Original Article

# Effects of Coping Skills Training on Quality of Life, Disease Biomarkers, and Clinical Outcomes in Patients With Heart Failure

## A Randomized Clinical Trial

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***Background***—Heart failure (HF) is a chronic disease that compromises patients' quality of life (QoL). Interventions designed to reduce distress and improve disease self-management are needed. We evaluated the efficacy of a telephone-based coping skills training (CST) intervention.

***Methods and Results***—This randomized clinical trial involved 180 HF outpatients with reduced ejection fraction. Participants ranged in age from 29 to 87 years (mean=58 years); 27% were women, and 47% were nonwhite. Participants were randomized to either a CST intervention or heart failure education, both delivered over 16 weeks. The primary outcomes were (1) postintervention effects on QoL and HF disease biomarkers (both with $\alpha$=0.01), and (2) a composite measure of time to death or first hospitalization (with $\alpha$=0.03) over a median follow-up period of 3 years. CST resulted in greater improvements in QoL compared with heart failure education ($P$<0.01), including the Kansas City Cardiomyopathy Questionnaire ($P$=0.009), depressive symptoms ($P$=0.027), and the 6-minute walk test ($P$=0.012). However, it did not differentially improve HF disease biomarkers or reduce risk of all-cause hospitalizations or death (hazard ratio=0.84 [95% confidence interval, 0.59–1.12]). Interestingly, exploratory analyses showed that participants randomized to CST experienced a reduction in the composite end point of worsening HF hospitalization or death during the 3-year follow-up period (hazard ratio=0.65 [95% confidence interval, 0.44–0.98]; $P$=0.040).

***Conclusions***—CST improved QoL in patients with HF. Monitoring and improving QoL is emerging as an important aspect of the clinical management of HF that can reduce disease burden and may help improve clinical outcomes in this vulnerable patient population.

***Clinical Trial Registration***—URL: https://www.clinicaltrials.gov. Unique identifier: NCT00873418.

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**Key Words:** adult ■ chronic disease ■ depression ■ hospitalization ■ quality of life



An estimated 5.7 million American adults are living with heart failure (HF), and another 870 000 new cases are diagnosed each year.[1] HF is the most costly diagnosis in the Medicare population and is the most common cause for hospitalization in patients over the age of 65 years. Although medical management helps control symptoms and stabilizes patients, HF is nonetheless an inherently unstable condition, with frequent hospitalizations being one manifestation of this instability. The associated annual direct and indirect costs for HF patient care in the United States are estimated to be in excess of $39 billion.[1,2]

### See Clinical Perspective

HF is a chronic condition with broad-ranging impact, affecting almost every important aspect of patients' lives. Consequently, psychological distress is prevalent in patients with HF and quality of life (QoL) is often markedly impaired. Major depressive disorder is a common manifestation of the difficulties in coping with distress experienced by patients with HF.[3] Impaired QoL and elevated depressive symptoms are associated with an adverse HF disease trajectory and poor clinical outcomes.[4,5]

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Traditional behavioral interventions designed to help HF patients remain in stable health and avoid preventable hospital admissions have focused on patient education, diet and medication adherence, and physical activity.[6] Overall, the evidence supporting these disease management strategies has been mixed, but some have resulted in prolonged event-free survival, decreased the number of hospital admissions, and improved QoL.[7,8] Although the most effective interventions have involved regular home visits by a nurse, telephone-based interventions also have been found to be effective and because they are more convenient for patients and relatively inexpensive compared with face-to-face encounters, there is a need to further develop and refine these approaches.[9]

Coping effectively with chronic disease can require significant behavioral change. Coping skills training (CST) is a cognitive-behavioral approach to disease self-management that transforms maladaptive coping styles into more constructive behaviors, facilitates compliance with medical treatment recommendations, and improves psychological well-being.[10] CST has been shown to both enhance self-management and improve patient health and QoL in many chronic diseases, including diabetes mellitus and pulmonary disease.[10,11] However, the CST approach to disease management has not been studied widely in patients with HF.[12] Because HF is a chronic disease that requires rigorous medical self-management, health behavior change, and psychological adjustment, a CST intervention focused on both disease self-management and alleviating psychological distress has the potential to be of significant value for HF patients.

The objective of this trial was to evaluate the efficacy of a CST intervention, delivered over the telephone to HF patients, on 3 outcomes: postintervention QoL, HF disease biomarkers, and longer term clinical outcomes defined by hospitalization or death. To achieve equipoise, a HF education (HFE) intervention was selected as the control condition.

# Methods

## Trial Overview

COPE-HF (Coping Effectively With Heart Failure) was a single-site randomized clinical trial in which 180 men and women with HF were randomized to either CST or HFE. Participants were enrolled between September 2009 and January 2014. Details of the study design, assessments, and interventions were published previously.[13]

## Participants

The study sample consisted of 180 men and women with documented HF. Patients were recruited from the HF Programs at Duke University Medical Center, the UNC Health Care system, and the Durham VA Medical Center. The protocol was approved by the respective institutional review boards at these centers, and written informed consent was provided by each participant. Inclusion criteria were: men or women aged ≥18 years; New York Heart Association class II–III HF of at least 3-month duration; and left ventricular ejection fraction (LVEF) ≤40% documented within 6 months of study enrollment. Exclusion criteria were: myocardial infarction or coronary artery revascularization within 3 months of enrollment; HF caused by a correctable cause or condition, such as uncorrected primary valvular disease; alcohol or drug abuse within 12 months; illnesses such as malignancies that are associated with a life expectancy of <12 months; current pregnancy; and inability to provide informed consent.

## Stratification and Randomization

Participants were randomized in a 1:1 ratio to either CST or HFE. A conditional randomization procedure (PROC PLAN in SAS 9.2) was used to stratify participants according to cause of HF (ischemic versus nonischemic) and age (<60 years versus ≥60 years). To maintain allocation concealment, group assignments were placed in sealed envelopes and opened sequentially at the time of randomization.

## Outcome Measures

The primary outcomes were as follows: (1) postintervention effects on QoL and HF disease biomarkers and (2) a composite measure of time to either all-cause death or hospitalization. The primary measure of HF disease biomarkers was a global score of B-type natriuretic peptide,[14] LVEF,[15] 24-hour heart rate variability indexed by the SD of normal R-R intervals,[16] flow-mediated dilation of the brachial artery,[17] and plasma C-reactive protein.[18] The primary QoL index was a global score of the Kansas City Cardiomyopathy Questionnaire (KCCQ),[19] Beck Depression Inventory II (BDI-II),[20] Speilberger State-Trait Anxiety Inventory,[21] HF Attitudes About Impairment questionnaire,[22] and the 6-minute walk test. Hospitalizations were categorized as all-cause‘, cardiovascular, and HF (worsening HF) based on medical records. Death was verified from hospital and EMS records.

Secondary outcomes were the components of the HF disease and QoL global score measures. Health behaviors important for HF self-management were assessed before randomization and immediately on completion of the intervention. Routine daily physical activity was assessed using an accelerometer (Actiwatch-64, Mini Mitter Co, Inc, Bend, OR) worn on the wrist of the nondominant arm for 24 hours. Medication adherence was assessed using the Medication Event Monitoring System bottle cap in-home for 10 days. Dietary sodium intake was estimated from a 24-hour standardized dietary recall with a nutritionist and by 24-hour urinary sodium excretion. In addition, we administered an established questionnaire that was designed to assess self-care in HF patients, defined by a combination of maintenance, symptom perception, and management behaviors.[23] Post-treatment assessments were performed within 2 weeks after completing the intervention. All outcome assessments were performed by research team members blinded to group assignment.

## Interventions

### *Coping Skills Training*

CST was delivered by a clinical psychologist (B.M.H.) and comprised 16 weekly 30-minute individual phone calls. Cognitive behavioral techniques were patterned after previous studies involving pulmonary[11,24] and cardiac[25] patients. Motivational interviewing was used to enhance adherence to prescribed health behaviors. All CST participants received the same set of topics. For the initial 4 sessions involving health behaviors (diet and salt restriction, daily weighing, physical activity, and medication adherence), participants could prioritize the order in which each health behavior was covered. The remaining 12 sessions were presented in the same sequence and including specific coping techniques (relaxation training, cognitive restructuring, visualization, problem solving, and activity pacing). Two optional modules addressing depression and assertiveness training were incorporated into the intervention at the discretion of the interventionist based on patient needs.

### *Heart Failure Education*

The HFE intervention was delivered by a Physician’s Assistant and also involved 16 weekly individual phone calls of ≤30-minute duration, providing a control for weekly patient contact, but focused on the provision and discussion of medical issues important for HF self-management without teaching behavioral skills to improve coping. The interventionist (J.S.) provided information about HF health behaviors, including symptom monitoring, importance of daily weighing, adherence to medications, physical activity, and optimal diet.

All study participants continued with their regular medical care, including their routine cardiology visits and management of any episodes of escalating symptoms or disease progression.

## Statistical Analysis

All analyses were performed with SAS 9.3 (Cary, NC), and the evaluation of all intervention effects were based on the principle of intention-to-treat, with missing post-treatment data managed using multiple imputations within PROC MI, using 100 imputations. The effects of treatment on the QoL and HF disease severity variables were assessed using 2 separate general linear models in which a rank-based global score of all QoL and HF disease markers served as the respective outcome variable, as suggested by O'Brien[26] for the examination of multiple end points.[27] This general analytic approach has previously been used in multiple cardiac trials and is recommended for examining multiple, related outcome variables within a domain of interest simultaneously.[28] Consistent with this gatekeeper methodology, if a global score analysis showed evidence of a treatment group difference, we conducted subsequent analyses examining the individual outcomes in a secondary, explanatory step.

Evaluation of treatment effects on clinical outcomes used separate Cox proportional hazards models. These analyses addressed all-cause first hospitalization or death as primary and cardiovascular hospitalization or death as supportive. Additional supportive analyses addressed worsening HF hospitalization or death, and death. For these analyses, the time of event was the index date, and participants with no dates were censored at the time of last contact with study staff or documentation in their medical record. All proportional hazards models controlled for age, HF cause, baseline B-type natriuretic peptide, LVEF, and number of hospitalizations within the past year. We also examined the impact of treatment on HF hospitalization and death using the Wei–Lin–Weissfeld method, which allows deaths after HF hospitalization to be taken into account.[29] This approach has been advocated for use among patients with chronic diseases because of the multiple natures of most hard clinical events in these populations, which are often clustered within individuals.[30]

An additional set of proportional hazards analyses were conducted in which changes in QoL served as the predictor of interest. Within this model, time to first HF hospitalization or death, and time to death, using the Wei–Lin–Weissfeld approach served as the outcome with change in QoL (post-treatment residualized for pretreatment) as the predictor of interest and baseline QoL, B-type natriuretic peptide, LVEF, age, cause of HF, and number of hospitalizations within the past year as control variables. Only events occurring after post-treatment assessments were considered in these models. These exploratory analyses also examined individual QoL indices.

## Power Calculation

With respect to the global HF severity and QoL scores, we estimated power assuming an attrition rate of ≈20% and multiple imputations for missing data. We identified a standardized effect size of about a half SD as clinically meaningful for the HF biomarker and QoL global scores.[31] For testing a given global index at 0.01, so as to account for multiple comparisons, ≈100 patients in each treatment arm provides ≈0.90 power to detect a standardized effect size of 0.60.

Power for the Cox regression model was estimated assuming an event rate of 70% in the control group, 42 months for patient accrual, a median follow-up time of 3 years and a minimum follow-up time of 15 months. With ≈100 patients in each group, we estimated power of ≈0.90 to detect a hazard ratio of 0.50 by a 2-sided test at 0.05. For testing at 0.03, to account for multiple comparisons, the power is 0.90 to detect a hazard ratio of 0.47.

# Results

## Participant Flow

Figure 1 displays the flow of participants during the trial. Of 584 men and women referred for potential participation, 199 were consented, 190 completed pretreatment assessments, and 180 were randomized. One participant randomized to CST died before receiving any treatment and was excluded in the analysis. The intent-to-treat analyses were, therefore, based on a study sample of 179 participants.

## Participant Characteristics

Demographic, clinical, and baseline characteristics are presented in Table 1. Although treatment groups were comparable on most background characteristics, the HFE group tended to have a higher percentage of participants with implantable cardiac defibrillators at baseline and lower LVEF.

## Treatment Adherence

Treatment adherence during the study intervention was excellent, with 95% of participants completing postintervention assessments. Average duration of the weekly telephone intervention calls were 10 minutes for HFE and 26 minutes for CST. Among individuals in the CST group, participants were present for an average of 14.5 (SD=3.5) sessions and 80% of these participants attended ≥14 sessions. Among individuals in the HFE group, participants were present for an average of 15.7 (SD=1.6) sessions, and 90% of individuals participated in all 16 sessions. Post-treatment data were available on all but 9 patients (8 in the CST group and 1 in the HFE group).

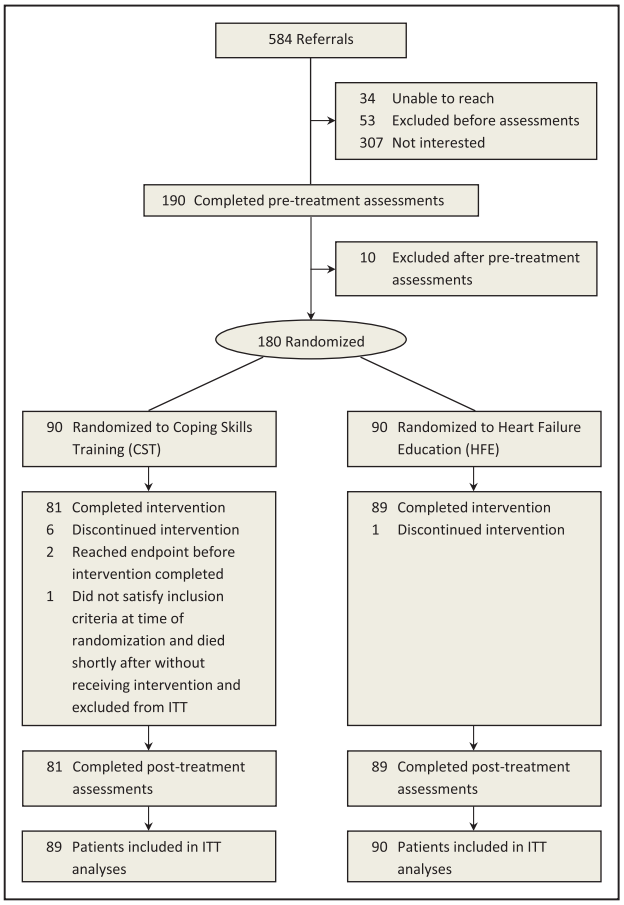


**Figure 1.** CONSORT chart (Consolidated Standards of Reporting Trials) of trial enrollment. ITT indicates intention to treat.

**Table 1. Background Characteristics of Study Sample**

| Variable | CST (n=89) | HFE (n=90) | Cohort (n=179) | *P* Value |
|---|---|---|---|---|
| Age, y | 57.6 (11.1) | 57.9 (11.9) | 57.7 (11.5) | 0.90 |
| Female sex, n (%) | 27 (30) | 21 (23.3) | 48 (26.7) | 0.29 |
| White, n (%) | 50 (55.6) | 46 (51.1) | 96 (53.3) | 0.50 |
| Ischemic cause, n (%) | 35 (38.9) | 37 (41.1) | 72 (40) | 0.81 |
| Laboratory results | | | | |
| Serum creatinine, mg/dL | 1.18 (0.37) | 1.23 (0.42) | 1.2 (0.40) | 0.44 |
| Hemoglobin, g/dL | 13.5 (1.7) | 13.4 (1.5) | 13.4 (1.6) | 0.66 |
| Urinary sodium, mg/24 hour | 3550 (1734) | 3882 (2055) | 3717 (1903) | 0.25 |
| Dietary sodium, mg/d | 2993 (1461) | 2806 (1653) | 2899 (1559) | 0.43 |
| Medications | | | | |
| ACEI, n (%) | 64 (72) | 69 (77) | 134 (74) | 0.47 |
| ARB, n (%) | 21 (23) | 16 (18) | 37 (21) | 0.34 |
| Aldosterone antagonists, n (%) | 47 (52) | 47 (52) | 94 (52) | 0.99 |
| Anticoagulants, n (%) | 26 (29) | 27 (30) | 54 (30) | 0.91 |
| Aspirin, n (%) | 58 (64) | 60 (67) | 118 (65) | 0.83 |
| β-Blocker, n (%) | 87 (98) | 85 (94.4) | 173 (96) | 0.25 |
| Antidepressant, n (%) | 21 (23) | 33 (37) | 54 (30) | 0.06 |
| Cholesterol drug, n (%) | 62 (69) | 64 (71) | 126 (70) | 0.83 |
| Diuretic, n (%) | 78 (88) | 84 (93) | 163 (91) | 0.19 |
| Nitrate, n (%) | 21 (23) | 25 (28) | 46 (25) | 0.52 |
| Medical history | | | | |
| Hypertension, n (%) | 65 (73) | 67 (74) | 132 (74) | 0.83 |
| Diabetes mellitus, n (%) | 41 (46) | 49 (54) | 90 (50) | 0.26 |
| Hyperlipidemia Dx, n (%) | 57 (64) | 64 (71) | 122 (68) | 0.31 |
| BiV pacemaker, n (%) | 32 (37) | 44 (49) | 77 (43) | 0.08 |
| ICD, n (%) | 63 (71%) | 75 (83%) | 139 (77%) | 0.05 |
| Quality of life | | | | |
| BDI score | 14.2±9.5 | 13.5±10.4 | 13.9±9.9 | 0.64 |
| AAI score | 47.3 (10.0) | 48.0 (10.7) | 47.6 (10.3) | 0.66 |
| STAI score | 28.1 (7.4) | 31.3 (9.9) | 29.7 (8.9) | 0.03 |
| KCCQ score | 58.1 (21.5) | 55.6 (21.9) | 56.8 (21.6) | 0.43 |
| 6-min walk distance, m | 376 (98) | 353 (114) | 365 (107) | 0.16 |
| Heart failure disease biomarkers | | | | |
| BNP, pg/mL | 284.4 (485) | 241.5 (318) | 262.8 (409) | 0.49 |
| LVEF, % | 31.7 (10.3) | 28.4 (8.7) | 30.0 (9.6) | 0.02 |
| HRV, SDNN | 88.8 (28.1) | 81.8 (29.2) | 85.7 (28.7) | 0.19 |
| Flow-mediated dilation, % | 4.1 (4.1) | 3.9 (4.2) | 4.0 (4.2) | 0.78 |
| CRP, mg/L | 3.7 (3.4) | 4.0 (3.4) | 3.8 (3.4) | 0.57 |

Values are presented as mean (SD) unless otherwise indicated. Hypertension, diabetes mellitus, or hyperlipidemia were defined as present if a diagnosis appeared in participants' medical records during the year preceding prerandomization baseline assessments. AAI indicates Attitudes About Impairment; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BDI, Beck Depression Inventory; BiV, biventricular; BNP, B-type natriuretic peptide; CRP, C-reactive protein; HRV, heart rate variability; ICD, implantable cardioverter defibrillator; KCCQ, Kansas City Cardiomyopathy Questionnaire; LVEF, left ventricular ejection fraction; SDNN, SD of normal to normal heart beat intervals; and STAI, State Anxiety.

Among the 9 patients with missing post-treatment assessments, 7 discontinued their randomly assigned intervention before its completion (6 in the CST group and 1 in the HFE group). Among the other 2 patients in the CST group with missing post-treatment assessments, 1 died before completion of the CST intervention and 1 completed the CST intervention but did not participate in the post-treatment assessment. In relation to the 3-year follow-up of clinical outcomes, there was 0% attrition.

## Primary Outcomes

### *Quality of Life*

Examination of postintervention changes in QoL demonstrated that the CST group exhibited significantly greater improvements in the QoL global score compared with HFE ($P<0.01$; Table 2). Further evaluation of the QoL global score components showed that the CST group exhibited greater improvements in the KCCQ and 6-minute walk test distance, and a greater reduction in depressive symptoms measured by the BDI-II compared with HFE. The remaining QoL components (Attitudes About Impairment and State-Trait Anxiety Inventory) showed trends toward greater improvements in the CST group. Follow-up analyses of changes in depressive symptoms also revealed a baseline depression by treatment group interaction ($P=0.001$), such that individuals exhibiting clinically elevated symptoms at baseline (BDI ≥14; n=77 [37 in HFE, 40 in CST]) showed reductions in depressive symptoms that were greater among individuals in CST (8.3 [1.4–5.6]) relative to HFE (3.8 [5.8–10.8]; $P=0.023$).

### *HF Biomarkers*

Although HF biomarkers showed improvement over time (data not shown), post-treatment comparisons for HF disease biomarkers revealed no significant differences between CST and HFE ($P=0.114$; Table 2).

### *Follow-Up Clinical Events*

Over a median 3-year follow-up (range: 0.2–5.7 years), 127 participants experienced at least one criterion clinical event (all-cause hospitalization or death), 106 experienced at least one cardiac event (myocardial infarction, stroke, cardiac revascularization, or death), and 80 experienced at least one HF hospitalization (n=65) or died (n=15). In this latter set of analyses, 24 participants whose first event was a HF hospitalization subsequently died. As shown in Table 3, compared with HFE, the CST intervention exhibited trends toward reduced risk of first all-cause hospitalization or death (hazard ratio [HR]=0.84 [95% confidence interval {CI}=0.59–1.12]; $P>0.03$) and first cardiovascular hospitalization or death (HR=0.78 [95% CI=0.53–1.16]; $P>0.03$). CST participants were more clearly less likely to experience a worsening HF hospitalization or die during follow-up (HR=0.63 [95% CI=0.40–1.01]; $P=0.055$); this effect seemed to be driven by the CST group tending to have a lower mortality rate (HR=0.53 [95% CI=0.27–1.06]; $P=0.072$). Follow-up analyses, integrating both of the latter models using the Wei–Lin–Weissfeld method, demonstrated that the CST group was less likely to experience a worsening HF hospitalization or die during follow-up (HR=0.65 [0.44–0.98]; $P=0.040$), with 3-year worsening HF hospitalization or death rates of 37% for the CST group and 50% for the HFE group (Table 3; Figure 2). Mortality rates in the CST group were ≈50% less than that observed in HFE, with a 3-year mortality rate of only 8% in the CST group compared with 15% in the HFE group.

## Secondary Outcomes

### *Health Behaviors and HF Self-Management*

All participants showed postintervention improvements in HF self-management scores: HF management (mean increase 8.6 [6.7–10.5]; $P=0.024$), HF maintenance (mean increase 7.6

**Table 2. Changes (Mean Change With Confidence Intervals) in Measures of QoL and Heart Failure Disease Biomarkers**

| Variable | Coping Skills Training (n=89) | Heart Failure Education (n=90) | *P* Value |
|---|---|---|---|
| QoL | | | |
| Attitudes about impairment | 3.7 (2.2 to 5.3) | 1.8 (0.3to 3.2) | 0.070 |
| Beck Depression Inventory | −4.5 (−5.8 to −3.1) | −2.4 (−3.7 to −1.1) | 0.027 |
| KCCQ total score | 8.3 (5.0 to 11.5) | 2.3 (−0.8 to 5.4) | 0.009 |
| 6-min walk distance, m | 15.8 (4.8 to 26.7) | −3.5 (−13.9 to 7.0) | 0.012 |
| State Anxiety | −2.6 (−4.4 to −0.8) | −0.2 (−1.9 to 1.6) | 0.057 |
| Heart failure disease biomarkers | | | |
| B-type natriuretic peptide, pg/mL | −23.5 (−63.6 to 16.2) | −25.0 (−62.9 to 12.8) | 0.958 |
| Left ventricular ejection fraction, % | 0.2 (−0.9 to 1.4) | −1.3 (−2.4 to −0.2) | 0.066 |
| Heart rate variability (SDNN) | 2.0 (−4.7 to 8.7) | −3.7 (−11.0 to 3.5) | 0.246 |
| Flow-mediated dilation, % | 0.2 (−0.5 to 0.9) | 0.0 (−0.7 to 0.7) | 0.733 |
| C-reactive protein, mg/L | −0.3 (−0.9 to 0.2) | 0.3 (−0.2 to 0.9) | 0.102 |

Values are adjusted for age, cause of heart failure (ischemic vs nonischemic), and the pretreatment level of the respective predictor. FMD analyses were also adjusted for baseline arterial diameter. FMD indicates flow-mediateddilation; KCCQ, Kansas City Cardiomyopathy Questionnaire; QoL, quality of life; and SDNN, SD of normal to normal heartbeat intervals.

**Table 3. Treatment Effects on All-Cause Hospitalization or Death and Wei–Lin–Weissfeld Integrated Model of Heart Failure Hospitalizations or Death**

| Variables | All-Cause Hospitalization or Death (127 Events) | | HF Hospitalization or Death (80 Events) | |
|---|---|---|---|---|
| Model | Hazard Ratio (95% CI) | *P* Value | Hazard Ratio (95% CI) | *P* Value |
| Age (>60 vs <60 y) | 1.07 (0.75–1.54) | 0.714 | 1.01 (0.67–1.53) | 0.949 |
| Cause (ischemic vs nonischemic) | 1.00 (0.69–1.43) | 0.986 | 0.77 (0.48–1.17) | 0.203 |
| BNP at baseline (1000 pg/mL) | 2.32 (1.58–3.40) | <0.001 | 3.48 (2.31–5.12) | <0.001 |
| Ejection fraction at baseline (10%) | 1.00 (0.83–1.21) | 0.992 | 0.92 (0.75–1.13) | 0.437 |
| Hospitalizations in past year (ref=0): 1–2≥3 | 0.82 (0.55–1.22)<br>1.77 (1.01–3.07) | 0.337<br>0.045 | 0.84 (0.52–1.34)<br>1.77 (1.06–2.97) | 0.462<br>0.031 |
| Coping skills training | 0.84 (0.59–1.21) | 0.352 | 0.65 (0.44–0.98) | 0.040 |

Analyses of heart failure and death included 80 first events and 24 subsequent events (ie, 24 individuals whose first event was a heart failure hospitalization subsequently died). BNP indicates B-type natriuretic peptide; and HF, heart failure.



[6.3–8.8]; *P*=0.036), and HF self-care (mean increase=10.4 [9.0–11.7]; *P*<0.001), and reduced urinary sodium excretion (mean reduction 339 [126–552]; *P*=0.028) and increased physical activity levels (mean increase in arbitrary actigraphy units 18 252 [5814–30 690]; *P*=0.005). However, there were no significant intervention group differences in these improvements, nor were there treatment group differences in medication adherence.

### *Association Between QOL Improvements and Clinical Outcomes*

Postintervention improvements on our global score measure of QoL were associated with a reduced likelihood of HF hospitalization or death (*P*=0.001). Examination of individual QoL components revealed that greater improvements in the KCCQ (*P*=0.007), 6MWD (*P*=0.012), AII (*P*=0.045), and State-Trait Anxiety Inventory (*P*=0.05) were most strongly associated with reduced clinical events, whereas the BDI-II (*P*=0.088) showed a somewhat weaker association.

## Discussion

The COPE-HF randomized clinical trial demonstrated that a coping skills training (CST) intervention resulted in marked and broad-ranging improvements in QoL for patients with HF. Among the most notable improvements were health-related QoL, assessed by the KCCQ, which increased by an average of >8 points in patients randomized to CST, reflecting a significant improvement in patients' clinical status.[32] Functional capacity assessed by the 6-minute walk test also increased by >15 meters in the CST group, which is indicative of the favorable clinical changes produced by the CST intervention.[32] By comparison, the HF-ACTION trial reported that 3 months of aerobic exercise training also resulted in a similar 15 m increase in the 6-minute walk test but a more modest increase in the KCCQ of <2 points, compared with usual care.[33,34] Depressive symptoms, assessed by the BDI-II were reduced by >4 points in participants randomized to CST, and other measures of psychological well-being also showed favorable trends toward improvement compared with the HFE control group. Importantly, postintervention QoL was associated with improved event-free survival. These findings underscore the perspective that QoL in HF patients should be considered an important treatment target.

Although participants in the CST intervention showed no greater improvement in HF disease biomarkers compared with patients randomized to the education control condition, there was some indication that it lowered the risk of death or hospitalization for worsening HF over an average follow-up period of 3 years. The CST intervention was not associated with reduced all-cause hospitalizations or mortality, but participants in the CST group did show a notable 35% reduction in risk of HF hospitalization or death compared with HFE participants. Importantly, the improved survival benefits found for the CST intervention are compared with a HF education control intervention that itself is also likely to have had a favorable impact on event-free survival, as patient education and the nonspecific effects of attention and support have been shown to be beneficial.[6] Moreover, the CST intervention involved weekly phone calls for 16 weeks, but its benefits persisted years after its completion, suggesting that the skills and techniques mastered during the intervention were retained over the course of the follow-up period.

Because health behaviors that are relevant to HF self-management are important to HF outcomes, we examined

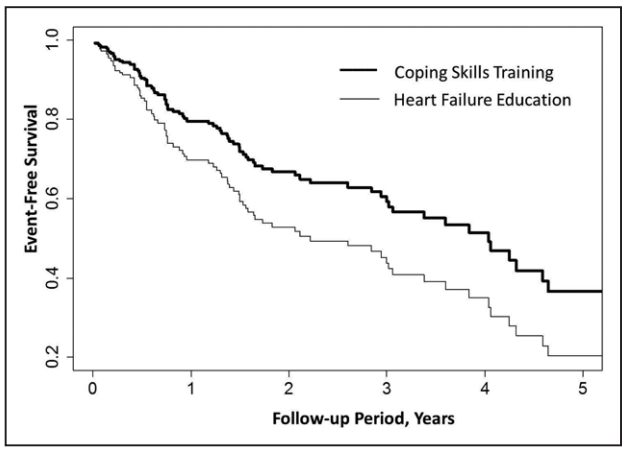


**Figure 2.** Adjusted Cox proportional hazards model comparing coping skills training (CST) and heart failure education (HFE) from randomization to 3-year follow-up. CST participants exhibited a lower rate of heart failure hospitalizations and death (hazard ratio=0.65 [95% confidence interval=0.44–0.98]; *P*=0.040) after adjustment for age, ejection fraction, B-type natriuretic peptide, and hospitalizations in the year preceding randomization.

the impact of treatment on important HF health behaviors. Our measures of dietary sodium intake indicated that a postintervention reduction was evident in both CST and HFE groups. Medication adherence was generally high in all participants and did not improve further as a result of the interventions, whereas self-reported HF self-management behaviors improved in both intervention groups. Therefore, although both treatment groups demonstrated improvements in health behaviors, such improvements do not account for the greater benefits of CST on QoL and reduced likelihood of hospitalization or death because of worsening HF.

Consistent with previous reports,[35] >40% of HF patients in our study sample had clinically significant depressive symptoms (BDI-II≥14). Of this subsample, those randomized to the CST intervention exhibited a marked and clinically significant 8-point average reduction in BDI-II score. These findings are consistent with those of a recent report showing cognitive behavior therapy to be an effective treatment for depression in HF patients with major depressive disorder.[12] Unfortunately, evidence about the efficacy of antidepressants for treating depressive symptoms and improving outcomes in HF patients has been disappointing.[36] We and others have previously shown that elevated depressive symptoms, and depressive symptoms that worsen over time regardless of initial severity, are associated with adverse clinical outcomes in HF, independent of HF disease severity and comorbidity.[5]

For patients with chronic diseases, patient-centered outcomes and QoL are gaining widespread recognition as being important treatment targets for optimal patient management. QoL is a complex construct consisting of multiple health-related and disease-specific domains for which there are no universally accepted measures.[37–39] Nonetheless, QoL measures have been shown to predict long-term clinical outcomes and survival in cancer patients[40] and in kidney transplant recipients.[41] Several studies of HF patients also have linked QoL, measured by HF disease-specific health-related QoL self-report scales, to survival, but only one recently conducted secondary analysis of data from the COACH study (Coordinating Study Evaluating Outcomes of Advising and Counseling in Heart Failure) demonstrated that this relationship remained robust after controlling for HF disease severity using HF biomarkers in hospitalized HF patients.[4] Our study confirms and extends this finding by further demonstrating that QoL is an important and independent aspect of HF that is related to long-term clinical outcomes in HF outpatients who were on a stable medical regimen. Moreover, our results showed that an intervention designed to reduce psychological distress in HF patients can improve QoL and also help lower the risk of death or hospitalization because of worsening HF.

The present study was relatively small, and the follow-up was for an average of only 3 years, limiting the power to detect differences in mortality and hospitalizations between treatment groups. Although our patients came from diverse clinical HF programs, they were recruited from only 3 sites, which may limit the generalizability of our findings. A further limitation is that participants in the CST condition had a similar number of phone calls, but sessions were longer compared with HFE. Although the duration of telephone intervention calls was unrelated to any outcome measure within each intervention group, the longer call duration for the CST condition cannot be ruled out as a potential confounding factor. It is of further note that a HF telemonitoring system that had previously demonstrated success in smaller scale trials, failed to scale successfully to a large-scale multisite randomized controlled trial.[42] Therefore, the present findings should be interpreted with caution; a larger scale trial spanning diverse clinical settings may be needed to establish the benefits and cost effectiveness of coping skills training for HF patients. Nonetheless, the COPE-HF trial findings are encouraging and are supported by the inclusion of a HFE control group that not only controlled for patient contact and attention but also provided equipoise in terms of anticipated outcome benefits to participants. It is also noteworthy that although the CST intervention was completed in 16 weekly phone calls, its benefits seemed to persist for years after its completion.

In summary, in a clinical efficacy trial, we found that a CST intervention delivered remotely by telephone showed promising results for improving overall QoL and reducing the risk of worsening HF hospitalizations and mortality in patients with HF. The present findings suggest that CST interventions also may be a feasible approach to reduce the burden on the healthcare system associated with managing this chronic disease. Our observations also underscore the importance of addressing the distress associated with living with HF and providing patients with approaches and strategies to improve their ability to cope with their disease and reduce their distress. Remote interventions of this kind may increasingly play an important role for patients with chronic debilitating diseases who may not have access to mental health facilities and may not be receptive to traditional mental health treatments.

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## Disclosures

None.

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## CLINICAL PERSPECTIVE

Heart failure is a chronic, debilitating condition that requires comprehensive medical management by physicians, including pharmacological and device therapies designed to limit and help reverse its severity. Unhealthy behaviors are often important causal factors in the development and progression of heart failure, and adoption of healthy lifestyle practices is, therefore, an important aspect of successful heart failure management. Findings from the present study confirm and extend growing evidence that implementing strategies designed to enhance patient self-management and improve coping may have beneficial effects on patient-centered outcomes. A novel finding from the study is that coping skills training delivered remotely by telephone improved quality of life more than health behavior education alone. These findings underscore the importance of addressing psychological distress associated with heart failure and providing patients with strategies to improve their ability to cope with their disease. Improving quality of life for heart failure patients also may help reduce the risk of hospitalizations or death because of worsening heart failure. Remote interventions of this kind could play an increasingly important role among heart failure patients and may help reduce the systemic healthcare burden associated with managing this complex, chronic disease.

# Effects of Coping Skills Training on Quality of Life, Disease Biomarkers, and Clinical Outcomes in Patients With Heart Failure: A Randomized Clinical Trial

Andrew Sherwood, James A. Blumenthal, Gary G. Koch, Benson M. Hoffman, Lana L. Watkins, Patrick J. Smith, Christopher M. O'Connor, Kirkwood F. Adams, Jr, Joseph G. Rogers, Carla Sueta, Patricia P. Chang, Kristy S. Johnson, Jeanne Schwartz and Alan L. Hinderliter

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# CONSORT 2010 checklist of information to include when reporting a randomised trial*

| Section/Topic | Item No | Checklist item | Reported on page No |
|---|---|---|---|
| **Title and abstract** | | | |
| | 1a | Identification as a randomised trial in the title | 1 |
| | 1b | Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts) | 2 |
| **Introduction** | | | |
| Background and objectives | 2a | Scientific background and explanation of rationale | 3-4 |
| | 2b | Specific objectives or hypotheses | 4 |
| **Methods** | | | |
| Trial design | 3a | Description of trial design (such as parallel, factorial) including allocation ratio | 4-6 |
| | 3b | Important changes to methods after trial commencement (such as eligibility criteria), with reasons | NA |
| Participants | 4a | Eligibility criteria for participants | 4-5 |
| | 4b | Settings and locations where the data were collected | 4 |
| Interventions | 5 | The interventions for each group with sufficient details to allow replication, including how and when they were actually administered | 6-7 |
| Outcomes | 6a | Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed | 6-7 |
| | 6b | Any changes to trial outcomes after the trial commenced, with reasons | NA |
| Sample size | 7a | How sample size was determined | 8-9 |
| | 7b | When applicable, explanation of any interim analyses and stopping guidelines | NA |
| Randomisation: | | | |
| Sequence generation | 8a | Method used to generate the random allocation sequence | 5 |
| | 8b | Type of randomisation; details of any restriction (such as blocking and block size) | 5 |
| Allocation concealment mechanism | 9 | Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned | 5 |
| Implementation | 10 | Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions | 5 |
| Blinding | 11a | If done, who was blinded after assignment to interventions (for example, participants, care providers, those | 6 |

| | | | |
|---|---|---|---|
| | | assessing outcomes) and how | |
| | 11b | If relevant, description of the similarity of interventions | 6-7 |
| Statistical methods | 12a | Statistical methods used to compare groups for primary and secondary outcomes | 7-8 |
| | 12b | Methods for additional analyses, such as subgroup analyses and adjusted analyses | 7-13 |
| **Results** | | | |
| Participant flow (a diagram is strongly recommended) | 13a | For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome | 9-10 |
| | 13b | For each group, losses and exclusions after randomisation, together with reasons | 9-10 |
| Recruitment | 14a | Dates defining the periods of recruitment and follow-up | 4-5 |
| | 14b | Why the trial ended or was stopped | NA |
| Baseline data | 15 | A table showing baseline demographic and clinical characteristics for each group | 23 |
| Numbers analysed | 16 | For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups | 9-10 |
| Outcomes and estimation | 17a | For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval) | 9-13 |
| | 17b | For binary outcomes, presentation of both absolute and relative effect sizes is recommended | |
| Ancillary analyses | 18 | Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory | 10-11 |
| Harms | 19 | All important harms or unintended effects in each group (for specific guidance see CONSORT for harms) | NA |
| **Discussion** | | | |
| Limitations | 20 | Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses | 14 |
| Generalisability | 21 | Generalisability (external validity, applicability) of the trial findings | 15 |
| Interpretation | 22 | Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence | 13-16 |
| **Other information** | | | |
| Registration | 23 | Registration number and name of trial registry | 1 |
| Protocol | 24 | Where the full trial protocol can be accessed, if available | 4 |
| Funding | 25 | Sources of funding and other support (such as supply of drugs), role of funders | 16 |

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.