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Right ventricular assist device results in worse post-transplant survival

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BACKGROUND: To our knowledge, how the need for a right ventricular assist device (RVAD) with a left ventricular assist device (LVAD) affects outcomes after orthotopic heart transplantation has not been studied in a multi-institutional database.

METHODS: The United Network for Organ Sharing (UNOS) database was queried for all adult orthotopic heart transplantations from the period 2005–2012. Patients requiring a RVAD + LVAD as a bridge to transplant were compared with patients requiring a LVAD only and patients requiring no ventricular assist device (VAD).

RESULTS: During the study period, 16,955 orthotopic heart transplantations were performed. Of these, 13,209 (77.9%) patients did not require a VAD, 3,270 (19.3%) required a LVAD only, and 457 (2.7%) required a RVAD + LVAD. The RVAD + LVAD group had the longest length of stay (25.7 days) compared with the no VAD group (20.8 days) and the LVAD-only group (21.1 days) ($p < 0.001$). On multivariate analysis, requirement of a RVAD + LVAD before transplantation was independently associated with post-transplant mortality (hazard ratio 1.22, 95% confidence interval 1.01–1.49, $p = 0.04$). Other variables associated with mortality included donor age, pulsatile flow LVAD as a bridge to transplant, prolonged ischemic time, worsening renal function, black race, history of diabetes in recipient, class II panel-reactive antibody >10%, sex mismatch, and extracorporeal membrane oxygenation or mechanical ventilation as a bridge to transplant.

CONCLUSIONS: The requirement of a RVAD in addition to a LVAD before orthotopic heart transplantation is associated with worse post-transplant outcomes and increased mortality.

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A significant portion of patients with a left ventricular assist device (LVAD) subsequently develop right ventricular failure.[1,2] The need for a right ventricular assist device (RVAD) is known to result in worse survival in patients with LVADs before transplantation.[3,4] However, how the implantation of a RVAD + LVAD affects outcomes after heart transplantation is unclear. Although prior studies showed similar survival in patients with implantation of a RVAD + LVAD after transplantation,[5] this topic to our knowledge has not been examined in a large, multi-institutional database. The goal of this study was to use the United Network for Organ Sharing (UNOS) database to determine if patients with a RVAD + LVAD as a bridge to transplant have worse survival after orthotopic heart transplantation. We hypothesized that patients with implantation of a LVAD + RVAD have worse post-transplant survival.

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Methods

Data source

After approval from the local institutional review board, public-use Standard Transplant Analysis and Research data files were obtained from the UNOS registry. The UNOS database was queried for all adult (≥18 years old) primary orthotopic heart transplants performed from January 2005 to December 2012. The analysis was started in 2005 because data on mechanical circulatory support devices became consistently available in this year. Patients with a RVAD + LVAD were compared with patients with a LVAD only and patients without any type of ventricular assist device (VAD). For our survival analysis, the LVAD-only group was divided into a pulsatile-flow LVAD group and a continuous-flow LVAD group. The primary end-point measured was risk-adjusted all-cause mortality. Secondary end-points included acute rejection episodes during index hospitalization and length of stay.

Statistical analysis

Student's *t*-test, analysis of variance, and chi-square test were used to examine continuous and categorical variables. Continuous variables are presented as mean ± SD, and categorical variables are reported as percentages of the total number of data points available for that field. Cox proportional regression analysis was performed in 2 steps. First, covariates were run in a univariate analysis as predictors of mortality. Next, covariates with a *p*-value < 0.20 were entered simultaneously in the Cox model. There were 1,212 (7.2%) patients excluded from the final multivariate analysis because of missing data. In addition, 2-way interactions were tested between recipient requirement of a RVAD + LVAD and recipient age, recipient sex, donor age, donor sex, and ischemic time. Because none of these interactions were significant, they were not retained in the final model. Covariates missing >15% of data in the registry were excluded from the analysis. Survival curves were generated using the Kaplan-Meier method and compared with the log-rank test.

Results

Recipient characteristics

During the study period, 16,955 orthotopic heart transplantations were performed. Of these, 13,209 (77.9%, mean) patients did not require a LVAD or RVAD, 3,270 (19.3%, mean) patients required a LVAD only, and 457 (2.7%, mean) patients required a RVAD + LVAD. Baseline recipient characteristics are compared in Table 1. The LVAD-only group was oldest (52.0 years), followed by the RVAD + LVAD group (46.9 years) and the no VAD group (43.1 years) ($p < 0.001$). The LVAD-only group also had the highest body mass index (28.0) compared with other groups ($p < 0.001$). The RVAD + LVAD group was most likely to require mechanical ventilation (6.8%) before transplantation followed by the no VAD group (5.5%) and the LVAD-only group (2.6%, mean) ($p < 0.001$). Median follow-up time for the study was 773.0 days.

Of the patients in the LVAD-only group, 2,286 (73.5%, mean) had a continuous-flow LVAD. The remaining 826 (26.5%, mean) patients were implanted with a pulsatile-flow LVAD. In addition, 19 (0.1%) patients with a RVAD only were excluded from the final survival analysis.

Donor characteristics

Donor characteristics are summarized in Table 2. Donors in the LVAD-only group were oldest (31.0 years, mean), followed by the RVAD + LVAD group (30.3 years, mean)

Table 1 Comparison of Recipient Characteristics

	No VAD ($n = 13,209$)	LVAD only ($n = 3,270$)	RVAD + LVAD ($n = 457$)	*p*-value
Age (years)	43.1 ± 21.9	52.0 ± 12.4	46.9 ± 13.9	<0.001
Male sex	8,885 (67.3)	2,552 (78.0)	341 (74.6)	<0.001
White	8,780 (66.5)	2,210 (67.6)	307 (67.2)	0.47
Black	2,541 (19.2)	717 (21.9)	77 (16.9)	0.001
Hispanic	1,275 (9.7)	224 (6.9)	47 (10.3)	<0.001
Asian	430 (3.3)	91 (2.8)	21 (4.6)	0.09
Native American/Alaskan	40 (0.3)	10 (0.3)	1 (0.2)	0.95
Hawaiian/Pacific Islander	41 (0.3)	6 (0.2)	2 (0.4)	0.03
Multiracial	102 (0.8)	12 (0.4)	2 (0.4)	<0.001
Recipient BMI	24.9 ± 6.1	28.0 ± 5.0	25.7 ± 4.8	<0.001
Cardiac output (liter/min)	4.27 ± 1.59	4.87 ± 1.58	4.38 ± 1.71	<0.001
Mean PVR (Wood units)	2.63 ± 2.83	2.25 ± 1.84	2.30 ± 1.84	<0.001
Class I PRA	6.20 ± 17.5	9.09 ± 20.90	9.75 ± 20.84	<0.001
Class II PRA	5.55 ± 17.48	5.32 ± 16.83	6.08 ± 17.76	0.54
Creatinine before transplant (mg/dl)	1.29 ± 0.80	1.44 ± 0.61	1.23 ± 1.04	0.02
Mechanical ventilation before transplant	728 (5.5)	86 (2.6)	31 (6.8)	<0.001
Inhaled nitric oxide before transplant	46 (0.4)	8 (0.2)	0 (0)	0.48
ECMO before transplant	254 (1.9)	23 (0.7)	12 (2.6)	<0.001

BMI, body mass index, ECMO, extracorporeal membrane oxygenation; LVAD, left ventricular assist device; PRA, panel-reactive antibody; PVR, pulmonary vascular resistance; RVAD, right ventricular assist device; VAD, ventricular assist device. Values are mean +/− SD, and n (%).