Contemporary Reviews in Cardiovascular Medicine

Palliative Care in the Treatment of Advanced Heart Failure

Eric D. Adler, MD; Judith Z. Goldfinger, MD; Jill Kalman, MD; Michelle E. Park, BA; Diane E. Meier, MD

Heart failure is epidemic in developed countries and is expanding rapidly worldwide. Roughly 5% of patients with heart failure have end-stage disease that is refractory to medical therapy (stage D heart failure). Palliative care consultation relieves symptoms, improves patient satisfaction, and decreases the costs of care for these patients. Despite this, only a small fraction of end-stage heart failure patients receive palliative care consultation. In recognition of this, palliative/hospice care referral was recommended for end-stage heart failure (Level of Evidence 1A) in the most recent American College of Cardiology/American Heart Association heart failure guidelines.2

To identify evidence-based studies of palliative care in heart failure, we searched the Medline database for literature with the medical subject headings “heart failure” and “palliative care,” “supportive care,” or “symptom management” and found 394 results. We identified 92 systematic reviews, 44 of which were English-language systematic reviews published within the past 5 years.

The Burden of Advanced Heart Failure

More than 5 million Americans have heart failure, with a yearly incidence estimated to be >500,000. The number of deaths due to heart failure in 2004 was 284,365, which exceeds the deaths due to lung cancer, breast cancer, prostate cancer, and HIV/AIDS combined (Table 1).3–5 Even as the national death rate decreased by 2% from 1994 to 2004, deaths due to heart failure increased by 28%.

The yearly cost of heart failure was roughly $30 billion in 2006. The mean hospital length of stay is almost 6 days, and more than one third of patients are admitted for more than 5 days. Nearly half of the hospitalizations for heart failure exceed Medicare diagnosis-related groups reimbursement.7 Compared with all other patients, heart failure patients incur greater costs through increased physician visits, hospital admissions, and the need to spend twice as many days in intensive care units.8

End-stage heart failure has one of the largest effects on quality of life of any advanced disease.9 Patients living with serious illness have identified the following as their top-priority needs from the healthcare system: adequate pain and symptom management, avoidance of inappropriate prolongation of dying, achievement of a sense of control, relief of the burden on others, and a strengthening of relationships with loved ones.10 Although heart failure patients are often assumed principally to suffer from fatigue and dyspnea, a majority have pain, and depression is extremely common.11 Other sources of suffering include edema, insomnia, anxiety, confusion, anorexia, and constipation.12,13

Overview of Palliative Care

The palliative care movement began in the 1970s as a grassroots community hospice movement aimed at caring for cancer patients in their homes. Medicare added hospice services to its benefits in 1982.14 Patients who choose hospice must agree to forego curative or life-prolonging medical treatments. The mean length of stay for the more than 1.3 million patients who received hospice services in 2006 was 59 days, and the median length of stay was only 20.6 days.15 Nearly half of the patients enrolled in hospice have cancer as a primary diagnosis, and only 12.2% have a primary diagnosis of cardiac disease.16

Nonhospice palliative medicine is aimed at improving quality of life and supporting patients and the families of patients with serious and complex chronic illnesses in whom prognosis is uncertain or may be measured in years. Thus, the hospice care palliative model is based on patient prognosis, and the nonhospice palliative care model is based on patient and family needs, independent of prognosis. Palliative care aims to relieve suffering by a multidisciplinary and holistic approach that addresses patients’ and caregivers’ physical, emotional, spiritual, and logistical needs. Heart failure is associated with a notoriously variable prognosis, which is a barrier to timely hospice referral. Hence, it is important to ensure access to nonhospice palliative care in this patient population.

Relationship of Nonhospice Palliative Care to Hospice Palliative Care

Palliative care consultations increase referrals to hospice and result in earlier referrals to hospice. Late referrals to hospice correlate with lower overall family satisfaction, lower satisfaction with hospice services, more unmet needs, lack of awareness about what to expect at time of death, lower confidence in participating in patient care at home, and more concerns about coordination of care. In half of all cases of
late referral, family members reported that physicians were a barrier to earlier hospice referral.19 It can be difficult to determine when to transition from nonhospice palliative care to hospice, and this should be a group decision made among patient, family members, and healthcare providers. An ongoing assessment by the physician using prognostic models can help make it clear when death is likely to occur in less than 6 months. Furthermore, an increase in the frequency of hospitalizations may be a sign that hospice is appropriate. Traditional medical models view the curing of disease and the providing of comfort care as mutually exclusive. An integrative model, in which palliation occurs while life-prolonging therapies are administered, is more appropriate. Palliative therapies gradually expand as illnesses progress. Hospice is ultimately administered according to the patient’s wishes or when the harm of therapies outweighs their benefits (Figure 1).

**Palliative Care Effects on Clinical Outcomes**

Palliative care improves outcomes, including patient and family satisfaction with care and symptom management.20–26 Patients who receive in-home palliative care are more likely to die at home. This is consistent with the expressed wishes of most patients27 and leads to decreases in expenditures. Palliative care promotes patient well-being and dignity, communication with healthcare providers, emotional and spiritual support for the patient and the family, and access to community support services.17,19,21 In a recent nonrandomized study of hospice care, patients with end-stage heart failure paradoxically had an improvement in survival of 81 days compared with those who did not receive hospice.27 The study authors speculated that this increased longevity may be due to the avoidance of procedures and hospital stays with their attendant risk of nosocomial infection and adverse events, or because heart failure patients in the study may have benefited from the hospice focus on symptom relief, support for exhausted caregivers, and close attention to prevention of complications.

**Impact of Palliative Care on Healthcare Utilization and Costs**

Inpatient palliative care consultations decrease the number of procedures or interventions performed near the end of life,28,29 the length of stay in inpatient wards,17,24,30–33 the length of stay in intensive care wards,25,34,35 hospital direct costs including pharmacy and imaging, and the overall cost of care,24,25,30,32,33 A recent large study of 8 well-established hospital palliative care programs in the United States demonstrated that patients receiving palliative care services had an adjusted net savings of $4908 in direct costs per admission (P=0.003) and $374 in direct costs per day (P<0.001) compared with propensity-score–matched control subjects.36 Hospice has demonstrated an ability to provide significant cost savings as well. Hospice programs can save up to 40% of healthcare costs during the last month of life and up to 17% during the last 6 months of life, by an average of $2309 per hospice user.37,38 A 1995 study by Pyenson et al showed that enrollment in hospice resulted in a reduction in mean Medicare cost per heart failure patient from $53 528 to $46 792.39

**Guideline Recommendations for Palliation in End-Stage Heart Failure**

The 2005 American College of Cardiology and American Heart Association guidelines now include ongoing discussion with patients and families about prognosis for functional capacity and survival, advance directives, palliative care and hospice care, the option to deactivate implantable cardiac defibrillators (ICDs), and the provision of care geared toward symptom management, including use of opiates.2 The guidelines state that aggressive procedures performed in the last several months of life that do not contribute to recovery or improve quality of life, including intubation and implantation of a cardiac defibrillator, are not appropriate.

Guidelines do not specifically address when to refer end-stage heart failure patients for hospice/nonhospice palliative care.40 Unlike many cancers, which are characterized by a steep linear decline in performance status during the last few months of life, heart failure is characterized by unpredictable decompensations and improvements, with a subtler decline over time.41,42 This makes it difficult for doctors to recognize when it is appropriate to refer a patient to hospice. A sample algorithm for management of end-stage heart failure patients is found in Figure 2.

### Table 1. Incidence of and Number of Deaths Due to Heart Failure Compared With Other Common Causes of Death in the United States

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Incidence</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart failure</td>
<td>~500,000</td>
<td>284,365</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>196,252</td>
<td>158,006</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>188,587</td>
<td>41,316</td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>189,075</td>
<td>29,002</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>37,726</td>
<td>16,395</td>
</tr>
</tbody>
</table>

Figure 1. Palliative care integrative model. Palliative care is initiated when patients are diagnosed with any serious or advanced chronic illness. As illness progresses, the ratio of palliative care to life-prolonging care gradually increases. Ultimately, life-prolonging care is discontinued according to patient’s wishes or when the harm of treatment outweighs its benefit. At this point, the transition to hospice care is made. After death, palliative care services continue and help family members with bereavement.
Prognostication in Heart Failure

Prognostic tools and models developed for heart failure may be useful to help patients and care providers determine when to refer patients to hospice. There is a large body of evidence for prognostic prediction in heart failure, including single-item predictors such as the 6-minute walk test, evidence for prognostic prediction in heart failure, including advance directives, especially the appointment of a healthcare proxy decision maker, preferably early in the course of their disease. They must also be assured that such preferences can always be changed. Patients and families should be reminded that resuscitation only applies to a situation of cardiac or pulmonary arrest.

Central to a palliative approach to patient care is the establishment of shared decision making among the patient, families/caretakers, and the medical team. Goals of care, established by the patient, should specifically address circumstances under which a patient would prefer comfort measures to life-prolonging measures. Discussion of specific interventions such as a ventilator or cardiopulmonary resuscitation is less useful than helping patients articulate a condition they often consider to be worse than death, which is inability to communicate with loved ones. This is most commonly described as circumstances of permanent cognitive impairment, rendering communication with loved ones impossible.

Effective dialogue includes the following: “Some of my patients tell me that if they were permanently comatose or severely brain injured and unable to recognize or interact with loved ones, they would want care focused only on making sure they were comfortable. Other patients of mine tell me they would want all life-prolonging technologies, no matter how brain damaged they were. Which would you choose?” Recording a patient’s response to this kind of question provides guidance for future care decisions. Discussions about cardiopulmonary resuscitation should involve a clear recommendation from the physician. The patient should also be encouraged to identify a healthcare proxy who can make decisions on behalf of the patient if the patient is unable to do so. Table 3 contains general guidelines for communicating with patients about end-of-life issues.

Sources of Suffering in Advanced Heart Failure

The most common symptoms and comorbidities among patients with end-stage heart failure include dyspnea, pain, depression, fatigue, and edema. Evidence-based palliative approaches to these symptoms can be found below and are summarized in Table 4.

Dyspnea

The use of diuretics is the cornerstone of therapy. Patients with end-stage heart failure may develop increasing levels of diuretic resistance; in such patients, aquapheresis may be safe and beneficial. Afterload reduction with long-acting nitrroglycerin formulations such as isosorbide dinitrate, with or without the vasodilator hydralazine, may provide relief, but their use may be limited by hypotension. Inotropes may be appropriate in select patients. Multiple studies demonstrate the efficacy and safety of opioids for dyspnea. Doses are typically a small fraction of those required for analgesia, such as 2.5 mg of morphine or 1 mg of oxycodone. Benzodiazepines may help with symptoms of panic associated with breathlessness. Some evidence exists for less frequently used techniques for dyspnea, including neuroelectrical muscle stimulation, chest wall vibration, exercise and breathing training, and hawthorn extract. Insufficient data exist to judge the benefit of...
Table 2. Comparison of Heart Failure Prognostic Tools

<table>
<thead>
<tr>
<th>Model</th>
<th>Components</th>
<th>End Point</th>
<th>Validation C-Statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Failure Survival Score</td>
<td>• Ischemic cardiomyopathy, Resting heart rate, Ejection fraction, Mean resting blood pressure, Intraventricular conduction delay, Maximal oxygen consumption, Serum sodium, AND pulmonary capillary wedge pressure in the invasive model</td>
<td>Death at 1 y</td>
<td>0.79 (first 7 components; noninvasive model); 0.81 (8 components; invasive model)</td>
</tr>
<tr>
<td>Zugck 2-variable model</td>
<td>• Ejection fraction, Maximal oxygen consumption or 6-min walk test</td>
<td>Death at 1 y</td>
<td>0.84 (ejection fraction and maximal oxygen consumption); 0.85 (ejection fraction and 6-min walk test)</td>
</tr>
<tr>
<td>Bouvy model</td>
<td>• Age, Male sex, History of diabetes, History of renal insufficiency, Ankle edema, Body weight, Blood pressure, Use of β-blockers, New York Heart Association class, Minnesota Heart Failure Questionnaire</td>
<td>Death at 18 mo</td>
<td>0.85</td>
</tr>
<tr>
<td>Heart Failure Risk Scoring System</td>
<td>On admission: • Age, Respiratory rate, Systolic blood pressure, Blood urea nitrogen, Serum sodium, Comorbid conditions: cerebrovascular disease, dementia, chronic obstructive pulmonary disease, cirrhosis, cancer, anemia</td>
<td>Death at 30 d and 1 y</td>
<td>0.80 (at 30 d), 0.77 (at 1 y)</td>
</tr>
<tr>
<td>Digitalis Investigation Group model</td>
<td>• Age, Ejection fraction, New York Heart Association class, Cardiothoracic ratio &gt;50%, Clinical signs/symptoms, Serum creatinine, Body mass index, Blood pressure, Nitrate use, If diabetes, cause of heart failure</td>
<td>Death at 1 y and 3 y</td>
<td>Not reported</td>
</tr>
<tr>
<td>Acute Decompensated Heart Failure National Registry</td>
<td>• Systolic blood pressure, Blood urea nitrogen, Creatinine</td>
<td>Death in hospital</td>
<td>0.687</td>
</tr>
<tr>
<td>Seattle Heart Failure model</td>
<td>• Age, Sex, New York Heart Association class, Weight, Ejection fraction, Systolic blood pressure, Cause of heart failure, Medication use, Diuretic dose, Anemia, % Lymphocytes, Uric acid, Total cholesterol, Serum sodium, Intraventricular conduction delay, Use of devices</td>
<td>Death at 1 y, 2 y, 3 y</td>
<td>0.729</td>
</tr>
<tr>
<td>Munich score</td>
<td>• Cause of heart failure, Systolic blood pressure, Left ventricular end-diastolic diameter, Maximum workload, Percent worsening of fractional shortening</td>
<td>Death at 1 y, 2 y</td>
<td>Not reported</td>
</tr>
</tbody>
</table>
Table 3. Guidelines for Communication With Patients About Heart Failure Prognosis and Plan of Care

| Assessment: | Ask the patient what he or she understands about his or her condition. |
| Prognosis: | Be conscious that prognostic uncertainty is no excuse for a failure to communicate about the implications of advanced heart disease. |
| Preparation: | Prepare the patient emotionally for what to expect. |
| Preferences: | Discuss healthcare proxy, goals if patient is permanently brain injured, cardiopulmonary resuscitation, ventilators, and location of care. |
| Planning for the worst: | Suggest getting financial and emotional affairs in order. |

Acupuncture/acupressure or distractive auditory stimuli, such as music.

Pain

Pain is common and often undertreated in end-stage heart failure. Pharmacological agents that treat the underlying cause of pain, such as bisphosphonates for fractures and antianginals for angina, should be used when appropriate. Intracoronary stenting may be appropriate for select patients whose anginal pain is recalcitrant to pharmacotherapy. Nonsteroidal antiinflammatory drugs should be avoided, because the risks of gastrointestinal bleeding, renal failure, and fluid retention are high. Alternative therapies, such as acupuncture, exercise training, and music, may be beneficial, although they have not been studied extensively in heart failure patients.

Opioids should be used as first-line agents for moderate to severe pain. Combination agents, such as oxycodeone/acetaminophen, are generally not recommended because the adjuvant agents may prevent dose escalation. For long-lasting pain, it is best to initiate therapy with a short-acting agent such as morphine or codeine, then switch to sustained-release preparations after total daily requirements have been determined. Short-acting agents can still be used for breakthrough pain. Methadone is useful for long-term pain but may increase the QT interval. Meperidine, morphine, and codeine should be used with caution in patients with renal dysfunction. Agents can be given transdermally (fentanyl) or subcutaneously (morphine or hydromorphone) when patients can no longer tolerate oral agents.

Fearing addiction, providers and patients are often wary of opioids. Although opioids will predictably induce tolerance and physical dependency, studies suggest true addiction in terminally ill patients is rare. Manipulative behavior or dramatic demands for opioids should initially be assumed to be a result of undertreatment and will generally respond to appropriate analgesia.

Depression

Depression occurs in 21% to 36% of patients with heart failure. More severe heart failure correlates with increased rates of depression. Patients who report severe depression have increased rates of clinical events and rehospitalization and incur a higher death rate and economic cost. Large, well-designed trials of depression management in heart failure are lacking. To manage depression, uncontrolled symptoms, including pain and dyspnea, must be addressed. Psychotherapy and cognitive behavioral therapy may play a role. Exercise and acupuncture may benefit some patients, although evidence is generally lacking to support the latter.

When pharmacotherapy is begun, it is important to strike a balance between relieving symptoms of depression without adding onerous side effects. This may be particularly difficult in this patient population because of polypharmacy and concomitant liver and renal diseases that reduce medication clearance. Physicians may need to try several medications before identifying an effective and tolerable agent. Selective serotonin reuptake inhibitors (SSRIs) are generally used as first-line agents for pharmacotherapy because they are relatively efficacious and have few side effects. A low dose should be used initially, such as citalopram 10 mg or duloxetine 15 mg daily. Drugs with a high risk of drug–drug interaction, such as fluoxetine, should be avoided. Tricyclic antidepressants may be useful in patients with chronic pain, but antimuscarinic side effects are relatively common. They also may cause QT prolongation and arrhythmias. The serotonin norepinephrine reuptake inhibitors (SNRIs) show promise and may be used as an alternative to tricyclic antidepressants because they have similar effects but fewer side effects.

Edema

Edema can be a significant cause of discomfort in patients. As with dyspnea, it is treated principally with diuretics. Compression stockings may be effective for lower-extremity edema. Patients with refractory ascites may benefit from paracentesis, which also may improve renal function in patients with elevated intra-abdominal pressure.

Medical Therapy Discontinuation

As heart failure progresses, the focus shifts away from life-extending therapeutics to a focus on quality of life. In certain situations, the discontinuation of medical therapy may result in an improvement in quality of life. β-Blockers may need to be withdrawn in patients with refractory fluid overload or symptomatic bradycardia. Discontinuation of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers...
may be warranted if end-stage patients develop azotemia or symptomatic hypotension. The development of circulatory or renal limitations to the use of these drugs may be a prognostic sign that disease is progressing.90–92

**Inotropes in End-Stage Heart Failure**

Clinical trials of inotropic agents used to treat refractory symptoms of heart failure and low cardiac output have not demonstrated improvement in survival, but inotropic agents may provide symptomatic relief for prolonged periods of time.93 In a recent retrospective study of end-stage patients given continuous-infusion milrinone or dobutamine, the 6-month and 1-year survival rates were 58% and 44%, respectively.94 Both inotropes were associated with a decrease in hospitalizations. Of note, dobutamine had an overall cost-saving effect at 1 year, but milrinone was significantly more costly than standard therapy. Given the lack of survival benefit, the American College of Cardiology/American Heart Association guidelines classify intravenous inotropes as a Class IIB indication for end-stage heart failure. Some hospices, either inpatient or home based, provide intravenous inotrope therapy; however, cost considerations prevent many agencies from providing them.

**ICDs and Cardiac Resynchronization Therapy**

ICDs reduce the likelihood of death by decreasing sudden cardiac death due to arrhythmias.95 As heart failure worsens, patients are likely to receive more frequent shocks, which cause significant pain and anxiety.96 Clinicians infrequently discuss ICD deactivation with patients, and most devices remain active until death.97 Qualitative studies have shown that patients may not fully understand how their ICDs work and develop complex psychological relationships with their devices that may contribute to a reluctance to deactivate the ICDs.98 For end-stage heart failure patients, deactivation of ICDs when death is near is advisable to avoid repeated shocks.

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**Table 4. Common Heart Failure Symptoms and Palliative Treatment Options**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Class of Recommendation*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>IIA IIB IIC Insufficient</td>
</tr>
<tr>
<td>Pain</td>
<td>Opioids</td>
</tr>
<tr>
<td>Depression</td>
<td>Selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Treat secondary causes (anemia, infection, sleep apnea, etc)</td>
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<td>Fatigue</td>
<td>Treat secondary causes (anemia, infection, sleep apnea, etc)</td>
</tr>
</tbody>
</table>

*Based on authors’ recommendations, not established specific guidelines.

Class I: Conditions for which there is evidence for and/or general agreement that the procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

Class IIa: The weight of evidence or opinion is in favor of the procedure or treatment.

Class IIb: Usefulness/efficacy is less well established by evidence or opinion.

Class III: Conditions for which there is evidence and/or general agreement that the procedure or treatment is not useful/effective and in some cases may be harmful.

Insufficient: Insufficient evidence to make recommendation.
in a dying patient. Particular care should be taken to make sure that such dialogue occurs early on, while the patient is still capable of participating in the discussion, and that it is clearly documented in the medical record.\textsuperscript{99} Unlike defibrillators, cardiac resynchronization therapy has been shown to improve quality of life.\textsuperscript{100\textendash}102 Therefore, it may be appropriate to continue biventricular pacing for patients even when the decision has been made to turn off ICDs.

**Ventricular Assist Devices**

The Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure trial demonstrated that ventricular assist devices (VADs) improve quality of life and survival compared with inotropes.\textsuperscript{103} Subsequent analyses demonstrated that VADs improve exercise tolerance, normalize hemodynamics, and improve end-organ dysfunction and emotional well-being.\textsuperscript{104} Nevertheless, they are associated with high rates of bleeding, infection, and stroke.\textsuperscript{105,106} These complications are particularly prevalent in the elderly.\textsuperscript{107} Although patients often experience significant improvement in some of their symptoms, many other symptoms, including physical pain, major depression, and organic mental syndromes, may remain or occur de novo after VAD implantation.\textsuperscript{108} Patients may also require significantly more support from caregivers. Therefore, palliative care may need to be continued or initiated after VAD placement. Recent estimates suggest that the quality-adjusted life-year cost for the devices is between $36,000 and $60,000.\textsuperscript{109}

The management of VAD patients near the end of life poses unique challenges to the patient, family, and care provider. Patients may have abrupt VAD mechanical dysfunction that leads to a sudden decrease in cardiac output and rapid decompensation. Alternatively, the device may continue to function while the patient develops other complications or pathologies (eg, infectious, embolic, or renal). Machines may continue to work even after the patient is clinically brain dead, or they may prolong the dying process. It is critical that the patient establish advance directives before implantation that outline the conditions under which he or she desires the device to be turned off.

**Conclusions: A Mandate for Further Study and Education**

Palliative care and hospice have the potential to improve quality of life for heart failure patients, family members, and care providers. In addition, costs decrease significantly for payers, hospitals, patients, and families. Evidence suggests that these options are underused; when they are used, it is often so late in the course of illness that the potential of these options is undermined and their efficacy decreased.

Several strategies may be fruitful in making the implementation of palliation more common. Studies that randomize patients with end-stage heart failure to receive usual care versus obtaining palliative care consultations could help elucidate the effectiveness of palliative care consultations in improving symptoms and patient and family satisfaction with care and decreasing costs. Specific heart failure metrics, including the Minnesota Living With Heart Failure Questionnaire, could be used as well. The addition of palliative care education to the curriculum of fellows training in cardiology would likely increase the implementation of palliation. Given the tremendous physical, psychological, and economic burdens of end-stage heart failure, there is an increasing need for the use of palliation as an integral part of the treatment plan.

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