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Effect of a Collaborative Care Intervention vs Usual Care on Health Status of Patients With Chronic Heart Failure
The CASA Randomized Clinical Trial

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Supplemental content

IMPORTANCE Many patients with chronic heart failure experience reduced health status despite receiving conventional therapy.

OBJECTIVE To determine whether a symptom and psychosocial collaborative care intervention improves heart failure–specific health status, depression, and symptom burden in patients with heart failure.

DESIGN, SETTING, AND PARTICIPANTS A single-blind, 2-arm, multisite randomized clinical trial was conducted at Veterans Affairs, academic, and safety-net health systems in Colorado among outpatients with symptomatic heart failure and reduced health status recruited between August 2012 and April 2015. Data from all participants were included regardless of level of participation, using an intent-to-treat approach.

INTERVENTIONS Patients were randomized 1:1 to receive the Collaborative Care to Alleviate Symptoms and Adjust to Illness (CASA) intervention or usual care. The CASA intervention included collaborative symptom care provided by a nurse and psychosocial care provided by a social worker, both of whom worked with the patients' primary care clinicians and were supervised by a study primary care clinician, cardiologist, and palliative care physician.

MAIN OUTCOMES AND MEASURES The primary outcome was patient-reported heart failure–specific health status, measured by difference in change scores on the Kansas City Cardiomyopathy Questionnaire (range, 0-100) at 6 months. Secondary outcomes included depression (measured by the 9-item Patient Health Questionnaire), anxiety (measured by the 7-item Generalized Anxiety Disorder Questionnaire), overall symptom distress (measured by the General Symptom Distress Scale), specific symptoms (pain, fatigue, and shortness of breath), number of hospitalizations, and mortality.

RESULTS Of 314 patients randomized (157 to intervention arm and 157 to control arm), there were 67 women and 247 men, mean (SD) age was 65.5 (11.4) years, and 178 (56.7%) had reduced ejection fraction. At 6 months, the mean Kansas City Cardiomyopathy Questionnaire score improved 5.5 points in the intervention arm and 2.9 points in the control arm (difference, 2.6; 95% CI, –1.3 to 6.6; P = .19). Among secondary outcomes, depressive symptoms and fatigue improved at 6 months with CASA (effect size of –0.29 [95% CI, –0.53 to –0.04] for depressive symptoms and –0.30 [95% CI, –0.55 to –0.06] for fatigue; P = .02 for both). There were no significant changes in overall symptom distress, pain, shortness of breath, or number of hospitalizations. Mortality at 12 months was similar in both arms (10 patients died receiving CASA, and 13 patients died receiving usual care; P = .52).

CONCLUSIONS AND RELEVANCE This multisite randomized clinical trial of the CASA intervention did not demonstrate improved heart failure–specific health status. Secondary outcomes of depression and fatigue, both difficult symptoms to treat in heart failure, improved.

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Many of the 5.8 million Americans with heart failure live with bothersome symptoms, reduced function, and poor quality of life, which together comprise health status. For example, common symptoms reported by patients with heart failure include breathlessness (44%-85%), fatigue (66%-85%), pain (38%-58%), and depression (19%-55%).[1-3] This morbidity occurs regardless of left ventricular ejection fraction and despite the use of guideline-directed therapies. Patient-reported health status is important because it reflects the patient's experience of illness and is associated with subsequent hospitalization and mortality.[4] Interventions that improve the health status of patients with heart failure are needed.

Depression is associated with heart failure–specific health status,[5] and combining treatment of depression with palliative management of persistent, burdensome symptoms of heart failure could improve health status.[6,7] Palliative care for patients with heart failure is recommended by professional societies, the National Academy of Medicine, and the World Health Organization,[8-10] and palliative care provided by specialists shows promise in improving the health status of patients with heart failure.[11-14] Existing studies have largely examined the role of palliative care among patients hospitalized with heart failure; however, many outpatients with heart failure report reduced health status.[4] Despite the promise of palliative care for heart failure, there are not enough palliative care specialists to treat all patients with heart failure and reduced health status. Furthermore, interventions to improve the health status of patients with heart failure are unlikely to be successful unless they can be integrated earlier in the course of the illness into ongoing outpatient heart failure care and be scalable to the large numbers of patients with reduced health status.

To address these challenges, the Collaborative Care to Alleviate Symptoms and Adjust to Illness (CASA) intervention was developed.[15] The CASA intervention uses a collaborative care health care delivery model to improve health status by concomitantly addressing persistent bothersome symptoms, adjustment to illness, and depression.[6,7] To increase scalability, the CASA health delivery model leverages nurses and social workers to provide telephonic care of symptoms and depression. By combining palliative approaches to symptoms with psychosocial care for depression, we hypothesized that the CASA intervention would improve the health status of outpatients with heart failure.

The multisite CASA trial evaluated the effect of the CASA intervention on the primary outcome of heart failure–specific health status in a population of patients with poor health status. Secondary outcomes included common symptoms (fatigue, pain, shortness of breath, anxiety, and depression), hospitalizations, and mortality.

Methods

Study Design

The CASA trial was a National Institutes of Health–funded single-blind, 2-arm, randomized clinical trial that compared

Key Points

Question Can a symptom and psychosocial collaborative care intervention improve the patient-reported health status (symptoms, function, and quality of life) of patients with chronic heart failure?

Findings In this randomized clinical trial of 314 adults with heart failure comparing a collaborative care intervention with usual care, the primary outcome of heart failure–specific health status did not change with the intervention. Among secondary outcomes, depressive symptoms and fatigue improved with the intervention, but pain and shortness of breath did not.

Meaning A symptom and psychosocial collaborative care intervention was not significantly better than usual care for improving heart failure–specific health status.

the CASA intervention with usual care in 3 health systems (urban safety net, Veterans Affairs, and academically affiliated health systems). This article reports the primary outcome and main secondary outcomes previously described in the study conceptual model.[7] The methods have been previously reported.[7] The study protocol in the Supplement was approved by the Colorado Multiple institutional review board, and the trial was regularly reviewed by an independent data and safety monitoring committee. Patients provided written informed consent.

Population

The eligibility criteria aimed to enroll patients with chronic heart failure and reduced health status who were likely to need the additional resources provided by the intervention. Patients with heart failure were identified through the study sites' electronic health records. The diagnosis was defined using previously validated administrative data[16] supplemented with data on required diuretic dosing (furosemide ≥80 mg/d or equivalent), left ventricular ejection fraction of 40% or less, brain-type natriuretic peptide (BNP) levels of 250 pg/mL or more (to convert to nanograms per liter, multiply by 1.0), or N-terminal prohormone level of BNP of 1000 pg/mL or more. During the study screening process, patients who reported reduced heart failure–specific health status (a Kansas City Cardiomyopathy Questionnaire Short Version[17] [KCCQ] score of ≤70) or reported at least 1 of the study's target symptoms (fatigue, shortness of breath, pain, and/or depression) were targeted for enrollment. Patients with active substance abuse or serious mental illness were excluded. Receipt of guideline-indicated therapy was not an eligibility criterion. Early in the study, the cutoffs for diuretic dosing and BNP were relaxed (furosemide level of ≥20 mg/d, BNP level of ≥100 pg/mL, or N-terminal prohormone level of BNP of ≥500 pg/mL), and both reduced heart failure–specific health status and 1 of the target symptoms were required to increase the eligible study population while still enrolling symptomatic patients.

Eligible patients who provided informed consent completed baseline measures and were then randomized to receive the CASA intervention or usual care. The randomization sequence was computer-generated using random block

sizes and stratification by study site and was concealed from study personnel. Randomization occurred between August 2012 and April 2015, and ended when the goal sample size was accrued. All participants were compensated $10 to $15 at each data collection time point.

CASA Intervention

The CASA intervention included 3 components. A registered nurse addressed symptoms, a social worker provided structured psychosocial care, and a team (including the nurse and social worker, a primary care clinician [C.F.M.], palliative care specialist [D.B.B.], and cardiologist [B.H.]) reviewed patients' care and provided orders for tests and medications to patients' clinicians for review and signature. The registered nurse and social worker were trained to provide the CASA intervention; they were not specialist palliative care clinicians.

The patient and nurse selected an initial symptom on which to focus from a choice of pain, breathlessness, fatigue, or depression.[7] These symptoms were chosen because most patients with heart failure experience at least 1 of these symptoms as burdensome and because each symptom is associated with patient-reported health status.[2,3] The nurse assessed and managed symptoms using structured guidelines developed for the study, including disease-specific, behavioral, and palliative approaches.[7] Additional symptoms, including those beyond the symptoms with structured guidelines, were revisited later during the intervention if needed. The nurse was trained in helping communication (1 hour), motivational interviewing (4 hours), and the symptom guidelines (3 hours).

Six nurse intervention follow-up assessments by telephone (1-2 per month) were planned using a structured symptom rating scale. The symptom rating scale assessed severity, burden, and management capability of pain, shortness of breath, and fatigue using a 10-point Likert scale. It also assessed depression and anxiety using the 4-item Patient Health Questionnaire.[18] These data were used by the intervention team for ongoing management of symptoms that were not improving. The nurse applied motivational interviewing to promote changes in health behaviors (eg, medication adherence, diet, and physical activities) that could improve patient symptoms.[19] The nurse had access to a PhD-level clinical nurse specialist to discuss difficult issues regarding symptom management.

The social worker provided a structured telephone-based psychosocial intervention to help patients with heart failure adjust to living with illness and address depression symptoms, if present.[20] The psychosocial intervention was operationalized in a treatment manual and was based on interpersonal and behavioral activation psychotherapies.[21,22] The following topics were included in approximately 6 counseling sessions (each of which could be split over multiple visits): grief and loss, change in role, behavioral activation, and pacing. The social worker also provided support to patients' informal caregivers as needed. The social worker received 8 hours of psychosocial intervention training and follow-up supervision.

The nurse and the social worker discussed the patients in weekly collaborative care team meetings with a primary care clinician, a cardiologist, and a palliative care physician. This team

Table 1. Comparison of CASA Intervention and Usual Care

Characteristic	CASA	Usual Care
Staff	Core staff: nurse and social worker. Collaborative care team provided case review and supervision.	Primary care physician or nurse practitioner. All practices had a nurse, and almost all had a social worker or access to a social worker.
Visits	Twice monthly.	As needed, generally every 3-6 mo.
Symptom assessment and management	Routine, structured assessment every visit by nurse. Structured guidelines to manage common symptoms.	As needed. Unstructured.
Psychosocial assessment and management	Routine, structured initial assessment by social worker. Structured psychosocial intervention.	Assessment and management on referral to social work or mental health.
Palliative care specialist	Part of collaborative care team; case review of every patient.	Involved only if consulted and then by in-person visit.
Cardiologist	Part of collaborative care team; case review of every patient.	Many patients already had cardiologists.
Telephone and between-visit care	Core to the intervention; most visits were by telephone.	Ad hoc.

Abbreviation: CASA, Collaborative Care to Alleviate Symptoms and Adjust to Illness.

was part of the CASA intervention and not part of usual care (Table 1 illustrates how CASA differs from usual care) because patients' current care clinicians could not feasibly participate in team meetings. The collaborative care team was used because this model of care is scalable and effective in improving depression and other symptoms in medically ill patients.[23-25] Based on review of patients' medical records and discussion with the nurse and social worker, the team recommended medications and tests (and wrote orders for them when feasible at the site) for the patients' usual care clinicians to review and give final approval. The nurse communicated with patients and their clinicians to follow up on these recommendations. A single intervention team provided care for patients in 3 different health systems.

Usual Care

Patients in the usual care group received care at the discretion of their clinicians, which could include care from cardiology, palliative care, and mental health (Table 1). Patients were also given an information sheet developed for the study that outlined self-care for heart failure. Finally, patients in the usual care arm who had significant depressive symptoms were notified of this, and their clinicians were also contacted. Referring clinicians then assumed responsibility for depression care at their discretion, with no constraints on treatment or referrals.

Outcomes

Patient-reported measures included the KCCQ (primary outcome), a valid, reliable measure of heart failure–specific health status that is responsive to change.[26,27] The scale range is from 0 to 100; lower scores indicate poorer health status, and a change of 5 is thought to be a clinically meaningful difference.[27]

Figure. Collaborative Care to Alleviate Symptoms and Adjust to Illness Trial CONSORT Diagram

PCP indicates primary care professional; RN, registered nurse; and SW, social worker.
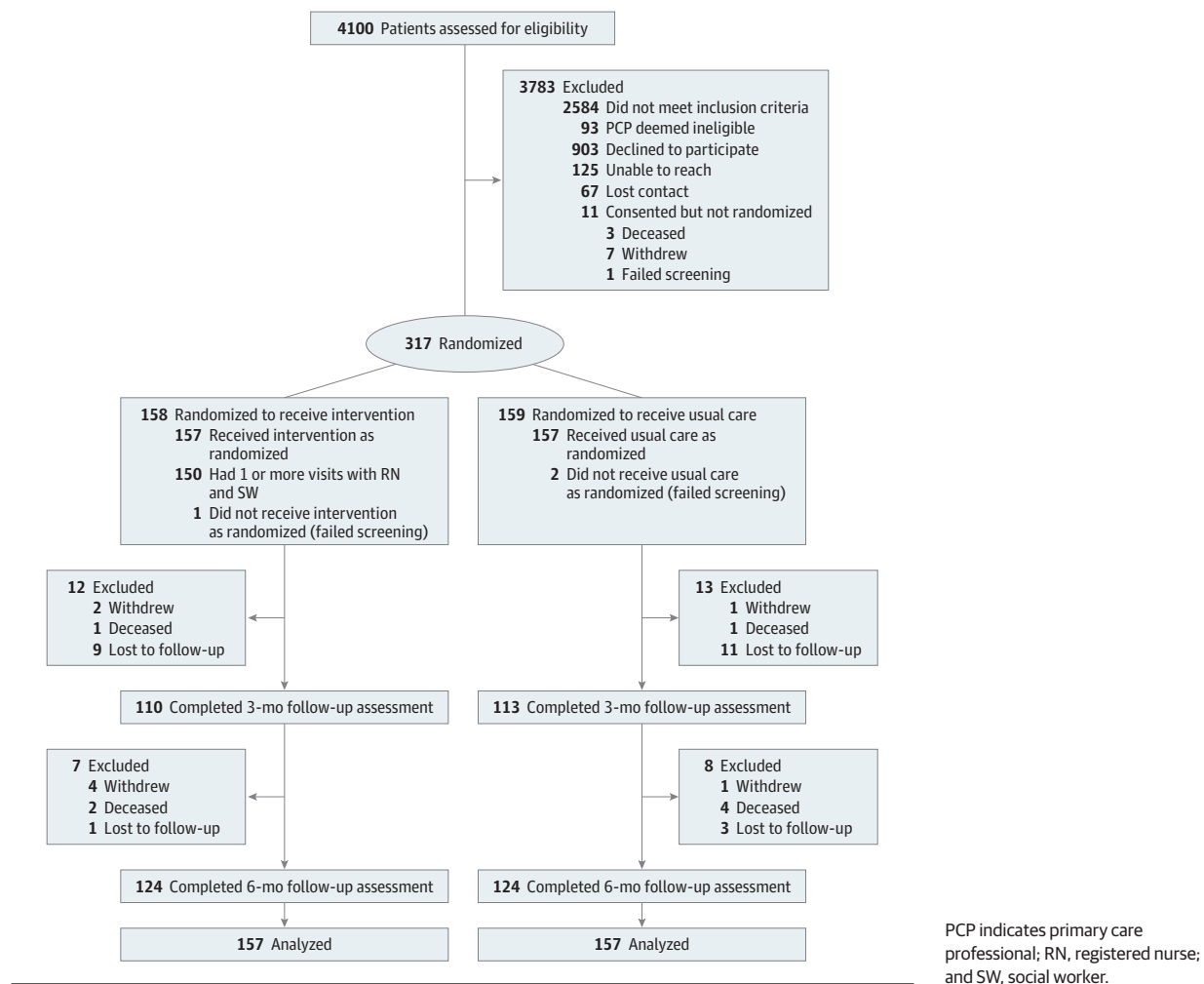
The 9-item Patient Health Questionnaire measured depression (range, 0-27; higher indicates more depressive symptoms).[28-30] The single-item General Symptom Distress Scale measured overall symptom distress (range 0-10; higher score indicates more distress).[31] The PEG (3 items, derived from the Brief Pain Inventory) measured pain intensity (P), interference with enjoyment of life (E), and interference with general activity (G) (range, 0-30; higher score indicates more pain).[32] We assessed shortness of breath using the same response items as the PEG. The Patient-Reported Outcomes Measurement Information System Short Form 8a measured fatigue (range, 0-48; higher score indicates more fatigue). We added the 7-item Generalized Anxiety Disorder to measure anxiety as an exploratory outcome.[33] Measures were completed in person, by mail, or by telephone at baseline and at 3, 6, and 12 months by personnel who did not provide the intervention and were unaware of treatment arm assignment and intervention activities. Hospitalizations and all-cause mortality were assessed by data in the medical records in each health system, supplemented with patient or family self-report. Hospitalizations and mortality were reported (blinded) during the study to the data and safety monitoring committee.

Sample Size

The primary study hypothesis was that patients receiving the CASA intervention would show greater improvement in heart failure–specific health status at 6 months compared with those receiving usual care. We planned a sample size of 312 to detect a change in KCCQ score of 6 to 8 points, greater than the clinically meaningful 5-point difference.[26] We anticipated a 25% dropout rate owing to death and other reasons. As the SD for the KCCQ has ranged from 15 to 20 in prior studies, with this sample size, we had 86% power to detect a change of 6 points (assuming an SD of 15) or 8 points (assuming an SD of 20) (2-sided test, α = .05).

Statistical Analysis

Data from all participants were included regardless of the level of participation, using an intent-to-treat approach. Baseline characteristics of patients were assessed by study group using t tests for continuous variables and χ^2 tests for categorical variables. Analyses of the repeated measures was performed using the maximum likelihood estimation for incomplete data (SAS Proc Mixed; SAS Institute). Effect sizes (Cohen d) are reported to enhance interpretability and allow comparison of

intervention effects across measures. An effect size of 0.20 is small, 0.50 is moderate, and 0.80 is large.[34] The number of all-cause hospitalizations and deaths was compared between study arms using the Mantel-Haenszel χ^2 test. $P < .05$ was considered significant.

Results

Of 317 patients randomized, 3 failed screening; thus, 314 were included in the intent-to-treat analysis (**Figure**). Baseline characteristics were balanced between groups, except those in the intervention group were significantly more likely to have a biventricular pacemaker and to be less short of breath compared with those in the control group (**Table 2**). Patients were predominantly male (247 [78.7%]), the mean (SD) age was 65.5 (11.4) years, and 178 (56.7%) had reduced ejection fraction. There was diversity in race (88 [28.0%] nonwhite), educational level (95 [30.2%] graduated high school or had less education), and income (230 [64.6%] with household income≤$40 000). Patients had comorbidities common in heart failure.

At baseline, the mean (SD) KCCQ overall summary scores were 48.6 (17.4) in the intervention group and 45.3 (21.0) in the usual care group, indicating high symptom burden and poor functional status and quality of life. Most patients were seeing a cardiologist (236 [75.2%]), and few were seeing a pain specialist (34 [10.8%]), mental health care clinician (41 [13.1%]), or palliative care (16 [5.1%]) specialist. Throughout the study, participation was comparable in the 2 groups (Figure).

In the intervention arm, 106 of 157 patients (67.5%) chose fatigue or breathlessness as an initial symptom of focus, 29 (18.5%) chose pain, and 17 (10.8%) chose depression (**Table 3**). The nurse spoke with patients a mean (SD) of 13.1 (5.7) times and the social worker spoke with patients 10.1 (4.0) times. Most of the team medical recommendations were to add, change, or discontinue medications (150 of 347 [43.2%]) or to order tests or laboratory studies (125 of 347 [36.0%]). A mean of 285 of 347 team orders (82.1%) were completed by primary care clinicians.

The primary outcome of difference in change scores on the KCCQ at 6 months did not differ significantly between groups: the mean KCCQ score improved 5.5 points in the intervention arm and 2.9 points in the control arm (difference, 2.6; 95% CI, –1.3 to 6.6; $P = .19$) (**Table 4**). Intervention effect on KCCQ differed by site (site 1 [n = 191]: effect size, 0.10; site 2 [n = 84]: effect size, 0.07; site 3 [n = 42]: effect size, 0.60) and ejection fraction (heart failure with reduced ejection fraction: effect size, 0.28; heart failure with preserved ejection fraction: effect size, –0.03). Among secondary outcomes, depressive symptoms improved with CASA (the effect size was –0.34 at 3 months [$P = .01$] and –0.29 at 6 months [$P = .02$]). This effect persisted at 12 months (effect size, –0.36; $P = .006$). Fatigue also improved with CASA at 6 months (effect size, –0.30; $P = .02$), yet this change did not persist at 12 months (effect size, –0.18; $P = .16$). Anxiety improved with CASA at 3 months (effect size, –0.28; $P < .001$), although the improvement at 6 months did not reach statistical significance (effect size, –0.21; $P = .09$). There were no changes in overall symptom distress, pain, or shortness of breath.

Characteristic	Participants, No. (%)	
	CASA Intervention (n = 157)	Usual Care (n = 157)
Age, mean (SD), y	64.5 (10.9)	66.5 (11.8)
Male sex	128 (81.5)	119 (75.8)
White race	111 (70.7)	115 (73.2)
Employment status		
Retired	73 (46.5)	72 (45.9)
Disabled	50 (31.8)	48 (30.6)
Employed	18 (11.5)	22 (14.0)
Educational level		
Less than high school graduate	6 (3.8)	13 (8.3)
High school graduate or GED	46 (29.3)	30 (19.1)
Some college	58 (36.9)	62 (39.5)
College graduate	28 (17.8)	28 (17.8)
Any postgraduate education	19 (12.1)	23 (14.6)
Income, $		
≤20 000	62/149 (41.6)	66/150 (44.0)
20 001-40 000	39/149 (26.2)	36/150 (24.0)
40 001-60 000	29/149 (19.5)	27/150 (18.0)
>60 000	19/149 (12.8)	21/150 (14.0)
Medical history		
Hypertension	131 (83.4)	123 (78.3)
Diabetes	84 (53.5)	88 (56.1)
Obstructive sleep apnea	72 (45.9)	70 (44.6)
Atrial fibrillation or atrial flutter	59 (37.6)	60 (38.2)
Myocardial infarction	57 (36.3)	55 (35.0)
Chronic obstructive pulmonary disease	54 (34.4)	57 (36.3)
Depression	52 (33.1)	61 (38.9)
Percutaneous coronary intervention	38 (24.2)	35 (22.3)
Coronary artery bypass graft	33 (21.0)	21 (13.4)
Stroke or transient ischemic attack	17 (10.8)	24 (15.3)
Implantable cardiac defibrillator	21 (13.4)	19 (12.1)
Biventricular implantable cardiac defibrillator[a]	24 (15.3)	11 (7.0)
Heart failure characteristics		
Ischemic cause	73 (46.5)	69 (43.9)
Left ventricular ejection fraction[b]		
Normal	57/150 (38.0)	64/149 (43.0)
Mildly reduced	28/150 (18.7)	18/149 (12.1)
Moderately reduced	30/150 (20.0)	22/149 (14.8)
Severely reduced	35/150 (23.3)	45/149 (30.2)
New York Heart Association class		
1	5 (3.2)	12 (7.6)
2	55 (35.0)	46 (29.3)
3	75 (47.8)	75 (47.8)
4	20 (12.7)	24 (15.3)
Medications		
ACE inhibitor or ARB	125 (79.6)	118 (75.2)
β-Blocker[c]	142 (90.4)	124 (79.0)
Aldosterone receptor antagonist	54 (34.4)	47 (29.9)
Opiate	52 (33.1)	51 (32.5)
Antidepressant	45 (28.7)	46 (29.3)

(continued)

Table 2. Characteristics of Participants (continued)

Characteristic	Participants, No. (%)	
	CASA Intervention (n = 157)	Usual Care (n = 157)
Specialty care		
Cardiologist	120/155 (77.4)	116/150 (77.3)
Pain specialist	20/155 (12.9)	14/150 (9.3)
Mental health	22/155 (14.2)	19/150 (12.7)
Palliative care	9/155 (5.8)	7/150 (4.7)
Health status, depression, and symptoms		
KCCQ score mean, (SD)[d]	48.6 (17.4)	45.3 (21.0)
Positive results of depression screening[e]	75 (47.8)	74 (47.1)
PHQ-9 score, median (IQR)	9 (5-14)	9 (5-14)
Positive result of anxiety screening[f]	32 (20.4)	39 (24.8)
Lack of energy[g]	88 (56.1)	90 (57.3)
Shortness of breath[g]	64 (40.8)	89 (56.7)
Pain[g]	66 (42.0)	70 (44.6)

Abbreviations: ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CASA, Collaborative Care to Alleviate Symptoms and Adjust to Illness; GED, General Educational Development; KCCQ, Kansas City Cardiomyopathy Questionnaire; PHQ-9, 9-item Patient Health Questionnaire.

[a] P = .02.

[b] Left ventricular ejection fraction was available for 150 patients in the usual care group and 149 patients in the intervention group (normal, ≥50%; mildly reduced, 40%-49%; moderately reduced, 30%-39%; severely reduced, <30%).

[c] P = .005.

[d] The KCCQ overall summary score range is from 0 to 100; higher numbers indicate better health status.

[e] Depression was measured using the PHQ-9; a score of 10 or higher is considered a positive screening result for depression.

[f] Anxiety was measured using the Generalized Anxiety Disorder Questionnaire-7; a score of 10 or higher is considered a positive screening result for anxiety.

[g] Lack of energy, shortness of breath, and pain measured using single items from the Memorial Symptom Assessment Scale; percentage of participants reporting the symptom "quite a bit" or "very much bothersome." P = .005 for difference in proportion of those with bothersome shortness of breath.

Mortality at 12 months was similar in both arms (10 of 157 patients died receiving CASA, and 13 of 157 patients died receiving usual care; P = .52). The distribution of the number of hospitalizations among patients was not statistically different between arms (CASA, 18 patients with 1 hospitalization and 9 with ≥2 hospitalizations; usual care, 30 patients with 1 hospitalization and 6 with ≥2 hospitalizations; P = .61). There were no harmful adverse events attributed to the intervention.

Discussion

To our knowledge, the CASA trial is the first clinical trial of a palliative and psychosocial collaborative care intervention for patients with heart failure. Study strengths included the relatively large number of patients with heart failure and reduced health status, the diverse patient population enrolled from disparate health systems, and the use of a central team that provided care to patients at the 3 health systems. In this

Table 3. Intervention Process

Characteristic	Value
Initial target symptom, No. (%)	
Fatigue or breathlessness[a]	106 (67.5)
Pain	29 (18.5)
Depression	17 (10.8)
Other	5 (3.2)
Nurse visits	
Visits per patient, mean (SD)	13.1 (5.7)
Time per visit, mean (SD), min	25.3 (23.9)
Social worker visits	
Visits per patient, mean (SD)	10.1 (4.0)
Time per visit, mean (SD), min	33.6 (26.0)
Recommendations, No./Total No. (%)	
Add, change, or discontinue medication	
Recommended	150/347 (43.2)
Completed	130/150 (86.7)
Order test (eg, imaging, ECG, pulmonary function tests) or laboratory (eg, metabolic panel, thyrotropin, testosterone)	
Recommended	125/347 (36.0)
Completed	105/125 (84.0)
Consult another service (physical or occupational therapy, mental health, nutrition)	
Recommended	72/347 (20.8)
Completed	50/72 (69.4)
Overall	
Recommended	347 (100)
Completed	285/347 (82.1)

Abbreviation: ECG, electrocardiogram.

[a] Breathlessness and fatigue were combined, as they had similar assessments.

multisite trial of 314 patients with heart failure and reduced health status, the CASA intervention did not demonstrate improved overall heart failure–specific health status compared with usual care. Among secondary outcomes, depressive symptoms and fatigue improved with the intervention at 6 months (anxiety improved at 3 months), while overall symptom distress, pain, and shortness of breath did not improve.

Several reasons could account for the lack of intervention effect on heart failure–specific health status. The intervention may not have been of adequate intensity. Although the rate of medical order completion was high, it was less than 100%, which may have diminished the intervention effect. The heart failure–specific health status measure, the KCCQ, is weighted toward symptoms and function and may not have captured the effect demonstrated by other palliative care interventions on measures weighted more toward the social, family, and emotional components of quality of life.[35,36] The cohort, while demonstrating significantly reduced baseline health status, had relatively low rates of death and hospitalization compared with large ambulatory cohorts of patients with heart failure. This difference may have limited modifiable heart failure-related contributors that could be affected by the intervention. The baseline KCCQ score was lower in the control arm, which may have led to more regression to the mean, limiting

Table 4. Change Scores Relative to Baseline and the Regression-Estimated Differences in Change Scores Between Groups

Characteristic	Intervention Group (n = 157)		Control Group (n = 157)		Difference Between Change Scores (95% CI)	P Value	Effect Size (95% CI)[a]
	Participants, No.	Mean Observed Change From Baseline	Participants, No.	Mean Observed Change From Baseline			
Heart failure–specific health status, KCCQ score[b]							
At 3 mo	106	4.8	108	3.0	1.8 (−1.9 to 5.6)	.34	0.12 (−0.13 to 0.38)
At 6 mo	121	5.5	121	2.9	2.6 (−1.3 to 6.6)	.19	0.16 (−0.08 to 0.41)
Depressive symptom, PHQ-9 score[c]							
At 3 mo	105	−2.1	105	−0.5	−1.6 (−2.7 to −0.4)	.01	−0.34 (−0.60 to −0.08)
At 6 mo	121	−2.2	119	−0.8	−1.4 (−2.6 to −0.2)	.02	−0.29 (−0.53 to −0.04)
Anxiety symptom, GAD-7 score[d]							
At 3 mo	110	−1.4	108	−0.3	−1.1 (−2.06 to −0.11)	<.001	−0.28 (−0.53 to −0.03)
At 6 mo	124	−1.5	124	−0.6	−0.9 (−2.0 to 0.13)	.09	−0.21 (−0.45 to 0.03)
Overall symptom distress, GSDS score[e]							
At 3 mo	108	−0.3	108	−0.5	0.2 (−0.4 to 0.8)	.57	0.08 (−0.17 to 0.33)
At 6 mo	124	−0.4	122	−0.5	0.1 (−0.5 to 0.7)	.80	0.03 (−0.21 to 0.27)
Pain, PEG score[f]							
At 3 mo	110	−0.5	107	−0.8	0.3 (−0.3 to 0.9)	.30	0.14 (−0.12 to 0.39)
At 6 mo	123	−0.5	124	−0.8	0.3 (−0.3 to 0.9)	.35	0.11 (−0.13 to 0.36)
Fatigue, PROMIS score[g]							
At 3 mo	107	−2.3	107	−1.1	−1.2 (−2.7 to 0.4)	.14	−0.20 (−0.46 to 0.06)
At 6 mo	121	−2.8	127	−0.8	−2.0 (−3.6 to −0.4)	.02	−0.30 (−0.55 to −0.06)
Dyspnea score[h]							
At 3 mo	110	−0.7	113	−0.6	−0.1 (−0.7 to 0.4)	.67	−0.05 (−0.31 to 0.20)
At 6 mo	124	−0.4	124	−0.5	0.1 (−0.5 to 0.7)	.76	0.00 (−0.20 to 0.28)

Abbreviations: GAD-7, 7-item Generalized Anxiety Disorder Questionnaire; GSDS, General Symptom Distress Scale; KCCQ, Kansas City Cardiomyopathy Questionnaire; PEG, pain intensity (P), interference with enjoyment of life (E), and interference with general activity (G); PHQ-9, 9-item Patient Health Questionnaire; PROMIS, Patient-Reported Outcomes Measurement Information System.

[a] Effect sizes are Cohen d; an effect size of 0.20 is small, 0.50 is moderate, and 0.80 is large.

[b] Heart failure–specific health status score range is from 0 to 100; a higher number means better health status.

[c] Depressive symptom scores range from 0 to 27; a higher number means more

depressive symptoms.

[d] Anxiety symptom score range from 0 to 21; a higher number means more anxiety symptoms.

[e] Symptom distress scores range from 0 to 10; a higher number means more overall distress from symptoms.

[f] Pain scores range from 0 to 10; a higher number means more pain.

[g] Fatigue scores range from 0 to 32; a higher number means more fatigue.

[h] Dyspnea scores range from 0 to 10; a higher number means more shortness of breath.

our ability to detect an intervention effect. Finally, it is possible that the study was underpowered to detect a more modest intervention effect.

The improvement in depression without improvement in heart failure–specific health status raises questions about the relationship between these 2 facets of the patient experience. Longitudinal studies demonstrate that depression and heart failure–specific health status are connected in patients with heart failure[5]; however, in both this trial and a previous trial,[37] improvements in depression were not associated with improvements in heart failure–specific health status, a key component of the study conceptual model. The link between depression and quality of life outcomes is strongest in randomized clinical trials that enroll only patients with depression.[24,38] This link should be considered in future study designs.

Depression and fatigue, both secondary outcomes, improved with the CASA intervention. Anxiety also improved at

3 months, yet this effect did not reach statistical significance at 6 months. Limited treatments exist for these common, bothersome symptoms in patients with heart failure.[39-42] For example, 2 randomized clinical trials of serotonin-specific reuptake inhibitors failed to show improved depressive symptoms in patients with heart failure.[39,40] The effect of the CASA intervention on depressive symptoms is at the upper end of effect sizes described in a meta-analysis of 37 collaborative care trials for primary care patients with depression (mean effect size, 0.025; 95% CI, 0.18-0.32).[23] These findings should be considered in the context of the CASA study population, which included patients with varying degrees of severity of depressive symptoms (half the patients screened positive for depressive disorder and 23% had depressive disorder, according to the 9-item Patient Health Questionnaire). The effect on depressive symptoms persisted at 12 months, which, for many patients, was 9 months after the intervention completed.

The CASA trial studied a structured, scalable intervention that could be integrated into outpatient care and could be provided earlier in the course of the illness prior to the end of life by nurses and social workers who collaborated with physicians. The CASA intervention differed from heart failure disease management and palliative care interventions by implementing a structured, manualized psychosocial care protocol, using a collaborative care model and structured guidelines to address common burdensome symptoms chosen by patients. The next steps in research could include (1) testing intervention components on specific outcomes (eg, psychosocial care intervention for patients with depressive disorder or fatigue); (2) studying the intervention in a higher-risk or more ill population, as another study using specialist palliative care has done,[11] or an underserved or rural population; and (3) using health information technology (eg, videoconference) to increase the reach, intensity, or scalability of the intervention. It is possible that further refinement of the intervention could improve disease-specific health status.

Limitations

The generalizability of the study findings may be limited because recruitment occurred in 1 US region and because the study population had a high proportion of men. Because of the nature of the intervention, participants could not be blinded. The missing patient-reported data rate of 21% at 6 months, equivalent in both arms, is similar to other studies of seriously ill populations.[11,36,38] Because we did not use an attention control group or measure usual care clinician time spent with patients, we cannot infer that the improvements in depression and fatigue were related to specific components of the intervention rather than nonspecific benefits from clinician attention or participation in the psychosocial intervention. Finally, there is a chance that specialist palliative care consultation in the usual care arm may have improved outcomes in the usual care group.

Conclusions

This multisite randomized clinical trial of the CASA intervention did not demonstrate improved heart failure–specific health status. Secondary outcomes of depression and fatigue, both difficult symptoms to treat in heart failure, improved. Further research is needed to test scalable models of outpatient palliative care in heart failure to improve patient outcomes.

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REFERENCES

1. Walke LM, Gallo WT, Tinetti ME, Fried TR. The burden of symptoms among community-dwelling older persons with advanced chronic disease. *Arch Intern Med*. 2004;164(21):2321-2324.

2. Blinderman CD, Homel P, Billings JA, Portenoy RK, Tennstedt SL. Symptom distress and quality of life in patients with advanced congestive heart failure. *J Pain Symptom Manage*. 2008;35(6):594-603.

3. Bekelman DB, Havranek EP, Becker DM, et al. Symptoms, depression, and quality of life in patients with heart failure. *J Card Fail*. 2007;13(8):643-648.

4. Heidenreich PA, Spertus JA, Jones PG, et al; Cardiovascular Outcomes Research Consortium. Health status identifies heart failure outpatients at risk for hospitalization or death. *J Am Coll Cardiol*. 2006;47(4):752-756.

5. Rumsfeld JS, Havranek E, Masoudi FA, et al; Cardiovascular Outcomes Research Consortium. Depressive symptoms are the strongest predictors of short-term declines in health status in patients with heart failure. *J Am Coll Cardiol*. 2003;42(10):1811-1817.

6. Bekelman DB, Hutt E, Masoudi FA, Kutner JS, Rumsfeld JS. Defining the role of palliative care in older adults with heart failure. *Int J Cardiol*. 2008;125(2):183-190.

7. Bekelman DB, Allen LA, Peterson J, et al. Rationale and study design of a patient-centered intervention to improve health status in chronic heart failure: the Collaborative Care to Alleviate Symptoms and Adjust to Illness (CASA) randomized trial. *Contemp Clin Trials*. 2016;51:1-7.

8. IOM (Institute of Medicine). *Dying in America: Improving Quality and Honoring Individual Preferences Near the End of Life*. Washington, DC: The National Academies Press; 2014.

9. Yancy CW, Jessup M, Bozkurt B, et al; WRITING COMMITTEE MEMBERS. 2016 ACC/AHA/HFSA focused update on new pharmacological therapy for heart failure: an update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force

on Clinical Practice Guidelines and the Heart Failure Society of America. *Circulation*. 2016;134(13):e282-e293.

10. Sepúlveda C, Marlin A, Yoshida T, Ullrich A. Palliative care: the World Health Organization's global perspective. *J Pain Symptom Manage*. 2002; 24(2):91-96.

11. Rogers JG, Patel CB, Mentz RJ, et al. Palliative care in heart failure: The PAL-HF randomized, controlled clinical trial. *J Am Coll Cardiol*. 2017;70 (3):331-341.

12. Brännström M, Boman K. Effects of person-centred and integrated chronic heart failure and palliative home care: PREFER: a randomized controlled study. *Eur J Heart Fail*. 2014;16(10):1142-1151.

13. Wong FK, Ng AY, Lee PH, et al. Effects of a transitional palliative care model on patients with end-stage heart failure: a randomised controlled trial. *Heart*. 2016;102(14):1100-1108.

14. Sidebottom AC, Jorgenson A, Richards H, Kirven J, Sillah A. Inpatient palliative care for patients with acute heart failure: outcomes from a randomized trial. *J Palliat Med*. 2015;18(2):134-142.

15. Bekelman DB, Hooker S, Nowels CT, et al. Feasibility and acceptability of a collaborative care intervention to improve symptoms and quality of life in chronic heart failure: mixed methods pilot trial. *J Palliat Med*. 2014;17(2):145-151.

16. Go AS, Yang J, Ackerson LM, et al. Hemoglobin level, chronic kidney disease, and the risks of death and hospitalization in adults with chronic heart failure: the Anemia in Chronic Heart Failure: Outcomes and Resource Utilization (ANCHOR) Study. *Circulation*. 2006;113(23):2713-2723.

17. Spertus JA, Jones PG. Development and validation of a short version of the Kansas City Cardiomyopathy Questionnaire. *Circ Cardiovasc Qual Outcomes*. 2015;8(5):469-476.

18. Löwe B, Wahl I, Rose M, et al. A 4-item measure of depression and anxiety: validation and standardization of the Patient Health Questionnaire-4 (PHQ-4) in the general population. *J Affect Disord*. 2010;122(1-2):86-95.

19. Rubak S, Sandbaek A, Lauritzen T, Christensen B. Motivational interviewing: a systematic review and meta-analysis. *Br J Gen Pract*. 2005;55(513): 305-312.

20. Turvey CL, Klein DM. Remission from depression comorbid with chronic illness and physical impairment. *Am J Psychiatry*. 2008;165(5): 569-574.

21. Stuart S, Robinson M. *Interpersonal Psychotherapy: A Clinician's Guide*. London, England: Edward Arnold; 2003.

22. Hopko DR, Lejuez CW, Ruggiero KJ, Eifert GH. Contemporary behavioral activation treatments for depression: procedures, principles, and progress. *Clin Psychol Rev*. 2003;23(5):699-717.

23. Gilbody S, Bower P, Fletcher J, Richards D, Sutton AJ. Collaborative care for depression: a cumulative meta-analysis and review of longer-term outcomes. *Arch Intern Med*. 2006;166 (21):2314-2321.

24. Katon WJ, Lin EH, Von Korff M, et al. Collaborative care for patients with depression and chronic illnesses. *N Engl J Med*. 2010;363(27): 2611-2620.

25. Kroenke K, Bair MJ, Damush TM, et al. Optimized antidepressant therapy and pain self-management in primary care patients with depression and musculoskeletal pain: a randomized controlled trial. *JAMA*. 2009;301(20):2099-2110.

26. Green CP, Porter CB, Bresnahan DR, Spertus JA. Development and evaluation of the Kansas City Cardiomyopathy Questionnaire: a new health status measure for heart failure. *J Am Coll Cardiol*. 2000;35(5):1245-1255.

27. Spertus J, Peterson E, Conard MW, et al; Cardiovascular Outcomes Research Consortium. Monitoring clinical changes in patients with heart failure: a comparison of methods. *Am Heart J*. 2005;150(4):707-715.

28. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16(9):606-613.

29. Thombs BD, Ziegelstein RC, Whooley MA. Optimizing detection of major depression among patients with coronary artery disease using the Patient Health Questionnaire: data from the Heart and Soul Study. *J Gen Intern Med*. 2008;23(12): 2014-2017.

30. Löwe B, Unützer J, Callahan CM, Perkins AJ, Kroenke K. Monitoring depression treatment outcomes with the Patient Health Questionnaire-9. *Med Care*. 2004;42(12):1194-1201.

31. Badger TA, Segrin C, Meek P. Development and validation of an instrument for rapidly assessing symptoms: the General Symptom Distress Scale. *J Pain Symptom Manage*. 2011;41(3):535-548.

32. Krebs EE, Lorenz KA, Bair MJ, et al. Development and initial validation of the PEG, a three-item scale assessing pain intensity and interference. *J Gen Intern Med*. 2009;24(6):733-738.

33. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166 (10):1092-1097.

34. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Hillsdale, NJ: L. Erlbaum Associates; 2006.

35. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med*. 2010;363 (8):733-742.

36. Zimmermann C, Swami N, Krzyzanowska M, et al. Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. *Lancet*. 2014;383(9930):1721-1730.

37. Bekelman DB, Plomondon ME, Carey EP, et al. Primary results of the Patient-Centered Disease Management (PCDM) for Heart Failure Study: a randomized clinical trial. *JAMA Intern Med*. 2015; 175(5):725-732.

38. Rollman BL, Belnap BH, LeMenager MS, et al. Telephone-delivered collaborative care for treating post-CABG depression: a randomized controlled trial. *JAMA*. 2009;302(19):2095-2103.

39. O'Connor CM, Jiang W, Kuchibhatla M, et al; SADHART-CHF Investigators. Safety and efficacy of sertraline for depression in patients with heart failure: results of the SADHART-CHF (Sertraline Against Depression and Heart Disease in Chronic Heart Failure) trial. *J Am Coll Cardiol*. 2010;56(9): 692-699.

40. Angermann CE, Gelbrich G, Störk S, et al; MOOD-HF Study Investigators and Committee Members. Effect of escitalopram on all-cause mortality and hospitalization in patients with heart failure and depression: the MOOD-HF randomized clinical trial. *JAMA*. 2016;315(24):2683-2693.

41. Freedland KE, Carney RM, Rich MW, Steinmeyer BC, Rubin EH. Cognitive behavior therapy for depression and self-care in heart failure patients: a randomized clinical trial. *JAMA Intern Med*. 2015; 175(11):1773-1782.

42. Perez-Moreno AC, Jhund PS, Macdonald MR, et al. Fatigue as a predictor of outcome in patients with heart failure: analysis of CORONA (Controlled Rosuvastatin Multinational Trial in Heart Failure). *JACC Heart Fail*. 2014;2(2):187-197.