inhibitors on admission to the hospital, and only 53% (median) at discharge.[19] ACE inhibitor use in the community setting is even lower, with only about 26% (median) of patients receiving them.[19] In addition, it appears that the dosages of ACE inhibitors are often substantially lower than those proven efficacious in trials.[19,20]

Even in those patients prescribed ACE inhibitors at the optimal doses, medication adherence may be a further problem. Although there are few published quantitative data on medication adherence in patients with HF, poor adherence has been identified as a common cause of HF hospitalizations.[21–23] Therefore, interventions to improve adherence should be included in programs designed to improve HF therapy and outcomes.

Because of the high prevalence and poor outcomes of patients with HF, several interventions have been evaluated. Clinical practice guidelines,[8,9] specialized HF clinics,[24] and multidisciplinary disease management programs[24–27] have been tried. It is widely thought that clinical practice guidelines do little to influence clinical practice. A recent evaluation of strategies to implement the Canadian guidelines for HF resulted in no improvement in ACE inhibitor use.[28] Although specialized HF clinics can certainly optimize treatment of patients with HF,[24,29,30] they can only serve a limited proportion of the population at risk. A systematic review of 11 randomized trials of disease management programs for patients with HF showed a reduction in hospitalizations and cost savings.[31]

Although there is a clear need for new efficacious therapies for HF, simply optimizing treatment with available therapies, in conjunction with patient education, may have as great an impact as any single new therapy. Given the clinical and economic importance of HF, widely applicable strategies to improve patient outcomes are needed. The purpose of the Review of Education on ACE inhibitors in Congestive Heart Failure Treatment (REACT) Study was 2-fold: first, to determine the effect of an in-hospital intervention program on ACE inhibitor use in patients with HF; and second, to determine the effect of a outpatient education and support program for patients with HF on medication adherence, clinical outcomes, and costs of care.

Methods

Study Design and Patient Eligibility

REACT was a multicenter 2-stage trial consisting of an in-hospital intervention in all patients (Stage 1), followed by a randomized trial of a patient support program (Stage 2). Ten hospitals participated in REACT (Appendix A). Before study commencement, the local research coordinators (a hospital pharmacist or nurse) attended a training workshop to review current HF management guidelines[8,9] and study procedures to ensure consistency in the delivery of the patient support program among participating hospitals. The study protocol was approved by the Research Ethics Board of all participating hospitals.

Consecutive patients older than age 18 years, admitted to a hospital with a most responsible, primary, secondary, or complicating diagnosis of HF were eligible to participate in the study. The presence of HF was confirmed by the attending physician. Patients were excluded from the study if they had known secondary causes of HF (ie, correctable causes as anemia or hyperthyroidism), preserved systolic function, were taking an angiotensin-II antagonist because of known intolerance or contraindication to ACE inhibitors, had a terminal illness with a life expectancy less than 6 months, cognitive impairment, were unable to communicate because of language barriers, were attending a specialized HF clinic for medical management, or were participating in a HF clinical trial. In Stage 2, the following additional exclusion criteria were applied: absolute contraindication to ACE inhibitors, patients residing outside the region of the participating hospital, those discharged to a setting where patients were not responsible for administration of their own medication, or those who did not provide written informed consent to participate.

Stage 1

In Stage 1, hospitalized patients with HF were identified through review of admitting databases, pharmacy records, or review of hospital charts (Fig. 1). After identification, patients' medical charts were reviewed to determine eligibility for the study. If the patient was not prescribed an ACE inhibitor, the local research coordinator evaluated their suitability for this therapy based on the published guidelines[8,9] and made recommendations to the attending physician. Patients already receiving an ACE inhibitor were evaluated to determine if a dosage increase was appropriate. As well, all medications were reviewed and recommendations made to optimize other HF therapies and monitored daily thereafter. Near to the time of hospital discharge, patients were approached for consent to participate in Stage 2 of the trial.

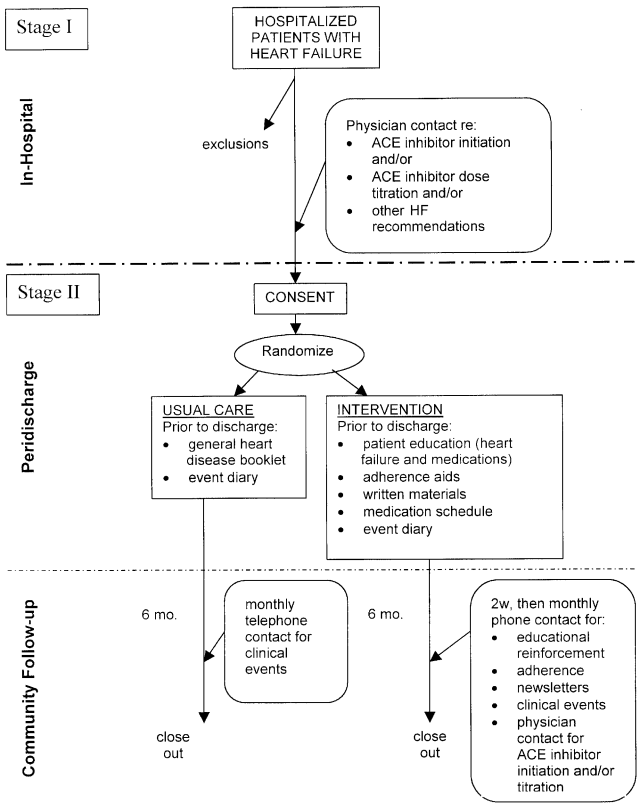

Fig. 1. Trial protocol.

Stage 2

In Stage 2, patients were randomized via a telephone call to the project office (Epidemiology Coordinating and Research Centre, University of Alberta) to the patient support program or usual care groups. Randomization was conducted by a computer-generated sequence using block randomization (block size of 4), stratified by study site (hospital).

The essential components of the patient support program were simplified into 5 basic areas: salt and fluid restriction, daily weighing, exercise alternating with rest periods, proper medication use, and knowing when to call their physician (early recognition of worsening symptoms). Educational materials were developed based on findings from focus groups of patients with HF[32] and consisted of information about HF (definition, causes, symptoms), nondrug treatment, medication information (with special emphasis on proven benefits of therapies), and self-monitoring—all written at a grade 8 reading level. The materials are available for downloading from the EPICORE Centre website (www.epicore.ualberta.ca; see projects, REACT).

The local research coordinator educated patients assigned to the intervention group on a 1-to-1 basis, before discharge, using the written educational package. Patients also received adherence aids including a medication organizer, medication administration schedule, and daily weight log. Patients were encouraged to contact the local research coordinator for ongoing community support.

Community follow-up of the patient support program patients consisted of telephone contact by the local research coordinator at 2 weeks, 4 weeks, then monthly thereafter for 6 months after discharge. The purpose of the telephone contact was to reinforce education and adherence relating to HF and other self-care activities, focusing on the 5 essential components as described previously. This was further supplemented by a monthly newsletter "Living with Congestive HF." Each issue featured an article about one of the essential components along with patient success stories, salt content of foods, low-salt recipes, and compliance tips. Information on ACE inhibitor use and clinical events (physician visits, emergency room (ER) visits, and hospital readmissions) were also collected during the telephone follow-up. The local research coordinator could also recommend the patient consult his or her physician for ACE inhibitor dosage titration or if a medical problem arose that required further attention.

Patients randomized to usual care received a general heart disease pamphlet before discharge, but no formal counseling beyond that of what was routine at the hospital. Follow-up consisted of monthly telephone contact for a period of 6 months to ascertain clinical events.

Study Endpoints and Statistical Analysis

The primary outcome for Stage 1 was the proportion of patients receiving ACE inhibitors at hospital admission compared with that at hospital discharge. The secondary outcome measure was the dosage of ACE inhibitor at hospital admission compared with that at discharge. For the purposes of this endpoint, all ACE inhibitor doses were converted to enalapril equivalents based on the following criteria: 1 mg enalapril = 7.5 mg captopril, 0.25 mg cilazapril, 1 mg fosinopril, 1 mg lisinopril, 2 mg quinapril, 0.5 mg ramipril, and 0.2 mg trandolapril. Changes in ACE inhibitor use were analyzed using chi-square analysis; changes in ACE inhibitor dosing was analyzed using a 2-sided paired *t*-test.

For Stage 2, the primary outcome was medication adherence, as measured by pharmacy records. A medication possession ratio[33] was calculated based on the number of days of ACE inhibitor dispensed divided by the number of days of follow-up (180 days). Clinical events, the secondary outcome, were recorded by patient report and through examination of hospital records. Differences in medication adherence was analyzed using 2-sided paired *t*-test. The Mann-Whitney U test was used for the comparison of clinical outcomes. All analyses were by intention to treat.

Sample size for Stage 1 was estimated assuming 60% utilization of ACE inhibitors at admission (based on previous studies[19]) and an anticipated increase to 70% at hospital discharge. Using a 2-sided alpha of .05, a total enrollment of 300 patients would provide 95% power to detect this difference. Sample size for Stage 2 was estimated assuming a 50% adherence rate in the usual care group and an anticipated increase to 70% in the patient support program group at 6 months after discharge. Using a 2-sided alpha of .05, 250 patients (125 per group) would be required to have 90% power to detect this difference. Because recruitment of patients for Stage 2 was dependent on Stage 1, it was decided to increase the sample size for Stage 1 to 750 to allow for recruitment of sufficient patients into Stage 2.

Economic Analysis

The economic impact of the patient support program was determined by a cost analysis, assessing the degree of health care resource utilization between the 2 study arms over 6 months. Each resource utilization component (drug therapy, physician visits, ER visits, and readmissions) was assessed by self-report during the scheduled telephone follow-up and confirmed with hospital and pharmacy records. For each readmission, the length of stay was determined. Physician visits were identified as general practitioner or specialist for costing purposes. Readmissions, ER visits, and physician visits were identified as CV- or non-CV related. CV-related events were defined as vascular instability (hypotension/hypertension), coronary ischemia, dysrhythmias, HF (dyspnea, pulmonary edema, low cardiac output), diabetes, and cerebrovascular ischemia. For drug therapy, only ACE inhibitors were included in the cost analysis; all other drug therapies were assumed to be equal.

Costs were estimated from the perspective of a Canadian provincial health care system using standard cost estimate approaches.[34] Average unit costs were estimated for the 3 provinces involved in the study (Table 1). Hospital costs were estimated by the product

Table 1. Unit Costs for Health Care Resources

	Saskatchewan	Alberta	British Columbia	Average
Prescription mark-up	10.00%	—*	7.00%	5.68%
Dispensing fee	$7.15	$9.70	$7.55	$8.13
No. days dispensed	30	30	30	30
Hospitalization cost/day	$627.00	$835.00	$650.00	$704.00
Emergency room cost/visit	$110.00	$110.00	$110.00	$110.00
Physician cost—general practitioner	$23.50	$22.19	$30.52	$25.40
Physician cost—specialist	$87.00	$107.78	$121.07	$105.28

All costs in Canadian dollars.

*Allow $0.20 for prescriptions costing less than $75.00, $0.75 for prescriptions costing less than $150.00, and $2.15 for prescriptions costing more than $150.00.

of the length of stay and the estimated standard per diem rate ($CDN 704/day). Standard costs were used for physician fee schedules and drug benefit lists published for each of the 3 provinces. Provincial physician fee schedule amounts for general practitioner visits and for specialists were applied for each visit. ACE inhibitor costs were estimated by a weighted unit price of all approved ACE inhibitors available on the provincial formularies as of June 2000. The weights for drug costs were determined by the actual distribution of ACE inhibitors used by study subjects during the follow-up period. Total costs for the 6-month follow-up were determined by summing the individual component costs, and categorized as all-cause or CV-related. Average costs per patient were calculated by dividing the total costs by the number of subjects enrolled into each study arm.

Results

Recruitment took place between September 1999 and April 2000. A total of 766 patients were entered into Stage 1 (Fig. 2). The baseline characteristics of the patients entered into Stage 1 are indicated in Table 2. These patients represent a typical hospitalized patient population with HF with 55% males and an average age of 74. The majority of patients were in New York Heart Association functional class II and III and the majority of patients had an ischemic etiology of their HF. Eighty percent of patients were treated with furosemide, and about half were treated with acetylsalicylic acid (ASA), nitrates, and digoxin. Thirty-six percent of patients were receiving a β-blocker on admission, and 14% were receiving spironolactone. Only 4% of patients were receiving an angiotensin II antagonist.

ACE inhibitor use increased from 58% of patients on admission to 83% of patients on discharge ($P < .0001$).

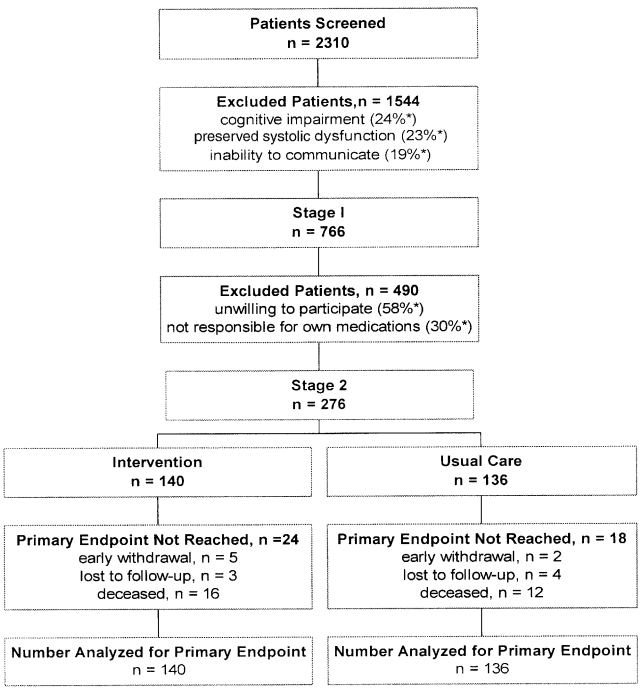

Fig. 2. Trial profile. *Percent of total exclusions.

Table 2. Baseline Characteristics, Stage 1 Patients (n = 766)

Males, n (%)	417 (55)
Mean age, years (±SD)	74 (12)
Mean ejection fraction, % (±SD)*	31 (12)
New York Heart Association Functional Class, %	
I	8
II	49
III	38
IV	5
Duration of heart failure, n (%)	
New onset	185 (24)
≤6 months	93 (12)
7–12 months	63 (8)
13–24 months	72 (9)
25–48 months	67 (9)
>48 months	179 (23)
Unknown	107 (14)
Medical history, n (%)	
Coronary artery disease	557 (76)
Hypertension	448 (50)
Myocardial infarction	381 (50)
Diabetes	295 (39)
Atrial fibrillation	246 (32)
Hypercholesterolemia	158 (21)
Peripheral vascular disease	154 (20)
Cerebrovascular disease	151 (20)
Ventricular tachycardia	65 (9)
Primary etiology of heart failure, n (%)	
Coronary artery disease	451 (59)
Hypertension	96 (13)
Idiopathic dilated cardiomyopathy	57 (8)
Valvular heart disease	48 (6)
Alcohol	16 (2)
Other	27 (3)
Unknown	67 (9)
Medications, n (%)	
Furosemide	609 (80)
Acetylsalicylic acid	355 (47)
Nitrate (oral or topical)	348 (46)
Digoxin	336 (44)
β-blocker	277 (36)
Cholesterol-lowering agent	129 (17)
Spironolactone	109 (14)
Angiotensin II antagonist	28 (4)
Hydralazine	12 (2)

*n = 437.

The average daily ACE inhibitor dose at hospital admission/drug initiation was 11.3 ± 8.8 mg enalapril equivalents. This increased to 14.5 ± 8.8 mg/day at hospital discharge ($P < .0001$).

From the 766 patients entered into Stage 1, 276 patients were enrolled in Stage 2. The baseline characteristics of patients enrolled in Stage 2 were similar to that of Stage 1 (Table 3), although 65% of the patient support program patients had an ischemic etiology compared with only 51% in the usual care group ($P = .03$). Eighty-five percent of patients in Stage 2 were receiving ACE inhibitors as a result of the intervention in Stage 1.

The main results for Stage 2 are shown in Table 4. ACE inhibitor adherence over the 6 months after discharge was 86.2 ± 29% in the usual care group versus 83.5 ± 29% in the patient support program group (P = NS). Although there were no differences in the number of all-cause physician visits, ER visits, or readmissions between treatment groups, there was a significant reduction in total length of hospital

Table 3. Baseline Characteristics, Stage 2 Patients (n = 276)

	Usual care	Patient support program
Total number	136	140
Males, n (%)	79 (58)	81 (58)
Mean age, y (±SD)	72 ± 12	71 ± 12
Ejection fraction, % (±SD)	31 ± 11	32 ± 12
New York Heart Association Functional Class, %		
I	14	12
II	52	48
III	30	35
IV	3	5
Primary etiology of heart failure, n (%)		
Coronary artery disease	71 (51)	91 (65)*
Hypertension	21 (15)	17 (12)
Medications, n (%)		
Angiotensin-converting enzyme inhibitor	115 (85)	119 (85)
Furosemide	109 (80)	105 (75)
β-blocker	55 (40)	63 (45)
Digoxin	52 (38)	58 (41)
Spironolactone	17 (13)	20 (14)

*P = .03.

stay (627 days versus 1,082 days, $P < .001$) and average length of hospital stay (6.6 ± 5.5 days versus 11.0 ± 9.2 days, $P < .001$) between the patient support program and usual care groups, respectively. There was no difference between groups in the proportion of patients readmitted at least once; 51 (37.5%) in the usual care group versus 59 (42.1%) in the patient support program. A significant reduction in CV-related ER visits (49 versus 20, $P = .030$) was observed. As well, patients in the usual care group were more likely to have an ER visit because of a CV event than were those in the intervention group (21.3% versus 12.1%, $P = .041$). The total length of hospital stay, in relation to a CV event (812 days versus 341 days, $P = .003$) and average length of hospital stay (11.6 ± 10.3 days versus 6.4 ± 6.0 days, $P = .003$) was also significantly reduced in the patient support program.

The economic analysis of Stage 2 is shown in Table 5. The total cost of care for CV-related events over the 6-month follow-up period of this study, was $CDN 4548 for usual care patients compared with $CDN 2017 for patient support program patients, for a cost difference of $CDN 2531 per patient. For all-cause events, the cost difference per patient was $CDN 2463 ($CDN 6154 for usual care and $CDN 3691 for the patient support program).

Discussion

As a highly prevalent condition with high mortality and morbidity,[1–3,5–7] even small increments in the improvement of the care of patients with HF may have large public health implications. The results of this study indicate that a dedicated HF program using hospital pharmacists and nurses can result in an improvement in ACE inhibitor usage and dosing, with reductions in clinical events and costs.

Stage 1, In-Hospital Intervention

The patients enrolled in Stage 1 were representative of hospitalized patients with HF, with many patients older than 70 years of age and with an almost even split of males and females. At baseline, it is notable that only 36% of patients were receiving a β-blocker, which also have very important effects on mortality and morbidity in HF. As well, almost three quarters of the patients had coronary artery disease, yet only 47% were receiving ASA and only 17% were receiving a cholesterol-lowering agent.

The study intervention resulted in an increase in the usage of ACE inhibitors from 58% on admission to 83% at the time of hospital discharge. The rate of ACE inhibitor utilization on admission is comparable with previous work by our group[35] and as reported by other investigators.[19] Whether 83% utilization represents the "ceiling" for ACE inhibitor utilization remains unknown. McAlister et al[36] reported ACE inhibitor utilization to be 83% in a specialty

Table 4. Stage 2 Results

	Usual care (n = 136)	Patient support program (n = 140)	P value
ACE inhibitor adherence % (±SD)	86.2 ± 29.0	83.5 ± 31.2	.691
Clinical events: all-cause			
Physician visits, n	904	933	.795
Emergency room visits, n	69	41	.206
Hospital readmissions, n	98	95	.635
Total length of hospital stay (days)	1082	627	<.001
Patients with at least 1 emergency room visit, n (%)	38 (27.9)	31 (22.1)	.266
Patients with at least 1 hospital readmission, n (%)	51 (37.5)	59 (42.1)	.431
Clinical events: cardiovascular related			
Physician visits, n	260	220	.366
Emergency room visits, n	49	20	.030
Hospital readmissions, n	70	53	.597
Total length of hospital stay (days)	812	341	.003
Average length of hospital stay (days ± SD)	11.6 ± 10.3	6.4 ± 6.0	.003
Patients with at least 1 emergency room visit, n (%)	29 (21.3)	12 (12.1)	.041
Patients with at least 1 hospital readmission, n (%)	38 (27.9)	37 (26.4)	.778

Table 5. Stage 2 Economic Analysis: Cardiovascular-Related Costs per Patient

Component	Usual care ($CDN)	Patient support program ($CDN)
Medications	169	168
Physician visits	136	118
Emergency room visits	40	16
Hospital readmissions	4203	1715
Total 6-month costs of care per patient	4548	2017

HF clinic. Because of our exclusion of patients with contraindications to ACE inhibitors and known preserved systolic dysfunction, it cannot be determined if this represents the highest possible utilization of these agents.

The average daily dose of ACE inhibitor also increased as a result of the Stage 1 intervention from the time of hospital admission/drug initiation to discharge (11.8 ± 8.8 mg to 14.5 ± 8.8 mg, enalapril equivalents). The dosage attained in this study is similar to that found to be efficacious in the randomized trials (15 mg in Vasodilator Heart Failure Trial [V-HeFT],[10] 16.6 mg in Studies of Left Ventricular Dysfunction [SOLVD] Treatment,[12] 12.7 mg in SOVLD Prevention,[13] 18.4 mg in Continental North Scandinavian Enalapril Survival Study [CONSENSUS][11]). Given that the dosages of ACE inhibitors used in the "real world" appear to be substantially lower than those in randomized trials,[19] interventions specifically targeting upward dosage titration are important in realizing the full benefits of ACE therapy. As well, high-dose ACE inhibitor therapy was found to be superior to low-dose therapy in reducing the composite endpoint of mortality and hospitalizations in a large randomized trial.[20]

Stage 2, Patient Support Program

In general, the baseline characteristics of patients enrolled in Stage 2 were similar to that of Stage 1. Surprisingly, ACE inhibitor adherence in both groups was quite high, with no significant difference between groups. Rich et al[37] evaluated the effect of a multidisciplinary treatment approach on medication adherence in patients with HF. Adherence, assessed by pill counts at 30 days, was also high in both the intervention and usual care groups (87.9% versus 81%, $P = .003$). In contrast, the findings of 1 small study that used pharmacy claims for a 10- to 17-month period noted that only 50% of patients with HF had an average ACE inhibitor mean possession ratio of >0.8.[38] There are several explanations for the high adherence rate observed our study. First, the follow-up period was rather short at only 6 months. Because patients often receive a 3-month supply of their medications, this represents only 2 refill cycles. Because the method of determination of adherence was a possession ratio (ie, number of tablets dispensed compared with number of days elapsed), this is prone to error depending on when the patient refilled his or her second prescription. Second, there is no gold standard for the measurement of adherence (all methods have limitations). Third, patients with cognitive impairment (and at risk for poor adherence) were excluded from the study. Fourth, even patients in the usual care group had frequent contact with the study coordinators. Although this contact was not intended to be educational, it may have reminded patients that they were in an "adherence study," which may have prompted them to take their medications as prescribed. Finally, a frequent problem with adherence studies is that of volunteer bias, whereby only patients who display interest in self-care of their condition consent to participate in such studies.

The clinical event rate in this group of patients was, as expected, rather high. Although there were no differences in CV-related physician visits or readmissions, there was a marked reduction in the need for ER visits and total length of hospital stay in patients randomized to the patient support program. Applying economic analyses to these figures shows a cost difference of $CDN 2531 per patient over the 6-month follow-up period. Given the prevalence of HF, this may have important public health implications. A recent evaluation of the burden of illness in HF showed that it is associated with more than 106,000 hospitalizations each year in Canada.[7] Therefore, the potential cost savings in terms of ER visits and hospitalizations in even a medium-size hospital (about 1000 admissions with HF per year) could be substantial.

It is unclear as to why the total numbers of readmissions did not differ between treatment groups, although there was a marked reduction in the total length of hospital stay (which is the primary driver of costs). We had originally hypothesized that the patient support program would lead to improved medication adherence with ACE inhibitors, resulting in improved clinical outcomes and therefore reduced costs of care. Although we observed substantial savings in the short follow-up, it did not appear to be a direct result of improved adherence to ACE inhibitors. It is quite likely, however, that the regular follow-up contact with the local research coordinators strongly reinforced all of the other aspects of self-management (eg, diet, daily weighing), which led to reductions in the use of hospital services. As a multifaceted intervention it is not possible to determine which component(s) are the most important. This will be studied further by our group.

Our study provides further evidence that disease management programs improve patient and economic outcomes in patients with HF. Disease management programs that have been shown to improve outcomes in randomized trials, however, vary substantially in terms of manpower resources (specialized multidisciplinary teams versus individual coordinator), educational content, comprehensive medical management (including medication adjustment by nurses as per protocol, individualized dietary plans), and mode/frequency of community follow-up of patients (telephone versus in person). In a recent systematic review of 11 randomized trials,[31] those programs involving patient education, multidisciplinary teams, and specialized follow-up procedures reduced the risk of hospitalization and were cost-saving. In contrast, telephone-based systems designed to enhance

follow-up with primary care providers did not appear to be effective.

Two additional trials have since been published. Kasper et al[27] conducted a randomized trial in 2 centers that included intensive medical management (active initiation and titration of medications by nurses) and follow-up by a multidisciplinary team. A reduction in a composite endpoint of hospital readmissions and mortality over 6 months ($P = .09$) was observed, but no difference in cost of care. Krumholz et al[26] evaluated the effect of a patient education and support program, without a medical management component, in a randomized trial of 88 patients. A significant reduction in the incidence of readmission or death was observed at 1 year (RR = .69, $P = .01$). As well, the cost of care was substantially lower in the intervention group. Unlike our study, the beneficial outcomes were not apparent until after 180 days of follow-up.

To the best of our knowledge, our study is the largest multicenter trial conducted to date, in both academic and community centers, demonstrating the improved outcomes using a simple patient support program. The use of a multicenter design increases the external validity. As well, our program is less resource intensive, in terms of manpower and follow-up procedures, as compared with other disease management programs[27,31] and focuses predominately on education and adherence rather than direct medical management. For these reasons, this program is more readily adaptable to a variety of settings to improve the outcomes of the growing number of patients with HF.

Limitations

There are a number of limitations of this study. Stage 1 used a nonrandomized, before-after design. Although this design provides a lower level of causal inference, it was selected for practical and ethical reasons (it was felt to be unethical not to attempt to get patients on ACE inhibitors). In Stage 2, the limitations of our adherence measure have been discussed previously. The long-term impact (beyond 6 months) of the Stage 2 patient support program is not known and will be evaluated in a subsequent study. Of note, local research coordinators indicated that one of the most time-consuming aspects of this study was finding patients with HF who could benefit from this program. Most hospitals do not have a system in place for real-time identification of patients with HF, which is a rate-limiting step in application of such beneficial programs. Finally, this study was conducted in the context of the Canadian health care system so the applicability to other systems is unknown. However, the consistent benefit on patient outcomes is more important than the exact cost savings.

Conclusion

A simple and practical in-hospital HF disease management program improved the utilization of ACE inhibitors by almost 50% and also promoted the usage of higher doses of ACE inhibitors. A 6-month patient education and support program for outpatients with HF had little impact on ACE inhibitor adherence however reduced utilization of health care resources, resulting in a cost reduction of $CDN 2531 per patient for CV-related events. Given the high prevalence and poor outcomes in this patient population, strong consideration should be given to implementation of such programs on a wider scale.

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Appendix A

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