Improving outcomes with long-term "destination" therapy using left ventricular assist devices

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Objective: Destination therapy experience using long-term left ventricular assist devices was analyzed relative to the benchmark Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure trial to evaluate the potential for improving outcomes with this groundbreaking therapy for advanced heart failure.

Methods: The largest single-center experience with destination therapy in the United States (Utah Artificial Heart Program, LDS Hospital, Salt Lake City, UT) was retrospectively analyzed. All destination therapy recipients (n = 23) presented with chronic, advanced heart failure, meeting indications for destination therapy adopted from the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure trial. All received HeartMate left ventricular assist devices (Thoratec Corp, Pleasanton, Calif), with 87% receiving an improved XVE model. Advanced practice guidelines were implemented using a multidisciplinary approach. Survivals (Kaplan–Meier, log-rank analyses) and adverse events (Poisson regression) were compared with those of the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure left ventricular assist device group (n = 68).

Results: Survival in the destination therapy group was significantly increased ($P = .007$), with an overall reduction in mortality of 66%. The 2-year survival was 77% for destination therapy compared with 29% for the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure left ventricular assist device group ($P < .0001$). The 1-year survival was 77% for destination therapy compared with the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure left ventricular assist device rate of 52% ($P = .036$). Adverse events decreased by 38% (3.90 per patient-year in the destination therapy group compared with the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure left ventricular assist device rate of 6.32). Factors related to severity of illness met Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure-like criteria for both groups.

Conclusions: This analysis provides evidence that long-term destination therapy can be improved well beyond the pioneering experience of the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure trial. With continued evolution of devices, management, and patient selection, outcomes approaching those of heart transplantation may be possible.

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Presented at the 31st Annual Meeting of the Western Thoracic Surgical Association, June 22–25, 2005, Victoria Conference Center and Fairmount Empress Hotel, Victoria, BC, Canada.

James Long and Karl Nelson report lecture fees from Thoratec and consulting fees and equity ownership in WorldHeart. Thoratec provided statistical resources for the study.

Received for publication April 3, 2006; revisions received Aug 16, 2006; accepted for publication Sept 5, 2006.

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J Thorac Cardiovasc Surg 2008;135:1353-61

0022-5223/$34.00

doi:10.1016/j.jtcvs.2006.09.124

Heart failure has become a major public health concern, with an incidence of 4.9 million cases in the United States and 550,000 new cases every year.[1] Heart failure is generally progressive, ultimately reaching an advanced end stage requiring organ replacement or substitution. Heart transplantation is a standard of care, but the availability of donor hearts has leveled at 2100 per year,[1] which is well short of projected needs.

Mechanical circulatory support (MCS) offers hope for the treatment of advanced heart failure. MCS has been used successfully over short to medium-term durations of support for bridging to heart transplantation.[2,3] As favorable outcomes have been observed over progressively longer durations of support with left ventricular assist devices (LVADs), interest has grown in using these devices for the long-term treatment of heart failure.[4]

The Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial evaluated the efficacy and safety of long-term support with the HeartMate VE LVAD (Thoratec Corp, Pleasanton, Calif) compared with optimal medical management (OMM) in patients with advanced, chronic heart failure New York Heart Association class IV who were unable to undergo transplantation.

Evidence of superior survival with acceptable safety and quality of life led to the first Food and Drug Administration approval in 2002 of LVADs for long-term destination therapy (DT) with the HeartMate models VE and XVE. The evidence has been compelling enough to justify reimbursement from payers, including the Centers for Medicare and Medicaid Services.

The initial report of the REMATCH trial results identified a significant survival benefit of LVAD therapy compared with OMM.[5] Survivorship at 1 year of 52% in the LVAD arm compared favorably with 25% in the OMM group. At 2 years, survival was 23% with an LVAD, whereas survival was only 8% with OMM. Overall, there was a 48% reduction in the risk of death from any cause in the LVAD arm compared with the OMM group. In addition, quality of life was better with an LVAD than OMM.

Despite the remarkable impact on survival, the greatest of any heart failure therapy previously studied, LVAD therapy during REMATCH was associated with considerable mortality and morbidity. This is not too surprising given the pioneering initiatives with a new therapy in a high-risk patient population. Nevertheless, for DT with LVADs to succeed, improvements will be necessary with (1) devices, (2) patient management, and (3) patient selection.

The overall experience with DT since the REMATCH trial remains modest. Only a few centers have individual experience beyond 10 patients. To date, there has been only 1 publication reporting DT outcomes outside of the REMATCH trial.[6] Given the complexities of this therapy with a significant learning curve, information about performance is vital for improvement and responsible dissemination.

Abbreviations and Acronyms

CVA = cerebrovascular accident
DT = destination therapy
LVAD = left ventricular assist device
OMM = optimal medical management
MCS = mechanical circulatory support
REMATCH = Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure
VO_2 max = maximum oxygen consumption

This study was conducted to evaluate DT outcomes within the largest single-center experience to date to better understand the potential for improving outcomes with this evolving therapy for advanced heart failure.

Materials and Methods

Patient Selection

Patients receiving DT from the Utah Artificial Heart Program at LDS Hospital, Salt Lake City, Utah (LDSH DT cohort) were studied and compared with LVAD recipients from the REMATCH trial. The REMATCH cohort consisted of the 68 patients from the LVAD arm of the REMATCH trial with 89 patient-years of experience. The LDSH DT cohort consisted of all patients in the DT LVAD group not randomized to the LVAD arm of the REMATCH trial and receiving an implant before March 14, 2005: a total of 23 patients with 26.8 patient-years of experience.

The selection of patients receiving DT incorporated REMATCH trial enrollment criteria,[7] Food and Drug Administration-approved indications, and Centers for Medicare and Medicaid Services qualifications.[8] Inclusion criteria included (1) New York Heart Association class IV end-stage heart failure during the last 3 months despite OMM, (2) maximum oxygen consumption (VO_2 max) of less than 12 $mL/kg^{-1}/min^{-1}$ (reduced from REMATCH criteria of 14 $mL/kg^{-1}/min^{-1}$) or dependence on intravenous inotropes, and (3) left ventricular ejection fraction less than 25%. Exclusion criteria included (1) eligibility for heart transplantation; (2) the presence of comorbid factors, other than those due to heart failure, precluding survival of at least 2 years; and (3) body size too small for the HeartMate VE or XVE LVAD (body surface area $< 1.6\ m^2$).

All patients who were in the LDSH DT cohort fit REMATCH qualifications with the exception of 1 patient who would have been excluded from the REMATCH trial by the presence of chronic renal failure requiring dialysis.

Patients from LDSH who were randomized to the LVAD arm of the REMATCH trial remained a part of the REMATCH cohort and were not included in the LDSH DT group.

Appropriate institutional review board approvals were obtained.

Management

DT recipients were guided through the complex management process characteristic of DT in this era by a multidisciplinary team located both at LDSH and in remote locations where the patients lived.

Candidacy was established after conducting reviews from multiple perspectives in consideration of surgical issues, heart failure/