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A Randomized Trial of the Efficacy of Multidisciplinary Care in Heart Failure Outpatients at High Risk of Hospital Readmission

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OBJECTIVES We sought to determine whether a multidisciplinary outpatient management program decreases chronic heart failure (CHF) hospital readmissions and mortality over a six-month period.

BACKGROUND Hospital admission for CHF is an important problem amenable to improved outpatient management.

METHODS Two hundred patients hospitalized with CHF at increased risk of hospital readmission were randomized to a multidisciplinary program or usual care. A study cardiologist and a CHF nurse evaluated each patient and made recommendations to the patient's primary physician before randomization. The intervention team consisted of a cardiologist, a CHF nurse, a telephone nurse coordinator and the patient's primary physician. Contact with the patient was on a prespecified schedule. The CHF nurse followed an algorithm to adjust medications. Patients in the nonintervention group were followed as usual. The primary outcome was the composite of the number of CHF hospital admissions and deaths over six months, compared by using a log transformation t test by intention-to-treat analysis.

RESULTS The median age of the study patients was 63.5 years, and 39.5% were women. There were 43 CHF hospital admissions and 7 deaths in the intervention group, as compared with 59 CHF hospital admissions and 13 deaths in the nonintervention group ($p = 0.09$). The quality-of-life score, percentage of patients on target vasodilator therapy and percentage of patients compliant with diet recommendations were significantly better in the intervention group. Cost per patient, in 1998 U.S. dollars, was similar in both groups.

CONCLUSIONS This study demonstrates that a six-month, multidisciplinary approach to CHF management can improve important clinical outcomes at a similar cost in recently hospitalized high-risk patients with CHF. (J Am Coll Cardiol 2002;39:471–80) © 2002 by the American College of Cardiology

Improving the outpatient management of patients with chronic heart failure (CHF) is an important challenge. The majority of patients with CHF do not receive or comply with optimal pharmacologic, dietary or physical activity regimens (1–7). Elderly patients with CHF may benefit from a focused multidisciplinary management approach designed to improve treatment, patient compliance and outcomes (8,9). We conducted a randomized clinical trial to determine whether a program designed to implement optimal medical therapy, increase patient understanding and compliance and reduce financial barriers to care, coupled with frequent telephone monitoring and clinic follow-up, could decrease deaths and hospital readmissions, as well as improve compliance and quality of life, at no extra cost in patients with CHF at increased risk of early hospital readmission.

METHODS

Study design. This was a prospective, randomized trial performed at The Johns Hopkins Hospital and The Johns Hopkins Bayview Medical Center. The Maryland Medical Research Institute independently collected and analyzed all data. An independent Oversight, Data, Safety and Monitoring Committee reviewed the protocol before the beginning of the study, monitored the progress of the study and assessed the occurrence of adverse events by treatment group. The Joint Committee on Clinical Investigation at The Johns Hopkins Medical Institutions approved the study, and each patient provided written, informed consent before randomization.

Eligibility of patients. English-speaking patients admitted with a primary diagnosis of New York Heart Association (NYHA) functional class III/IV CHF and judged to be at high risk of CHF readmission were eligible for study participation. At randomization, patients were usually no

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Abbreviations and Acronyms

ACE = angiotensin-converting enzyme
CHF = chronic heart failure
LV = left ventricular
LVEF = left ventricular ejection fraction
NYHA = New York Heart Association

longer in NYHA functional class III/IV (Table 1). High risk of hospital readmission was defined by the presence of one or more of the following criteria, selected from the literature (4–7,10–13) and from our clinical experience: age >70 years, left ventricular ejection fraction (LVEF) <35%, at least one additional CHF hospital admission in the previous year, ischemic cardiomyopathy, peripheral edema at hospital discharge, <3 kg weight loss while in the hospital, peripheral vascular disease or hemodynamic findings (during the index admission) of pulmonary capillary wedge pressure >25 mm Hg, cardiac index <2.0 l/min/m^2, systolic blood pressure >180 mm Hg or diastolic blood pressure >100 mm Hg. Patients were ineligible if they had any of the following: valvular heart disease requiring surgical correction, active substance abuse, peripartum cardiomyopathy, hypertrophic cardiomyopathy with left ventricular (LV) outflow tract obstruction, restrictive cardiomyopathy, constrictive pericarditis, psychiatric disease or dementia

Table 1. Baseline Characteristics

	Intervention Group (n = 102)	Nonintervention Group (n = 98)
Demographic data		
Age (yrs)	60.2 ± 13.8 (25–87)	63.7 ± 15.0 (26–88)
Males	66 (64.7%)	55 (56.1%)
African American	34 (33.3%)	35 (35.7%)
White	65 (63.7%)	63 (64.3%)
Specialty of primary care physician		
Internal medicine	67 (65.7%)	71 (72.5%)
Cardiology	30 (29.4%)	25 (25.5%)
Baseline medical data		
Hypertension	68 (66.7%)	66 (67.3%)
Diabetes mellitus	40 (39.2%)	40 (40.8%)
LVEF <45%	89 (87.3%)	86 (87.8%)
Ischemic etiology	49 (48.0%)	49 (50.5%)
NYHA functional class		
II	38 (37.3%)	33 (33.7%)
III	57 (55.9%)	60 (61.2%)
Medications		
ACE inhibitor	92 (90.2%)	80 (81.6%)
Angiotensin II blocker	7 (6.9%)	10 (10.3%)
Beta-blocker	39 (38.2%)	39 (39.8%)
Digoxin	72 (70.6%)	64 (65.3%)
Diuretic	98 (96.1%)	96 (98.0%)
Hydralazine	4 (3.9%)	7 (7.2%)
Long-acting nitrate	14 (13.7%)	24 (24.5%)
Physical examination		
Pulse (beats/min)	82.5 ± 14.5 (47–112)	79.7 ± 14.6 (52–129)
BP (mm Hg)		
Systolic	118.0 ± 21.3 (79–188)	120.2 ± 20.7 (81–170)
Diastolic	69.0 ± 12.2 (42–100)	68.4 ± 10.9 (48–100)
Laboratory data		
LVEF (%)	27.1 ± 13.8 (10–70)	27.5 ± 13.9 (5–60)
Creatinine (mg/dl)	1.3 ± 0.5 (0.4–2.8)	1.3 ± 0.5 (0.5–2.9)
Sodium (mmol/l)	137.0 ± 3.9 (122–147)	137.1 ± 3.6 (127–146)
Quality-of-life scores		
Minnesota Living With Heart Failure Questionnaire		
Total	64.3, 68.5 (51–79)	62.4, 65.5 (52–78)
Physical	30.2, 34 (26–38)	30.6, 35 (27–38)
Emotional	14.6, 15 (9–21)	13.9, 16 (8–20)
Duke Activity Status		
Score	5.5, 5 (3–7)	5.0, 4.5 (3–7)
Index	20.0, 17 (7–29)	17.0, 13 (7–24)

Data are presented as the mean value ± SD (range; for age, physical examination and laboratory data), number (%) of patients or mean and median values (25th to 75th percentile; for quality-of-life scores). There were no statistically significant differences.

ACE = angiotensin-converting enzyme inhibitor; BP = blood pressure; NYHA = New York Heart Association.

likely to limit compliance, concurrent noncardiac illness likely to cause repeat hospital admissions, heart transplantation likely to occur within six months, uncorrected thyroid disease, serum creatinine ≥265 μmol/l (3.0 mg/dl), long-term intravenous inotropic therapy at home, cardiac surgery or myocardial infarction during the index admission, active participation in another research trial or unwillingness to provide informed consent. Residence in a nursing home, rehabilitation facility or outside the area served by the clinical sites was also an exclusion criterion. After permission from the patient's primary physician, patients were approached at the end of the index hospital period.

Baseline evaluation. Baseline evaluation included a history and physical examination performed by cardiologists specialized in the management of heart failure. Echocardiography was performed to document LV function if it had not been performed in the previous six months. Recommendations, including those regarding medication, diet and exercise management, were documented in the patient's medical record before randomization.

Treatment assignment. The coordinating center made treatment assignments by using an automated telephone response system, after the baseline evaluation and recommendations were recorded in the patients' chart. Random number schedules were prepared before initiation of patient recruitment and were unknown to the clinical investigators. Randomization was stratified by site and by the presence of LV systolic dysfunction, defined by LVEF <45%.

Intervention group. The four members of the intervention team were the telephone nurse coordinator, the CHF nurse, the CHF cardiologist and the patient's primary physician. The telephone nurse coordinator made follow-up calls to patients from a central site located in Rockville, Maryland. Telephone calls were placed within 72 h of hospital discharge, then weekly for one month—twice in the second month and monthly thereafter, unless a problem occurred that required more frequent contact. The telephone nurse coordinator followed a set script and pursued problems as clinically indicated, but did not adjust medications over the telephone.

The CHF nurses were assigned to assist the intervention group and helped to implement the therapeutic plan designed by the CHF cardiologists. Patients had at least monthly follow-up with these nurses. Most visits occurred in CHF clinics located at each site, but some occurred in the patient's home. The CHF nurses adjusted medications under the directions of the CHF cardiologists, following a prespecified algorithm, which included initiation and titration of angiotensin-converting enzyme (ACE) inhibitors, beta-blockers and diuretics. The algorithm included a 2-g sodium-restricted diet, as well as a recommendation to exercise by walking for 20 min at least four days per week. The treatment plan was individualized for each patient. In the course of the study, the algorithm was updated to include, for example, the use of beta-blockers. All members of the team, except for the patients' primary physicians, participated in weekly patient care meetings.

The CHF cardiologists designed and documented a treatment plan for all study patients before randomization and saw the patients at baseline and six months. They designed the prespecified algorithm according to available CHF guidelines and clinical experience.

The primary physicians approved of their patients' participation, as well as medication, dietary, activity and follow-up regimens. They managed all problems not related to CHF, received regular updates from the CHF nurses and were notified of abnormal laboratory values. Most of the primary physicians were internists (Table 1).

Patients in the intervention group with limited financial resources were provided, if needed, a scale, a 3-g sodium "Meals on Wheels" diet, medications, transportation to the clinic and a telephone. All patients in the intervention group were supplied with a pill sorter, a list of correct medications, a list of dietary and physical activity recommendations, a contact number available 24 h/day and patient education material. The intervention continued for six months.

Nonintervention group. Patients assigned to the nonintervention group were cared for by their primary physicians. The baseline therapeutic plan designed by the CHF cardiologist was documented in the patient's chart, without further intervention.

Outcome collection. No patient withdrew from the study. Follow-up data were collected on every patient. Transplantation was performed in two patients during the six-month study period, and another had a prolonged pretransplant hospital stay during the study period and underwent successful transplantation shortly thereafter. Outcome data were obtained at the six-month visit, and the patients were then followed for an additional three months. The CHF cardiologist, along with the CHF nurse, saw all patients during the six-month visit.

Several methods were used to obtain complete ascertainment of study outcomes. The importance of reporting all hospital admissions was explained to each patient; patients were asked to keep a diary of all hospital admissions, and the diaries were sent to the coordinating center monthly. An independent central telephone data collector, who had no knowledge of the patients' treatment assignment, collected data monthly from all patients during the nine months after enrollment. Medical document coordinators blinded to treatment assignment searched the on-line medical records of The Johns Hopkins Hospital and The Johns Hopkins Bayview Medical Center for admissions during the study period. If a hospital admission was found at another hospital, medical document collectors searched that hospital's medical records for additional admissions during the study period.

The diaries, telephone interviews and medical records were used to enumerate all hospital admissions and deaths. Medical document collectors obtained copies or abstracts of the medical records. The coordinating center deleted from

all documents and records information that revealed personal identity or treatment assignment.

Outcomes. A committee composed of three cardiologists, who had no knowledge of the treatment assignment, categorized each hospital admission and death using documents prepared by the coordinating center. Two members independently evaluated all cases. In the event of a discrepant classification, the third member reviewed the report and assigned the final classification.

The primary outcome variable was the composite of death from any cause and the total number of CHF hospital admissions. Planned secondary outcome variables included death, CHF hospital admissions, total hospital admissions, changes in quality of life (measured by the Minnesota Living With Heart Failure Questionnaire [14]) and activity status (measured by the Duke Activity Status Index [15]). The best score on the Minnesota Living With Heart Failure Questionnaire is 0 and the worst is 105. The best score on the Duke Activity Status is 12 and the worst is 0. Similarly, the weighted best score on the Duke Activity Status Index is 58.2. The questionnaires were completed by the patients and analyzed by the coordinating center in a blinded fashion. Additional secondary end points assessed by the CHF nurse included NYHA functional class, the patient's global assessment of how he or she felt and the amount of ankle edema.

Planned secondary outcomes also included several indexes of the quality of care, such as the percentage of patients with systolic dysfunction who were receiving target vasodilators, defined as ACE inhibitor therapy according to published guidelines (16,17), or, if intolerant of ACE inhibitor therapy, those taking either losartan (50 mg/day) or a combination of isosorbide dinitrate (up to 160 mg/day) and hydralazine (up to 300 mg/day). Target beta-blocker doses were not defined in the initial protocol, because at that time, no beta-blockers were approved by the U.S. Food and Drug Administration for use in patients with CHF. Additional planned analyses included the degree of compliance with dietary recommendations, as well as the percentage of patients who were euvolemic according to the goal weight. Goal weight was defined as that weight at which the jugular venous pressure was <8 cm of water above the right atrium, with a stable serum creatinine value <221 μmol/l (2.5 mg/dl) in the absence of ankle edema and symptomatic orthostasis. The goal weight, assessed by the CHF nurse, could be adjusted depending on the patient's clinical condition. Compliance with dietary recommendations was assessed using a locally developed dietary sodium score, which was completed by the patient at baseline and at the final visit.

The cost of the personnel included direct and indirect components. Salaries are consistent with those in the published data and with average salaries in the mid-Atlantic region (18–20). Salaries were adjusted for the recorded actual time spent caring for the patients in the intervention group and supervising the CHF nurse over the 2.5 years required to complete the study for the nurses and physicians, respectively. Pharmacy cost included all outpatient medications recorded during the study period, using wholesale, generic outpatient drug costs taken from the *Drug Topics Red Book,* 1997 to 1999 (21–23). Supplies included scales, 3-g sodium "Meals on Wheels" diet, medications, transportation to the clinic, pill sorters and telephones. Inpatient costs (excluding professional fees) for readmission to the two primary hospitals were measured in constant 1998 U.S. dollars by applying state-regulatory cost-to-charge ratios and annual inflation factors to actual charges. Costs for inpatient stays at other hospitals were imputed by multiplying the mean daily cost at the two primary hospitals by the length of stay at other hospitals. Inpatient costs and length of stay do not include two patients who underwent heart transplantation and one patient who had a prolonged pretransplant hospital stay during the six-month study period; these patients were randomized to the intervention group.

Statistical methods. Patient characteristics are presented as counts and percentages and were compared using tests of difference for two proportions for dichotomous data (24) and the Mantel-Haenszel method (25) for data in multiple categories. The Fisher exact test was used for characteristics with a prevalence $<5\%$ (26). Survival and survival-free of hospital admission were compared according to the Kaplan-Meier method (27), using the log-rank test for statistical inference (28).

Data measured on continuous scales were compared using the t test (29) and the Wilcoxon rank-sum statistic (30). Because cost and length of stay inherently have a severely skewed distribution, with a median value of 0, these data were expressed in percentiles and analyzed with the two-tailed nonparametric Wilcoxon test. The Duke Activity Index and Minnesota Living With Heart Failure scores were analyzed using both unweighted and published weighting methods.

The primary outcome, the combination of deaths and the total number of CHF admissions, was analyzed using a log transformation of counts of the primary outcome per patient (0.5 was added to the count of the primary outcome to accommodate patients with no hospital admissions in the analysis, and death was counted as an event), and comparisons were made by using the t test. A Poisson model comparison (29) was also performed, as suggested by a statistician of the Oversight, Data and Safety Monitoring Committee at their initial meeting before patient enrollment. Analyses were based on the intention-to-treat principle.

The planned sample size was 100 patients per treatment group, based on an alpha value of 0.05 and a power of 80% for alternative hypotheses of a 35% relative reduction in the primary outcome. One interim analysis was planned, setting the critical value at $p = 0.001$ and adjusting the final, primary-analysis critical value at $p = 0.0487$. For secondary analyses in which 40% to 50% of patients had the outcome

Table 2. Events Within Six Months of Study Entry

	Intervention Group (n = 102)	Nonintervention Group (n = 98)	p Value
Death (life-table rate)	7 (6.9%)	13 (13.4%)	0.14 (LR)
Distribution of CHF hospital admissions or death			
0	72 (70.6%)	58 (59.2%)	
1	20 (19.6%)	26 (26.5%)	
2	6 (5.9%)	6 (6.1%)	
3	1 (1.0%)	2 (2.0%)	
4	1 (1.0%)	3 (3.1%)	
5	1 (1.0%)	2 (2.0%)	
6	1 (1.0%)	1 (1.0%)	
Mean	0.5	0.7	
Total	50	72	0.09 (L), 0.03 (P)
Distribution of hospital admissions or death			
0	55 (53.9%)	43 (43.9%)	
1	26 (25.5%)	32 (32.7%)	
2	13 (12.7%)	8 (8.2%)	
3	4 (3.9%)	5 (5.1%)	
4	1 (1.0%)	6 (6.1%)	
5	2 (2.0%)	2 (2.0%)	
6	1 (1.0%)	2 (2.0%)	
Mean	0.8	1.1	
Total	84	109	0.13 (L), 0.04 (P)

Data are presented as the number (%) of patients.
CHF = chronic heart failure; L = log transformation *t* test; LR = log-rank test; P = Poisson model comparison.

of interest and alpha = 0.01, the estimated power was 80% for relative reductions in the range of 37.5% to 50%.

RESULTS

Patients. From December 1996 until December 1998, 200 patients were enrolled in the study. There were 104 patients randomized at The Johns Hopkins Hospital and 96 at The Johns Hopkins Bayview Medical Center. There were 1,252 patients screened and found to be ineligible. Of these, 476 (36.6%) did not have NYHA functional class III/IV CHF on admission or did not meet the high-risk inclusion criteria. In addition, there were 776 high-risk patients admitted with NYHA functional class III/IV CHF who had one or more of the exclusion criteria. The causes of exclusion include renal dysfunction (14.3%), dementia or substance abuse (10.7%) and planned cardiac revascularization or heart transplantation (10.2%), and 10.2% had cardiac exclusions such as hypertrophic cardiomyopathy, restrictive cardiomyopathy, amyloidosis and valvular heart disease. Of excluded patients, 15.5% were participating in another research protocol, 7% lived beyond our area and 5.1% lived in a nursing home or were discharged on an intravenous inotrope. A variety of noncardiac disorders thought likely to cause repeated hospital admissions led to the exclusion of 12.8% of the patients. Finally, 11.9% of the patients refused to participate, and 2.3% were excluded because their primary-care physicians declined to participate.

The demographic and clinical characteristics of the two randomized groups were statistically similar at baseline (Table 1). The median age of the patients was 63.5 years (range 25 to 88). The Minnesota Living With Heart Failure and the Duke Activity Status Index scores are consistent with a moderate impairment in quality of life and functional capacity, respectively. At randomization, 94% of the patients were in NYHA functional class II/III.

Hospital admission and mortality. Thirteen patients in the nonintervention group and seven in the intervention group died during the six-month study period. There were 59 hospital admissions for CHF among 35 patients in the nonintervention group, and 43 hospital admissions among 26 patients in the intervention group ($p = 0.09$ by the log-transformation *t* test and $p = 0.03$ by Poisson model comparison). There were fewer hospital admissions for any reason in the intervention group, as well (Table 2). Treatment effects were most marked after the third month, and the event rates continue to separate through six months (Fig. 1). A continued separation of the event rates in the two groups was not seen in the three months after the end of the intervention.

Baseline predictors of the primary end point on univariate analysis were diabetes ($p = 0.003$) and an ischemic cause of CHF ($p = 0.001$). Atrial fibrillation, LVEF <45%, the presence of an internal cardioverter-defibrillator, age ≥65 years, NYHA functional class ≥III at discharge from the index hospitalization and a Minnesota Living With Heart Failure total score ≥65 were not predictive of the primary end point on univariate analysis.

Quality of care. The telephone nurse coordinator made 973 calls to patients in the intervention group, averaging 9.5 calls per patient. The CHF nurses made 862 patient visits, or 8.5 visits per patient. The mean (±SD) duration of a

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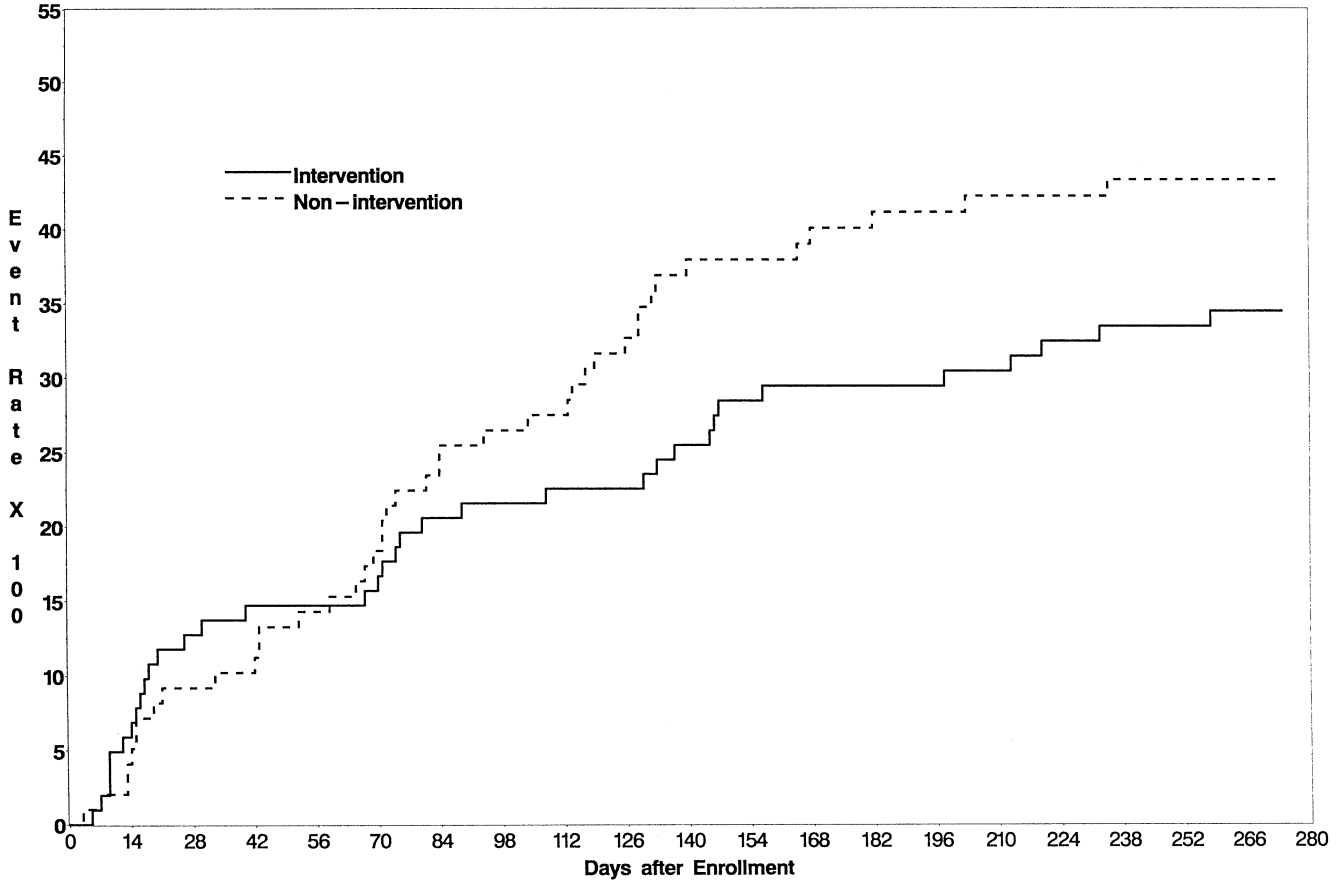

Figure 1. Life-table first event rates for death or readmission for chronic heart failure. The trial end point was 180 days or six months ($p = 0.12$ by log-rank). This was not the primary end point, which was death or all readmissions for chronic heart failure.

telephone call was 16 ± 9 min, whereas the average length of a visit by a CHF nurse was 57 ± 21 min. The average visit with the CHF cardiologist lasted 22 ± 12 min in both the intervention and nonintervention groups.

After six months, patients with systolic dysfunction in the intervention group were more likely to be prescribed target doses of vasodilators (74 of 80 patients vs. 43 of 71 patients in the nonintervention group, $p < 0.001$). Similarly, dietary compliance was more likely to be described as "good" or "average" in patients in the intervention group versus the nonintervention group, based on a review of dietary history (65 of 94 patients vs. 38 of 85 patients, $p = 0.002$). The intervention patients were also more likely to be at their goal weight, as compared with the nonintervention patients (47 of 94 patients vs. 17 of 85 patients, $p = 0.001$). There was no difference in medication compliance.

Quality of life. At the final visit, patients in the intervention group were less symptomatic, according to NYHA functional class (Table 3). Patients in the intervention group were more likely to report stable or improved symptoms, as compared with those in the nonintervention group (81of 94 patients vs. 55 of 85 patients, $p = 0.003$) and were less likely to have ankle edema (18 of 89 patients vs. 35 of 85 patients, $p = 0.003$). Quality of life, measured by the Minnesota Living With Heart Failure Questionnaire, improved in both groups, but patients in the intervention group improved more (Table 3). Improvement occurred in total score as well as in both physical and emotional dimensions.

Cost. The most costly component of the intervention was personnel (Table 4). The intervention, including salaries and supplies, cost $904 per patient in the intervention group. The mean outpatient pharmacy cost per patient was similar in both groups: $1,353 in the intervention group and $1,405 in the nonintervention group. The median number of outpatient physician visits was four in both groups. The greatest overall cost was readmission (Table 4). The costs of readmission are consistent with the published costs of admission due to CHF, which range from $4,397 to $10,148 (31–35). Inpatient costs for all study patients ranged from $0 to $239,760 (mean $10,085), and the length of stay ranged from 0 to 132 days (mean 5.5). There was no significant difference in inpatient or outpatient resource use between the intervention and nonintervention groups (Table 4).

In the analysis of cost, we excluded two patients who underwent transplantation during the study and one who did shortly thereafter. The first two were patients with the highest and third highest inpatient costs. The third patient had a relatively low inpatient cost. All were randomized to the intervention group. If included, the mean length of stay

Table 3. Clinical Data at Six-Month Final Visit

	Intervention Group (n = 102)	Nonintervention Group (n = 98)	p Value
Data available	94	85	
NYHA functional class			
I	7 (8%)	9 (11%)	
II	62 (67%)	34 (40%)	
III	18 (20%)	35 (41%)	
IV	5 (5%)	7 (8%)	0.03 (CMH)
Missing	2 (2%)	0	
Patient-assessed CHF symptoms			
Stable	41 (44%)	29 (35%)	
Improved	40 (43%)	26 (31%)	
Worse	11 (12%)	29 (35%)	0.003
Missing	2 (2%)	1 (1%)	
Ankle edema	18/89 (20%)	35 (41%)	0.003
At goal weight	47 (50%)	17 (20%)	0.001
Diet compliance			
Good	32 (34%)	12 (14%)	
Average	33 (35%)	26 (31%)	
Poor	25 (27%)	44 (52%)	0.002
Missing	4 (4%)	3 (4%)	
Medications			
ACE inhibitor	78 (82.9%)	60 (70.6%)	0.07
Angiotensin II blocker	12 (12.8%)	7 (8.2%)	0.33
Beta-blocker	43 (45.7%)	32 (37.6%)	0.27
Digoxin	67 (71.3%)	51 (60.0%)	0.11
Diuretic	87 (92.6%)	75 (88.2%)	0.32
Hydralazine	5 (5.3%)	7 (8.2%)	0.44
Long-acting nitrate	14 (14.9%)	17 (20.0%)	0.37
Quality-of-life scores			
Minnesota Living With Heart Failure Questionnaire			
At final visit			
Total	35.7, 33 (14–52)	45.3, 51 (22–64)	0.01 (W)
Physical	14.7, 14 (5–21)	21.3, 25 (11–32)	0.0006 (W)
Emotional	9.0, 6 (2–15)	10.6, 10 (2–19)	0.33 (W)
Change from baseline			
Total	−28.3, −28	−15.7, −15	0.001 (W)
Physical	−15.4, −17	−8.7, −8	0.0004 (W)
Emotional	−5.3, −4	−2.5, −1	0.03 (W)
Duke Activity Status			
At final visit			
Score	6.8, 6 (5–9)	6.0, 6 (4–8)	0.05 (W)
Index	25.7, 21 (15–37)	21.8, 19 (10–31)	0.04 (W)
Change from baseline			
Score	1.1, 1	0.8, 1	0.44 (W)
Index	5.5, 4.5	3.9, 2.7	0.52 (W)

Data are presented as the number (%) of patients or mean and median values (25th to 75th percentile).
CMH = Cochran-Mantel-Haenszel test for trend; W = Wilcoxon test; other abbreviations as in Tables 1 and 2.

in the intervention group increased to 8.7 days (75th percentile, 4 days), and the mean inpatient cost increased to $16,182 (75th percentile, $6,527). However, there remains no significant difference in inpatient or outpatient resource use between the intervention and nonintervention groups.

DISCUSSION

Readmission for CHF. Heart failure is common and associated with high mortality and morbidity. Hospital admission for CHF is frequent, and readmission rates of up to 44% within six months are reported (10). Treatment regimens for CHF are increasingly complex and require considerable expertise and time on the part of physicians, who are usually not heart failure experts. Numerous studies indicate that factors related to patient behavior account for large numbers of hospital admissions (4–7,36). Other barriers to effective CHF management include a lack of coordination among various providers and the cost of medications and special diets.

The intervention. The program we describe was designed to overcome the aforementioned barriers to improved outpatient CHF management. A 55-page CHF algorithm,

Table 4. Resource Use Per Patient by Treatment Assignment in Constant 1998 U.S. Dollars

	Intervention Group	Nonintervention Group
Telephone coordinator	$129	$0
CHF nurse	$541	$0
CHF cardiologist	$196	$0
Supplies	$38	$0
Outpatient pharmacy (mean)	$1,353	$1,405
Inpatient length of stay (days)*		
Mean	6.3	4.8
75th percentile	3	7
Inpatient cost†		
Mean	$11,315	$8,789
75th percentile	$5,952	$10,898

*p = 0.17 and †p = 0.20, favoring the intervention group.
CHF = chronic heart failure.

incorporating detailed descriptions of the initiation, titration and monitoring of medical, dietary and activity therapies, formed the basis for recommendations provided by the multidisciplinary team. The CHF algorithm was based on randomized clinical trials, published guidelines and our personal expertise and experience. The algorithm provided "guardrails to practice decisions" (37), but did not provide a protocol of a common standard therapy for patients with CHF.

In our study, CHF experts were available to provide guidance, but did not see the patients between the initial and final visits. Nurses supervised by cardiologists, along with primary-care physicians, provided most of the care, adjusted medications and provided dietary and physical activity guidance. It is important to note that primary-care physicians were not excluded from CHF disease management, but rather were integrated into the team care of their patients.

Primary end point analysis. The multidisciplinary approach is associated with a clinically important decline in death or CHF hospital admissions over the six-month intervention period (p = NS). The primary end point of death plus hospital admissions for CHF was chosen because patients may have multiple admissions for CHF, all of which are important to prevent. The data were also analyzed in terms of the time to first event (Fig. 1), with similar results. Differences in the primary outcome between the two groups widened beginning in the third month. During the three months after termination of the intervention, the curves no longer separate, suggesting that the intervention should be continued. There were significant differences in quality of life, assessed by the Minnesota Living With Heart Failure Questionnaire, and quality of care, assessed by both the proportion of patients on target vasodilator therapy and the proportion of patients at their goal weight. Although the primary outcome is of borderline statistical significance, an overall view of the data suggests that the intervention was beneficial.

Predictors of readmission or death. Only diabetes and an ischemic cause of CHF independently predicted readmission for CHF or death—the primary end point. Both diabetes and coronary disease are associated with a poor prognosis (38–41).

Comparison with previous studies. Management programs for CHF have received wide acceptance, primarily on the basis of uncontrolled studies. There are several randomized trials of disease management in patients with CHF and two review articles (42,43). A recently published meta-analysis of 11 randomized trials supports a reduction in CHF hospital admissions for patients participating in some programs (44). Of the randomized trials, there are two assessing the effectiveness of interventions designed to improve care delivery. At baseline, the patients in our trial were younger, were more often male, had a lower average LVEF and were less likely to have coronary disease, as compared with the patients enrolled in the two most similar randomized trials. To the best of our knowledge, this is both the first multicenter trial of CHF disease management and the first trial with active initiation and titration of medications by nurse practitioners.

Rich et al. (8) reported that intensive patient education, coupled with three-month follow-up using home-care services, improved hospital admission-free survival in patients with a median age of 79 years. Our findings extend the benefits of this approach to a longer intervention period and to a younger population. We emphasized the involvement of the patient's primary physician, as well as active initiation and titration of medications by nurses.

Stewart et al. (9) reported that a single visit by a cardiac nurse 7 to 14 days after hospital discharge, followed by a report to the patient's physician, was associated with improved survival, without unplanned hospital admission over a six-month period in patients with CHF with a mean age of 75 years. The only other contacts with the study team were telephone calls at three and six months. Our intervention program was different in that it included extensive patient contact and education, intensive pharmacologic intervention and involvement of the patient's physician; also, our patients were younger.

In our trial, the patient's primary physician, regardless of randomization, received expert recommendations at the time of the patient's enrollment. This is reflected by the higher utilization of ACE inhibitors and beta-blockers at baseline in our trial, as compared with the other two trials. This may explain the lower event rate in the current trial and why the differences between the two groups were most apparent after the third month, whereas in both the Rich et al. (8) and Stewart et al. (9) trials, the differences were present almost immediately after randomization.

Cost. This was a relatively expensive program, although the cost of the hospital period dwarfed the cost of the program itself. There was no significant difference in resource use between the two groups (Table 4), but our sample size was too small for reliable conclusions, especially because overall resource use by patients with CHF is sensitive to high-cost outliers. This is demonstrated in

Table 4 by the difference between the mean and 75th percentile for both inpatient length of stay and inpatient cost. Although there were fewer admissions in the intervention group, the average admission was more expensive. This suggests that the intervention decreases admission for relatively less severe and hence less expensive problems.

Study limitations. Several limitations should be noted. First, the program was multidisciplinary and not designed to analyze the relative contributions of its various components. Second, physicians caring for patients in the nonintervention group received expert recommendations at the time that their patients were discharged from the index hospital period and knew their patients were in a randomized trial assessing CHF treatment. Thus, the comparison was not to a strict usual care group, and these factors may have decreased the event rate in the nonintervention arm. Third, some but not all of the secondary outcomes were collected in an unblinded manner by the CHF nurse, and not all of the tools utilized to assess medication and dietary compliance have been validated. This may have introduced bias in those unblinded secondary end points. Fourth, these results may not be applicable to all patients with CHF, because we specifically targeted patients thought to be at high risk of readmission. Finally, it is likely that not all patients with CHF require such an extensive intervention. We are unable to determine, from our data, which patient subgroups benefited from participation. Many commercial CHF management programs do not involve cardiologists or CHF nurses, but rely only on telephone management. It is unclear, from our data, whether telephone management alone results in a benefit. A significant component of future investigation will be to determine which patient subsets benefit most from this intervention strategy.

Conclusions. Our results indicate that a multidisciplinary approach to the management of high-risk outpatients with CHF, utilizing an expert knowledge algorithm, frequent monitoring, intensive and continuing patient education and close interaction with the patient's primary physician, improves quality of life, with a trend toward improvement in the primary end point of death and total number of CHF hospital admissions over a six-month intervention period. Future studies are needed to determine which physiologic and behavioral characteristics best predict the need for specific intervention strategies.

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