Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure - REMATCH

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Description:

Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure.

Hypothesis:

LVADs reduce mortality 33% in non-transplantable ESHF patients over 2 years compared to optimal medical management (OMM) patients; LVAD patients' QOL equals or exceeds OMM control patients.

Study Design:

Patients Enrolled: 129
Mean Follow Up: 2 years

Primary Endpoints:

Total mortality; quality of life.

Secondary Endpoints:

Adverse events; hospitalization; cost; cost-effectiveness.

Drug/Procedures Used:

Mechanical assistance vs. medical management to reduce mortality and extend quality of life (QOL) in end stage heart failure (ESHF) patients.
Concomitant Medications:

OMM included digoxin, diuretics, angiotensin-converting enzyme (ACE) inhibitors (unless contraindicated); beta-blockers, spironolactone at investigator discretion.

Principal Findings:

Results from the OMM control group confirmed the high mortality in this population: by 1 year, only 25% of control patients were alive; at 2 years, only 8% of control patients were alive.

In contrast, the LVAD patients experienced considerable improvement in survival, with 1-year survival of 52% (p=0.002) and 2-year survival of 23% (p=0.09).

There was a 48% decrement in relative risk of death over the 2-year observation period (p=0.001).

The predominant cause of death among OMM patients was due to heart failure; the highest number of deaths among LVAD patients was from sepsis, followed by device failure.

Quality of life was measured by multiple highly validated indices on a prospective basis. At 1 year, the LVAD patients showed significantly higher SF-36 scores in physical functioning (p=0.01) and emotional role scores (p=0.03) than the OMM patients. In comparing Beck Depression Inventory scores, LVAD patients again showed a significant improvement compared to controls (p=0.04). One year after enrollment, control patients remained NYHA class IV, while LVAD patients were NYHA class II (p=0.01). There was no statistical significance in Minnesota Living with Heart Failure scores, although there was a trend favoring the device patients.

Despite the improvement in survival and quality of life, LVAD patients still faced serious adverse events that required hospitalization. The relative risk of all adverse events was 2.35 times higher in LVAD patients compared to OMM patients, with a predominance of infection, bleeding, and device malfunction.

Nearly three-fourths of patients had no neurologic events. When they occurred, neurologic events in LVAD patients were due to toxic and metabolic causes. Only 10% of LVAD patients suffered an ischemic stroke.

The median survival of LVAD patients was 408 days vs. 150 in the control group; 25 patients remain alive in the LVAD group compared to 5 in OMM. Days out of hospital was more than 3 times as long for the LVAD group vs the OMM patients (median 340 vs. 106 days). For LVAD patients, the index hospitalization of 29 days was approximately the length of a heart transplant hospitalization. However, LVAD patients did spend almost a median of 88 days in the hospital because of readmission for complications vs a median of 24 days in hospital for the OMM group.

The severity of illness in the REMATCH patient population far exceeded previous heart failure randomized clinical trials. Control patient mortality was 4 times that observed in recently reported beta-blocker trials for severe heart failure.

Based on the data, investigators estimate that implantation of LVADs would avert 270 deaths annually per 1000 patients treated. This is nearly 4 times the observed impact of beta blockers and ACE inhibitors, and almost 30 times the impact of thrombolytic therapy for acute myocardial infarction.

Although patient QOL was not restored to normalcy, the QOL of LVAD patients was clearly improved compared to that reported for ESHF patients; physical function scores were similar to hemodialysis and ambulatory heart failure patients. Emotional role scores were better than those of patients with clinical depression patients and similar to patients with ambulatory heart failure.

In terms of adverse events, LVAD morbidity is still considerable. Infections and mechanical failure can be improved, although at 10%, the rate of neurologic events was very encouraging and sets a possible new benchmark for this type of therapy with devices.

The investigators concluded that man-made circulatory support devices can now provide clinically meaningful survival and QOL benefits in non-transplantable ESHF patients.

Interpretation:

Heart failure affects almost 5 million Americans, and half of patients with newly diagnosed with heart failure will die in less than 5 years. In contrast, half of heart transplant patients will survive almost 10 years. The lack of donor organs precludes everyone from receiving a transplant, but study results provide a very strong motivation to develop alternative myocardial replacement therapies. LVAD technology was first conceived in fact as an alternative to biologic replacement of the heart primarily to circumvent the mandatory need for immunosuppression in transplantation as well as the grossly inadequate donor supply. However, these devices are primarily used as a bridge to transplantation, where they are both reliable and effective. Observations from bridging led investigators to consider whether such devices can be used as a long-term destination therapy for patients with end stage heart disease. Data certainly suggest that wearable LVADs allow for extended periods out of the hospital, although at the cost of considerable morbidity. Patients do enjoy a reasonable qualify of life. The REMATCH Trial represents a natural progression to use LVADs for their originally designed purpose. The findings demonstrate that these devices can prolong life and improve QOL, particularly in the extremely sick group of patients observed in this study. With heart failure deaths on the rise, these results are significant for an expanding target population. However, despite the significant improvement in survival and QOL by LVAD patients in this study, with less than one-fourth of LVAD patients alive at 2 years may not be of sufficient magnitude to convince the medical community and insurance companies that this technology (or at least this particular device) can be considered a reasonable alternative to transplantation. Improvements are needed aimed at reducing the frequency of device failure as well as mortality and complication rates. During that presentation at the AHA 2002 annual meeting, discussant Sharon Hunt noted that she believes that the REMATCH study represents a “landmark report” and “the most widely regarded benchmark for all future trials of mechanical heart replacement.”

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Clinical Topics: Cardiac Surgery, Heart Failure and Cardiomyopathies, Invasive Cardiovascular Angiography and Intervention, Cardiac Surgery and Heart Failure, Acute Heart Failure, Heart Transplant, Mechanical Circulatory Support

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- See more at: http://www.acc.org/Latest-in-Cardiology/Clinical-Trials/2010/02/23/19/16/REMATCH#sthash.5uOQMbn2.dpuf