Comparative Effectiveness of Left Ventricular Assist Device (LVAD) and Medical Management in end-stage heart failure

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Abstract

Heart Failure (HF) is a complex clinical condition caused by structural or functional cardiac disorders that impair the ability of one or both ventricles to fill with or eject blood. Although many conditions may lead to HF, the predominant causes are myocardial ischemia and high blood pressure. (1) Heart transplantation remains the gold standard therapy for end-stage HF. Nevertheless, for patients who are ineligible for transplant, the available management options include: destination therapy with left ventricular assist device (LVAD) or medical therapy(5). The purpose of this research is to determine whether LVAD or medical therapy is more effective in decreasing mortality and increasing functional status (measured by 6 min walk distance) in patients with end-stage HF. A search strategy was developed and applied in both PubMed and Scopus. Key terms such as, heart failure, LVAD, medical therapy, functional status, fluid retention and quality of life were used. Exclusion criteria such as year and language of publication were applied to further refine the search results. The ten most relevant publications were used for the purpose of this research. HF affects an estimated five million patients in the United States. Of those, 60% have heart failure with left ventricular dilation and reduced ejection fraction. LVAD is a mechanical device that is surgically implanted into a patient's chest to help restore blood flow and thus relieve symptoms such as fatigue and shortness of breath. On the other hand, medical therapy includes aggressive use of angiotensin converting enzyme inhibitors, beta blockers, digoxin, and diuretics to relieve lung congestion, create fluid balance and improve patient symptoms. Studies show therapy with permanent LVAD device doubled the one-year survival rate of patients with end-stage heart failure as compared with medical treatment alone. Furthermore, LVAD patients experienced 340 days alive out of the hospital, compared with 106 for patients on medical therapy.(2)

Methods

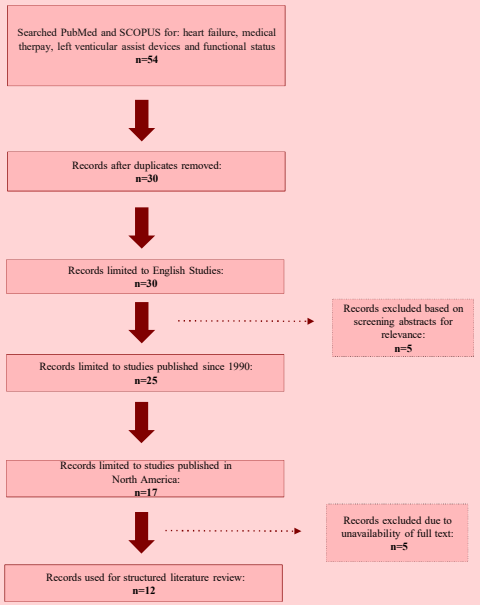

Figure 1. Methodology

Introduction

Heart failure (HF) is a complex syndrome in which structural or functional cardiac disorders impair the ability of one or both ventricles to fill with or eject blood. HF is considered to be a chronic condition with periods of worsening symptoms that may require medical attention. It may present acutely within just 24 hours in the form of pulmonary edema or even cardiogenic shock. To diagnose HF, three criteria need to be present: including shortness of breath at rest or during exertion and/or fatigue, signs of fluid retention such as pulmonary congestion and/or ankle swelling, and objective evidence of a decrease in myocardial performance at rest which is demonstrated using echocardiography.(1)

HF is currently one of the fastest growing problems in cardiovascular medicine. Although drug therapy for patients with chronic HF has improved over the years, mortality still remains high.(3) It is relatively high in the first few weeks after the occurrence of HF thereafter the survival curve shows a much more gradual slope. (1) HF patients are usually classified according to the severity of their symptoms. The New York Heart Association (NYHA) divide the heart failure into four classes. Class I, no limitation of physical activity. Ordinary physical activity does not cause fatigue, palpitation, dyspnea. Class II, slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea. Class III, marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnea. Finally, class IV, unable to carry on any physical activity without discomfort. Symptoms of heart failure seen at rest. If any physical activity is undertaken, discomfort increases.(3)

HF is a leading cardiac disorder that is showing an age-dependent increase in both prevalence and incident as well as the leading cause of death and hospitalization among the elderly. Generally speaking, the prevalence of HF can be estimated at 1% to 2% in Western countries and the incidence approaches 5 to 10 per 1000 persons per year. Data on the occurrence of HF in the developing world are largely absent. (1) As a consequence of the worldwide increase in life expectancy, and due to improvements in the treatment of heart failure in recent years, the proportion of patients that reach an advanced phase of the disease, also known as the end stage, refractory or terminal heart failure, is steadily growing. (4)

Heart transplantation remains the gold standard therapy for end-stage heart failure. Unfortunately, only 2,200 heart transplants are performed annually. Since 75% of patients with heart failure are more than 65 years old, the vast majority are ineligible for cardiac transplantation. One promising therapy for patients who are ineligible for cardiac transplantation is destination therapy with left ventricular assist device (LVAD). (5,6) LVAD is a mechanical pump that restores normal hemodynamics and thus end organ perfusion in patients with profound myocardial dysfunction. This therapy has the unique advantage of not being limited by donor organ availability. (7)

In terms of optimal medical management (OMM), angiotensin-converting enzyme (ACE) inhibitors are recommended as first-line treatment in all patients with reduced left ventricular (LV) systolic function. In patients with symptomatic chronic HF who do not tolerate ACE inhibitors, angiotensin II type I receptor blockers (ARBs) can be used as an alternative to improve morbidity and mortality. However, the higher rate of hypotension, renal dysfunction, and hyperkalemia with such a combination therapy warrants close monitoring of these parameters. As patients with end stage heart failure frequently show signs of fluid retention or have a history of such, inhibitors of the renin-angiotensin system should be co-administered with diuretics, most commonly loop diuretics, which usually leads to rapid symptomatic improvement of dyspnea and exercise tolerance while lacking significant effects on survival. In addition to standard treatment with ACE inhibitors and diuretics, patients with symptomatic stable systolic heart failure should be treated with b-adrenergic receptor blockers unless there are contraindications. Additionally aldosterone receptor antagonists are recommended in addition to ACE inhibitors, b-adrenergic receptor blockers, and diuretics, unless contraindicated. (3)

Research Question:

What is more effective, LVAD or medical management in improving functional status and decreasing mortality rate in end-stage heart failure?

Results

Article	Research Design	Population	Measurements/ Statistical Analyses	Findings
Jerry D, Estep et al. (2015)	Observational Study	•Included a total of 200 patients (97 LVAD, 103 OMM) meeting the inclusion criteria included ≥1 hospitalization for HF in the last 12 months and 6-min walk distance (6MWD) <300 m. The primary composite endpoint was survival on original therapy with improvement in 6MWD ≥75 m at 12 months. -LVAD patients were more severely ill	• Two baseline surveys were used, one on health-related quality of life (including the visual analog scale) and a depression-screening questionnaire. • Differences between groups were analyzed by using the Fisher exact test. • Actuarial survival as-treated was determined with the Kaplan-Meier method - Survival was also determined under the intention-to-treat principle. Differences between groups were determined with the log-rank test. • A 2-sided p value <0.05 was considered significant	• More LVAD patients met the primary endpoint (39% LVAD vs. 21% OMM; odds ratio: 2.4 [95% confidence interval: 1.2 to 4.8]; p = 0.012). • On the basis of as-treated analysis, 12-month survival was greater for LVAD versus OMM (80 ± 4% vs. 63 ± 5%; p = 0.022) patients. • Health-related quality of life (HRQol) and depression improved from baseline more significantly with LVADs than with OMM (Δ visual analog scale: 29 ± 25 vs. 10 ± 22 [p < 0.001]. (9)
Rogers et al. (2010)	Observational Study	•Data from advanced heart failure patients enrolled in the LVAD bridge to transplantation (n = 281) and destination therapy (n = 374) trials were analyzed.	•Functional status 6-min walk distance, patient activity scores) • Quality of life questionnaires were collected before and after LVAD implantation.	• Use of a continuous flow LVAD in advanced heart failure patients results in clinically relevant improvements in functional capacity and heart failure-related quality of life. (10)
Gaddam et al. (2009)	Systematic review	•Patients with advanced heart failure receiving LVAD or medical management	Clinical presentation and evaluation of patients with advanced heart failure	• Diuretics have not been shown to affect mortality in patients with heart failure. Electrolyte abnormalities and renal insufficiency often complicate treatment • Beta blockers and angiotensin converting enzyme inhibitors (ACEIs) (angiotensin receptor blockers in patients intolerant to ACEIs) should be maximized as tolerated. Aldosterone antagonists (spironolactone or eplerenone) have been shown to improve survival and decrease the frequency of hospitalization in patients with New York Heart Association (NYHA) class III–IV symptoms when added to ACEIs, beta blockers, and diuretics. •The 1-year survival rate was significantly higher in the LVAD group than in the medical therapy group. (11)
Rose et al. (2001)	Cohort Study	• Random assignment of 129 patients with end stage heart failure to receive a LVAD (68 patients) or OMM (61)	• Kaplan-Meier survival analysis • HRQol survey Cox proportional-hazards regression log-rank statistic.	•Reduction by 48% in the risk of death from any cause in the LVAD group as compared with the medical-therapy group (relative risk, 0.52; 95 percent confidence interval, 0.34 to 0.78; P=0.001). •Survival rates at one year were 52% in LVAD group and 25% in medical-therapy group (P=0.002), and the rates at two years were 23% and 8% percent (P=0.09), respectively. (12)

Figure 2. Summary of Literature Review

Discussion

Findings:

- There is great clinical homogeneity in the conclusions of the studies
- The use of LVAD in patients with advanced heart failure resulted in a clinically meaningful survival benefit and an improved quality of life.

Limitations of the Study:

- Only English studies were assessed.
- Only two search engines were used to search for literature .
- Slight variance in medications being used for OMM throughout studies
- Selection bias was not unexpected, as seen in the baseline characteristics, which indicated that OMM patients were appropriately less ill than LVAD patients. Thus, the risk/benefit analyses presented may underestimate the benefit and overestimate the risk of LVAD versus OMM

Future research:

This study was performed in a selected patient population, and applicability to the broader population of noninotropic-dependent patients with HF, including those with less hemodynamic and functional compromise would make good candidates for further research in this field.

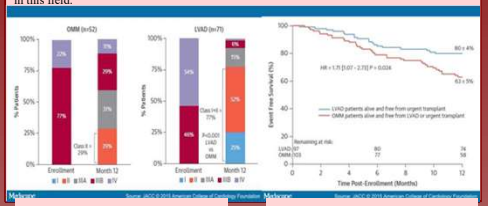

Figure 3: At 1 year survival as treated. (9)

Figure 4: At 1 year survival as treated. (9)

Conclusion

Compared with baseline, LVAD patients demonstrated early and sustained improvements in functional status and quality of life. Most patients in these studies had NYHA functional class IV symptoms at baseline. Following implant, 80%-82% of patients at 6 months and 79% at 24 months improved to NYHA functional class I or II. Mean 6-min walk distance in DT patients was 204 m in patients able to ambulate at baseline, which improved to 350 and 360 m at 6 and 24 months. Survival with improved functional status was better with LVAD compared with OMM. Despite experiencing more frequent adverse events, LVAD patients improved more in health-realted quality of life, and depression.

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