

## Palliative Care in the Treatment of Advanced Heart Failure

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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).<sup>1</sup> 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.<sup>2</sup>

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.<sup>3</sup> 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).<sup>3-5</sup> 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.<sup>6</sup> 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.<sup>7</sup> 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.<sup>8</sup>

End-stage heart failure has one of the largest effects on quality of life of any advanced disease.<sup>9</sup> 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.<sup>10</sup> Although heart failure patients are often assumed principally to suffer from fatigue and dyspnea, a majority have pain, and depression is extremely common.<sup>11</sup> Other sources of suffering include edema, insomnia, anxiety, confusion, anorexia, and constipation.<sup>12,13</sup>

### 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.<sup>14</sup> 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.<sup>15</sup> 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.<sup>16</sup>

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.<sup>17</sup> 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.<sup>18</sup> In half of all cases of

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

Cause of Death	Incidence	Deaths
Heart failure <sup>3</sup>	≈500 000	284 365
Lung cancer <sup>4</sup>	196 252	158 006
Breast cancer <sup>4</sup>	188 587	41 316
Prostate cancer <sup>4</sup>	189 075	29 002
HIV/AIDS <sup>5</sup>	37 726	16 395

late referral, family members reported that physicians were a barrier to earlier hospice referral.<sup>19</sup>

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.<sup>20–26</sup> Patients who receive in-home palliative care are more likely to die at home. This is consistent with the expressed wishes of most patients<sup>27</sup> 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.<sup>17,19,21</sup> 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.<sup>27</sup> 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

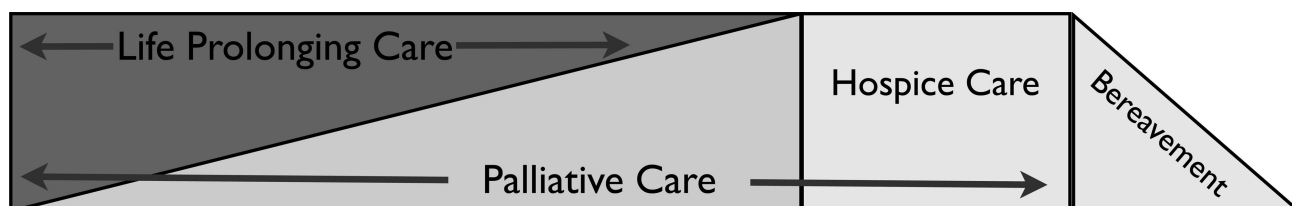
Inpatient palliative care consultations decrease the number of procedures or interventions performed near the end of life,<sup>28,29</sup> the length of stay in inpatient wards,<sup>17,24,30–33</sup> the length of stay in intensive care wards,<sup>25,34,35</sup> hospital direct costs including pharmacy and imaging, and the overall cost of care.<sup>24,25,30,32,33</sup> 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.<sup>36</sup>

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.<sup>37,38</sup> 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.<sup>39</sup>

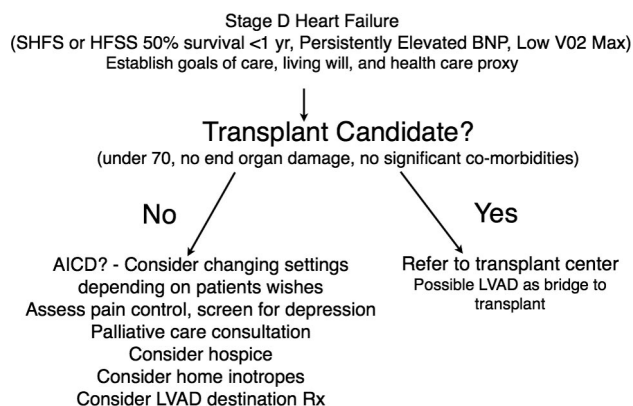
### Guideline Recommendations for Palliation in End-Stage Heart Failure

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.<sup>2</sup> 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.<sup>40</sup> 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.<sup>41,42</sup> 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.



**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.



**Figure 2.** Sample algorithm for treatment of end-stage heart failure. Prognostic scores are used to help evaluate which patients with optimally treated heart failure have stage D disease. Goals of care should be established in all patients. Appropriate patients should be referred for transplant/LVAD centers for evaluation. Pain should be addressed at every visit. Palliative care consultation and/or hospice care may be considered. SHFS indicates Seattle Heart Failure Score; HFSS, Heart Failure Survival Score; BNP, brain natriuretic peptide; AICD, automated ICD; LVAD, left ventricular assist device; and Rx, therapy.

### 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.<sup>16,43</sup> There is a large body of evidence for prognostic prediction in heart failure, including single-item predictors such as the 6-minute walk test,<sup>44</sup> maximal oxygen consumption,<sup>45</sup> B-type natriuretic peptide,<sup>46</sup> and creatinine levels,<sup>47</sup> as well as more complex multivariable models.<sup>43,48–55</sup> A summary of these models is presented in Table 2. Factors that predict an increased likelihood of death include frequent emergency department visits or hospitalizations, symptoms at rest, a dependency in activities of daily living, weight loss >10%, albumin <2.5 g/dL, ejection fraction <20%, symptomatic arrhythmia, prior cardiopulmonary resuscitation, prior syncope, and embolic stroke.

Although all of the models have particular strengths and weaknesses, the Seattle Heart Failure Score includes the greatest number of variables, such as adjustments for specific pharmacological and device-based therapies. It also provides prognostic data at 1, 2, and 5 years and has been validated thoroughly in a large patient population. Other less comprehensive systems, such as the ADHERE (Acute Decompensated Heart Failure National Registry) database scoring system, may be easier to use at the bedside.

### Communication in End-Stage Heart Failure

Bereaved family members of heart failure patients with nonsudden cardiac deaths reported minimal communication from physicians about what to expect. Specifically, only 37% were aware of a poor prognosis, only 8% of patients and 44% of family members were told by a physician that time was short, and 36% of these patients died alone.<sup>56</sup>

A crucial component of communication in heart failure is advanced care planning. Patients and families should discuss 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.<sup>57–59</sup> Evidence-based palliative approaches to these symptoms can be found below and are summarized in Table 4.<sup>60–82</sup>

#### Dyspnea

The use of diuretics is the cornerstone of therapy.<sup>60</sup> Patients with end-stage heart failure may develop increasing levels of diuretic resistance; in such patients, aquapheresis may be safe and beneficial.<sup>61</sup> Afterload reduction with long-acting nitroglycerin formulations such as isosorbide dinitrate, with or without the vasodilator hydralazine, may provide relief, but their use may be limited by hypotension.<sup>61</sup> Inotropes may be appropriate in select patients.<sup>64</sup> Multiple studies demonstrate the efficacy and safety of opioids for dyspnea.<sup>62,63</sup> 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.<sup>70</sup> Some evidence exists for less frequently used techniques for dyspnea, including neuroelectrical muscle stimulation, chest wall vibration, exercise and breathing training, and hawthorn extract.<sup>66–68</sup> Studies suggest oxygen is no better than room air for dyspnea in patients without hypoxia.<sup>69</sup> Insufficient data exist to judge the benefit of

**Table 2. Comparison of Heart Failure Prognostic Tools**

Model	Components	End Point	Validation C-Statistic
Heart Failure Survival Score <sup>48</sup>	<ul style="list-style-type: none"> <li>• Ischemic cardiomyopathy</li> <li>• Resting heart rate</li> <li>• Ejection fraction</li> <li>• Mean resting blood pressure</li> <li>• Intraventricular conduction delay</li> <li>• Maximal oxygen consumption</li> <li>• Serum sodium</li> <li>• AND pulmonary capillary wedge pressure in the invasive model</li> </ul>	Death at 1 y	0.79 (first 7 components; noninvasive model); 0.81 (8 components; invasive model)
Zugck 2-variable model <sup>49</sup>	<ul style="list-style-type: none"> <li>• Ejection fraction</li> <li>• Maximal oxygen consumption or 6-min walk test</li> </ul>	Death at 1 y	0.84 (ejection fraction and maximal oxygen consumption); 0.85 (ejection fraction and 6-min walk test)
Bouvy model <sup>50</sup>	<ul style="list-style-type: none"> <li>• Age</li> <li>• Male sex</li> <li>• History of diabetes</li> <li>• History of renal insufficiency</li> <li>• Ankle edema</li> <li>• Weight</li> <li>• Blood pressure</li> <li>• Use of <math>\beta</math>-blockers</li> <li>• New York Heart Association class</li> <li>• Minnesota Heart Failure Questionnaire</li> </ul>	Death at 18 mo	0.85
Heart Failure Risk Scoring System <sup>51</sup>	<p>On admission:</p> <ul style="list-style-type: none"> <li>• Age</li> <li>• Respiratory rate</li> <li>• Systolic blood pressure</li> <li>• Blood urea nitrogen</li> <li>• Serum sodium</li> <li>• Comorbid conditions: cerebrovascular disease, dementia, chronic obstructive pulmonary disease, cirrhosis, cancer, anemia</li> </ul>	Death at 30 d and 1 y	0.80 (at 30 d), 0.77 (at 1 y)
Digitalis Investigation Group model <sup>52</sup>	<ul style="list-style-type: none"> <li>• Age</li> <li>• Ejection fraction</li> <li>• New York Heart Association class</li> <li>• Cardiothoracic ratio &gt;50%</li> <li>• Clinical signs/symptoms</li> <li>• Serum creatinine</li> <li>• Body mass index</li> <li>• Blood pressure</li> <li>• Nitrate use</li> <li>• If diabetes, cause of heart failure</li> </ul>	Death at 1 y and 3 y	Not reported
Acute Decompensated Heart Failure National Registry <sup>53</sup>	<ul style="list-style-type: none"> <li>• Systolic blood pressure</li> <li>• Blood urea nitrogen</li> <li>• Creatinine</li> </ul>	Death in hospital	0.687
Seattle Heart Failure model <sup>54</sup>	<ul style="list-style-type: none"> <li>• Age</li> <li>• Sex</li> <li>• New York Heart Association class</li> <li>• Weight</li> <li>• Ejection fraction</li> <li>• Systolic blood pressure</li> <li>• Cause of heart failure</li> <li>• Medication use</li> <li>• Diuretic dose</li> <li>• Anemia</li> <li>• % Lymphocytes</li> <li>• Uric acid</li> <li>• Total cholesterol</li> <li>• Serum sodium</li> <li>• Intraventricular conduction delay</li> <li>• Use of devices</li> </ul>	Death at 1 y, 2 y, 3 y	0.729
Munich score <sup>55</sup>	<ul style="list-style-type: none"> <li>• Cause of heart failure</li> <li>• Systolic blood pressure</li> <li>• Left ventricular end-diastolic diameter</li> <li>• Maximum workload</li> <li>• Percent worsening of fractional shortening</li> </ul>	Death at 1 y, 2 y	Not reported

**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.

Provide approximate time estimates (eg, months or years?).

Talk about some likely scenarios.

**Preferences:**

Discuss healthcare proxy, goals if patient is permanently brain injured, cardiopulmonary resuscitation, ventilators, and location of care.

Discuss deactivation of ICD/cardiac resynchronization therapy/VAD, if applicable.

**Planning for the worst:**

Suggest getting financial and emotional affairs in order.

Help to mobilize community and family supports (eg, palliative care, home care, hospice referrals).

acupuncture/acupressure or distractive auditory stimuli, such as music.<sup>67</sup>

**Pain**

Pain is common and often undertreated in end-stage heart failure.<sup>59</sup> Pharmacological agents that treat the underlying cause of pain, such as bisphosphonates for fractures<sup>1</sup> and antianginals for angina,<sup>72</sup> should be used when appropriate. Intracoronary stenting may be appropriate for select patients whose anginal pain is recalcitrant to pharmacotherapy.<sup>72</sup> Non-steroidal antiinflammatory drugs should be avoided, because the risks of gastrointestinal bleeding, renal failure, and fluid retention are high.<sup>71</sup> Alternative therapies, such as acupuncture, exercise training, and music, may be beneficial, although they have not been studied extensively in heart failure patients.<sup>73–75</sup>

Opioids should be used as first-line agents for moderate to severe pain. Combination agents, such as oxycodone/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 dependence, studies suggest true addiction in terminally ill patients is rare.<sup>83</sup> 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.<sup>84,85</sup> 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.<sup>86</sup> Large, well-designed trials of depression management in heart failure are lacking.<sup>85,86</sup> To manage depression, uncontrolled symptoms, including pain and dyspnea, must be addressed. Psychotherapy and cognitive behavioral therapy may play a role.<sup>77</sup> Exercise and acupuncture may benefit some patients, although evidence is generally lacking to support the latter.<sup>78,79</sup>

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.<sup>87</sup> 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.<sup>87</sup> 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.<sup>88</sup>

**Fatigue**

The foundation for treatment of fatigue is the identification and treatment of secondary causes such as anemia, infection, dehydration, electrolyte abnormalities, thyroid dysfunction, and depression. Pharmacological options for primary fatigue include stimulants, such as methylphenidate, as well as nonpharmacological techniques, such as training in energy conservation and aerobic exercise.<sup>80,81</sup> Sleep apnea may lead to fatigue and can be treated with noninvasive ventilation.<sup>82</sup>

**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.<sup>89</sup>

**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.  $\beta$ -Blockers may need to be withdrawn in patients with refractory fluid overload or symptomatic bradycardia.<sup>90,91</sup> Discontinuation of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers

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

Symptom	Class of Recommendation*				
	I	IIA	IIB	III	Insufficient
Dyspnea	Loop diuretics with or without thiazides <sup>60</sup> Nitrates <sup>61</sup> Low-dose opioids <sup>62,63</sup>	Inotropes <sup>64</sup> Aquapheresis (if diuretic resistance) <sup>65</sup> Walking aids <sup>66</sup> Breathing training <sup>66</sup> Exercise training <sup>67</sup> Hawthorn extract <sup>68</sup>	Oxygen (without hypoxia) <sup>69</sup>	Benzodiazepines <sup>70</sup>	Acupuncture/ acupressure <sup>67</sup> Distractive auditory stimuli, ie, music <sup>67</sup> Relaxation techniques <sup>67</sup> Psychotherapy <sup>67</sup> Fans <sup>67</sup> Nebulized opioids <sup>64</sup>
Pain	Opioids <sup>71</sup> Bone pain: bisphosphonates <sup>71</sup> Anginal pain: nitrates, $\beta$ -blockers, calcium channel blockers, ranolazine, coronary revascularization <sup>72</sup>	Psychological interventions: cognitive behavioral therapy, counseling, or supportive therapy <sup>77</sup>	Acupuncture <sup>73</sup> Exercise training <sup>74</sup> Music <sup>75</sup>	Nonsteroidal antiinflammatory drugs <sup>71</sup>	
Depression	Selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants <sup>76</sup>		Exercise <sup>78</sup>		Acupuncture <sup>79</sup>
Fatigue		Treat secondary causes (anemia, infection, sleep apnea, etc) <sup>80-82</sup> Stimulants <sup>80,81</sup> Exercise training <sup>81</sup> Hawthorn extract <sup>68</sup>		Increased rest and reduction of physical activity <sup>81</sup>	Anti-inflammatory agents <sup>81</sup> L-carnitine <sup>81</sup> Nutritional supplements or appetite stimulants <sup>81</sup>

\*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.

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.<sup>90-92</sup>

### 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.<sup>93</sup> 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.<sup>94</sup> 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.<sup>95</sup> As heart failure worsens, patients are likely to receive more frequent shocks, which cause significant pain and anxiety.<sup>96</sup> Clinicians infrequently discuss ICD deactivation with patients, and most devices remain active until death.<sup>97</sup> 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.<sup>98</sup> For end-stage heart failure patients, deactivation of ICDs when death is near is advisable to avoid repeated shocks

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.<sup>99</sup> Unlike defibrillators, cardiac resynchronization therapy has been shown to improve quality of life.<sup>100–102</sup> 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.<sup>103</sup> Subsequent analyses demonstrated that VADs improve exercise tolerance, normalize hemodynamics, and improve end-organ dysfunction and emotional well-being.<sup>104</sup> Nevertheless, they are associated with high rates of bleeding, infection, and stroke.<sup>105,106</sup> These complications are particularly prevalent in the elderly.<sup>107</sup> 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.<sup>108</sup> 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.<sup>109</sup>

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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### Disclosures

None.

### References

1. Costanzo MR, Mills RM, Wynne J. Characteristics of "stage D" heart failure: insights from the Acute Decompensated Heart Failure National Registry Longitudinal Module (ADHERE LM). *Am Heart J*. 2008;155:339–347.
2. Hunt SA, Abraham WT, Chin MH, Feldman AM, Francis GS, Ganiats TG, Jessup M, Konstam MA, Mancini DM, Michl K, Oates JA, Rahko PS, Silver MA, Stevenson LW, Yancy CW, Antman EM, Smith SC Jr, Adams CD, Anderson JL, Faxon DP, Fuster V, Halperin JL, Hiratzka LF, Jacobs AK, Nishimura R, Ornato JP, Page RL, Riegel B; American College of Cardiology; American Heart Association Task Force on Practice Guidelines; American College of Chest Physicians; International Society for Heart and Lung Transplantation; Heart Rhythm Society. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure): developed in collaboration with the American College of Chest Physicians and the International Society for Heart and Lung Transplantation: endorsed by the Heart Rhythm Society. *Circulation*. 2005;112:e154–e235.
3. Rosamond W, Flegal K, Furie K, Go A, Greenlund K, Haase N, Hailpern SM, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell C, Roger V, Sorlie P, Steinberger J, Thom T, Wilson M, Hong Y; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics: 2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2008;117:e25–e146.
4. US Cancer Statistics Working Group. United States cancer statistics (USCS): 1999–2004 incidence and mortality. Web-based report. Atlanta, Ga: US Dept of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2007. Available at: [www.cdc.gov/uscs](http://www.cdc.gov/uscs). Accessed June 13, 2008.
5. Centers for Disease Control and Prevention. HIV/AIDS surveillance report, 2006. Vol 18. Atlanta, Ga: US Dept of Health and Human Services, Centers for Disease Control and Prevention; 2008. Available at: [www.cdc.gov/uscs](http://www.cdc.gov/uscs). Accessed June 13, 2008.
6. Thom T, Haase N, Rosamond W, Howard VJ, Rumsfeld J, Manolio T, Zheng ZJ, Flegal K, O'Donnell C, Kittner S, Lloyd-Jones D, Goff DC Jr, Hong Y, Adams R, Friday G, Furie K, Gorelick P, Kissela B, Marler J, Meigs J, Roger V, Sidney S, Sorlie P, Steinberger J, Wasserthiel-Smoller S, Wilson M, Wolf P; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics: 2006 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2006;113:e85–e151.
7. Hauptman PJ, Swindle J, Burroughs TE, Schnitzler MA. Resource utilization in patients hospitalized with heart failure: insights from a contemporary national hospital database. *Am Heart J*. 2008;155:978–985.e1.
8. Liao L, Anstrom KJ, Gottdiener JS, Pappas PA, Whellan DJ, Kitzman DW, Aurigemma GP, Mark DB, Schulman KA, Jollis JG. Long-term

- costs and resource use in elderly participants with congestive heart failure in the Cardiovascular Health Study. *Am Heart J*. 2007;153:245–252.
9. Bekelman DB, Havranek EP, Becker DM, Kutner JS, Peterson PN, Wittstein IS, Gottlieb SH, Yamashita TE, Fairclough DL, Dy SM. Symptoms, depression, and quality of life in patients with heart failure. *J Card Fail*. 2007;13:643–648.
  10. Singer PA, Martin DK, Kelner M. Quality end-of-life care: patients' perspectives. *JAMA*. 1999;281:163–168.
  11. Goodlin SJ. Palliative care for end-stage heart failure. *Curr Heart Fail Rep*. 2005;2:155–160.
  12. McCarthy M, Lay M, Addington-Hall J. Dying from heart disease. *J R Coll Physicians Lond*. 1996;30:325–328.
  13. Lynn J, Teno JM, Phillips RS, Wu AW, Desbiens N, Harrold J, Claessens MT, Wenger N, Kreling B, Connors AF Jr. Perceptions by family members of the dying experience of older and seriously ill patients: SUPPORT Investigators: Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments. *Ann Intern Med*. 1997;126:97–106.
  14. Connor SR. Development of hospice and palliative care in the United States. *Omega (Westport)*. 2007;56:89–99.
  15. Taylor DH Jr, Ostermann J, Van Houtven CH, Tulskey JA, Steinhauser K. What length of hospice use maximizes reduction in medical expenditures near death in the US Medicare program? *Soc Sci Med*. 2007;65:1466–1478.
  16. Fox E, Landrum-Mcniff K, Zhong Z, Dawson NV, Wu AW, Lynn J. Evaluation of prognostic criteria for determining hospice eligibility in patients with advanced lung, heart, or liver disease: SUPPORT Investigators: Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments. *JAMA*. 1999;282:1638–1645.
  17. Campbell ML, Frank RR. Experience with an end-of-life practice at a university hospital. *Crit Care Med*. 1997;25:197–202.
  18. Schockett ER, Teno JM, Miller SC, Stuart B. Late referral to hospice and bereaved family member perception of quality of end-of-life care. *J Pain Symptom Manage*. 2005;30:400–407.
  19. Teno JM, Clarridge BR, Casey V, Welch LC, Wetle T, Shield R, Mor V. Family perspectives on end-of-life care at the last place of care. *JAMA*. 2004;291:88–93.
  20. Connor SR, Teno J, Spence C, Smith N. Family evaluation of hospice care: results from voluntary submission of data via website. *J Pain Symptom Manage*. 2005;30:9–17.
  21. Casarett D, Pickard A, Bailey FA, Ritchie C, Furman C, Rosenfeld K, Shreve S, Chen Z, Shea JA. Do palliative consultations improve patient outcomes? *J Am Geriatr Soc*. 2008;56:593–599.
  22. Gries CJ, Curtis JR, Wall RJ, Engelberg RA. Family member satisfaction with end-of-life decision making in the ICU. *Chest*. 2008;133:704–712.
  23. Finlay IG, Higginson IJ, Goodwin DM, Cook AM, Edwards AG, Hood K, Douglas HR, Normand CE. Palliative care in hospital, hospice, at home: results from a systematic review. *Ann Oncol*. 2002;13(suppl 4):257–264.
  24. Higginson IJ, Finlay I, Goodwin DM, Cook AM, Hood K, Edwards AG, Douglas HR, Norman CE. Do hospital-based palliative teams improve care for patients or families at the end of life? *J Pain Symptom Manage*. 2002;23:96–106.
  25. Gade G, Venohr I, Conner D, Mcgrady K, Beane J, Richardson RH, Williams MP, Liberson M, Blum M, Penna RD. Impact of an inpatient palliative care team: a randomized control trial. *J Palliat Med*. 2008;11:180–190.
  26. Higginson IJ, Romer AL. Measuring quality of care in palliative care services. *J Palliat Med*. 2000;3:229–236.
  27. Connor SR, Pyenson B, Fitch K, Spence C, Iwasaki K. Comparing hospice and nonhospice patient survival among patients who die within a three-year window. *J Pain Symptom Manage*. 2007;33:238–246.
  28. Field BE, Devich LE, Carlson RW. Impact of a comprehensive supportive care team on management of hopelessly ill patients with multiple organ failure. *Chest*. 1989;96:353–356.
  29. Tse DM, Chan KS, Lam WM, Leu K, Lam PT. The impact of palliative care on cancer deaths in Hong Kong: a retrospective study of 494 cancer deaths. *Palliat Med*. 2007;21:425–433.
  30. Carlson RW, Devich L, Frank RR. Development of a comprehensive supportive care team for the hopelessly ill on a university hospital medical service. *JAMA*. 1988;259:378–383.
  31. Campbell ML, Guzman JA. Impact of a proactive approach to improve end-of-life care in a medical ICU. *Chest*. 2003;123:266–271.
  32. Smith TJ, Coyne P, Cassel B, Penberthy L, Hopson A, Hager MA. A high-volume specialist palliative care unit and team may reduce in-hospital end-of-life care costs. *J Palliat Med*. 2003;6:699–705.
  33. Bruera E, Neumann CM, Gagnon B, Brenneis C, Quan H, Hanson J. The impact of a regional palliative care program on the cost of palliative care delivery. *J Palliat Med*. 2000;3:181–186.
  34. Lilly CM, De Meo DL, Sonna LA, Haley KJ, Massaro AF, Wallace RF, Cody S. An intensive communication intervention for the critically ill. *Am J Med*. 2000;109:469–475.
  35. Norton SA, Hogan LA, Holloway RG, Temkin-Greener H, Buckley MJ, Quill TE. Proactive palliative care in the medical intensive care unit: effects on length of stay for selected high-risk patients. *Crit Care Med*. 2007;35:1530–1535.
  36. Morrison RS, Penrod JD, Cassel JB, Caust-Ellenbogen M, Litke A, Spragens L, Meier DE. Cost savings associated with US hospital palliative care consultation programs. *Arch Intern Med*. 2008;168:1783–1790.
  37. Emanuel EJ. Cost savings at the end of life: what do the data show? *JAMA*. 1996;275:1907–1914.
  38. Taylor DO, Edwards LB, Boucek MM, Trulock EP, Aurora P, Christie J, Dobbels F, Rahmel AO, Keck BM, Hertz MI. Registry of the International Society for Heart and Lung Transplantation: twenty-fourth official adult heart transplant report—2007. *J Heart Lung Transplant*. 2007;26:769–781.
  39. Pyenson B, Connor S, Fitch K, Kinzbrunner B. Medicare cost in matched hospice and non-hospice cohorts. *J Pain Symptom Manage*. 2004;28:200–210.
  40. Hauptman PJ, Havranek EP. Integrating palliative care into heart failure care. *Arch Intern Med*. 2005;165:374–378.
  41. Teno JM, Weitzen S, Fennell ML, Mor V. Dying trajectory in the last year of life: does cancer trajectory fit other diseases? *J Palliat Med*. 2001;4:457–464.
  42. Davis MP, Albert NM, Young JB. Palliation of heart failure. *Am J Hosp Palliat Care*. 2005;22:211–222.
  43. Huynh BC, Rovner A, Rich MW. Identification of older patients with heart failure who may be candidates for hospice care: development of a simple four-item risk score. *J Am Geriatr Soc*. 2008;56:1111–1115.
  44. Bittner V, Weiner DH, Yusuf S, Rogers WJ, McIntyre KM, Bangdiwala SI, Kronenberg MW, Kostis JB, Kohn RM, Guillolette M: SOLVD Investigators. Prediction of mortality and morbidity with a 6-minute walk test in patients with left ventricular dysfunction. *JAMA*. 1993;270:1702–1707.
  45. Mancini D, Lejemtel T, Aaronson K. Peak  $VO_2$ : a simple yet enduring standard. *Circulation*. 2000;101:1080–1082.
  46. Doust JA, Pietrzak E, Dobson A, Glasziou P. How well does B-type natriuretic peptide predict death and cardiac events in patients with heart failure: systematic review. *BMJ*. 2005;330:625.
  47. Smith GL, Vaccarino V, Kosiborod M, Lichtman JH, Cheng S, Watnick SG, Krumholz HM. Worsening renal function: what is a clinically meaningful change in creatinine during hospitalization with heart failure? *J Card Fail*. 2003;9:13–25.
  48. Aaronson KD, Schwartz JS, Chen TM, Wong KL, Goin JE, Mancini DM. Development and prospective validation of a clinical index to predict survival in ambulatory patients referred for cardiac transplant evaluation. *Circulation*. 1997;95:2660–2667.
  49. Zugck C, Kruger C, Kell R, Korber S, Schellberg D, Kubler W, Haass M. Risk stratification in middle-aged patients with congestive heart failure: prospective comparison of the Heart Failure Survival Score (HFSS) and a simplified two-variable model. *Eur J Heart Fail*. 2001;3:577–585.
  50. Bouvy ML, Heerdink ER, Leufkens HG, Hoes AW. Predicting mortality in patients with heart failure: a pragmatic approach. *Heart*. 2003;89:605–609.
  51. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. *JAMA*. 2003;290:2581–2587.
  52. Brophy JM, Dagenais GR, McSherry F, Williford W, Yusuf S. A multivariate model for predicting mortality in patients with heart failure and systolic dysfunction. *Am J Med*. 2004;116:300–304.
  53. Fonarow GC, Abraham WT, Yancy CW, Boscardin WJ; ADHERE Scientific Advisory Committee, Study Group, and Investigators. Risk stratification for in-hospital mortality in acutely decompensated heart failure: classification and regression tree analysis. *JAMA*. 2005;293:572–580.



54. Levy WC, Mozaffarian D, Linker DT, Sutradhar SC, Anker SD, Cropp AB, Anand I, Maggioni A, Burton P, Sullivan MD, Pitt B, Poole-Wilson PA, Mann DL, Packer M. The Seattle Heart Failure Model: prediction of survival in heart failure. *Circulation*. 2006;113:1424–1433.
55. Stempfle HU, Alt A, Stief J, Siebert U. The Munich score: a clinical index to predict survival in ambulatory patients with chronic heart failure in the era of new medical therapies. *J Heart Lung Transplant*. 2008;27:222–228.
56. McCarthy M, Hall JA, Ley M. Communication and choice in dying from heart disease. *J R Soc Med*. 1997;90:128–131.
57. Goodlin SJ, Hauptman PJ, Arnold R, Grady K, Hershberger RE, Kutner J, Masoudi F, Spertus J, Dracup K, Cleary JF, Medak R, Crispell K, Pina I, Stuart B, Whitney C, Rector T, Teno J, Renlund DG. Consensus statement: palliative and supportive care in advanced heart failure. *J Card Fail*. 2004;10:200–209.
58. Lorenz KA, Lynn J, Dy SM, Shugarman LR, Wilkinson A, Mularski RA, Morton SC, Hughes RG, Hilton LK, Maglione M, Rhodes SL, Rolon C, Sun VC, Shekelle PG. Evidence for improving palliative care at the end of life: a systematic review. *Ann Intern Med*. 2008;148:147–159.
59. Nordgren L, Sorensen S. Symptoms experienced in the last six months of life in patients with end-stage heart failure. *Eur J Cardiovasc Nurs*. 2003;2:213–217.
60. Faris R, Flather MD, Purcell H, Poole-Wilson PA, Coats AJ. Diuretics for heart failure. *Cochrane Database Syst Rev*. 2006;CD003838.
61. Cotter G, Metzkor E, Kaluski E, Faigenberg Z, Miller R, Simovitz A, Shaham O, Marghitay D, Koren M, Blatt A, Moshkovitz Y, Zaidenstein R, Golik A. Randomised trial of high-dose isosorbide dinitrate plus low-dose furosemide versus high-dose furosemide plus low-dose isosorbide dinitrate in severe pulmonary oedema. *Lancet*. 1998;351:389–393.
62. Jennings AL, Davies AN, Higgins JP, Gibbs JS, Broadley KE. A systematic review of the use of opioids in the management of dyspnoea. *Thorax*. 2002;57:939–944.
63. Abernethy AP, Currow DC, Frith P, Fazekas BS, McHugh A, Bui C. Randomised, double blind, placebo controlled crossover trial of sustained release morphine for the management of refractory dyspnoea. *BMJ*. 2003;327:523–528.
64. Packer M. Effect of vasodilator and inotropic drugs on clinical symptoms and long-term survival in chronic congestive heart failure. *Eur Heart J*. 1988;9(suppl H):105–108.
65. Costanzo MR, Guglin ME, Saltzberg MT, Jessup ML, Bart BA, Teerlink JR, Jaski BE, Fang JC, Feller ED, Haas GJ, Anderson AS, Schollmeyer MP, Sobotka PA; UNLOAD Trial Investigators. Ultrafiltration versus intravenous diuretics for patients hospitalized for acute decompensated heart failure. *J Am Coll Cardiol*. 2007;49:675–683.
66. Bausewein C, Booth S, Gysels M, Higginson I. Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases. *Cochrane Database Syst Rev*. 2008;CD005623.
67. Pozehl B, Duncan K, Hertzog M. The effects of exercise training on fatigue and dyspnea in heart failure. *Eur J Cardiovasc Nurs*. 2008;7:127–132.
68. Pittler MH, Guo R, Ernst E. Hawthorn extract for treating chronic heart failure. *Cochrane Database Syst Rev*. 2008;CD005312.
69. Booth S, Anderson H, Swannick M, Wade R, Kite S, Johnson M. The use of oxygen in the palliation of breathlessness: a report of the expert working group of the Scientific Committee of the Association of Palliative Medicine. *Respir Med*. 2004;98:66–77.
70. Currow DC, Abernethy AP. Pharmacological management of dyspnoea. *Curr Opin Support Palliat Care*. 2007;1:96–101.
71. Qaseem A, Snow V, Shekelle P, Casey DE, Cross JT, Owens DK; Clinical Efficacy Assessment Subcommittee of the American College of Physicians; Dallas P, Dolan NC, Forciea MA, Halasyamani L, Hopkins RH, Shekelle P. Evidence-based interventions to improve the palliative care of pain, dyspnea, and depression at the end of life: a clinical practice guideline from the American College of Physicians. *Ann Intern Med*. 2008;148:141–146.
72. Fraker TD, Fihn SD, Gibbons RJ, Abrams J, Chatterjee K, Daley J, Deedwania PC, Douglas JS, Ferguson TB, Gardin J, O'Rourke RA, Williams SV, Smith SC, Jacobs AK, Adams CD, Anderson JL, Buller C, Creager MA, Ettinger SM, Halperin JL, Hunt SA, Krumholz H, Kushner FG, Lytle BW, Nishimura R, Page RL, Riegel B, Tarkington LG, Yancy C. 2007 Chronic angina focused update of the ACC/AHA 2002 guidelines for the management of patients with chronic stable angina: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines Writing Group to develop the focused update of the 2002 guidelines for the management of patients with chronic stable angina. *J Am Coll Cardiol*. 2007;50:2264–2274.
73. Lee H, Schmidt K, Ernst E. Acupuncture for the relief of cancer-related pain: a systematic review. *Eur J Pain*. 2005;9:437–444.
74. Knols R, Aaronson NK, Uebelhart D, Franssen J, Aufdemkampe G. Physical exercise in cancer patients during and after medical treatment: a systematic review of randomized and controlled clinical trials. *J Clin Oncol*. 2005;23:3830–3842.
75. Cepeda MS, Carr DB, Lau J, Alvarez H. Music for pain relief. *Cochrane Database Syst Rev*. 2006;CD004843.
76. Rutledge T, Reis VA, Linke SE, Greenberg BH, Mills PJ. Depression in heart failure: a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes. *J Am Coll Cardiol*. 2006;48:1527–1537.
77. Lane DA, Chong AY, Lip GY. Psychological interventions for depression in heart failure. *Cochrane Database Syst Rev*. 2005;CD003329.
78. Ströhle A. Physical activity, exercise, depression and anxiety disorders. *J Neural Transm*. 2009;116:777–784.
79. Smith CA, Hay PP. Acupuncture for depression. *Cochrane Database Syst Rev*. 2005;CD004046.
80. Harris JD. Fatigue in chronically ill patients. *Curr Opin Support Palliat Care*. 2008;2:180–186.
81. Radbruch L, Strasser F, Elsner F, Goncalves JF, Loge J, Kaasa S, Nauck F, Stone P; Research Steering Committee of the European Association for Palliative Care (EAPC). Fatigue in palliative care patients: an EAPC approach. *Palliat Med*. 2008;22:13–32.
82. Ponikowski P, Anker SD, Chua TP, Francis D, Banasiak W, Poole-Wilson PA, Coats AJ, Piepoli M. Oscillatory breathing patterns during wakefulness in patients with chronic heart failure: clinical implications and role of augmented peripheral chemosensitivity. *Circulation*. 1999;100:2418–2424.
83. Kanner RM. Opioids for severe pain: little change over 15 years. *J Pain Symptom Manage*. 2001;21:3.
84. Koenig HG. Physician attitudes toward treatment of depression in older medical inpatients. *Aging Ment Health*. 2007;11:197–204.
85. Faris R, Purcell H, Henein MY, Coats AJ. Clinical depression is common and significantly associated with reduced survival in patients with non-ischaemic heart failure. *Eur J Heart Fail*. 2002;4:541–551.
86. Sullivan M, Simon G, Spertus J, Russo J. Depression-related costs in heart failure care. *Arch Intern Med*. 2002;162:1860–1866.
87. Solai LK, Mulsant BH, Pollock B. Selective serotonin reuptake inhibitors for late-life depression: a comparative review. *Drugs Aging*. 2001;18:355–368.
88. Degner D, Grohmann R, Bleich S, Ruther E. New antidepressant drugs: what side effects and interactions are to be expected? *MMW Fortschr Med*. 2000;142:35–38, 40.
89. Mullens W, Abrahams Z, Francis GS, Taylor DO, Starling RC, Tang WH. Prompt reduction in intra-abdominal pressure following large-volume mechanical fluid removal improves renal insufficiency in refractory decompensated heart failure. *J Card Fail*. 2008;14:508–514.
90. Packer M, Bristow MR, Cohn JN, Colucci WS, Fowler MB, Gilbert EM, Shusterman NH; US Carvedilol Heart Failure Study Group. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. *N Engl J Med*. 1996;334:1349–1355.
91. Fonarow GC, Abraham WT, Albert NM, Stough WG, Gheorghiadu M, Greenberg BH, O'Connor CM, Sun JL, Yancy CW, Young JB; OPTIMIZE-HF Investigators and Coordinators. Influence of beta-blocker continuation or withdrawal on outcomes in patients hospitalized with heart failure: findings from the OPTIMIZE-HF program. *J Am Coll Cardiol*. 2008;52:190–199.
92. Kittleson M, Hurwitz S, Shah MR, Nohria A, Lewis E, Givertz M, Fang J, Jarcho J, Mudge G, Stevenson LW. Development of circulatory-renal limitations to angiotensin-converting enzyme inhibitors identifies patients with severe heart failure and early mortality. *J Am Coll Cardiol*. 2003;41:2029–2035.
93. Sindone AP, Keogh AM, Macdonald PS, McCosker CJ, Kaan AF. Continuous home ambulatory intravenous inotropic drug therapy in severe heart failure: safety and cost efficacy. *Am Heart J*. 1997;134:889–900.
94. Hauptman PJ, Mikolajczak P, George A, Mohr CJ, Hoover R, Swindle J, Schnitzler MA. Chronic inotropic therapy in end-stage heart failure. *Am Heart J*. 2006;152:1096.e1–1096.e8.

95. Moss AJ, Hall WJ, Cannom DS, Daubert JP, Higgins SL, Klein H, Levine JH, Saksena S, Waldo AL, Wilber D, Brown MW, Heo M; Multicenter Automatic Defibrillator Implantation Trial Investigators. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. *N Engl J Med.* 1996;335:1933–1940.
96. Sears SF Jr, Conti JB. Quality of life and psychological functioning of ICD patients. *Heart.* 2002;87:488–493.
97. Goldstein NE, Lampert R, Bradley E, Lynn J, Krumholz HM. Management of implantable cardioverter defibrillators in end-of-life care. *Ann Intern Med.* 2004;141:835–838.
98. Goldstein NE, Mehta D, Siddiqui S, Teitelbaum E, Zeidman J, Singson M, Pe E, Bradley EH, Morrison RS. “That’s like an act of suicide” patients’ attitudes toward deactivation of implantable defibrillators. *J Gen Intern Med.* 2008;23(suppl 1):7–12.
99. Nohria A, Lewis E, Stevenson LW. Medical management of advanced heart failure. *JAMA.* 2002;287:628–640.
100. Cleland JG, Daubert JC, Erdmann E, Freemantle N, Gras D, Kappenberger L, Tavazzi L; Cardiac Resynchronization-Heart Failure (Care-Hf) Study Investigators. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med.* 2005;352:1539–1549.
101. Bristow MR, Saxon LA, Boehmer J, Krueger S, Kass DA, De Marco T, Carson P, Dicarolo L, Demets D, White BG, Devries DW, Feldman AM; Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (Companion) Investigators. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med.* 2004;350:2140–2150.
102. Epstein AE, Dimarco JP, Ellenbogen KA, Estes NA, Freedman RA, Gettes LS, Gillinov AM, Gregoratos G, Hammill SC, Hayes DL, Hlatky MA, Newby LK, Page RL, Schoenfeld MH, Silka MJ, Stevenson LW, Sweeney MO, Smith SC, Jacobs AK, Adams CD, Anderson JL, Buller CE, Creager MA, Ettinger SM, Faxon DP, Halperin JL, Hiratzka LF, Hunt SA, Krumholz HM, Kushner FG, Lytle BW, Nishimura RA, Ornato JP, Page RL, Riegel B, Tarkington LG, Yancy CW; American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices); American Association for Thoracic Surgery; Society of Thoracic Surgeons. ACC/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices) developed in collaboration with the American Association for Thoracic Surgery and Society of Thoracic Surgeons. *J Am Coll Cardiol.* 2008;51:e1–e62.
103. Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, Long JW, Ascheim DD, Tierney AR, Levitan RG, Watson JT, Meier P, Ronan NS, Shapiro PA, Lazar RM, Miller LW, Gupta L, Frazier OH, Desvigne-Nickens P, Oz MC, Poirier VL; Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) Study Group. Long-term mechanical left ventricular assistance for end-stage heart failure. *N Engl J Med.* 2001;345:1435–1443.
104. Wray J, Hallas CN, Banner NR. Quality of life and psychological well-being during and after left ventricular assist device support. *Clin Transplant.* 2007;21:622–627.
105. Lietz K, Long JW, Kfoury AG, Slaughter MS, Silver MA, Milano CA, Rogers JG, Naka Y, Mancini D, Miller LW. Outcomes of left ventricular assist device implantation as destination therapy in the post-REMATCH era: implications for patient selection. *Circulation.* 2007;116:497–505.
106. Holman WL, Park SJ, Long JW, Weinberg A, Gupta L, Tierney AR, Adamson RM, Watson JD, Raines EP, Couper GS, Pagani FD, Burton NA, Miller LW, Naka Y; REMATCH Investigators. Infection in permanent circulatory support: experience from the REMATCH trial. *J Heart Lung Transplant.* 2004;23:1359–1365.
107. Huang R, Deng M, Rogers JG, Howser R, Portner PM, Pierson RN III, Butler J. Effect of age on outcomes after left ventricular assist device placement. *Transplant Proc.* 2006;38:1496–1498.
108. Shapiro PA, Levin HR, Oz MC. Left ventricular assist devices: psychosocial burden and implications for heart transplant programs. *Gen Hosp Psychiatry.* 1996;18:30S–35S.
109. Hutchinson J, Scott DA, Clegg AJ, Loveman E, Royle P, Bryant J, Colquitt JL. Cost-effectiveness of left ventricular-assist devices in end-stage heart failure. *Expert Rev Cardiovasc Ther.* 2008;6:175–185.

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