Palliative Care for Advanced Heart Failure in a Department of Veterans Affairs Regional Hospice Program: Patient Selection, a Treatment Protocol, and Clinical Course

George J. Taylor, MD,^{1,2} Dorothy M. Lee, ACNP,² Catalin F. Baicu, PhD,^{1,2} and Michael R. Zile, MD^{1,2}

Abstract

Background: Palliative care for advanced heart failure (HF) is generally recommended. However, few reports have focused on the particulars of treatment, or the clinical course of HF on a specific treatment regimen.

Objective: Palliation adequate to allow patients to avoid HF admission and die at home.

Methods: Patients from a veterans administration regional practice with multiple, recent hospital admissions were enrolled in community hospice programs. Treatment of HF with reduced left ventricular ejection fraction (HFrEF) included guidelines-directed medical therapy, digoxin, opioids, and oral bumetanide (with metolazone as needed) rather than intravenous diuretics. Levodopa (l-dopa) was added when conventional therapy failed to control symptoms. HF with preserved EF was also treated with bumetanide and opioids.

Results: Thirty male veterans, 23 of them with HFrEF, had 90 HF admissions in the 6 months before enrollment, and 3 HF admissions during follow-up of at least 14 months. Twenty-one patients died, 18 of them at home; 14 died within 5 months, and the rest lived much longer. Failure to improve with initial therapy predicted early death. Results were similar for those with reduced and preserved left ventricular ejection fraction. L-dopa was started in 13 patients and tolerated by 8 patients; functional class improved and B-type natriuretic peptide declined after treatment.

Conclusions: With this treatment protocol, there were few HF admissions and patients were able to die at home. It can be used as a guide to therapy, or as an approach that can be tested with additional study.

Keywords: bumetanide; digoxin; end-of-life; heart failure; hospice; hospital readmission; levodopa; opioids; palliative care; veterans administration

Introduction

RECURRENT DECOMPENSATION and frequent hospital admission are common in the late stage of heart failure (HF). Palliative care has been recommended, and most have suggested continuing guidelines-directed medical therapy (GDMT) because it is palliative as well as life prolonging.¹⁻³ There have been few reports describing the clinical course of HF in a palliative care program that provided details of both HF-specific and palliative treatment.¹⁻⁴

We hypothesized that a program embracing the principals of home-delivered palliative care could use both intensive GDMT and the application of other palliative therapies, including oral bumetanide in place of intravenous diuretics, digoxin, opioids, and levodopa (l-dopa) to improve care and

comfort, reduce the need for rehospitalization, and allow death at home.⁵⁻⁹ The patients were from a large geographical area, so we elected to develop this HF palliative care program using local home-hospice programs. It was implemented in February 2014. This report is a retrospective analysis of the experience with the initial 30 patients who have been followed for more than a year.

Methods

Patient selection and setting

Patients were enrolled in five existing home-hospice services in a veterans administration (VA) practice region that included Charleston, Myrtle Beach, Conway, and Beaufort, SC, as well as Savannah, GA. There are a number of clinical

¹Department of Medicine, Medical University of South Carolina, Charleston, South Carolina.

²Ralph H. Johnson Department of Veterans Affairs Medical Center, Charleston, South Carolina.

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variables associated with early HF mortality that could have been used for patient selection.¹⁰ A principal goal of this program—shared by patients and their caregivers—was to reduce the need for hospital readmission for those who reached the stage of HF marked by recurrent admission. For this reason, the enrollment criteria were multiple HF admissions in the previous six months and the patient's desire to avoid hospital admission.

The home-hospice nurse visited the patient weekly, or more frequently if needed, and was authorized to adjust medical therapy after consulting the program's cardiologist (G.J.T.). They discussed each patient weekly, and there was additional telephone consultation when instability required changes in therapy. Thus, the HF hospice cardiologist directed HF management, rather than the community hospice program's physician director.

At the time of enrollment, patients and caregivers made the following hospice agreement: avoiding hospital admission is a primary goal, and congestion and other symptoms will be managed at home. The hospice nurse is to be called with any change in condition. The five community-based programs applied the standard hospice approach to psychosocial and spiritual aspects of end-of-life care with active participation by social workers, chaplains, and volunteers.

When clinically indicated, patients had laboratory evaluation during follow-up including monitoring of electrolytes and creatinine, B-type natriuretic peptide (BNP), and digitalis levels.

Drug therapy

For HF with reduced ejection fraction (HFrEF), beta blockers, angiotensin converting enzyme inhibitors or receptor antagonists, sacubitril/valsartan, and mineralocorticoid receptor blockers were continued or started, and were titrated to GDMT doses as tolerated. In addition, other treatments were added for palliation. All with HFrEF were treated with digoxin. Opioids were added to ameliorate dyspnea and/or pain. By design, intravenous diuretics were avoided. Pulmonary congestion and peripheral edema were treated with oral bumetanide, with addition of metolazone as needed.

Patients treated with intravenous inotropes in hospital and who were considered for home inotrope infusion therapy were offered oral l-dopa as a substitute. L-dopa was also offered to others with diuretic-resistant congestion. Presently, l-dopa is available in combination with carbidopa (such as Sinemet), which prevents its decarboxylation to dopamine in the peripheral circulation. The pharmaceutical, l-dopa (without carbidopa), is available, and a local compounding pharmacy providing 250 and 500 mg capsules. The starting dose was 250 mg four times daily (qid), with gradual up-titration to a dose that resulted in effective diuresis or improved exercise tolerance. Once the patient was stable, the l-dopa dose was adjusted to the lowest effective dose. Because nausea is a common side effect of l-dopa, all received prophylactic antiemetic therapy.

The treatment protocol for HF with preserved EF (HFpEF) included blood pressure control, prevention of tachycardia, and adjustment of bumetanide for congestion.

Data analysis

This was a retrospective study, and institutional review board approval was obtained for the retrospective chart review. All statistical analyses were performed using SigmaStat 4.0 (Systat Software, Inc., San Jose, CA). Differences in NYHA class were tested for statistical differences using a Fisher exact test. Differences in effect of l-dopa on BNP were tested for statistical significance using a Mann-Whitney rank sum test. Significance was determined by $p < 0.05$. Data are presented as mean $\pm$ standard deviation, or median and range. The cause of hospitalization before and after enrollment was determined by the authors (G.J.T., D.M.L.) after review of hospital records. The mode of death was determined by the authors (G.J.T., D.M.L.) in consultation with the hospice nurse.

Results

Patient population

Beginning in February 2014, 32 male veterans with HF were offered treatment, and 30 were enrolled (Fig. 1). Frequent HF admission in the preceding six months was the indication for

FIG. 1. Consort diagram. Patient disposition, HFrEF versus HFpEF distribution, mortality, days in hospice. HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; *Days after enrollment (range, median).

TABLE 1. BASELINE CHARACTERISTICS, 30 MALE VETERANS

Age, years	48–94 (Median 70)
Race: black/white	11/19 Patients
Etiology of HF	
HFrEF: ICM	13 Patients
HFrEF: NICM	10 Patients
HFpEF	7 Patients (2 with cor pulmonale)
Comorbidities (30 pts)	No. of patients
Hypertension	12
Chronic lung disease	13
Diabetes	11
Elevated creatinine	7
Atrial fibrillation	10
Stroke	4
Ascites	4
Aortic stenosis	2
Mitral regurgitation	2
CABS/PCI	8/5
ICD/CRT	10/3
Treatment HFrEF (23 pts)	
Digoxin	7
ACE I/ARBs	20
Beta-blocker	22
Spironolactone	8
IV inotropes	9
Treatment HFpEF (7 pts)	
ACE I/ARBs	4
Beta-blocker	3

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker; CABS, coronary artery bypass surgery; CRT, cardiac resynchronization therapy; HF, heart failure; HFpEF, HF with preserved LVEF; HFrEF, HF with reduced left ventricular ejection fraction (LVEF); ICD, implantable cardiac defibrillator; ICM, ischemic cardiomyopathy; IV, intravenous; NICM, nonischemic cardiomyopathy; PCI, percutaneous coronary intervention; pts, patients.

enrollment for 28 of them, and the other 2 were enrolled after one admission because of dependence on inotrope infusion therapy. Table 1 provides a clinical profile including comorbidities. Enrollment diagnosis was HFrEF in 23 patients (all with EF <30%, and 14 with left ventricular ejection fraction (LVEF) <20%). Seven patients had HFpEF, including two with diuretic-resistant cor pulmonale.

Clinical course

Twenty-one of the 30 patients died from 7 to 781 days after enrollment (median, 90 days), and 18 of the 21 died at home (Fig. 1). One of them died after 18 hours in hospital, and two died in nursing homes. Five died within 30 days, and 14 (47%) within 5 months of enrollment. The other seven patients died more than 10 months after enrollment (312–781, median 357 days, Table 2). One patient died after stroke, one with gastrointestinal bleeding, and the other deaths were HF related. Of the 18 patients dying at home, 3 had terminal pulmonary congestion that was treated with high-dose morphine, 10 developed hypotension and coma and died without congestion, and 5 had sudden cardiac death. Nine patients are alive 437–859 days from enrollment (median 540 days; Fig. 1).

Most patients were decompensated and in functional class IV while in hospital at the time of enrollment; for example, they were unable to dress without symptoms.¹¹ With treat-

TABLE 2. PATTERNS OF SURVIVAL AFTER HOSPICE ENROLLMENT

	Death in <5 months of enrollment (n = 14)	Longer survival (n = 16) ^a
Age, years (range, median)	63–93 (71)	48–94 (62)
HFrEF, <i>n</i>	12	11
Ischemic cardiomyopathy, <i>n</i>	9	5
Duration of HF, years (range, median)	2–10 (5)	0.5–9 (1.6)**
Inotrope infusion in hospital, <i>n</i>	5	4
Number of HF admissions pre/postenrollment	37 (2.6/patient)/2	53 (3.3/patient)/1
L-dopa, <i>n</i>	2	6
Functional class IV after treatment, <i>n</i>	13	1**

^aSeven of them died later, 312–781 days after enrollment.

***p* < 0.001 versus death in <5 months of enrollment.

ment, most patients improved and 16 of them were in functional classes III and II (Fig. 2). The patients who died early, within five months of enrollment, as a group had no functional improvement with initial treatment (Fig. 2 and Table 2). They also had a longer clinical history of HF, were somewhat older, and were more likely to have ischemic cardiomyopathy (Table 2). The number of admissions in the six months before enrollment was unrelated to survival during follow-up.

Hospital admission

During the six months before enrollment, the 30 patients had 110 hospital admissions, 90 of them for HF (Table 3). After enrollment, there were 26 admissions, 3 of them for HF. The other admissions were for pulmonary disease (eight admissions), falls (six), mental status changes (three), stroke (two), gastrointestinal bleeding (two), poor diabetes control (one), and new atrial fibrillation (one). Two patients accounted for nine non-HF-related admissions.

Drug therapy

At the time of enrollment, most patients were on GDMT, and it was continued (Table 1). Oral bumetanide was used instead of furosemide for all patients. Congestion crises often required high-dose oral bumetanide, as much 4 mg thrice daily, and a three to five-day course of metolazone was commonly added.

Of the 23 patients with HFrEF, 7 (30%) were on digoxin at the time of enrollment. Eleven patients not on digoxin were treated with 0.125 mg daily. Eight patients on digoxin had elevated creatinine and were treated with reduced dosing frequency; digoxin levels were monitored and there was no digitalis toxicity.

Opioid therapy was offered as palliation for dyspnea or pain: 7 refused, 4 did not tolerate it, and the remaining 19

FIG. 2. Change in NYHA functional class with treatment. While in hospital at the time of enrollment, most were in functional class IV (unable to dress without symptoms). Fisher exact test showed statistically significant ($p < 0.001$) differences between pre-post NYHA class IV versus NYHA class III.

were treated with long-acting morphine (14 patients) or fentanyl,⁵ titrated to a tolerable dose.

L-dopa was given to 13 patients, 12 of the 23 with HFrEF, and 1 with cor pulmonale and right ventricular dysfunction. It was started one–five weeks after hospital discharge. Five of these 13 patients had been treated with IV inotrope infusion in hospital, 2 of them for cardiogenic shock, and the other 3 to enable diuresis. (Four other patients on inotrope infusion therapy declined l-dopa therapy.) Eight of the 13 patients had congestion resistant to digoxin and high-dose bumetanide plus metolazone, and were started on l-dopa as an alternative to intravenous inotrope therapy. The initial l-dopa dose was 250 mg qid, and it was raised at one-week intervals; most were

on a maintenance dose of 500–750 mg qid. It was not tolerated by 5 of the 13 patients (38%): 4 had nausea that could not be controlled with antiemetics and 1 had confusion. Seven of the eight who tolerated therapy remained on antiemetics.

Of the eight patients who tolerated l-dopa, seven had improved functional class and better control of congestion, and five of them were in the longer survival group (Table 2). Three patients on l-dopa died, 117, 132, and 325 days after starting therapy. Thus, all of the patients on maintenance l-dopa were alive at three months, and six of eight at six months. Ten of the 13 patients who started l-dopa had BNP measured pretreatment, and again after reaching a maintenance dose (2 subsequently stopped it because of nausea). BNP declined in all of them (Fig. 3), and all had resolution of edema on lower dose bumetanide. Four patients receiving l-dopa had ascites attributed to HF, three requiring large volume paracentesis. All had ascites resolve with l-dopa therapy.

One patient had an escalating insulin requirement with l-dopa that resolved when it was held. Hyperglycemia worsened when l-dopa was restarted. Glycemic control was achieved when l-dopa was given at 7 am and noon. Insulin resistance is a heretofore-unreported side effect.

TABLE 3. HOSPITAL ADMISSIONS

	<i>Six months pre-enrollment</i>	<i>During follow-up*</i>
All cause admission	110	26
HF admission	90	3

*Minimum follow-up was 14 months for patients still living.

FIG. 3. Change in BNP with l-dopa therapy in 10 patients. Mann–Whitney rank sum test showed statistically significant differences. * $p=0.014$ versus the pre-treatment value. BNP, B-type natriuretic peptide.

Discussion

At first glance, what is described in this report may seem to be a standard palliative care program, but it is not. It was a HF-specific hospice program centered on the idea of an exclusively outpatient care approach to end-of-life HF to avoid the suffering and high cost associated with hospital admission. It was accomplished using existing community hospice programs. The treatment approach is described in sufficient detail to allow its reproduction in other healthcare delivery settings. HF admission after enrollment was rare, suggesting that end-of-life HF can be treated as an outpatient illness. Control of suffering was adequate to allow 18 of the 21 patients who died to remain at home. The timing of death was bimodal, with about half dying early, but the rest living at least nine months (Table 2). The best predictors of early death were the duration of HF and the initial response to therapy. Patients who failed to improve to functional class III were apparently nearer end of life and died within five months.

Six months after beginning this program, the Swedish PREFER group reported six-month follow-up of a randomized trial of palliative care for HF.⁴ They found fewer all-cause hospital admissions in the palliative care group and lower costs, a result that documents the economic benefit of palliative care for advanced HF. There are differences comparing PREFER and the present report: the PREFER study population had less advanced disease; only 20% had LVEF <30%, and six-month mortality was 22%. PREFER was limited to patients whose primary care clinic was within 30 km of the program center, so a specialized HF team managed their patients. The present results complement PREFER, and further indicate that comparable results are possible for HF patients who are nearer end of life, and who are treated in existing community hospice programs.²

PREFER and others recommending HF palliative care continued GDMT to optimize survival.^{1–4} We did that, but with the following additional measures:

First, unlike PREFER, parenteral diuretics were not used to treat congestion crises. High-dose oral bumetanide proved

effective, often in combination with metolazone. A need for parenteral diuretics is the usual reason for admission with decompensated HF, and this experience suggests that it can be avoided if congestion is detected early and treated aggressively.

Second, all our patients with HFrEF were treated with digoxin. Only 30% of them were taking it when enrolled, similar to digoxin treatment rates in other HF studies as well as PREFER.^{4,12} The palliative benefit of digoxin for HF is established, because it has been shown to reduce hospital admission with advanced HF.^{6,13}

Third, we reintroduced the use of the oral inotropic agent, l-dopa. The hemodynamic benefits of oral l-dopa in patients with HF have been confirmed, but it has not been in clinical use for HF for decades.^{8,9} A possible reason for this is difficulty of use. Nausea is common, preventing continued use in 5 of our 13 patients who started it. Another may be the popularization of inotrope infusion therapy in the early 1980s, which, despite early enthusiasm, is now believed to hasten death.^{14,15} In this small series of eight patients who tolerated oral l-dopa maintenance therapy, early death was uncommon, possibly an effect of dose. The hemodynamic studies of oral l-dopa in HF tested a 1500 mg dose, twice the average dose given to our patients.⁸ At a lower dose, oral l-dopa—or other oral inotropes—could be a substitute for intravenous inotrope therapy, and could have a role in end-of-life management when conventional therapy is not working. It is a possibility worth pursuing because infusion therapy is inconvenient, uncomfortable, expensive, and possibly lethal (it is a therapy that begs for replacement).

The employment of community hospice programs allowed rapid start-up and the treatment of patients over a large geographic region. Hospice nurses are accustomed to treating critically ill patients at home, are authorized to make medicine adjustments, and in this program did so in consultation with the supervising cardiologist. In addition, the hospice programs' social workers, chaplains, and volunteers often made it possible for our patients to remain at home, because many of them were economically and geographically disadvantaged. The five community home-hospice programs caring for our patients quickly developed a HF track and expertise.

A question at the beginning was whether patients with terminal HF symptoms would remain at home. Trust in the hospice nurse allowed this. In addition, terminal pulmonary edema was uncommon. Others have observed that when congestion is adequately treated, death with advanced HF often is a pump failure syndrome with progressive hypotension and coma (e.g., dry pump failure).²

We recognize that palliative care for HF departs from the traditional hospice model. Life-extending treatment is continued, because GDMT is palliative as well.^{1–3} Extended survival is common. Half of our patients lived longer than six months and one-third more than a year. In contrast, about half died early, satisfying the enrollment criterion that death within six months is as likely as not. VA policy allowed prolonged care, and it appeared justified by the low readmission rate.

Despite these differences, we called it “HF hospice,” and our patients signed on for treatment in community hospice programs. Practical benefits of hospice status include the rationale for treating congestion crises outside the hospital, the use of novel therapies for palliation, and terminal care at home.

Most reports describing palliative care for HF are descriptive, and like this study are limited by the absence of a control group. In this case, the number of deaths during follow-up makes it unlikely that a change in the trajectory of illness explains the low HF admission rate. Still it is a descriptive case series, and the results should be considered hypothesis generating.

Conclusion

Palliative care is widely recommended for patients with HF nearing end of life, but there has been little focus on the particulars of HF management. This report describes the clinical course of VA patients treated in community hospice programs using a treatment protocol, including GDMT, oral bumetanide, digoxin, opioids, and l-dopa. After enrollment, HF admissions were rare, and patients were able to die at home. These results suggest that end-of-life HF can be an outpatient illness.

Author Disclosure Statement

No competing financial interests exist.

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Address correspondence to:

George J. Taylor, MD

Ralph H. Johnson VA Medical Center

109 Bee Street

Charleston, SC 29401

E-mail: gtaylormd@gmail.com