The impact of bridge-to-transplant ventricular assist device support on survival after cardiac transplantation

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Objective: To determine the impact of bridge-to-transplant ventricular assist device support on survival after cardiac transplantation.

Methods: From January 1, 1993, to April 30, 2009, a total of 525 cardiac transplants were performed. Ventricular assist devices were placed as a bridge to transplant in 110 patients. We focused our analysis on the 2 most common causes of end-stage heart failure requiring transplantation: idiopathic dilated cardiomyopathy (n = 201) and coronary artery disease (n = 213). Data including gender, age, date of transplant, cause of heart failure, prior heart transplant, placement of a ventricular assist device, type of ventricular assist device, and panel-reactive antibody sensitization were analyzed to derive Kaplan–Meier survival probabilities and multivariable Cox regression models.

Results: In patients with idiopathic dilated cardiomyopathy who received a ventricular assist device as a bridge to transplant, survival was decreased at 1 year ($P = .008$) and 5 years ($P = .019$), but not at 10 years, posttransplant. In patients with coronary artery disease, the use of a ventricular assist device as a bridge to transplant did not influence survival at 1, 5, and 10 tears posttransplant. In patients with idiopathic dilated cardiomyopathy who received a Heartmate I (Thoratec Corp, Pleasanton, Calif) ventricular assist device as a bridge to a cardiac transplant, elevation in the pretransplant panel-reactive antibody correlated with a decrease in long-term survival.

Conclusion: In patients with idiopathic dilated cardiomyopathy, placement of a Heartmate I ventricular assist device as a bridge to a cardiac transplant is associated with an elevation in the pretransplant panel-reactive antibody and a decrease in 1- and 5-year survivals after cardiac transplantation. (J Thorac Cardiovasc Surg 2010;140:169-73)

Cardiac transplantation remains the gold standard for the treatment of end-stage heart failure. The major factor limiting the number of heart transplants performed in the United States today is the availability of donor hearts. Ventricular assist devices (VADs) allow for the successful bridging of patients who otherwise would not be expected to survive long enough to receive a heart transplant.[1-3] Previous studies have reported equivalent survival at 1, 2, and 5 years in patients who were bridged with a VAD compared with the broader population of heart transplant recipients.[4,5] More recent studies, however, have found that bridge-to-transplant VADs are associated with an increase in mortality within 6 months and more than 5 years after cardiac transplantation.[6] We examined our experience with the use of bridge-to-transplant VADs, with particular attention to heart failure cause, to determine their impact on survival after cardiac transplantation.

MATERIALS AND METHODS

This study was reviewed and approved by the institutional review board at the University of Utah Health Sciences Center. All patients undergoing cardiac transplantation from January 1, 1993, to April 30, 2009, in the Utah Transplant Affiliated Hospitals (UTAH) heart transplant program were included in the analysis. The UTAH heart transplant program had its inception in 1985. The start date for this analysis is 1993 because this was the inception of the VAD program within the UTAH heart transplant program. Patients undergoing heart–lung transplantation were excluded from the analysis. Specific data regarding date of transplant, mortality, cause of death, gender, age, cause of heart failure, prior heart transplant, United Network for Organ Sharing status, previous cardiac surgery, placement of a VAD, type of VAD, transfusion of cellular blood products, duration of VAD support, panel-reactive antibody (PRA) sensitization, use of pretransplant and perioperative plasmapheresis for desensitization in patients with a PRA more than 90%, immunosuppressive agents, immunosuppression

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Abbreviations and Acronyms

CAD = coronary heart disease
CI = confidence interval
HR = hazard ratio
IDC = idiopathic dilated cardiomyopathy
LVAD = left ventricular assist device
PRA = panel-reactive antibody
UTAH = Utah Transplant Affiliated Hospitals
VAD = ventricular assist device

protocols, incidence and severity of acute cellular and humoral rejection posttransplant, and incidence of cardiac allograft vasculopathy were collected for each patient. Patients who did and did not receive a VAD as a bridge to a cardiac transplant were compared with regard to each of the above listed variables with a 2-sample *t* test for continuous variables and a chi-square or Fisher's exact test, as appropriate, for categoric variables. These 2 groups were then analyzed using multivariable Cox regression. Only 3 patients had 2 transplants in the dataset, which was not enough to introduce lack of independence among the observations. Therefore, there was no need to account for lack of independence with a shared frailty Cox regression, which is the Cox regression analog of a mixed-effects linear regression. On the basis of the limited sample size of this study, multivariable Cox regression rather than propensity score matching was used to control for the potentially confounding variables in the analysis. For this particular analysis, the use of propensity score matching in the limited sample size of the study would have required loose matching to maintain an adequate sample size, leaving several residual confounding variables in the analysis.

Given that the posttransplant follow-up was measured as a continuous variable, accurate to a day, rather than a predetermined time interval such as a year, the Kaplan–Meier approach was used to obtain survival estimates for specific time points, rather than the actuarial method, which is designed for data aggregated by time interval.

The data were analyzed to derive Kaplan–Meier survival probabilities and to fit the multivariable shared frailty Cox regression models. Hazard ratios (HRs), confidence intervals (CIs), and *P* values were calculated for each variable. The primary end point of the analysis was the impact of pretransplant VAD support on patient survival after cardiac transplantation. The secondary end point of the analysis was the impact of pretransplant PRA on patient survival after cardiac transplantation. Data are reported as the mean ± standard deviation.

RESULTS

From January 1, 1993, to April 30, 2009, a total of 525 cardiac transplants were performed in the UTAH heart transplant program. The most common indications for transplantation were ischemic cardiomyopathy as a result of coronary artery disease (CAD, n = 213) and idiopathic dilated cardiomyopathy (IDC, n = 201) (Table 1). Among the cardiac transplants, VADs were placed as a bridge to transplant in 110 patients. Among the 110 patients receiving VADs, the cause of heart failure was CAD (n = 59) or IDC (n = 45) in 104 patients (Table 1). We therefore focused our analysis on the patients with a history of CAD and IDC because these 2 subgroups had sufficient numbers of patients with and without VADs for statistical analysis.

For the entire cardiac transplant program, Kaplan–Meier survival probability at 1, 5, 10, and 15 years posttransplant was 90%, 77%, 59%, and 44% respectively. In patients with CAD, the use of a VAD as a bridge to transplant did not influence survival at 1, 5, and 10 tears posttransplant. In patients with IDC, the use of a VAD as a bridge to transplant was associated with a decrease in Kaplan–Meier survival probability at 1 year (84% vs 96%, $P = .008$) and 5 years (66% vs 82%, $P = .019$) posttransplant (Table 2, Figure 1). Specifically, the use of a Heartmate I (Thoratec Corp, Pleasanton, Calif) VAD was associated with a decrease in survival in patients with IDC at 1 year (HR = 4.33; CI, 1.46–12.90) and 5 years (HR = 2.25; CI, 1.14–4.42) posttransplant. There was no significant difference in survival, however, for patients with IDC at 10 years posttransplant when comparing patients with and without VADs (62% vs 67%, $P = .11$, Figure 1).

Patients with IDC receiving VADs as a bridge to transplant were more likely to have a PRA greater than 10% than the precardiac transplant population without VADs. In patients with IDC who received a VAD as a bridge to transplant, the pretransplant PRA was elevated to 35% ± 40% versus only 5% ± 14% in the patients without VADs ($P < .001$). In addition, among the patients with IDC, 40% of the patients who received a VAD had a PRA greater than 10%, compared with only 10% of the patients without VADs ($P < .001$). Some 32% of patients with IDC with a VAD had a PRA greater than 40% ($P < .001$), and 20% of patients with IDC with a VAD had a PRA greater than 75% ($P < .001$).

In both the IDC and CAD groups, the transfusion of cellular blood products, the duration of VAD support, and the use of pretransplant and perioperative plasmapheresis for desensitization in patients with a PRA greater than 90% did not affect long-term survival after transplantation. Similarly, United Network for Organ Sharing status and the incidence of reoperative cardiac surgery did not affect long-term survival. The incidence and severity of acute cellular and humoral rejection, immunosuppressive agents, immunosuppression protocols, and cardiac allograft vasculopathy did not differ between those with and without VADs in the IDC and CAD groups. Finally, although 1- and 5-year survivals were decreased for patients with VADs in the IDC group, the incidences of mortality cause (ie, acute rejection, infection, cardiac allograft vasculopathy, and malignancy) did not differ between patients with and without VADs.

During the time period analyzed, the predominant bridge-to-transplant VADs used in the UTAH heart transplant program were the Heartmate I and Heartmate II systems. The Heartmate I system was used exclusively until 2004, when the Heartmate II system also began to be placed as a bridge-to-transplant device. An interesting finding with regard to these 2 VAD systems is that PRA elevation greater than 10% was seen only in those patients who received