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Predictors of 30-day post-transplant mortality in patients bridged to transplantation with continuous-flow left ventricular assist devices—An analysis of the International Society for Heart and Lung Transplantation Transplant Registry

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BACKGROUND: Continuous-flow (CF) left ventricular assist devices (LVADs) are standard of care for bridging patients to cardiac transplantation. However, existing data about preoperative factors influencing early post-transplant survival in these patients are limited. We sought to determine risk factors for mortality using a large international database.

METHODS: All patients in the International Society for Heart and Lung Transplantation Transplant Registry who were bridged to transplantation with CF LVADs between June 2008 and June 2012 were included. Risk factors for mortality within 30 days of transplant were identified. Statistical analysis included multivariable analysis and Kaplan-Meier survival analysis.

RESULTS: During the study period, 2,152 patients with CF LVADs underwent heart transplantation. Post-transplant survival was 95.5% at 30 days. Risk factors for mortality during this window included ventilator support at transplant (hazard ratio [HR] = 5.00, 95% confidence interval [CI] = 1.51–16.58), female recipient/male donor (compared with all other combinations, HR = 3.29, 95% CI = 1.90–5.72), history of hemodialysis (HR = 2.51, 95% CI = 1.14–5.51), and history of coronary bypass grafting (HR = 1.89, 95% CI = 1.19–3.00). Increasing recipient age ($p = 0.002$), body mass index ($p = 0.002$), creatinine ($p = 0.004$), and total bilirubin ($p < 0.001$) also were associated with an increase in mortality.

CONCLUSIONS: In patients supported with CF LVADs, risk factors for early mortality can be identified before transplant, including ventilator support, female recipient/male donor, increasing recipient age, and body mass index. Despite the inherent complexities of a reoperative surgery, patients bridged to transplant with CF LVADs have excellent peri-operative survival.

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Continuous-flow left ventricular assist devices (CF LVADs) have emerged as the mainstay of therapy for patients who require bridging to heart transplantation.[1] Patients bridged with CF LVADs have been shown to have

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similar post-transplant survival as patients who are bridged with traditional pulsatile-flow LVADs.[2] CF devices have largely replaced pulsatile-flow devices because of decreased complication rates, improved mechanical performance, and smaller size.[3,4]

There has been considerable research regarding pulsatile-flow devices and the corresponding outcomes after heart transplant; however, less information is available regarding CF devices.[5–12] In particular, published data correlating CF LVAD use as it relates to transplant outcomes are largely derived from single-center analyses, stratify outcomes by a single variable (e.g., sex or age), or have multiple indications in the study cohort (destination therapy combined with bridge-to-transplant). At the present time, data derived from a large, multi-institutional analysis of pre-transplant risk factors influencing post-transplant mortality in patients bridged to heart transplantation with CF LVADs are sparse.[12,13] Some studies have described increased risk of early post-transplant mortality in patients bridged with CF LVADs.[12,14,15] However, to our knowledge, a comprehensive evaluation of risk factors that predispose patients to early, 30-day mortality after transplantation has not been done.

Large multi-institutional databases such as the International Society for Heart and Lung Transplantation (ISHLT) Transplant Registry provide an opportunity for large-scale investigation of post-transplant survival outcomes. Multiple pre-transplant data points are collected on patients bridged with CF LVADs, and post-transplant follow-up information is collected annually on each of these patients, which makes the registry a valuable tool for assessing the effects of pre-transplant variables on post-transplant outcomes. Using data from the ISHLT Transplant Registry, we sought to determine which pre-transplant risk factors influence early (30-day) post-transplant survival in patients bridged to transplantation with CF LVADs.

Methods

The University of Utah Institutional Review Board waived the need for formal approval and individual consent for this study. The ISHLT Transplant Registry was queried for all patients who underwent transplantation between July 1, 2008, and June 30, 2012, who were ≥18 years old at the time of transplant and were bridged to transplant with a durable CF LVAD (Table 1).

Table 1 Types of CF LVADs in Patients Bridged to Transplant Between July 1, 2008, and June 30, 2012 ($N = 2,152$)

VAD type	No.
HeartMate II (Thoratec)	1,883
Jarvik 2000 (Jarvik Heart)	33
DeBakey (MicroMed Technology)	1
HVAD (HeartWare)	139
DuraHeart (Terumo)	26
VentrAssist (Ventracor)	63
Levacor (WorldHeart)	7

CF, continuous-flow; LVAD, left ventricular assist device; VAD, ventricular assist device.

Patients with a prior transplant of any organ, biventricular support, or simultaneous transplant of any other organ were excluded. Patients were analyzed for survival at 30 days post-transplant.

Risk factors for early mortality, including recipient factors, donor factors, and transplant factors, were analyzed (Table 2). Some variables of interest were excluded from the analysis. Exercise oxygen consumption was excluded because of poor data quality, and donor and recipient human immunodeficiency virus status and human T-lymphotropic virus status were excluded because of insufficient sample size.

Demographic and clinical characteristics were analyzed using univariate analysis. Kaplan-Meier survival with log-rank analysis was used to evaluate post-transplant survival. Multivariable analysis in the form of Cox proportional hazards regression was used to evaluate the relationship between risk factors and mortality. Continuous risk factors were included in the models using a restricted cubic spline. This method assigns a hazard ratio (HR) of 1.0 to the median value of a particular risk factor, with HRs of other values for that risk factor compared relative to the median value. Continuous risk factors with missing values were imputed using multiple imputation. Variables that were found to be significant ($p < 0.05$) were designated as having an association with the given outcome.

Results

During the study period, 2,152 patients underwent transplantation while being supported by a CF LVAD. The frequency of risk factors, including donor and recipient characteristics and transplant process variables, is listed in Table 2. Patients were predominantly men (81.6%), had a median age of 56 years, and received hearts from donors with a median age of 29 years. Idiopathic cardiomyopathy was the most common cause of heart failure (43.6%), followed closely by ischemic cardiomyopathy (42.3%). Hypertension and diabetes were present in 49.4% and 30.1% of patients, respectively. Previous cardiac surgery had been performed in 70.9% of the patients. Overall survival to 30 days post-transplant in this population was 95.5% (Figure 1), with a 95% confidence interval (CI) of 94.6%–96.4%.

Among categorical risk factors tested, the need for ventilator use in a heart transplant candidate at the time of transplant had the highest HR for mortality within the first 30 days post-transplant, with a 5-fold increase in mortality risk compared with candidates without use of a ventilator (HR = 5.00, 95% CI = 1.51–16.58) (Figure 2). Other categorical risk factors for increased mortality within the first 30 days post-transplant after being bridged to transplant with a CF LVAD included being a female recipient of a male donor allograft vs all other combinations (HR = 3.29, 95% CI = 1.90–5.72), a history of pre-transplant dialysis (HR = 2.51, 95% CI = 1.14–5.51), and pre-transplant coronary artery bypass grafting (HR = 1.89, 95% CI = 1.19–3.00). The presence of diabetes in this study population appeared to be associated with a lower risk of mortality in the first 30 days post-transplant (HR = 0.61, 95% CI = 0.38–0.96).

Continuous risk factors from the recipient and the donor were found to be significant. Increasing recipient age