

Clinical Outcome of Patients with Chronic Heart Failure Followed in a Specialized Heart Failure Center

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ABSTRACT: **Background:** Patients with heart failure (HF) have a poor prognosis. Heart failure centers with specialized nurse-supervised management programs have been proposed to improve prognosis.

Objectives: To evaluate the clinical outcome of patients with HF treated at a multidisciplinary HF center of Clalit Health Services in Jerusalem in collaboration with Hadassah University Hospital.

Methods: We evaluated clinical outcome including hospitalizations and death in all HF patients followed at the HF center for 1 year.

Results: Altogether, 324 patients were included and followed at the HF center; 58% were males with a mean age of 76 ± 11 years, and 58% were in New York Heart Association (NYHA) functional class III-IV. The overall 1 year survival rate was 91% and the 1 year hospitalization rate 29%. Comparing patients in the HF center to the whole cohort of patients with a diagnosis of HF (N=6618) in Clalit Health Services in Jerusalem demonstrated a similar 1 year survival rate: 91% vs. 89% respectively but with a significantly reduced hospitalization rate: 29% vs. 42% respectively ($P < 0.01$). Cox regression analysis demonstrated that treatment in the HF center was a significant predictor of reduced hospitalization after adjustment for other predictors (hazard ratio 0.65, 95% confidence interval 0.53–0.80, $P < 0.0001$). A subset of patients that was evaluated (N=78) showed significantly increased compliance. NYHA class improved in these patients from a mean of 3.1 ± 0.1 to 2.6 ± 0.1 after treatment ($P < 0.0001$).

Conclusions: Supervision by dedicated specialized nurses in a HF center increased compliance, improved functional capacity in HF patients, and reduced hospitalization rate. HF centers should be considered part of the standard treatment of patients with symptomatic HF.

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Heart failure is a major epidemic today and a significant public health problem. It is associated with considerable morbidity and mortality [1,2]. The chronic and debilitating nature of the illness in patients who suffer from multiple comorbidities, are on complex drug regimens and must adhere to a strict diet poses a substantial challenge to HF patients and to their caregivers [3,4]. Heart failure centers with specialized nurse-supervised management programs may help to resolve this issue. These HF centers are led by specialized nurses who educate patients regarding their disease and instruct them with regard to self-care and self-management of the disease. In addition, the nurses closely follow the patients by telephone or clinic visit as required, depending on the clinical status of the patient. Close follow-up increases compliance, improves care and helps in the management of changes in clinical status, thereby preventing deterioration and reducing hospitalization.

A growing body of evidence suggests that specialized centers have a significant effect on outcome, reducing hospitalization rates and improving survival [5-8]. In addition, these centers may reduce costs, although the data supporting this are less conclusive [9,10]. Nevertheless, a recent large-scale multicenter randomized clinical study from the Netherlands failed to show a significant clinical benefit for a nurse-led HF management program [11]. Nurse-supervised management programs have been proposed to improve clinical outcomes; however, these programs vary among different countries and particular centers, depending on the specific program implemented, the particular nurse-supervision strategy employed, and the available resources allocated. These variations have an impact on the effectiveness of the program and should affect clinical outcome.

The purpose of the present study was to evaluate if a nurse-supervised management program strategy employed at Clalit Health Services, the largest of Israel's four health management organizations, would improve the clinical outcome of HF patients. We evaluated all patients with HF treated at a

HF = heart failure

multidisciplinary nurse-supervised HF center of Clalit Health Services in Jerusalem in collaboration with Hadassah University Hospital during a 2 year period. Patients were followed for clinical outcome including 1 year survival and hospitalization rate.

PATIENTS AND METHODS

All patients treated and followed at the HF center in Jerusalem during a 2 year period (2008–2009) were included in this analysis. Patients referred to the clinic were symptomatic HF patients (New York Heart Association functional class II–IV) with a recent hospitalization or considered by the treating physician to be unstable or deteriorating clinically. The patients included suffered from clinical heart failure as diagnosed by the treating HF specialist in the HF center, based on standard clinical criteria [12]. Three major principles determined the management of the patients: a) specialized nurse-supervised implementation of care; b) joint management of patients with the primary physician; and c) careful implementation of management guidelines, from lifestyle modification to pharmacological therapy and all applicable advanced technologies. A multidisciplinary team comprising a HF nurse, a cardiologist specialized in HF management and a dietician evaluated patients admitted to the HF center. Patients received detailed information about their disease from the cardiologist and the HF nurse. In addition, they received information and counseling regarding appropriate self-care behavior including a recommended low salt diet and a general diet, their medication regimen, as well as the importance of self-monitoring weight and awareness of changes in their clinical status. The nurse followed the patients regularly by telephone and/or by periodically scheduled clinic visits depending on the clinical status of the patient. In addition, regular follow-up clinic visits with the HF specialist were scheduled, depending on the patients' clinical status. We followed patients for 1 year after admission to the HF center for clinical outcome including cardiac related hospitalizations and death.

We compared the outcome of these patients to a large cohort of HF patients in Jerusalem during the same period. Patients were identified and their data retrieved electronically from the computerized database of Clalit Health Services in Jerusalem. Patients were enrolled if they had a recorded diagnosis of heart failure. Available relevant clinical data were retrieved from the computerized database and analyzed. All hospitalizations in cardiac and internal medicine departments including cardiac and internal intensive care units were retrieved and analyzed. Data on mortality were obtained from the National Census Bureau. The data analyzed included clinical events during a period of 1 year from July 2008 to the end of June 2009. The Institutional Committee for Human Studies of Clalit Health Services approved the study protocol.

A subset of patients seen at the HF center filled out detailed questionnaires regarding compliance data prior to starting treatment at the HF center and after treatment. Compliance data included adherence to a low salt diet, a general diet and medical therapy. NYHA functional status was also recorded.

STATISTICAL ANALYSIS

SPSS commercially available software was used in all analyses. Comparison between patients followed in the HF center versus HF patients not managed in the HF center was performed using the one-way ANOVA test for continuous variables and the chi-square test for categorical variables. Kaplan-Meier curves, with the log-rank test, were used to compare survival and hospitalization-free survival between the groups. Multivariate Cox regression analysis was used to evaluate independent variables that determined hospitalization and survival. Included in the multivariate analysis in one model were clinical parameters, such as age, gender, ischemic heart disease, hypertension, diabetes, hyperlipidemia, atrial fibrillation, serum sodium, hemoglobin and urea. In the second model, HF medication including angiotensin-converting enzyme inhibitor/angiotensin receptor blocker, beta blocker, spironolactone and furosemide were included in the Cox regression analysis. A *P* value of < 0.05 was considered statistically significant.

RESULTS

CLINICAL PARAMETERS

Altogether, 324 patients were included and followed at the HF center. The demographics and clinical parameters of these patients are presented in Table 1. The mean age of the patients was 76 ± 11 years and 58% were males. Mean NYHA class was 2.6 ± 0.6 with 58% in NYHA III–IV. We compared patients in the HF center to the whole cohort of patients in Clalit Health Services in Jerusalem with a diagnosis of HF (N=6618). Their clinical data are presented for comparison in Table 1. Age was comparable between the groups. However, there were more males in the HF center group, and the percentage of patients suffering from ischemic heart disease, hypertension and hyperlipidemia, atrial fibrillation, peripheral vascular disease and chronic obstructive lung disease was significantly higher in the HF center patients. In addition, HF center patients had on average lower blood pressure, lower serum sodium and estimated glomerular filtration rate, and increased urea. A significantly higher percentage of patients followed in the HF center were on standard heart failure medications at the beginning of treatment [Table 1]. NYHA class was not available for analysis in the whole cohort of patients. Echocardiographic data were available for analysis

NYHA = New York Heart Association

Table 1. Demographics, clinical characteristics and pharmacological treatment of patients in the heart failure center versus all patients with heart failure

	HF center patients (N=324)	All HF patients (N=6618)	P value*
Age (yrs)	76±11	75±15	0.11
Male	187 (58%)	3314 (50%)	< 0.01
Clinical characteristics			
Ischemic heart disease	252 (78%)	4778 (72%)	0.03
S/P coronary bypass surgery	65 (20%)	1130 (17%)	0.16
Hypertension	281 (87%)	5377 (81%)	0.01
Diabetes mellitus	165 (51%)	3070 (46%)	0.11
Hyperlipidemia	280 (86%)	5406 (82%)	0.03
Atrial fibrillation	129 (40%)	1620 (24%)	< 0.0001
S/P TIA or CVA	76 (23%)	1503 (23%)	0.75
Peripheral vascular disease	70 (22%)	1118 (17%)	0.03
COPD	44 (14%)	627 (9%)	0.01
Dementia	18 (6%)	669 (10%)	0.01
Dialysis	13 (4%)	295 (4%)	0.70
Reduced LV function**	72 (60%)	898 (55%)	0.25
NYHA class III-IV	174 (58%)	—	—
Body mass index (kg/m ²)	31 ± 6	30 ± 8	0.10
Systolic BP (mmHG)	124 ± 19	128 ± 19	< 0.001
Diastolic BP (mmHG)	69 ± 10	71 ± 10	0.01
Pulse pressure (mmHG)	55 ± 16	57 ± 17	0.01
Pulse (bpm)	73 ± 17	73 ± 13	0.60
Laboratory data			
Serum creatinine (μmol/L)	1.3 ± 0.6	1.3 ± 1.2	0.37
eGFR (ml/min/1.73 m ²)	60 ± 26	64 ± 30	0.01
Serum urea (mmol/L)	66 ± 38	58 ± 35	< 0.0001
Serum sodium (mEq/L)	139 ± 4	140 ± 3	0.02
Hemoglobin (g/dl)	12.6 ± 1.7	12.7 ± 1.8	0.42
Treatment			
ACE-inhibitor/ARB	284 (88%)	4808 (73%)	< 0.0001
Beta-blockers	241 (74%)	4358 (66%)	< 0.0001
Spirolactone	176 (54%)	1936 (29%)	< 0.0001
Furosemide	284 (88%)	4176 (63%)	< 0.0001
Thiazides	87 (27%)	1542 (23%)	0.14
Digoxin	50 (15%)	652 (10%)	< 0.0001
Anticoagulants	70 (22%)	1042 (16%)	< 0.0001
Aspirin	225 (69%)	4269 (65%)	0.07

* P value by one-way ANOVA for continuous variables and chi-square test for categorical variables.

** Reduced LV function vs. preserved LV function (ejection fraction ≥ 50%)

Data are presented as mean ± standard deviation for continuous variables and number of patients (percentages) for categorical variables

TIA = transient ischemic attack, CVA = cerebral vascular accident, COPD = chronic obstructive pulmonary disease, BP = blood pressure, eGFR = estimated glomerular filtration rate, ACE = angiotensin-converting enzyme, ARB = angiotensin receptor blocker

in 37% of the patients in the HF center (N=120) and in 25% of the total patient cohort (N=1645). In the HF center there was a slightly higher percentage of patients with any reduction in left ventricular function (60% vs. 55%), which was attributed to more patients with severely reduced LV function in the HF center group (30% vs. 26%); however, this was not statistically different from the whole cohort.

LV = left ventricular

EFFECT OF TREATMENT IN THE HF CENTER ON COMPLIANCE AND FUNCTIONAL CAPACITY

In a subset of the patients followed in the HF center (N=78), compliance to a recommended low salt diet, recommended diet and drug therapy was recorded at the start of treatment in the HF center and after intervention based on information given by the patient. In addition, NYHA class was recorded before and after intervention. Treatment at the HF center resulted in a significant increase in all measures of compliance. Adherence to a low salt diet increased significantly from 60% of the patients before supervision to 96% after supervision ($P < 0.001$). Adherence to an appropriate diet as recommended increased significantly from 66% before supervision to 88% after supervision ($P < 0.05$). A less dramatic increase was seen in adherence to medication, since 84% of the patients were taking medication regularly prior to enrollment in the program. Nevertheless, adherence to the medication regimen increased to 93% after supervision ($P = 0.1$). There was a significant improvement in functional capacity during follow-up. NYHA class improved from a mean of 3.1 ± 0.1 to 2.6 ± 0.1 after treatment ($P < 0.0001$). In addition, 60% of the patients reported that their functional status had improved due to supervision in the HF center.

CLINICAL OUTCOME

The 1 year survival rate in patients followed at the HF center was 91% and the 1 year hospitalization rate 29%. Comparing patients in the HF center to the whole cohort of patients with HF demonstrated a similar 1 year survival rate: 91% vs. 89% respectively ($P = 0.7$). Cox regression analysis after adjustment for other predictors did not show a significant difference in mortality (hazard ratio 0.93, 95% confidence interval 0.60–1.45, $P = 0.7$) [Figure 1A]. There was a significantly reduced hospitalization rate in patients treated in the HF center compared to the whole cohort of patients with HF: 29% vs. 42% respectively ($P < 0.01$). Cox regression analysis demonstrated that treatment in the HF center was a significant predictor of reduced hospitalization after adjustment for other predictors (HR 0.65, 95% CI 0.53–0.80, $P < 0.0001$) [Figure 1B and Table 2]. Inclusion of HF medication in the Cox regression analysis did not change the result significantly, with reduced hospitalization in the HF center group (HR 0.59, 95% CI 0.48–0.72, $P < 0.000001$).

DISCUSSION

The syndrome of heart failure has become a major epidemic in the western world, leading to significant morbidity and mortality and presenting a significant global health burden. There are many strategies for improving outcome in these patients. These include lifestyle-modifying interventions, pharmacological therapy and device-based therapies. Nurse-

HR = hazard ratio
CI = confidence interval

Figure 1. Adjusted survival rate **[A]** and cardiac-related hospitalization rate **[B]** of patients treated in the HF center versus all HF patients by Cox regression analysis. There was no significant difference in survival between the groups: hazard ratio 0.93, 95% confidence interval 0.60–1.45, $P = 0.7$. There was a significant reduction in hospitalization rate in patients treated in the HF center: HR 0.65, 95% CI 0.53–0.80, $P < 0.0001$

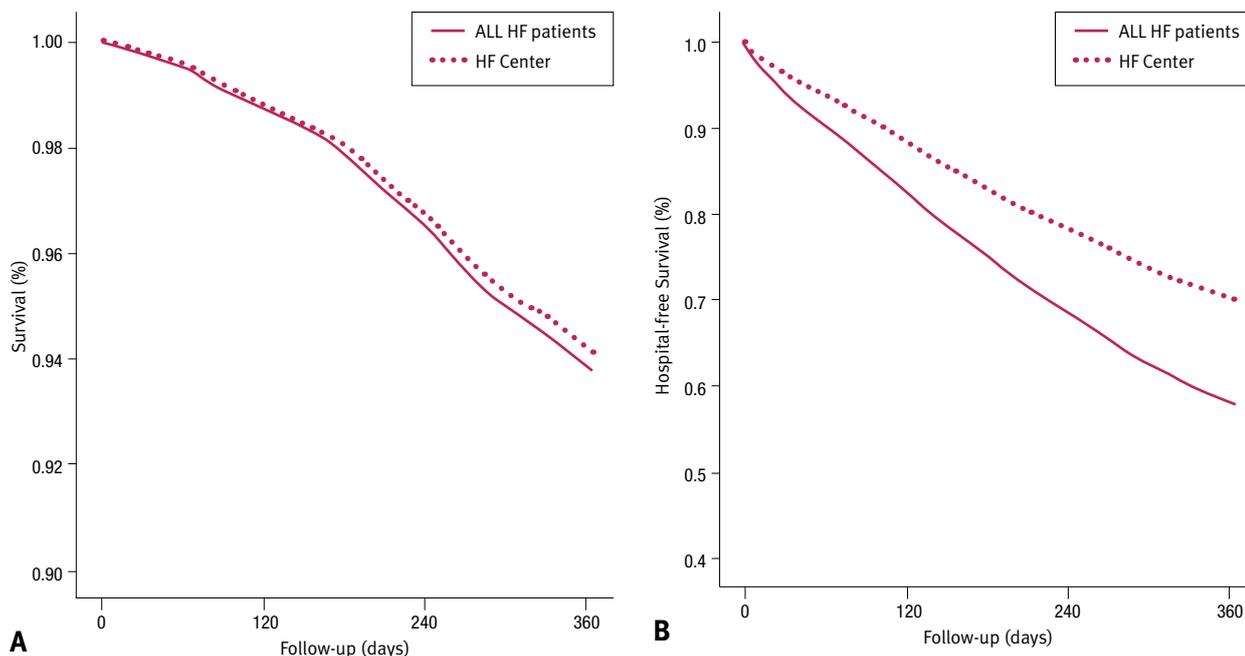


Table 2. Predictors of hospitalization by Cox regression analysis in the whole cohort

	HR (95% CI)	P value
Age (yrs)	1.00 (1.00–1.01)	0.006
Gender (male)	1.14 (1.05–1.24)	0.002
Ischemic heart disease	1.13 (1.03–1.24)	0.012
Diabetes mellitus	1.20 (1.10–1.30)	< 0.0001
Hyperlipidemia	0.86 (0.78–0.96)	0.009
Hypertension	1.21 (1.08–1.36)	0.002
Atrial fibrillation	1.28 (1.17–1.39)	< 0.0001
Hemoglobin (g/dl)	0.86 (0.84–0.89)	< 0.0001
Serum sodium (mEq/L)	0.98 (0.96–0.99)	< 0.0001
Serum urea*	1.42 (1.26–1.60)	< 0.0001
Heart failure center	0.65 (0.53–0.80)	< 0.0001

* Serum urea levels were divided into quartiles. The data (hazard ratio) denote a comparison of the highest quartile with the lowest quartile

supervised management programs in HF centers have been shown to improve prognosis in patients with HF, reducing hospitalizations and improving survival. Several meta-analyses have demonstrated that strategies incorporating a specialized multidisciplinary management program to treat heart failure reduce both hospital admission and all-cause mortality [5,7,8].

Present guidelines endorse such an interventional strategy and HF management programs are recommended for patients with HF recently hospitalized and for other high risk patients [13]. The present study evaluated this interventional approach in HF patients in Jerusalem. We found that patients followed in a multidisciplinary HF center with a specialized nurse-supervised management program had fewer hospital admissions compared to a large control group of patients with HF. Moreover, treatment in the HF center increased compliance and improved functional capacity.

We did not find a survival benefit in our patients compared to the comparative control group, although evidence in the literature suggests such a benefit in HF patients [5,8]. This is not unexpected since this was not a randomized study and patients referred to the HF center were patients with active and advanced disease who were hospitalized frequently. These patients were referred by their primary physician to the HF center because they were unstable or had more advanced disease and needed more intensive treatment. These patients would be expected to have a worse prognosis than stable patients comprising the comparison control group. Despite this, the survival rate in these patients was better than expected in patients with symptomatic HF. The control group was based on a computerized database of all patients with a diagnosis of HF. This would include the entire spectrum of patients with HF, including patients with very mild and stable clinical disease.

Although we performed a multivariate regression analysis in order to compensate for some of these differences, clinical data including NYHA class, previous hospitalizations and other variables pertaining to the clinical stability of the patients were missing from this analysis. Therefore, the included variables probably would not compensate for the inherent differences between the groups or for the selection bias. It is also possible that some of the patients included in the HF cohort had an erroneous diagnosis of HF.

Analysis of the patients' clinical data suggests that the HF center patients were generally more seriously ill and had an expected worse prognosis. Background diseases were more prevalent in the HF center patients, although the differences were relatively minor. A higher percentage of patients in the HF center were on heart failure medications. Notably, more patients were on loop-diuretics and spironolactone on entry to the HF center program, signifying that these patients had a more advanced disease. These patients had an increased serum urea, a strong predictor of reduced survival in patients with HF [14]. Serum urea encompasses and represents several key biological parameters pertaining to the overall status of the chronic patient with HF, such as renal function, fluid volume balance, hemodynamics and the neurohormonal axis. In addition, serum sodium was significantly reduced in these patients. Low serum sodium is a significant predictor of reduced survival [15] and is a sign of increased neurohormonal activation [16], which is associated with more advanced illness and reduced survival. Despite the expected worse prognosis in the HF center patients, the survival rate in both groups was comparable, suggesting a possible survival benefit in patients followed in the HF center.

Hospitalization is a major problem in patients with HF and a significant economic burden on HMOs. Hospitalization due to heart failure has tripled over the last few decades [17] and is expected to increase as the population ages. The rehospitalization rate after hospitalization is also extremely high, with a 1 year readmission rate of up to 50% of patients [18]. The economic implications of the increased hospitalization rates are enormous. HF management programs are specifically targeted to reduce the hospitalization rate of chronic HF patients and thus improve prognosis and reduce costs. Several recent meta-analyses [5,6,8] have shown that HF management programs reduced HF-related admission rates by 25–30% and all-cause admission rates by 12–20%, with even larger benefits reported by non-randomized studies. In the present study we did not analyze HF-related admission rates specifically as these were not readily available. We did, however, observe that cardiovascular-related hospitalization rates were reduced by 35% in the HF center compared to the total HF patient group. This is in line with the above

published data. Although the present study was a non-randomized observational study, the data suggest that the HF management program in Jerusalem achieves a similar benefit in reducing hospitalization rates in patients with HF as in previous published studies.

In the present study, the nurse-supervised interventional management program succeeded in improving measures of compliance, and in particular, increased compliance to a low salt diet. In addition, increased compliance to the recommended diet and drug therapy improved. Improved compliance and self-care behavior were shown previously in similar management programs [19–21] and are key to the success of nurse-supervised programs. This benefit is paramount, as non-compliance to a low salt diet is the most frequent preventable cause for hospital admission due to decompensated HF, which occurs in up to 40% of patients [22]. Patients followed in the HF center also had improved functional capacity. This has been reported in comparable nurse-supervised management programs [20,23–25] and could be related to increased compliance to the prescribed diet and pharmacological treatment, as seen in this study. Functional capacity not only reflects an amelioration of symptoms and improvement in quality of life, it has a significant prognostic impact and is associated with clinical outcome. All these improved measures demonstrate the importance and the central role of nurse supervision in the interventional management program of self-care behavior [19].

LIMITATIONS OF THIS STUDY

The present study was an observational study and the control group was not matched to the group treated in the HF center. In addition, data regarding the control group were taken from a computerized database with the inherent limitations of such data. In addition, echocardiography data were available in only a minority of patients, limiting complete characterization of these patients. Data on device-based treatments were also missing from the present analysis and may play a role in the improved clinical outcome of the HF center patients. These facts should be taken into account when interpreting the data. Nevertheless, the findings in the present study are in concordance with numerous studies reported in the literature and support the concept that nurse-led management programs from a wide range of settings and locations – whether Europe, the United States or Israel – have a clinical benefit in patients with HF.

CONCLUSIONS

Supervision by dedicated specialized nurses in a HF center in Jerusalem increased compliance, improved functional capacity in patients with HF, and reduced hospitalization rates. HF centers should be considered part of the standard treatment of patients with symptomatic HF.

HMO = health management organization

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