Posttransplant Outcomes Among Septuagenarians Bridged to Transplantation With Continuous-Flow Left Ventricular Assist Devices

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Background. **A bridge to transplant strategy with a continuous-flow left ventricular assist device is increasingly being offered to older patients. However, the upper patient age limit has not been defined.**

Methods. **The United Network of Organ Sharing (UNOS) database was used to identify 21,258 heart transplant recipients from 2004 to 2014. Of these, 4,850 (22.8%) were bridged with a continuous-flow left ventricular assist device. Recipients were stratified by age: group 1, aged 70 years or more (n = 115, 2.4%); and group 2, aged 18 to 69 years (n = 4,735, 97.6%).**

Results. **Elderly patients more likely had ischemic etiology than younger patients (69.6% versus 41.0%; $p < 0.001$), and received a heart from an older donor (35.8 versus 31.3 years, $p < 0.001$) or an expanded criteria donor (8.7% versus 2.4%; $p < 0.001$). Elderly patients had decreased 90-day survival (88.8% versus 93.2%; $p = 0.021$) and 3-year posttransplant survival (80.9% versus 85.7%; $p = 0.073$). However, analysis of a propensity matched cohort did not demonstrate survival difference at 90 days and 3 years. Among septuagenarians, the model for end-stage liver disease excluding international normalized ratio (MELD-XI) score was a predictor for 90-day mortality (hazard ratio 4.48, 95% confidence interval: 1.90 to 10.55; $p = 0.001$) and 3-year mortality (hazard ratio 2.27, 95% confidence interval: 1.51 to 3.41; $p < 0.001$), whereas functional independence was protective for 3-year mortality (hazard ratio 0.11, 95% confidence interval: 0.013 to 0.86; $p = 0.036$). Functionally independent patients showed a remarkably superior posttransplant survival compared with functionally dependent patients (96.7% versus 42.8% at 3 years; $p = 0.001$).**

Conclusions. **The continuous-flow left ventricular assist device supported septuagenarians did not have increased posttransplant mortality. Functional outcomes during device support may have important implications for organ allocation among the elderly.**

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Heart failure afflicts more than 5.8 million people in the United States and 23 million worldwide [1]. Its prevalence and incidence are strongly associated with age, and most patients with heart failure are aged 70 years or more [2]. With a general increase in life expectancy and growing elderly population, there will be undoubtedly an increased need for mechanical circulatory support (MCS) and heart transplantation in the elderly [3].

Heart transplantation today is the "gold standard" treatment for end-stage heart failure refractory to medical management. However, advanced age has traditionally been considered a contraindication to transplantation, owing to concerns for reduced survival and limited donor availability [4]. Recently, continuous-flow left ventricular assist device (CF-LVAD) use has rapidly grown, either as bridge to transplant (BTT) or destination therapy [5]. In contrast, life-threatening adverse events, including bleeding, stroke, ventricular arrhythmias, readmissions, pump thrombosis, and driveline infections have been unsolved issues [6, 7]. Cost effectiveness of destination therapy is also a concern given expensive device implant and costs for long-term equipment as well as repeated rehospitalizations due to device-related complications (DRCs) [7].

Although the results have been varied, several small, single-center series report favorable results for non-BTT heart transplantation in septuagenarians [8, 9]. Several centers, including our own, have broadened the criteria for transplants to include patients aged more than 65

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Abbreviations and Acronyms

BTT	=	bridge to transplant
CF-LVAD	=	continuous-flow left ventricular assist device
CI	=	confidence interval
DRC	=	device-related complications
HR	=	hazard ratio
KPS	=	Karnofsky performance score
LVAD	=	left ventricular assist device
MCS	=	mechanical circulatory support
MELD-IX	=	model for end-stage liver disease excluding international normalized ratio
OR	=	odds ratio
UNOS	=	United Network of Organ Sharing

years [4]. As the number of septuagenarians with heart failure rises, consideration of BTT strategy may become inevitable in some patients. Currently, our understanding of BTT strategy among patients aged 70 years or more is limited. Studying outcomes in this patient population will clarify whether BTT is an acceptable strategy for transplantation among septuagenarians.

Patients and Methods

Data Collection and Study Population

A retrospective review of deidentified data from the United Network of Organ Sharing (UNOS) thoracic registry identified a total of 25,139 heart transplant patients between January 1, 2004, and December 31, 2014. Of these, 4,850 (19.3%) were bridged with CF-LVAD (Fig 1). Recipients were stratified by age: group 1, aged 70 years or more (n = 115, 2.4%), and group 2, aged 18 to 69 years (n = 4,735, 97.6%). Clinical characteristics and outcomes were compared between groups. Follow-up ended on March 5, 2015. The DRCs in each group were provided

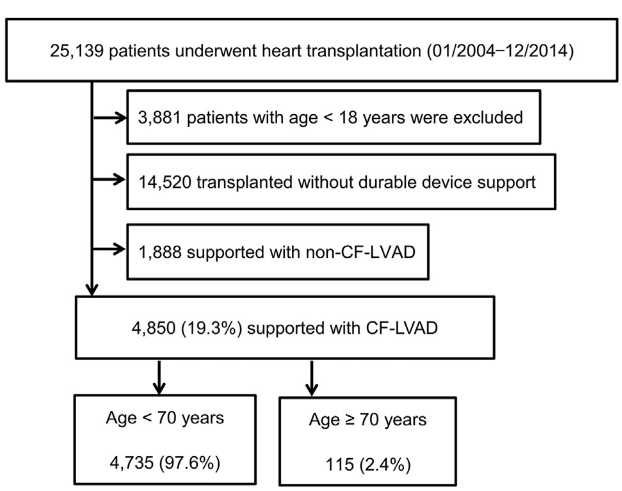

Fig 1. Cohort derivation. (CF-LVAD = continuous-flow left ventricular assist device.)

within the dataset. Organ Procurement and Transplantation Network policy defines DRC in five categories; thromboembolism, device infection, mechanical failure, life-threatening ventricular arrhythmias, and others. The UNOS dataset uses the Karnofsky performance score (KPS) [10] to determine the functional status of a recipient. In brief, KPS increases by 10 points from 0 to 100 as patient independence improves and symptoms resolve. Functional status in each patient was categorized based on a KPS of 80 to 100 (no assistance), 50 to 70 (some assistance), and 10 to 40 (total assistance). The model for end-stage liver disease excluding international normalized ratio (MELD-XI) score [11], a modification to the existing MELD, was calculated for each patient. The Columbia University Institutional Review Board approved all aspects of this study and waived informed consent as the database is deidentified and publicly available.

Statistical Analysis

Continuous variables are expressed as mean ± 1 SD. Categoric variables are presented as proportions and absolute numbers. Differences between groups were measured using the χ^2 or Fisher's exact test for categoric variables and Student's *t* test or the Mann-Whitney *U* test for continuous variables. Survival data were compared using Kaplan-Meier survival analysis and log rank test. All patients were subjected to propensity matching using the sequential nearest neighbor, caliper-constrained matching technique. Propensity matching used the following clinically relevant variables that did not have missing values in the dataset: MELD-XI score, body mass index, donor-recipient weight ratio, inotropic and mechanical ventilator support, sex mismatch, organ ischemic time, and donor age. On the estimation of propensity scores, a greedy matching algorithm matched the septuagenarian cohort (n = 113) to the cohort of patients aged 18 to 69 years (n = 226). Matching used a caliper size equal to 0.2 times the standard deviation of the estimated log propensity scores. For regression modeling, missing variables were imputed using a multiple imputation technique. Each missing data was imputed 10 times, resulting in 10 imputed data sets. All subsequent analyses were performed for each imputed dataset separately and combined to produce a final single set of parameter estimates. Clinical parameters before transplantation were analyzed to determine contributing factors for posttransplant mortality using logistic regression for 90-day mortality and Cox proportional hazards models for 3-year mortality. For multivariable analyses, variables with a *p* value of 0.25 or less on univariable analysis were included in a final multivariable model. Results are presented as odds ratio (OR) or hazard ratio (HR) with corresponding 95% confidence interval (CI). A *p* value less than 0.05 was considered to be statistically significant. All *p* values were results of two-tailed tests. The statistical analysis was performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corporation, Armonk, NY).