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Survival after biventricular assist device implantation: An analysis of the Interagency Registry for Mechanically Assisted Circulatory Support database

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BACKGROUND: Patients requiring biventricular assist device (BiVAD) for mechanical circulatory support (MCS) have substantially worse outcomes than patients requiring left VAD (LVAD) support only. Patient-specific risk factors have yet to be consistently identified in a large, multicenter registry, which may underlie the poorer outcomes for BiVAD patients. The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) is a registry of U.S. Food and Drug Administration–approved durable MCS devices used for bridge-to-transplantation, destination therapy, or recovery. The purposes of this study were to 1) identify the underlying pre-implant characteristics of the population requiring BiVAD support that contribute to reduced survival, and 2) identify differences in postoperative outcomes with respect to adverse events compared with patients supported with LVAD alone.

METHODS: From June 2006 to September 2009, 1,646 patients were entered into the INTERMACS database in which adverse events and outcomes were recorded for primary implants with LVAD or BiVAD. Competing outcomes methodology was used to estimate the time-related probability of death, transplant, or recovery. Overall survival for all groups was analyzed with Kaplan-Meier methods and Cox proportional regression analysis.

RESULTS: The distribution of primary device implants included 1,440 LVADs and 206 BiVADs. BiVAD patients presented with a lower INTERMACS profile 93% in INTERMACS 1 or 2, compared with 73% for LVAD patients ($p < 0.001$). Survival at 6 months was 86% for LVADs and 56% for BiVADs ($p < .0001$). Adverse event rates, expressed as episodes/100 patient-months for the BiVAD group compared with LVAD, were significantly higher for infection (33.2 vs 14.3), bleeding (71.6 vs 15.5), neurologic events (7.9 vs 2.6), and for device failure (4.9 vs 2.0).

CONCLUSIONS: Patients requiring BiVAD support at the time of durable MCS implant are more critically ill at the time of MCS implant. BiVAD patients experience worse survival than patients supported with LVAD alone and higher rates of serious adverse events. Characteristics of the population present at the time of BiVAD implant likely influence post-implant MCS outcomes.

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Improvements in outcomes with mechanical circulatory support (MCS) for patients requiring left ventricular assistance (LVAD) have been universally recognized during the past decade.[1–4] However, for patients requiring biventricular assistance (BiVAD), outcomes still remain far inferior to realized gains in LVAD therapies. Indeed, data from the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) show that the presence of a BiVAD confers a strong adverse effect on outcomes, with these patients facing twice the mortality risk.[5] The reasons for the increased mortality with BiVAD remain unknown, but indices of right ventricular (RV) dysfunction, such as increased bilirubin and higher right atrial pressure, also emerged as robust mortality risk factors in subsequent analysis.[6] Given the strong association of the need for BiVAD and these risk factors, one questions whether the BiVAD itself or clinical markers of severe RV dysfunction are the driving factors in determining the inferior outcomes of BiVAD patients.

The purpose of this study was to determine whether the BiVAD or the patient with right heart failure dictates poor outcomes in MCS support. To address this question, we used data from INTERMACS, a nationally audited registry for patients who receive a durable, U.S. Food and Drug Administration (FDA)–approved MCS device. INTERMACS indications for MCS support include bridge-to-transplant (BTT), destination therapy (DT) for patients who have contraindications to transplantation, and bridge to recovery or rescue of the native heart. Data from INTERMACS collected from June 2006 to September 2009 were prospectively analyzed and form the basis for the current report.

Methods

From June 23, 2006, to September 30, 2009, 89 institutions prospectively enrolled 1,881 patients into the INTERMACS registry. Participating centers are listed on the INTERMACS Web site (www.INTERMACS.org). Data were transmitted from sites using a Web-based system to a secure server administered by the United Network for Organ Sharing (UNOS). The study sites and central data processing and analyzing facilities received Institutional Review Board approval before collecting data. Data were managed according to Health Insurance Portability and Accountability Act (HIPAA) regulations. The Data Coordinating Center at University of Alabama at Birmingham provided analysis of these data.

MCS devices in the INTERMACS database included the AbioCor total artificial heart (TAH; Abiomed, Danvers, MA); the Heartmate IP, VE, VXE, and Heartmate II LVAD (Thoratec, Pleasanton, CA); the MicroMed Debakey Child left VAD (MicroMed, Houston, TX); the Novacor PC and PCq left VADs (Novacor, Oakland, CA); the Syncardia Cardiowest TAH (Syncardia Systems, Tucson, AZ); and the Thoratec IVAD and PVAD pumps (Thoratec).

The INTERMACS data were checked for completeness by the central collection facility (UNOS). Values that fell outside of predetermined limits were validated with their site of origin; however, source documents are not routinely checked against the data submitted to INTERMACS. Adverse event forms were reviewed by 2 physicians from the INTERMACS community. Differences of opinion between the initial 2 reviewers were adjudicated by members of the INTERMACS Adverse Event Committee before a final decision was made on the classification of individual adverse events.

Data elements describing pre-implant patient condition, indication for MCS, demographic profile, hemodynamics, laboratory values, adverse events, and outcomes were gathered. The analysis included all patients who had a primary device implant, and we analyzed only patients who had an LVAD and RVAD inserted in the same operation. The analysis excluded pediatric patients. Thus, all patients aged > 19 years at implant were included. Competing outcomes methodology was used to estimate the time-related probability of death, transplant, or recovery. Overall survival for all groups was analyzed with Kaplan-Meier methods and Cox proportional regression analysis.

Results

During the study period, 1,771 prospective patients were enrolled in INTERMACS; of which, 65 (4%) implants were not primary, thus 1,706 patients had primary implants. Of these 1,706 patients, 1,440 underwent LVAD implant, 206 underwent BiVAD implant, and 60 received a TAH. The analysis excluded patients not receiving a primary implant and patients receiving a TAH. Thus, 1,646 patients were available for analysis.

The pre-implantation demographics between LVAD and BiVAD patients demonstrated important differences (Table 1). BiVAD patients were generally younger and had a lower incidence of diabetes. Important differences in pre-implant laboratory values between LVAD and BiVAD groups included significantly higher levels of creatinine, blood urea nitrogen, and bilirubin; higher international normalized ratios (INRs), and higher white blood cell counts. The BiVAD group had lower serum albumin and pre-albumin levels.

The incidence of mechanical ventilation at the time of MCS implant was significantly higher for the BiVAD group. Important hemodynamic parameters significantly differed between LVAD and BiVAD groups. The BiVAD group had lower systolic blood pressure and lower cardiac index (Table 2). Compared with the LVAD group, right atrial pressure was higher in the BiVAD group and pulmonary systolic pressure was lower (Table 2).

Of the BiVAD cohort of 206 patients, 55% had clinical characteristics consistent with INTERMACS profile 1 (critical cardiogenic shock) at the time of MCS device implant compared with only 26% of patients in the LVAD group ($p < .0001$; Table 3), and 166 patients (77%) had support with durable devices supporting both ventricles. This configuration was represented by a Thoratec device on the left side and a planned Thoratec device on the right side in 162 patients. Four patients underwent implant with a Heart Mate II supporting the left side with a planned Thoratec device supporting the right side. A durable LVAD was present in 50 patients (23%) along with a temporary RVAD.

Survival while any device was in place at 6 months was 86% for the LVAD group and 56% for the BiVAD group (Figure 1). There was a trend for worse survival with lower INTERMACS patient profile for the BiVAD group, but