Long-term mechanical circulatory support (destination therapy): On track to compete with heart transplantation?

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Objectives: Average 2-year survival after cardiac transplantation is approximately 80%. The evolution and subsequent approval of larger pulsatile and, more recently, continuous flow mechanical circulatory support (MCS) technology for destination therapy (DT) offers the potential for triage of some patients awaiting cardiac transplantation to DT.

Methods: The National Heart, Lung, and Blood Institute Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) is a national multi-institutional study of long-term MCS. Between June 2006 and December 2011, 127 pulsatile and 1160 continuous flow pumps (24% of total primary left ventricular assist devices [LVADs]) carried an initial strategy of DT therapy.

Results: By multivariable analysis, risk factors ($P < .05$) for mortality after DT included older age, larger body mass index, history of cancer, history of cardiac surgery, INTERMACS level I (cardiogenic shock), dialysis, increased blood urea nitrogen, use of a pulsatile flow device, and use of a right ventricular assist device (RVAD). Among patients with a continuous flow LVAD who were not in cardiogenic shock, a particularly favorable survival was associated with no cancer, patients not in cardiogenic shock, and blood urea nitrogen less than 50 mg/dL, resulting in 1- and 2-year survivals of 88% and 80%.

Conclusions: (1) Evolution from pulsatile to continuous flow technology has dramatically improved 1- and 2-year survivals; (2) DT is not appropriate for patients with rapid hemodynamic deterioration or severe right ventricular failure; (3) important subsets of patients with continuous flow DT now enjoy survival that is competitive with heart transplantation out to about 2 years. (J Thorac Cardiovasc Surg 2012;144:584-603)

Durable mechanical circulatory support (MCS) systems have evolved into therapies suitable for multiyear support. In the United States, the historical development of such support devices was linked to cardiac transplantation, addressing the universal shortage of suitable donors for cardiac transplantation. The vast majority of durable devices have been implanted as bridge-to-transplant therapy, with a small subset implanted as a bridge-to-ventricular recovery. When MCS therapy in the United States was expanded to include the intent of long-term ''destination'' therapy (DT) in 2003,[1] Medicare and most other providers considered DT appropriate only for patients not considered eligible for cardiac transplantation, based on inferior demonstrated survival with MCS compared with transplantation.

However, the landscape of devices, their expected durability, and patient outcomes have rapidly evolved over the past 4 years. This study was undertaken to examine, through a national MCS database, the hypothesis that ''mechanical circulatory support as DT has evolved to a level that justifies consideration of selected patients for DT who are transplant eligible.''

MATERIALS AND METHODS

Interagency Registry for Mechanically Assisted Circulatory Support Database

Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) is a registry for durable (suitable for patient discharge) MCS devices approved by the US Food and Drug Administration (FDA) and implanted in the United States. The registry is sponsored by the National Heart, Lung, and Blood Institute (NHLBI). The term ''interagency'' emphasizes the unique collaboration between the NHLBI as the funding and scientific support agency, the FDA as the regulatory agency, and the Center for Medicaid and Medicare Services (CMS) as the federal reimbursement agency.[2] Information collected in the INTERMACS database

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Abbreviationsand Acronyms

CMS	= Center for Medicaid and Medicare Services
DT	= destination therapy
EQ	= EuroQol
FDA	= Food and Drug Administration
INTERMACS	= Interagency Registry for Mechanically Assisted Circulatory Support
LVAD	= left ventricular assist device
MCS	= mechanical circulatory support
NHLBI	= National Heart, Lung, and Blood Institute
NYHA	= New York Heart Association
RVAD	= right ventricular assist device
VAD	= ventricular assist device

includes patient profile data, implant and device data, scheduled follow-up information, and event-driven data. The occurrence of infection, device failure, neurologic events, and death trigger the acquisition of additional relevant data elements. Participation in INTERMACS is a requirement for hospitals to be reimbursed by CMS for the implantation of MCS devices intended for permanent or ''destination'' therapy (DT). Patient enrollment in INTERMACS was commenced on June 23, 2006. Between June 23, 2006, and December 31, 2011, a total of 5614 patients who received a durable ventricular assist device (VAD) or total artificial heart were entered into the INTERMACS database.

Study Group

Of these 5614 registry patients, 1287 patients received a VAD as DT (Figure 1). These 1287 patients are the subject of this analysis. The study inclusion criteria are listed in Table 1. At the time of implant, 1256 patients received a left VAD (LVAD) only, and 31 received biventricular support. In the overall experience, 127 DT implants were pulsatile devices and 1160 were continuous flow pumps (see again Figure 1).

Missing DT Patients From INTERMACS

Patients receiving MCS implants in the United States who are entered into INTERMACS must fulfill 2 criteria: (1) the device implanted must be FDA approved and (2) the patient must provide informed consent for entry of his or her data into INTERMACS. For FDA-approved devices, INTERMACS receives data on device implant and survival/mortality at 48 hours for all patients, even if consent is not obtained. Further follow-up is available only if patient consent is obtained. INTERMACS audits and screening logs indicate that 9.6% of patients suitable for INTERMACS were not entered with full data collection owing to failure to obtain informed consent. INTERMACS receives no information for patients who receive an investigational device as part of a clinical trial.

Follow-up

All patients are followed up as part of the requirements of INTERMACS until 1 of 3 end points is reached: death, transplant, or device explant for recovery. Data collection at routine follow-up intervals (see Appendix Table 1) occurs for a variety of routine clinical variables in addition to data forms that are ''triggered'' by specific adverse events. Among the 1287 DT patients, follow-up was available in greater than 99% at the follow-up date of December 31, 2011.

Adverse Event Definitions

Standardized definitions for adverse events were established during the initial phase of INTERMACS, developed with the participation and agreement of experts in the field, FDA, and industry. The adverse event definitions are included in Appendix Table 2.

INTERMACS Profiles

The INTERMACS profiles represent a reclassification of New York Heart Association (NYHA) class IV heart failure.[3] The profiles are listed in Appendix Table 3.

Statistical Methods

Standard Kaplan-Meier actuarial methods as well as parametric depictions were used to examine survival and freedom from other specific events. Standard methods were used to examine whether differences among variables were likely due to chance. Competing outcomes depictions used standard methodology as described by McGiffin and colleagues.[4] Risk

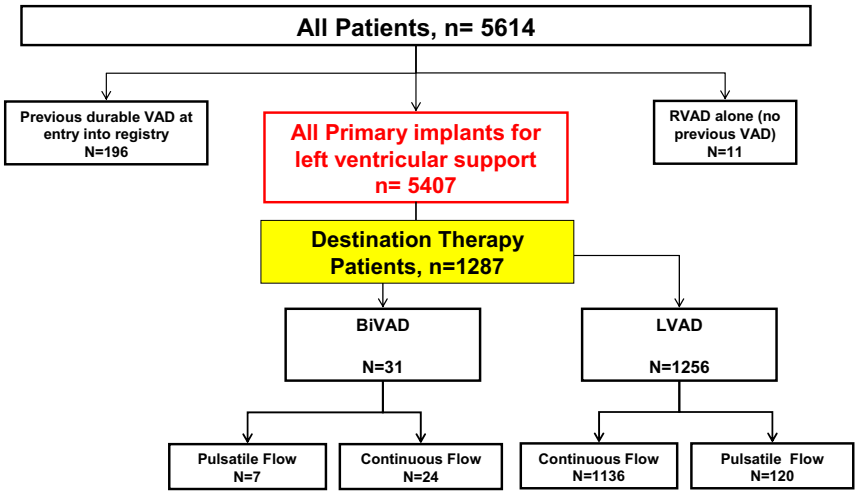

FIGURE 1. Categorization of all 5614 patients entered into INTERMACS between June 23, 2006, and December 31, 2011. The group Destination Therapy (n = 1287) constitutes the study group. *INTERMACS*, Interagency Registry for Mechanically Assisted Circulatory Support; *VAD*, ventricular assist device; *RVAD*, right ventricular assist device; *LVAD*, left ventricular assist device; *BiVAD*, biventricular assist device.