Economics of the Treatment of Heart Failure

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Summary

The number of patients who suffer from heart failure is growing dramatically. Heart failure patients have tremendous morbidity and mortality. The clinical application of medicines and devices in this particular group of patients is extraordinary and is expanding rapidly. Many of these therapies are life saving, yet we have limited healthcare resources in our economic environment today. Cost and effectiveness of therapy becomes an important issue in the heart failure (HF) population.

Key Points

- Pharmacologic and device therapies, which have been shown to reduce morbidity and mortality, should be used in HF patients at all stages as recommended by the ACC/AHA guidelines.
- Beta-blocker therapy has revolutionized the care of heart failure patients.
- Cost effectiveness, and the morbidity and mortality benefits of each intervention, should be considered.

APPROXIMATELY 5 MILLION PATIENTS IN the United States have heart failure (HF).[1] The morbidity and mortality rates with HF are enormous. Over 500,000 patients are diagnosed with HF each year.[1] Heart failure is the primary reason for over 15 million office visits and over 6.5 million hospital visits each year.[1] Eighty percent of men and seventy percent of women who have HF die within eight years.[1] Approximately seventy thousand patients die of HF each year.[1]

The incidence of HF is increasing not only in a larger group of patients, but is particularly increasing in the elderly. The incidence of HF approaches ten per 1,000 in the over-65 population. It is the most common Medicare diagnostic related group (DRG). More dollars are spent for the diagnosis and treatment of HF than any other diagnosis by Medicare.[1]

Heart failure is really a continuum disease state. Severity ranges from mild to severe. The cause of death differs with the progression from mild to severe. A HF patient with mild disease primarily dies of sudden death. As the patient progresses into more symptomatic stages of HF, the mode of death is a bit more agonizing. It is more prolonged, primarily because HF complications are the main cause of death in this growing patient population.

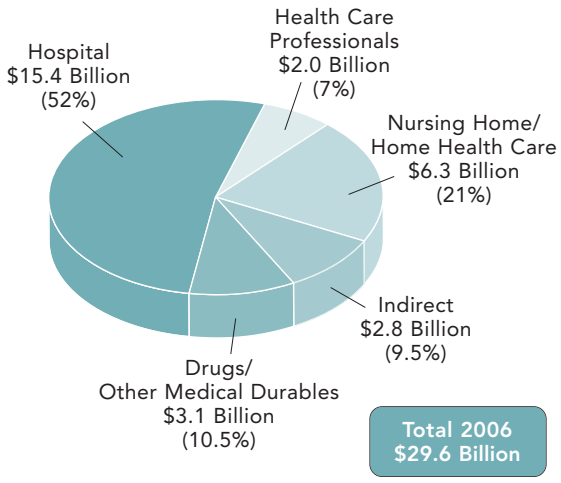
HF has overwhelming economic implications. Hospital discharges from HF increased 174 percent between the years 1979 and 2003.[1] This is due to the increased aging population, improved post-myocardial infarction survival, and wide ranges of treatments that are now available.[2] Repeat hospitalizations stemming from HF are common. Forty to 50 percent of patients are back in the hospital within six months after their first hospitalization.[3]

In 2006, the direct and indirect costs of HF were estimated at $30 billion dollars (Exhibit 1).[1] Less than 10 years ago, the total costs were half as much. More than half of the expense that this patient population incurs is hospitalization costs.

Unfortunately, there appears to be a risk to treatment mismatch with HF.[4] Data about the lowest-risk patients indicates they tend to be getting appropriate therapies, such as ACE inhibitor and beta-blocker therapy, at higher rates. These therapies have been proven to improve morbidity and mortality in HF patients. The patients who are sickest are getting the least access to the medications that can impact morbidity and mortality. The reasons for this disparity in clinical practice are unknown.

The most recent update of the American Heart Association/American College of Cardiology guidelines for HF management was published in 2005.[5]

Exhibit 1: Estimated Direct and Indirect Cost of HF



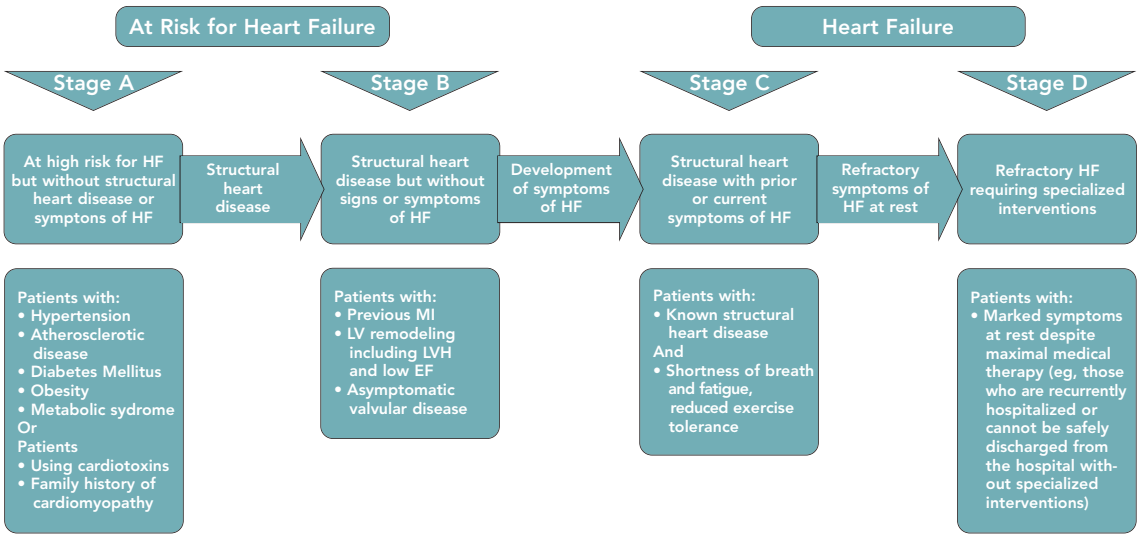
This update of the guidelines changed how HF patients are classified. The New York Heart Association classification is no longer used to stratify patients. The guidelines recommend staging patients as shown in (Exhibit 2).[5] Stage A and Stage B patients, the largest group of patients in this classification system, are at risk for HF. They have no symptoms but have numerous risk factors that will eventually lead to structural heart damage. This group benefits from many of the same therapies that the sicker group benefits from, including: angiotensin converting enzyme (ACE) inhibitor therapy in the diabetic patients and beta-blocker therapy in the diabetic and hypertensive patients. The Stage C and D patients are the sicker groups, who suffer from structural heart disease and symptoms.

In determining which therapies should be used in HF, the effectiveness of treating symptoms and preventing death and the cost implications must be examined for each strategy. The effectiveness of a strategy is classified based on the strength of evidence. One commonly used system places evidence in Classes I to III. A Class I therapy has benefits that far outweigh the risks. A Class III therapy is more risky than the benefits gained from instituting that therapy. The use of a Class III therapy is not recommended. Class II falls between classes I and III, with some data to support use but not an overwhelming amount.

It is a Class I indication to use ACE inhibitors for patients who have had current or prior symptoms of HF with a diminished left ventricular ejection fraction (LVEF). ACE inhibitors should never be used in combination with angiotensin receptor blockers (ARBs) and aldosterone antagonists as a treatment for HF (Class III). Three trials, the Consensus study, the SOLVD treatment trial and the SOLVD prevention study all demonstrated marked reductions in morbidity and mortality rates in patients receiving ACE inhibitors as compared to controls.[6]

Some cost-effectiveness data on the use of ACE inhibitors in HF has been published. Therapy with enalapril in the SOLVD study resulted in a 0.16 year of life gain and financial savings of $718.00.[7] During the patient's lifetime, there was a survival benefit of 0.4 year, a cost per year life savings of $80.00, and a cost per quality adjusted life year savings of $115.00.[7]

Exhibit 2: ACC/AHA 2005 Guideline: Staging of Heart Failure Patients



E=ejection fraction; HF=heart faliure; LVH=left ventricle hypertrophy; MI=myocardial infarction

Exhibit 3: Effect of Beta Blockade on Outcome of Heart Failure

Study	Drug	HF Severity	Target Dosage (mg/day)	Outcome
US Carvedilol	Carvedilol	Mild/ moderate	6.25 to 25 bid	↓ 48% disease progression (P = .001)
CIBIS-II	Bisoprolol	Moderate/ severe	10qd	↓ 34% mortality (P < .0001)
MERIT-HF	Metoprolol Succinate	Mild/ moderate	200 qd	↓ 34% mortality (P = .0062)
COPERNICUS	Carvedilol	Severe	25 bid	↓ 35% mortality (P = .0014)
COMET	Carvedilol Metoprolol	Mild/ moderate	25 bid, 50 bid	↓ 17% mortality (P = .0017)

This economic analysis indicated that a net savings and a gain in life expectancy were seen with an ACE inhibitor in the HF patient. Not only does this therapy improve morbidity and mortality, but it saves money long-term in the treatment of HF patients.

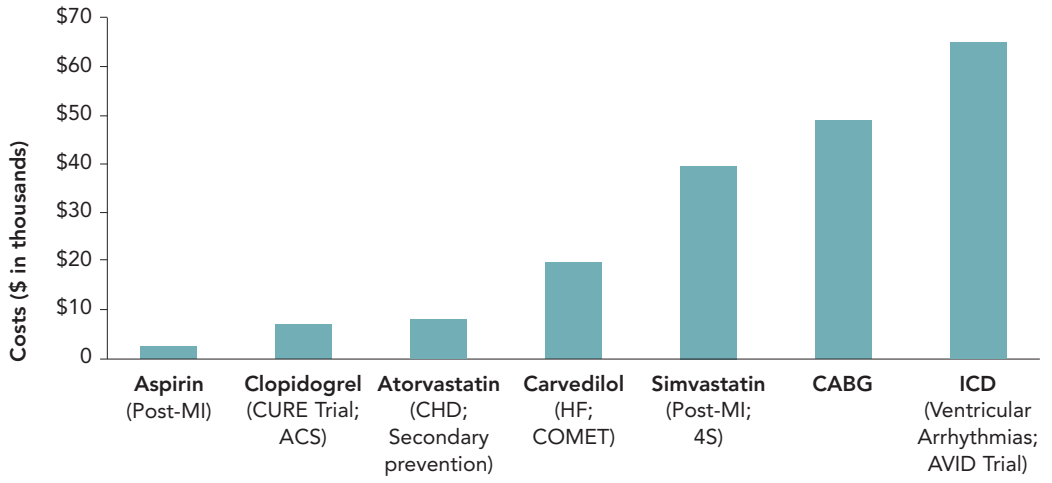
Angiotensin receptor blockers such as valsartan and losartan are different in some ways from ACE inhibitors. Angiotensin receptor blockers are approved for HF in patients with current or prior symptoms of HF and reduced left ventricular ejection fraction who have not tolerated an ACE inhibitor. They are a substitute for the ACE inhibitors. The CHARM study evaluated the role of candesartan in treating HF in ACE intolerant patients. This study found that candesartan, compared to placebo, decreased the risk of cardiovascular death and hospitalizations.[8] A cost effectiveness analysis based on the CHARM study has been published.[9] Use of candesartan was found to be an acceptable cost for the benefits achieved.[9]

Aldosterone antagonists are appropriate therapy for some patients. They are beneficial for patients with moderate or severe symptoms of HF and reduced left ventricular ejection fraction without significant renal dysfunction. The RALES study, which studied adding spironolactone, an inexpensive therapy, to standard of care therapy, demonstrated a significant mortality benefit.[10] Using data from the RALES study, spironolactone has been demonstrated to be cost-effective in HF management with a savings of $713.00 per life year gain.[11] The EPHESUS trial examined the addition of another aldosterone antagonist, eplerenone, to standard therapy in the post myocardial infarction patient who had demonstrated some degree of left ventricular systolic dysfunction.[12] Eplerenone reduced morbidity and mortality in this patient population.

Beta-blockers are recommended for all stable patients with current or prior symptoms of HF and reduced LVEF, unless contraindicated.[5] One of the three agents that have been proven to reduce mortality should be used (i.e., bisoprolol, carvedilol, and sustained release metoprolol succinate).[5] The major beta-blockers in HF studies are summarized in (Exhibit 3).[13-17] As an example, the U.S. Carvedilol study, which used carvedilol in the mild to moderate HF patients, showed a 48 percent decrease in morbidity and mortality.[13] The use of carvedilol resulted in a 29 percent risk reduction for all cause hospitalizations, a 28 percent risk reduction for cardiovascular hospitalizations, and a 38 percent risk reduction for HF hospitalizations.[18] It also resulted in significant reductions in per patient and per stay hospitalizations costs.[18] Data from the COPERNICUS study found that costs were reduced even when treating the patients with severe HF.[19] There was an 11 percent reduction in total costs, a 22 percent reduction in hospital admission costs, a 23 percent reduction in post-discharge medical care, and even a 15 percent reduction in nursing home costs.[19] If the costs per life year gained with carvedilol are compared to other HF interventions, carvedilol appears in the middle (Exhibit 4).[20-23]

Another way to compare carvedilol to other beta-blockers is to analyze health insurance claims data. An analysis of U.S. health insurance claims data, found a 22 percent risk reduction in mortality, a 23 percent risk reduction in all cause hospitalizations, and a 28 percent reduction in cardiovascular hospitalizations for patients on carvedilol as compared to metoprolol tartrate.[25] A $7,700 cost savings was found when carvedilol was used compared to metoprolol tartrate for cardiovascular hospitalizations.[25]

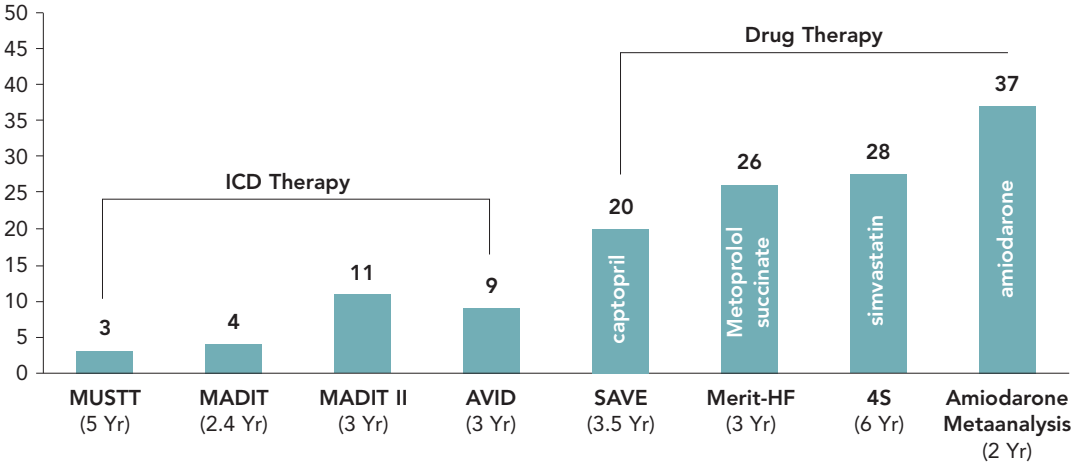
Exhibit 4: Cost Per Life-Year Gained: Use of Carvedilol in COMET vs Other Known Interventions



Data not representative of head-to-head analysis. All data expressed in US dollars.

Exhibit 5: Number Needed to Treat To Save A Life

NNTx years = 100 / (% Mortality in Control Group – % Mortality in Treatment Group)



The beta-blockers are a therapy that has completely revolutionized the care of the HF patient. There is data on the cost effectiveness and impact of morbidity and mortality rates for carvedilol, the morbidity and mortality benefits of bisoprolol, and the sustained release metoprolol.

Although hydralazine and isosorbide dinitrate were the mainstay of HF therapy many years ago, their use has declined with the introduction of ACE inhibitors and the discovery of beneficial effects of beta-blockers. There has been a resurgence of interest in hydralazine and isosorbide dinitrate with the introduction of a combination product (BiDil®). The addition of a combination of hydralazine and a nitrate is reasonable for patients who have persistent symptoms with reduced LVEF who are already taking an ACE inhibitor and beta-blocker for symptomatic HF. Data from the A-HeFT study demonstrated that this combination resulted in a 43 percent decrease in all causes of mortality.[26] The A-HeFT study was primarily designed to address the role of this therapy in select African-American patients and was terminated early because of the substantial benefits. The combination has also been shown to be cost-effective based on A-HeFT data.[27]

Devices in the treatment of HF patients are another area to examine for mortality benefits and

cost-effectiveness. Implantable cardioverter-defibrillators (ICDs) and resynchronization therapy are recommended for certain patients to prolong survival in severe HF and prevent sudden cardiac death. Each year sudden cardiac death kills more people than stroke, lung cancer, breast cancer, and AIDs all combined.[28] Four-hundred-and-fifty thousand sudden cardiac arrests occur in this country every year. Pharmacologic agents have been very effective in reducing total mortality and reducing the risk of sudden death. However, the risk of sudden death still remains relatively high—even in patients who are maximized on drug therapy.[29]

Trials published in recent years of devices looking at defibrillator therapy, resynchronization therapy with defibrillator therapy, or resynchronization therapy alone have shown marked reductions in overall death and arrhythmic death in both primary and secondary prevention groups.[30-33] Device therapy in a select patient population is powerful. It saves lives, provides symptom relief, and provides improvement in functional class. Compared with pharmacotherapy, device therapy requires a lower number of treatments to save a life (Exhibit 5).[34-40] Compared with other cardiovascular interventions, devices are considered cost effective.[41]

It is overwhelming how simple it is to utilize these various pharmacologic and device therapies and save lives. For example, only 14 patients with severe HF need to be treated with carvedilol before one year of life is saved.[16]

Conclusion

Heart failure affects a rapidly growing population with devastating morbidity and mortality. Management of HF patients represents a tremendous economic challenge. Cost effective management strategies beneficially impacting mortality for these patients exist and continue to expand. The economic impact of various management strategies has to be considered in the treatment paradigm of these patients. **JMCM**

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