Journal of the American College of Cardiology Vol. 53, No. 3, 2009

Published by Elsevier Inc.
ISSN 0735-1097/09/$36.00
doi:10.1016/j.jacc.2008.08.070

The Effect of Ventricular Assist Devices on Post-Transplant Mortality

An Analysis of the United Network for Organ Sharing Thoracic Registry

Vishnu Patlolla, MD, MPH,* Richard D. Patten, MD,† David DeNofrio, MD,† Marvin A. Konstam, MD,† Rajan Krishnamani, MD†

Worcester and Boston, Massachusetts

Objectives This study sought to determine the relationship between pre-transplant ventricular assist device (VAD) support and mortality after heart transplantation.

Background Increasingly, VADs are being used to bridge patients to heart transplantation. The effect of these devices on post-transplant mortality is unclear.

Methods Patients 18 years or older who underwent first-time, single-organ heart transplantation in the U.S. between 1995 and 2004 were included in the analyses. This study compared 1,433 patients bridged with intracorporeal and 448 patients bridged with extracorporeal VADs with 9,455 United Network for Organ Sharing status 1 patients not bridged with a VAD with respect to post-transplant mortality. Because the proportional hazards assumption was not met, hazard ratios (HRs) for different time periods were estimated.

Results Intracorporeal VADs were associated with an HR of 1.20 (95% confidence interval [CI]: 1.02 to 1.43; $p = 0.03$) for mortality in the first 6 months after transplant and an HR of 1.99 (95% CI: 1.44 to 2.75; $p < 0.0001$) beyond 5 years. Between 6 months and 5 years, the HRs were not significantly different from 1. Extracorporeal VADs were associated with an HR of 1.91 (95% CI: 1.53 to 2.37; $p < 0.0001$) for mortality in the first 6 months and an HR of 2.93 (95% CI: 1.19 to 7.25; $p = 0.02$) beyond 5 years. The HRs were not significantly different from 1 between 6 months and 5 years, except for an HR of 0.23 (95% CI: 0.06 to 0.91; $p = 0.04$) between 24 and 36 months.

Conclusions Extracorporeal VADs are associated with higher mortality within 6 months and again beyond 5 years after transplantation. Intracorporeal VADs are associated with a small increase in mortality in the first 6 months and a clinically significant increase in mortality beyond 5 years. These data do not provide evidence supporting VAD implantation in stable United Network for Organ Sharing status I patients awaiting heart transplantation. (J Am Coll Cardiol 2009;53:264–71) © 2009 by the American College of Cardiology Foundation

Ventricular assist devices (VADs) are increasingly used to successfully bridge patients to heart transplantation. Patients bridged with VADs typically show significant improvement in end-organ function after implantation (1,2). These observations have contributed to the notion that VAD therapy may therefore render patients more medically suitable to endure the rigors of cardiac transplantation. Despite the increase in use of VADs before transplantation, studies exploring the effect of VADs on post-transplant mortality have yielded conflicting results. Although some single-center studies analyzing outcomes from a limited number of patients have concluded that VAD therapy before heart transplantation is not related to post-transplant survival, others have shown that VAD therapy is associated with improved post-transplant survival (3–9). Furthermore, 1 study has observed diminished survival for patients bridged to transplant with a VAD (10).

See page 272

We conducted a retrospective analysis in 11,336 patients entered into the United Network for Organ Sharing

From the *Department of Medicine, Division of Cardiovascular Medicine, University of Massachusetts Medical School, Worcester, Massachusetts; and the †Division of Cardiology, Tufts Medical Center, Boston, Massachusetts. The data reported here have been supplied by the United Network for Organ Sharing as the contractor for the Organ Procurement and Transplantation Network. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by the Organ Procurement and Transplantation Network or the U.S. Government.

Manuscript received April 29, 2008; revised manuscript received July 14, 2008, accepted August 18, 2008.

(UNOS) Thoracic Registry to examine the relationship between intracorporeal and extracorporeal VAD implantation and post-transplant mortality.

Methods

This analysis was based on Organ Procurement and Transplantation Network data as of May 25, 2006. We limited our analysis to patients in the UNOS Thoracic Registry who were 18 years or older and who underwent heart transplantation between January 1995 and December 2004. The analysis was limited to first-time, single-organ heart transplant recipients. Patients with a history of malignancy were excluded. Patients were divided into 3 groups based on the support at the time of transplant. The UNOS status 1 group included UNOS status 1 patients without VAD support at the time of transplant. The intracorporeal VAD group included patients on a HeartMate (Thoractec Corporation, Pleasanton, California) or Novacor (World Heart Inc., Oakland, California) intracorporeal VAD. The extracorporeal VAD group included patients with a Thoratec (Thoractec Corporation) or Abiomed (Abiomed Inc., Danvers, Massachusetts) extracorporeal VAD. Patients in either VAD group who were also on an intra-aortic balloon pump (IABP) were excluded. Patients with both an intracorporeal and an extracorporeal VAD were included in the extracorporeal VAD group. The primary outcome was all-cause mortality.

Abbreviations and Acronyms

HR = hazard ratio
IABP = intra-aortic balloon pump
PRA = panel reactive antibodies
UNOS = United Network for Organ Sharing
VAD = ventricular assist device

Baseline characteristics were compared among the 3 groups using analysis of variance, with the Tukey method

Table 1 Baseline Characteristics

Characteristic	UNOS Status I (n = 9,455)	Intracorporeal VAD (n = 1,433)	Extracorporeal VAD (n = 448)	p Value*
Age (yrs)				
Recipient	52	50.6	47.6	<0.0001
Donor	31.5	31	32	0.20
Difference	20.6	19.6	15.5	<0.0001
Recipient male	78.1	86.3	72.5	<0.0001
Sex mismatch	19.5	16.6	14.1	0.0009
Time on wait list (days)	217	251	146	<0.0001
Ischemic cardiomyopathy	48.9	51.0	46.0	0.14
CMV mismatch (positive donor/negative recipient)	18.6	19.9	14.3	0.03
Ventilator	3.0	2.1	12.5	<0.0001
Inotropic support	83.2	20.1	38.2	<0.0001
Amiodarone	27.0	31.5	31.0	0.0009
Diabetes	19.0	22.4	14.4	0.0004
Serum creatinine	1.4	1.3	1.4	<0.0001
Total bilirubin	1.4	1.2	1.9	0.0003
Cold ischemia time (h)	3.0	3.2	3.4	<0.0001
Most recent PRA (%)	3.5	7.7	9.9	<0.0001
VAD type				
Novacor		10.2		
Heartmate		89.8		
Abiomed			24.6	
Thoratec			73.6	
Abiomed/Thoratec			0.2	
Abiomed/Heartmate			0.4	
Thoratec/Heartmate			1.1	
Status at last follow-up				
Alive	66.3	72.0	66.3	0.0002
Dead	32.5	27.5	31.9	
Repeat transplantation	1.1	0.6	1.8	
Year of transplantation				
1995–1996	21.6	2.6	0.9	<0.0001
1997–1998	22.4	6.1	1.3	
1999–2000	20.5	25.4	13.2	
2001–2002	18.5	36.8	44.6	
2003–2004	17.0	29.1	40.0	

Values are mean or %. *From analysis of variance or chi-square test as appropriate.
CMV = cytomegalovirus; PRA = panel reactive antibodies; UNOS = United Network for Organ Sharing; VAD = ventricular assist device.

JACC Vol. 53, No. 3, 2009
January 20, 2009:264–71

for controlling for multiple comparisons, for continuous variables, and the chi-square test for categorical variables. Survival curves were estimated using the Kaplan-Meier method, and equality of survival curves was tested using a log-rank test. The Cox proportional hazards regression model was used to estimate hazard ratios (HRs) of death in the intracorporeal and extracorporeal VAD groups compared with the UNOS status 1 group, after adjustment for covariates: donor and recipient age, recipient sex, sex mismatch (female donor–male recipient), time on waiting list, ischemic etiology of heart failure, cytomegalovirus-positive donor/cytomegalovirus-negative recipient, recipient use of ventilator, inotropes and amiodarone before transplant, recipient history of diabetes, recipient's serum creatinine and bilirubin, cold ischemia time, most recent panel reactive antibodies (PRA), and year of transplant. Proportional hazards assumption for each of the variables was examined using an interaction term with time. Ventilator use before transplant, serum bilirubin, PRA, and year of transplant showed a significant interaction with time, and the interaction term with time for these variables was retained in the final model. The relationship between intracorporeal or extracorporeal VAD use and mortality, using UNOS status 1 patients as the reference group, was found to be time dependent. Therefore, HRs for different time periods were estimated with the use of indicator variables that represented interaction between these groups and the different time periods. Values of missing variables were replaced by their median value for continuous variables and their most common value for categorical variables.

Secondary analysis was performed, treating various causes of death as competing risks in the Cox proportional hazards model, in selected time periods in which the mortality between the groups was different, to identify the cause responsible for the difference in mortality (11). The causes of death were grouped into 6 categories for this analysis: rejection, infection, cardiovascular, pulmonary, malignant, and other (Online Appendix). A separate Cox proportional hazards model for each of these categories of death was built, with adjustment for all of the variables as in the main analysis. In addition, malignancy in the donor was included as a covariate in the model for death due to malignancy. Statistical analysis was performed using SAS version 9.1 (SAS Institute, Cary, North Carolina).

Results

Patient population. There were 9,455 patients in the UNOS status 1 group, 1,433 patients in the intracorporeal VAD group, and 448 patients in the extracorporeal VAD group.

The median follow-up time was 49 months in the UNOS status 1 group, 36.5 months in the intracorporeal VAD group and 24.4 months in the extracorporeal VAD group.

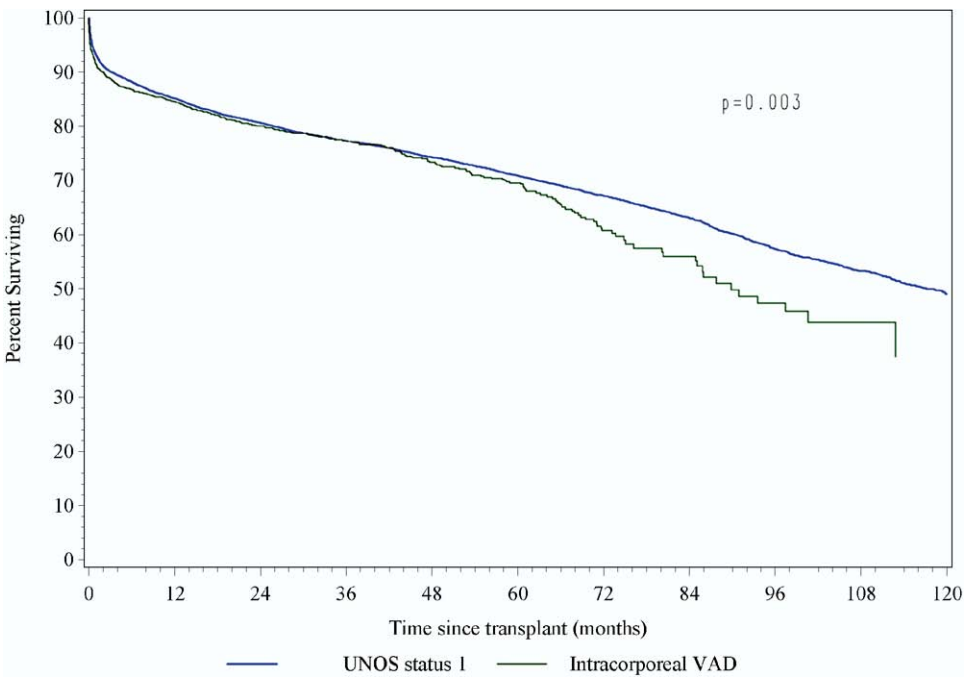

Figure 1 **Post-Transplant Survival of Patients on Intracorporeal VAD Support Compared With UNOS Status 1 Patients Without VAD Support**

Kaplan-Meier survival curves for survival after heart transplantation in each of the 2 groups. The p value is based on the log-rank test of equality. UNOS = United Network for Organ Sharing; VAD = ventricular assist device.

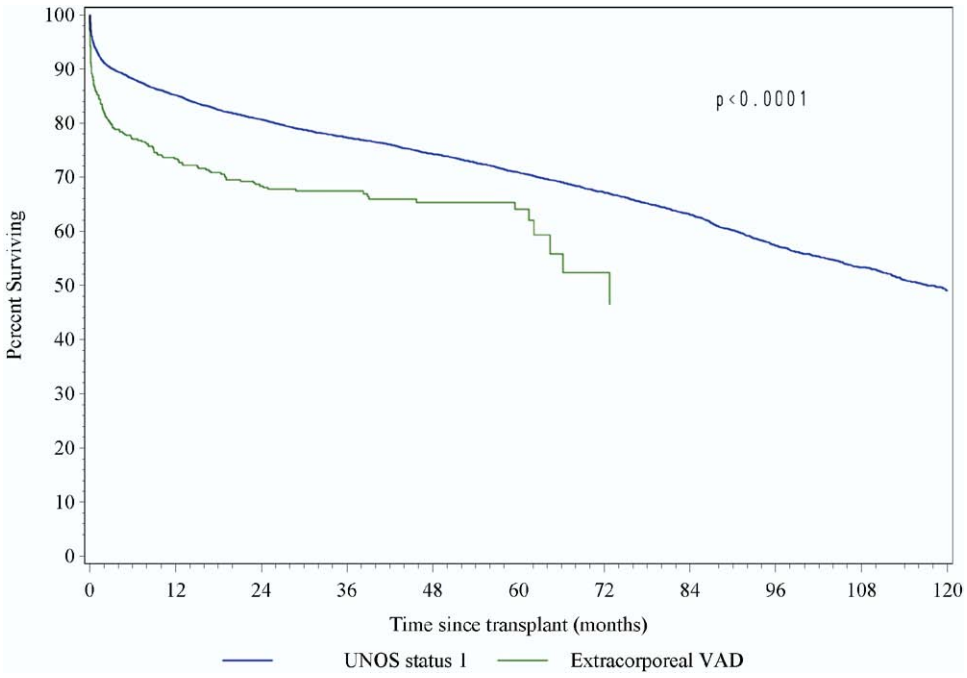

Figure 2 **Post-Transplant Survival of Patients on Extracorporeal VAD Support Compared With UNOS Status 1 Patients Without VAD Support**

Kaplan-Meier survival curves for survival after heart transplantation in each of the 2 groups. The p value is based on the log-rank test of equality. Abbreviations as in Figure 1.

Baseline characteristics. The baseline characteristics of the 3 groups are summarized in Table 1. The etiology of cardiomyopathy was similar between the groups. UNOS status 1 patients were older than intracorporeal VAD patients, who were older than the extracorporeal VAD patients. Time on the waiting list was shorter for the extracorporeal VAD patients compared with UNOS status 1 and intracorporeal VAD patients. Creatinine was lower in the intracorporeal VAD group than in the other 2 groups. Bilirubin was higher in the extracorporeal VAD group compared with the other 2 groups. The most recent PRA was highest in the extracorporeal VAD group, followed by the intracorporeal VAD group, followed by the UNOS status 1 group. Extracorporeal VAD patients were more likely to be on a ventilator compared with the other 2 groups. Inotropic support was more common in the UNOS status 1 group compared with the other 2 groups. Eight percent of patients in the UNOS status 1 group were supported with an IABP. The majority of patients in the extracorporeal and intracorporeal VAD groups were transplanted from 1999 to 2004, whereas patients in the UNOS status 1 group were more evenly derived from 1995 to 2004.

The effect of VAD therapy on post-transplant mortality. Figures 1 and 2 and Table 2 summarize the unadjusted survival in each of the 3 groups after transplantation. Survival curves in the intracorporeal VAD group and

Table 2 **Survival of Patients in the 3 Groups**

	Time in Months										
	0	6	12	24	36	48	60	72	84	96	120
UNOS status 1											
Survival (%)	100	89	86	81	78	75	72	68	64	58	51
Number left	9,455	8,313	7,849	6,886	5,912	4,981	4,117	3,265	2,473	1,670	444
Intracorporeal VAD											
Survival (%)	100	87	85	80	78	74	70	61	57	48	38
Number left	1,433	1,239	1,155	955	752	530	312	143	66	37	4
Extracorporeal VAD											
Survival (%)	100	78	75	70	69	67	66	53	48	48	—
Number left	448	345	312	237	180	110	49	11	3	2	0

Abbreviations as in Table 1.

JACC Vol. 53, No. 3, 2009
January 20, 2009:264–71

UNOS status 1 group were similar up to 48 months, when they started to diverge with decreased survival in the intracorporeal VAD group compared with the UNOS status 1 group. The overall p value for equality of survival between the groups was 0.033 (Fig. 1). The rate of decline in survival was steeper in the extracorporeal VAD group compared with the UNOS status 1 group in the first post-transplant year (Fig. 2). The decline in survival in the extracorporeal VAD group was equal to or less than that in the UNOS status 1 group between 12 and 60 months. The smaller number of patients with follow-up >60 months in the extracorporeal VAD group makes survival estimates after this time point in this group unreliable. The overall p value for equality of survival between these groups was <0.0001.

Intracorporeal and extracorporeal VAD groups were associated with nonproportional time-dependent hazards for mortality compared with the UNOS status 1 group. Thus, HRs were obtained for different time periods and are shown in Table 3. After adjusting for covariates mentioned in the Methods section, the intracorporeal VAD group was associated with an HR of 1.20 (95% confidence interval [CI]: 1.02 to 1.43) for mortality in the first 6 months after transplant compared with the UNOS status 1 group. Between 6 and 60 months, the HRs were not significantly different from 1, after which the HR for the intracorporeal VAD group was 1.99 (95% CI: 1.44 to 2.75) compared with the UNOS status 1 group. The extracorporeal VAD group had an HR of 1.91 (95% CI: 1.53 to 2.37) for mortality compared with the UNOS status 1 group in the first 6 months after transplant. Thereafter, HRs in this group decreased to 0.23 (95% CI: 0.06 to 0.91) at 24 to 36 months and remained diminished until 60 months, after which the extracorporeal VAD group was associated with an HR of 2.9 (95% CI: 1.19 to 7.25) for mortality compared with the UNOS status 1 group.

Causes of increased mortality. The results of the competing risks analysis to identify causes of increased mortality in the VAD groups in selected time periods are shown in Tables 4 and 5. In the first 12 months post-transplant, the intracorporeal VAD group showed a trend toward increased death caused by infection. During this period, the extracorporeal VAD group experienced increased risk of death caused by infections and due to other causes. Beyond 60 months post-transplant, the intracorporeal VAD group showed an increased risk of death caused by infection, malignancy, and other causes. The number at risk was small in the extracorporeal VAD group, yielding unreliable estimates in this time period.

Effect of VADs on post-transplant mortality by era of transplantation. We examined the effect of VADs on post-transplant mortality by era of transplantation (1995 to 1999 vs. 2000 to 2004) by introducing an interaction term of the VAD group and the period of transplantation into the model. No significant difference was noted in the effect of intracorporeal or extracorporeal VADs on post-transplant mortality between these time periods.

Table 3 Hazard Ratios for Post-Transplant Mortality

Variable	Hazard Ratio (95% CI)*	p Value
Intracorporeal VAD vs. UNOS status 1 (months)		
0–<6	1.20 (1.02–1.43)	0.03
6–<12	0.80 (0.56–1.16)	0.24
12–<24	1.06 (0.80–1.41)	0.7
24–<36	0.84 (0.57–1.24)	0.38
36–<48	1.18 (0.79–1.76)	0.42
48–<60	1.22 (0.77–1.92)	0.4
≥60	1.99 (1.44–2.75)	<0.0001
Extracorporeal VAD vs. UNOS status 1 (months)		
0–<6	1.91 (1.53–2.37)	<0.0001
6–<12	1.22 (0.72–2.06)	0.46
12–<24	1.26 (0.79–2.01)	0.33
24–<36	0.23 (0.06–0.91)	0.04
36–<48	0.73 (0.27–1.97)	0.54
48–<60	0.32 (0.05–2.30)	0.26
≥60	2.93 (1.19–7.25)	0.02
Recipient age	0.999 (0.996–1.002)	0.56
Donor age	1.01 (1.01–1.02)	<0.0001
Recipient male	0.83 (0.77–0.91)	<0.0001
Sex mismatch	1.08 (0.99–1.18)	0.07
Time on wait list (days)	1.00 (1.00–1.00)	0.11
Ischemic cardiomyopathy	1.08 (1.00–1.16)	0.04
CMV mismatch (positive donor/ negative recipient)	0.97 (0.88–1.05)	0.43
Ventilator	2.35 (1.96–2.82)	<0.0001
Ventilator × time (months)	0.99 (0.98–0.99)	0.0001
Inotrope use	0.94 (0.86–1.03)	0.16
Amiodarone	1.03 (0.96–1.12)	0.42
Diabetes	1.22 (1.13–1.33)	<0.0001
Serum creatinine (mg/dl)	1.04 (1.03–1.06)	<0.0001
Total bilirubin (mg/dl)	1.03 (1.02–1.04)	<0.0001
Bilirubin × time (months)	0.999 (0.999–1.00)	0.002
Cold ischemia time (h)	1.11 (1.07–1.15)	<0.0001
Most recent PRA (%)	1.01 (1.00–1.01)	<0.0001
Most recent PRA × time (months)	1.00 (1.00–1.00)	0.0007
Year of transplantation	0.95 (0.93–0.97)	<0.0001
Year × time (months)	1.00 (1.00–1.002)	0.005

*Adjusted for all variables in the table.
CI = confidence interval; other abbreviations as in Table 1.

Discussion

The treatment options for patients with advanced heart failure or those with deteriorating end-organ function on maximal medical management are limited to intravenous inotropes and mechanical assistance with IABP or VAD. Evidence from observational studies suggests that VADs are superior to IABP and inotropic support in successfully bridging patients to transplantation (8,9). VADs have been shown to improve cardiac output and end-organ function (1,2). A study by Deng et al. (12) compared mortality by the urgency of placement of a VAD including semielective, urgent, and emergent, and showed that the best outcomes were observed in patients who received VADs semielectively. Gronda et al. (13) showed that patients receiving intravenous inotropic support while awaiting transplanta-

Table 4 Risk of Cause-Specific Death Within the First 12 Months After Transplant

Cause of Death*	Number of Deaths			Hazard Ratio (95% CI)†	
	UNOS Status 1 (n = 9,455)	Intracorporeal VAD (n = 1,433)	Extracorporeal VAD (n = 448)	Intracorporeal VAD	Extracorporeal VAD
Rejection	173	21	10	0.91 (0.54–1.55)	1.34 (0.67–2.69)
Infection	276	49	23	1.41 (0.98–2.03)	2.17 (1.35–3.46)
Cardiovascular	246	33	19	0.89 (0.59–1.35)	1.55 (0.93–2.58)
Pulmonary	75	7	5	0.60 (0.25–1.41)	1.48 (0.56–3.91)
Malignancies	23	3	1	1.17 (0.28–4.83)	2.36 (0.28–19.96)
Other	568	104	54	1.07 (0.83–1.37)	1.66 (1.21–2.26)

*See the Online Appendix for details of classification. †Compared with the UNOS status 1 group. Adjusted for variables listed in the Methods section.
Abbreviations as in Table 3.

tion for more than 21 days had a >50% mortality post-transplant. These observational data lend support to the hypothesis that transitioning patients who are on inotropic support to VAD support may improve post-transplant survival. This idea, combined with the scarcity of donor organs, has led to an increasing number of transplant recipients being bridged to transplant with a VAD (14).

Several studies exploring effect of VADs on post-transplant outcomes have reported conflicting results, showing improved, neutral, or even worse survival for patients supported with VADs pre-transplant (3–10,14–19). One study that used data from the Cardiac Transplant Research Database reported no significant difference in post-transplant survival between 502 patients treated with a left ventricular assist device (including 85 patients on an extracorporeal left ventricular assist device) and 2,514 patients on intravenous inotropes bridged to transplant between 1990 and 1997 (20). In contrast, however, 4 of the last 6 annual reports from the International Society for Heart and Lung Transplantation registry reported increased early post-transplant mortality in patients supported with VADs (14–19). These data are in agreement with our own findings. Indeed, the primary strength of the current analysis is that it is a study with the largest number of patients to date to help address this important issue in the care of patients before cardiac transplantation. We found that patients bridged to transplant with intracorporeal VADs had a 20% higher risk of mortality in the first 6 months after transplant and a nearly 2-fold higher risk of mortality beyond 5 years compared with UNOS status 1 patients. In absolute terms this translates to 2% excess mortality at 6 months, 1% excess mortality at 1 year, and 7% to 10% excess mortality at 6 to 8 years. The difference at 6 months and 1 year is small and of unclear clinical significance, but the 7% to 10% excess mortality at 6 to 8 years in the intracorporeal VAD group is of considerable concern.

Patients bridged with extracorporeal VADs showed a nearly 2-fold increase in mortality in the first 6 months after transplant compared with UNOS status 1 patients not bridged with a VAD. These findings are consistent with the results from the registry of the International Society for Heart and Lung Transplantation (14,18,19,21). Beyond 6 months, however, patients bridged with extracorporeal VADs had a lower mortality compared with UNOS status 1 patients. This is probably the result of self-selection of patients who were able to survive the initial post-transplant period. Similar to the finding in patients with intracorporeal VADs, patients bridged with extracorporeal VADs had a higher mortality beyond 5 years of transplant compared with UNOS status 1 patients not bridged with a VAD, although the number of patients for this analysis was small.

Infection seems to mediate part of the excess mortality in the early post-transplant period in the extracorporeal and possibly in the intracorporeal VAD group. Although we did not have the data to look at, it is known that extracorporeal VAD patients are more likely to have biventricular failure and therefore a number of contributors to increased mortality, including poor nutritional status and increased ino-

Table 5 Risk of Cause-Specific Death More Than 60 Months After Transplant

Cause of Death*	Number of Deaths			Hazard Ratio (95% CI)†	
	UNOS Status 1 (n = 4,111)	Intracorporeal VAD (n = 311)	Extracorporeal VAD (n = 49)	Intracorporeal VAD	Extracorporeal VAD
Rejection	38	1	1	0.42 (0.05–3.6)	6.47 (0.64–65.34)
Infection	90	7	0	3.26 (1.34–7.93)	0 (0–∞)
Cardiovascular	143	3	0	1.02 (0.3–3.41)	0 (0–∞)
Pulmonary	30	2	0	1.47 (0.3–7.13)	0 (0–∞)
Malignancies	87	10	1	7.08 (3.24–15.48)	19.84 (2.19–179.6)
Other	284	19	3	2.06 (1.23–3.47)	4.06 (1.19–13.91)

*See the online Appendix for details of classification. †Compared with the UNOS status 1 group. Adjusted for variables listed in the Methods section.
Abbreviations as in Table 3.

trope use, which could potentially explain the higher mortality in this group compared with the intracorporeal VAD group in the immediate post-transplant period. The increase in mortality in the intracorporeal VAD group attributable to infection, malignancy, and other causes 5 years beyond transplant is an intriguing finding. It has been shown that patients with VADs have impaired cellular immunity (22,23). Although this can explain the trend toward increased infections in patients bridged with VADs in the early post-transplant period, the reason for increased infections in these patients 5 years after transplant is not clear. Further study into this aspect of VADs is warranted. The reason for increased death caused by malignancy in intracorporeal VAD patients is unclear. Ventricular assist devices are associated with allosensitization (21). However, we did not see increased mortality associated with rejection in VAD patients in our study. Allosensitization may play a role in a longer waiting time to transplant with intracorporeal VADs (21). It is not known whether this results in end-organ damage, which manifests as late increased mortality.

Study limitations. Survival to transplant is an important component of the overall effect of any intervention in patients awaiting transplantation. We could not assess the effect of VADs on survival to transplant and could only assess their effect post-transplant. We therefore cannot estimate the overall benefit or harm with VADs. Although we adjusted for a variety of indicators of the patient's illness at the time of transplant, it is possible that there were unmeasured differences between the groups that could potentially bias the results. We did not have the indication for VAD in the database and resorted to combining all patients on VAD. It was therefore not possible to determine the effect of VADs on post-transplant mortality by the reason for VAD implantation (i.e., elective vs. clinical instability). Because the data used predate the appearance of continuous flow devices, the results of this study cannot be generalized to these newer devices, which are gaining popularity (24). Only a randomized controlled trial can establish the overall effect of VADs in stable status 1 patients awaiting transplantation.

Conclusions

Patients who are unstable or symptomatic despite maximal medical therapy require VAD support as a bridge to transplant. One question raised by studies that have shown improved end-organ function with VADs is whether VADs improve post-transplant survival. Our results do not confirm this conclusion, but rather show that VADs are associated with increased early and late post-transplant mortality. Based on our results, we cannot recommend VAD implantation with a view to improving post-transplant survival for patients who are stable on intravenous inotropic therapy.

Reprint requests and correspondence: Dr. Rajan Krishnamani, Division of Cardiology, Tufts Medical Center, 800 Washington Street, Box 5931, Boston, Massachusetts 02111. E-mail: rkrishnamani@tuftsmedicalcenter.org.

REFERENCES

1. Farrar DJ, Hill JD, for the Thoratec Ventricular Assist Device principal investigators. Recovery of major organ function in patients awaiting heart transplantation with Thoratec ventricular assist devices. J Heart Lung Transplant 1994;13:1125–32.
2. Friedel N, Viazis P, Schiessler A, et al. Recovery of end-organ failure during mechanical circulatory support. Eur J Cardiothorac Surg 1992;6:519–22, discussion 523.
3. Massad MG, McCarthy PM, Smedira NG, et al. Does successful bridging with the implantable left ventricular assist device affect cardiac transplantation outcome? J Thorac Cardiovasc Surg 1996;112: 1275–81, discussion 1282–3.
4. Drakos SG, Kfoury AG, Long JW, et al. Effect of mechanical circulatory support on outcomes after heart transplantation. J Heart Lung Transplant 2006;25:22–8.
5. Baran DA, Gass AL, Galin ID, et al. Lack of sensitization and equivalent post-transplant outcomes with the Novacor left ventricular assist device. J Heart Lung Transplant 2005;24:1886–90.
6. Morgan JA, Park Y, Kherani AR, et al. Does bridging to transplantation with a left ventricular assist device adversely affect posttransplantation survival? A comparative analysis of mechanical versus inotropic support J Thorac Cardiovasc Surg 2003;126:1188–90.
7. Pagani FD, Dyke DB, Wright S, Cody R, Aaronson KD. Development of anti-major histocompatibility complex class I or II antibodies following left ventricular assist device implantation: effects on subsequent allograft rejection and survival. J Heart Lung Transplant 2001;20:646–53.
8. Frazier OH, Rose EA, McCarthy P, et al. Improved mortality and rehabilitation of transplant candidates treated with a long-term implantable left ventricular assist system. Ann Surg 1995;222:327–36, discussion 336–8.
9. Frazier OH, Rose EA, Oz MC, et al. Multicenter clinical evaluation of the HeartMate vented electric left ventricular assist system in patients awaiting heart transplantation. J Thorac Cardiovasc Surg 2001;122:1186–95.
10. Fernandez FG, Jaramillo A, Ewald G, et al. Blood transfusions decrease the incidence of acute rejection in cardiac allograft recipients. J Heart Lung Transplant 2005;24:S255–61.
11. Allison PD. Survival Analysis Using SAS: A Practical Guide. Cary, NC: SAS Institute Inc., 1995:185.
12. Deng MC, Weyand M, Hammel D, et al. Selection and management of ventricular assist device patients: the muenster experience. J Heart Lung Transplant 2000;19:S77–82.
13. Gronda EG, Barbieri P, Frigerio M, et al. Prognostic indices in heart transplant candidates after the first hospitalization triggered by the need for intravenous pharmacologic circulatory support. J Heart Lung Transplant 1999;18:654–63.
14. Taylor DO, Edwards LB, Boucek MM, et al. Registry of the international society for heart and lung transplantation: twenty-fourth official adult heart transplant report—2007. J Heart Lung Transplant 2007;26:769–81.
15. Hertz MI, Taylor DO, Trulock EP, et al. The registry of the international society for heart and lung transplantation: nineteenth official report–2002. J Heart Lung Transplant 2002;21:950–70.
16. Taylor DO, Edwards LB, Mohacsi PJ, et al. The registry of the international society for heart and lung transplantation: twentieth official adult heart transplant report–2003. J Heart Lung Transplant 2003;22:616–24.
17. Taylor DO, Edwards LB, Boucek MM, Trulock EP, Keck BM, Hertz MI. The registry of the international society for heart and lung transplantation: twenty-first official adult heart transplant report–2004. J Heart Lung Transplant 2004;23:796–803.
18. Taylor DO, Edwards LB, Boucek MM, et al. Registry of the international society for heart and lung transplantation: twenty-second official adult heart transplant report–2005. J Heart Lung Transplant 2005;24:945–55.

19. Taylor DO, Edwards LB, Boucek MM, et al. Registry of the international society for heart and lung transplantation: twenty-third official adult heart transplantation report–2006. J Heart Lung Transplant 2006;25:869–79.
20. Jaski BE, Kim JC, Naftel DC, et al. Cardiac transplant outcome of patients supported on left ventricular assist device vs. intravenous inotropic therapy. J Heart Lung Transplant 2001;20:449–56.
21. John R, Lietz K, Schuster M, et al. Immunologic sensitization in recipients of left ventricular assist devices. J Thorac Cardiovasc Surg 2003;125:578–91.
22. Kimball PM, Flattery M, McDougan F, Kasirajan V. Cellular immunity impaired among patients on left ventricular assist device for 6 months. Ann Thorac Surg 2008;85:1656–61.
23. Itescu S, Schuster M, Burke E, et al. Immunobiologic consequences of assist devices. Cardiol Clin 2003;21:119–33.
24. Miller LW, Pagani FD, Russell SD, et al. Use of a continuous-flow device in patients awaiting heart transplantation. N Engl J Med 2007;357:885–96.

Key Words: heart-assist devices ■ ventricular assist device ■ mortality ■ outcome ■ heart transplantation.

APPENDIX

For a classification of causes of death into categories, please see the online version of this article.