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Impact of Center Left Ventricular Assist Device Volume on Outcomes After Implantation

An INTERMACS Analysis

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ABSTRACT

OBJECTIVES This study examined patient outcomes after left ventricular assist device (LVAD) implantation across a range of center surgical volumes.

BACKGROUND In order for a center to qualify for reimbursement, Centers for Medicare and Medicaid Services (CMS) requires it to implant ≥10 LVADs or total artificial hearts over a 3-year period. The impact of center LVAD surgical volumes on patient outcomes has not been thoroughly scrutinized.

METHODS Center volumes were provided for 7,416 patients undergoing LVAD implantation who were enrolled in INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support). Center LVAD volume was categorized as either very low (≤10 implants/year, n = 617), low (11 to 30 implants/year, n = 2,561), medium (31 to 50 implants/year, n = 2,458), or high (>50 implants/year, n = 1,750). The main outcome of interest was patient survival based on center volume derived from Kaplan-Meier and multivariate Cox regression.

RESULTS Overall survival was associated with center volume (p = 0.003), as follows: 71 ± 1.8% (very low volume), 81 ± 0.8% (low volume), 83 ± 0.8% (medium volume), and 79 ± 1.0% (high volume) at 1 year. Compared with medium volume centers, the 90-day mortality was higher in very low volume (odds ratio [OR]: 1.35; p = 0.04) and high volume (OR: 1.28; p = 0.018) VAD centers. The adjusted hazard ratios (HRs) for mortality were 1.32 (95% confidence interval [CI]: 1.11 to 1.56), 1.07 (95% CI: 0.95 to 1.21), and 1.17 (95% CI: 1.03 to 1.30) for very low, low, and high volume centers, respectively. Center volume did not predict mortality (p = 0.25; n = 3,688) in INTERMACS profile 1 patients (patients who had sustained cardiogenic shock) and profile 2 patients (patients with progressive hemodynamic decline despite inotropes).

CONCLUSIONS Center volume correlates with post-VAD survival, with worse survival noted at very-low volume centers. These findings suggest that current U.S. VAD center standards warrant reconsideration. (J Am Coll Cardiol HF 2017;5:691–9)

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ABBREVIATIONS AND ACRONYMS

CF = continuous flow

ECMO = extracorporeal membrane oxygenation

IABP = intra-aortic balloon pump

LVAD = left ventricular assist devices

MCS = mechanical circulatory support

Various studies have demonstrated associations between mortality and surgical volumes following various cardiac operations (1-6). In an analysis of first-generation left ventricular assist devices (LVADs) implanted for destination therapy, Lietz et al. (7) found a correlation between mortality and lower center surgical volume, but center volume was not an independent predictor of death when other risks were considered. Using the U.S. National Inpatient Sample, Shah et al. (6) demonstrated that patients undergoing mechanical circulatory support implantation at low volume centers (<22 LVADs/year) had inferior inpatient survival compared with patients undergoing LVAD surgery at higher volume centers (6). In contrast, a study of 88 academic medical centers in the United States found no association between hospital LVAD surgical volume and inpatient mortality, but operative survival was greatest when the LVAD operation was performed by the highest volume surgeons (5). During the derivation of the HeartMate II Risk Score, it was noted that center volume was an independent correlate of operative mortality in multivariate analysis (8). Aside from age, center volume (hazard ratio [HR]: 1.6) was also the only predictor of longer-term survival after HeartMate II implantation (8). Granular analyses restricted to approved continuous flow (CF) devices are lacking, and the influence of center volume on long term outcomes is not clear.

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As more centers are opening for mechanical circulatory support (MCS) implantation, the impact (or lack thereof) of center volume on patient short- and long-term outcomes warrants study. Using data from patients entered in the INTERMACS (Interagency Registry of Assisted Circulatory Support), we compared patient outcomes based on centers' VAD volume.

METHODS

The full INTERMACS cohort consisted of 14,014 patients who underwent primary CF-LVAD or biventricular assist device (BiVAD) implantation between 2009 and 2015. Patients who received total artificial heart support or isolated right ventricular support were excluded (9). Center volume data were provided by INTERMACS administrators for 7,416 patients undergoing LVAD or BiVAD implantation between 2012 and 2014. Center volume was defined as the number of durable LVAD implants performed at the center in the same calendar year as the patient's LVAD implantation. Patients undergoing right ventricular assist device (RVAD) support simultaneously with LVAD operation were counted as 1 single event. To maintain center anonymity during analysis, center MCS volumes were subdivided by INTERMACS administrators prior to data release into the following thresholds of yearly implantations: ≤10 (very low volume), 11 to 20, 21 to 30, 31 to 50 (medium volume), and >50 (high volume). After further data analysis, survival and adjusted survival were deemed equivalent between centers implanting 11 to 20 VADs and 21 to 30 VAD per year; these patient groups were consolidated into 1 group (11 to 30 VADs per year) termed "low volume."

Pre-operative clinical characteristics, demographics and frequencies of pre-operative vasoactive medication use, hemodialysis, ventilator support, and application of extracorporeal membrane oxygenation (ECMO) and/or intra-aortic balloon pump (IABP) support were compared between the entire INTERMACS cohort (n = 14,014) and the center volume sample (n = 7,416). Then, these same variables were compared among thresholds of center volumes (very low, low, medium, and high volume).

To examine survival in patients who were critically ill at the time of LVAD implantation, we performed a subanalysis of center volume and outcomes exclusive to patients categorized as INTERMACS profile 1

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(patients who had sustained cardiogenic shock) and profile 2 (patients with progressive hemodynamic decline despite inotropes). Prior studies have shown marked heterogeneity in assigning profile 1 versus profile 2 in critically ill patients, so the consolidated grouping herein was believed to be appropriate (10).

OUTCOMES OF INTEREST. The main clinical outcome of interest was the difference in adjusted survival by center LVAD volume. Early mortality (defined as death within 90 days of MCS implantation) was a secondary outcome. The 90-day time frame for early mortality was chosen because prior INTERMACS analyses have shown this to be the post-operative time frame with the highest risk for adverse outcome following LVAD, after which the risk declines (11).

STATISTICAL ANALYSIS. SAS version 9.3 software (SAS, Cary, North Carolina) and SPSS version 24 software (SPSS, Chicago, Illinois) were used for analyses. Categorical variables were tallied as frequencies and compared using Fisher exact or Pearson chi-square tests for >2×2 comparisons. Continuous variables were assessed for normality using histograms and are reported as mean ± SEM or median (25th, 75th quartiles), as appropriate, unless otherwise specified. Possible differences among groups were assessed by using Student *t* or Mann-Whitney *U* test, as appropriate.

Odds ratios for 90-day mortality were generated using logistic regression. Kaplan-Meier survival estimates were calculated at each center volume threshold, censoring patients at the time of transplantation or explantation for recovery. For all survival analyses, differences among center volume groups were compared using log rank testing and then pairwise comparisons among center volume groups were made. To account for any bias in Kaplan-Meier estimates due to censoring for transplantation, a separate analysis was performed including only those patients who did not undergo transplantation.

Mortality HRs based on center volume for the whole cohort were calculated using Cox regression modeling. Mortality comparisons were adjusted for known clinical risks. Simultaneous Cox modelling included the following covariates: advanced patient age (>69 years of age), sex, previous cardiac surgery, bridge to transplant listed status, INTERMACS profile 1 and 2 status, pre-operative creatinine and albumin concentrations, pre-operative ventilator support (within 48 h), and concomitant surgery and/or implantation of RVAD support at the time of durable LVAD implantation (8,11–13). Device type (axial vs. centrifugal flow) was also forced into the model. Due to a large amount of missing data (>20%), social measurements (substance use, education level), vasopressor use, and temporary circulatory support modifier were not included in data analysis. Hazard ratios (and 95% confidence interval) were provided. For all analyses including multivariate regression candidate variable exit criteria, a p value of ≤0.05 was considered significant.

This study and manuscript were approved by the Data Access, Analysis, and Publication Committee of

TABLE 1 Characteristics in the Total INTERMACS CF-LVAD/BiVAD Sample and in the 2012-2014 Cohort

	INTERMACS Total CF-LVAD Sample (n = 14,014)	2012-2014 INTERMACS Cohort (n = 7,416)
Age group, yrs		
<50	3,536 (26)	1,834 (25)
50–59	3,863 (28)	1,967 (27)
60–69	4,595 (33)	2,488 (34)
≥70	1,920 (14)	1,127 (15)
Males	11,011 (79)	5,834 (79)
Ischemic myopathy	6,447 (46)	3,466 (47)
Congenital heart disease	70 (0.5)	36 (0.5)
Prior cardiac surgery	4,755 (34)	2,472 (33)
BTT listed	3,881 (28)	1,799 (25)
INTERMACS profile		
1	2,064 (15)	1,055 (14)
2	5,190 (37)	2,633 (36)
3	4,217 (30)	2,331 (32)
4–7	2,483 (18)	1,356 (18)
Pre-operative ECMO	355 (2.5)	188 (2.5)
IABP	3,487 (25)	1,626 (22)
Pre-operative vasopressor*	982 (7.3)	513 (7.2)
Ventilator support 48 h pre-surgery	840 (6.0)	382 (5.2)
Renal replacement†	317 (2.3)	147 (2.0)
Creatinine, mg/dl	1.41 ± 0.06	1.39 ± 0.01
INR	1.2 (1.1, 1.4)	1.2 (1.1, 1.4)
Albumin, g/dl	3.40 ± 0.01	3.41 ± 0.01
LVAD only	13,563 (96.8)	2,554 (95.8)
BiVAD (simultaneous)	451 (3.2)	34 (4.3)
Continuous flow		
CF-Af	12,051 (86)	6,004 (81)
CF-CF	1,963 (14)	1,412 (19)
Bypass time, min	96.2 ± 0.4	95.3 ± 0.6
Concomitant surgery	5,620 (40)	3,054 (41)
Total months support	11.7 (4.9, 24.8)	13.9 (7.2, 23.9)
90-day death	1,339 (10)	705 (10)
Survival, 1 yr	80 ± 0.4	81 ± 0.5

Values are n (%), mean ± SEM, or median (25th, 75th percentiles). *Defined as epinephrine or norepinephrine pre-operatively. †Defined as dialysis or ultrafiltration administered within 48 h prior to operation.

BiVAD = biventricular assist device; BTT = bridge to transplant; CF-Af = continuous flow, axial flow; CF-CF = continuous flow, centrifugal flow; ECMO = extracorporeal membrane oxygenation; IABP = intra-aortic balloon pump; INR = international normalized ratio; INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support; LVAD = left ventricular assist device.

TABLE 2 Characteristics of Patients by Center Volume of CF-LVAD Implants in 2012 to 2014

	Center Volume				
	≤10 (n = 617)	11–30 (n = 2,561)	31–50 (n = 2,488)	>50 (n = 1,750)	p Value
Age group, yrs					<0.001
<50	113 (18)	622 (24)	647 (26)	452 (26)	
50–59	131 (21)	672 (26)	682 (27)	482 (28)	
60–69	207 (34)	822 (32)	851 (34)	608 (35)	
≥70	166 (27)	445 (17)	308 (12)	208 (12)	
Males	487 (79)	2,039 (80)	1,951 (78)	1,357 (78)	0.57
Ischemic myopathy	321 (53)	1,202 (47)	1,122 (46)	821 (47)	0.021
Congenital heart disease	3 (0.6)	13 (0.5)	9 (0.4)	11 (0.6)	0.32
Prior cardiac surgery	216 (35)	824 (32)	860 (35)	572 (33)	0.23
BTT listed	95 (15)	617 (24)	604 (24)	483 (28)	<0.001
INTERMACS profile					<0.001
1	80 (13)	311 (12)	356 (15)	308 (18)	
2	204 (33)	979 (38)	841 (34)	609 (35)	
3	205 (33)	802 (31)	801 (33)	523 (30)	
4–7	125 (20)	463 (18)	460 (19)	308 (18)	
Support 48 h pre-operative ECMO	14 (2.3)	53 (2.1)	70 (2.8)	51 (2.9)	0.24
IABP	97 (16)	560 (22)	582 (23)	387 (22)	0.001
Ventilator	36 (5.8)	111 (4.3)	143 (5.7)	92 (5.3)	0.12
Vasopressor*	32 (5.3)	142 (5.8)	210 (8.8)	129 (7.8)	<0.001
Dialysis†	16 (2.6)	34 (1.3)	50 (2.0)	47 (2.7)	0.010
Creatinine, mg/dl	1.36 ± 0.02	1.39 ± 0.01	1.36 ± 0.02	1.44 ± 0.02	0.006
INR	1.30 ± 0.02	1.31 ± 0.01	1.31 ± 0.01	1.32 ± 0.01	0.65
Albumin, g/dl	3.35 ± 0.03	3.42 ± 0.01	3.40 ± 0.01	3.46 ± 0.02	0.003
LVAD only	609 (98.7)	2,494 (97.4)	2,408 (96.8)	1,686 (96.3)	0.014
BiVAD (simultaneous)	8 (1.3)	67 (2.6)	80 (3.2)	64 (3.7)	
Continuous flow					
CF-Af	582 (94)	2,153 (84)	1,935 (78)	1,334 (76)	<0.001
CF-CF	35 (5.7)	408 (16)	553 (22)	416 (24)	
Bypass time, min	107 ± 2.1	97 ± 1.0	96 ± 1.0	87 ± 1.1	<0.001
Concomitant surgery	256 (42)	968 (38)	1,017 (41)	799 (46)	<0.001
Total months of support	15 (7.1, 25.0)	13 (6.9, 23.0)	15 (8.0, 25.0)	13 (6.7, 23.0)	0.002

Values are n (%), mean ± SEM, or median (25th, 75th percentiles). *Defined as epinephrine or norepinephrine pre-operatively. †Defined as dialysis or ultrafiltration administered within 48 h prior to operation.

Abbreviations as in Table 1.

INTERMACS. Patient consent for INTERMACS data collection was obtained at enrolling centers according to local Review Board requirements.

RESULTS

Table 1 shows the pre-operative demographics, characteristics, and laboratory values for the entire INTERMACS cohort and those in the 2012 to 2014 INTERMACS sample. The 2012 to 2014 sample was similar to the full INTERMACS CF-LVAD cohort. Survival at 1 year was 80 ± 0.4% in the full INTERMACS CF-LVAD cohort and 81 ± 0.5% in the 2012 to 2014 sample.

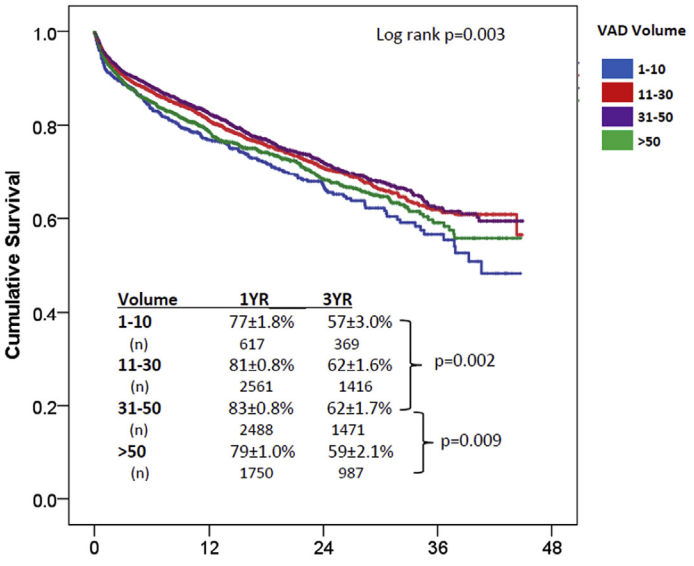
In the 2012 to 2014 INTERMACS sample (n = 7,416), 8.3% (n = 617) implants were from very-low volume centers, 34.5% (n = 2,561) were from low volume centers, 33.5% (n = 2,488) were from medium volume centers, and 23.6% (n = 1,750) were from high volume centers. Table 2 shows the baseline characteristics of patients by center volume category. Very-low volume centers implanted more patients of advanced age (≥70 years) and a destination therapy indication was more common. Very-low volume centers were less likely to implant a balloon pump pre-operatively; had longer bypass times intraoperatively; and were less likely to insert RVAD support intraoperatively. High volume centers performed implantations in more patients with an INTERMACS profile of 1 pre-operatively, but the frequency of ECMO and use of pre-operative ventilators were not greater. Patients at high volume centers were less likely to be of advanced age and had higher baseline serum creatinine and albumin concentrations.

SURVIVAL BASED ON 2012 TO 2014 CENTER VOLUMES. The median (25th, 75th percentiles) duration of support for the 2012 to 2014 sample was 415 (211, 718) days (mean 486 days). Using medium volume (n = 31 to 50 VADs/year) centers as a reference, early mortality (within 90 days, n = 708 total) occurred in 11.5% (OR: 1.35 [95% CI: 1.01 to 1.80]; p = 0.04), 10% (OR: 1.11 [95% CI: 0.92 to 1.30]; p = 0.29), 9.1% (reference), and 11.7% (OR: 1.28 [95% CI: 1.04 to 1.58]; p = 0.018) of very low, low, medium, and high volume centers (p = 0.029), respectively. Unadjusted overall survival (Figure 1) was also associated with center volume (p = 0.003), and 1-year survival rates were as follows: 77 ± 1.8% (very low volume), 81 ± 0.8% (low volume), 83 ± 0.8% (medium volume), and 79 ± 1.0% (high volume). A pairwise comparison of center volumes (Figure 1) showed overall survival was worse in the high volume than in the medium volume centers (HR: 1.17 [95% CI: 1.04 to 1.32]; p = 0.009). There were no differences in survival between high volume (>50 VADs/year) and very-low volume centers (p = 0.25). Very-low volume centers (<10 VADs/year) had worse survival than medium volume centers (HR: 1.29 [95% CI: 1.10 to 1.52]; p = 0.002). To account for the competing outcomes of transplantation, we examined survival in the 5,601 patients who did not undergo cardiac transplantation during the period of study. Significant survival differences persisted (p = 0.036) with 1-year survivals as follows: 74 ± 1.9% (very low volume), 75 ± 1.0% (low volume), 78 ± 1.0% (medium volume), and 73 ± 1.0% (high volume).

After we adjusted for known correlates of risk (see Methods), center volume remained predictive of adverse outcome (p = 0.005) (Table 3) (8,11–13). Compared with medium volume centers, the adjusted HR for mortality was 32% (adjusted HR: 1.32 [95% CI: 1.11 to 1.56]; p = 0.001), higher for patients who underwent implantation at very-low volume centers, and 17% (adjusted HR: 1.17 [95% CI: 1.03 to 1.30]; p = 0.016), higher for patients who underwent implantation at high volume centers. There were no differences in survival between medium volume centers and low volume centers. When we restricted the analysis to patients who did not undergo transplantation, center volume remained a significant predictor of outcome (p = 0.024). Compared with medium volume centers, very-low volume centers had an adjusted patient mortality of 1.27 (95% CI: 1.07 to 1.50; p = 0.006), and high volume centers had an adjusted mortality of 1.16 (95% CI: 1.02 to 1.31; p = 0.025).

SURVIVAL RESTRICTED TO PATIENT PROFILES 1 AND 2. There were 3,688 patients categorized as either INTERMACS profile 1 (those who had sustained cardiogenic shock) or 2 (those with progressive hemodynamic decline despite inotropes) pre-operatively. Baseline characteristics and demographics of these patients grouped by center volume are shown in Online Table 1. High volume centers operated on profile 1 and 2 patients who had

FIGURE 1 Survival in INTERMACS Patients (2012 to 2014) by Center VAD Volume



Significant differences were noted on pairwise comparison between medium volume (31 to 50 VADs/year) and high (>50 VADs/year), medium, and very low (<10 VADs/year) volume centers. VAD = ventricular assist device.

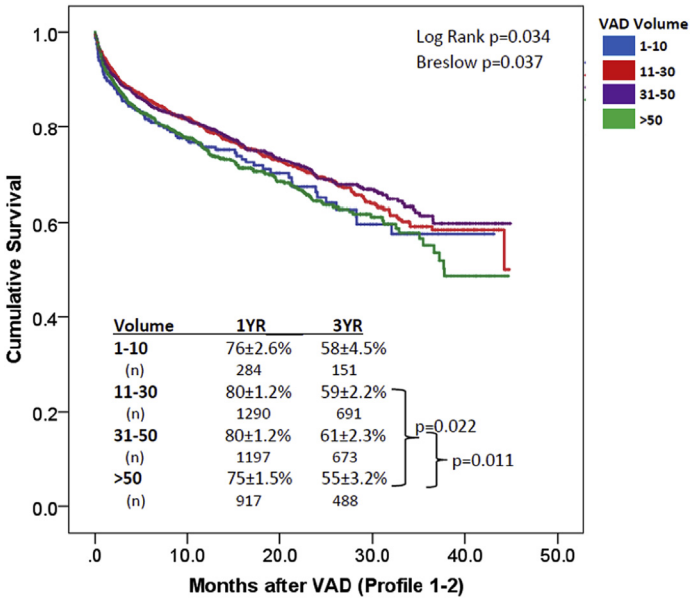
TABLE 3 Predictors of Mortality on Multivariate Analysis

	Hazard Ratio Mortality (95% CI)	p Value
Center volume		0.005
≤10	1.32 (1.11–1.56)	0.001*
11–30	1.07 (0.95–1.21)	0.25*
31–50	Reference	—
>50	1.17 (1.03–1.30)	0.016*
Age >69 yrs	1.64 (1.46–1.84)	<0.001
BTT (listed)	0.69 (0.59–0.80)	<0.001
Males	0.84 (0.75–0.94)	0.003
Previous cardiac surgery	1.42 (1.29–1.57)	<0.001
Pre-operative ventilator support	1.08 (0.88–1.32)	0.48
Patient profile 1 or 2	1.21 (1.10–1.34)	<0.001
Creatinine, mg/dl	1.18 (1.13–1.23)	<0.001
Albumin, g/l	0.88 (0.82–0.95)	0.001
CF-AF	0.82 (0.71–0.96)	0.012
Concomitant surgery	1.25 (1.13–1.38)	<0.001
BiVAD	2.22 (1.78–2.78)	<0.001

*p values were derived from comparisons with medium volume. All variables were added simultaneously in Cox modeling.

Abbreviations as in Table 1.

FIGURE 2 Survival in Profile 1 and 2 Patients Based on Center Volume



Survival was examined in profile 1 and 2 patients. The Breslow p value favors the early period of the curve (operative interval). Significant differences in survival were noted in pairwise comparisons between high centers (>50 VADs/year) and both medium (31 to 50 VADs/year) and low (11 to 30 VADs/year) volume centers. No differences were noted between very-low volume (<10 VADs/year) and medium volume centers. Abbreviation as in Figure 1.

sicker phenotypes, inclusive of a greater frequency of pre-operative cardiac arrests, higher serum creatinine, and greater need for pre-operative renal replacement therapy and IABP support. Higher volume centers had shorter cardiopulmonary bypass times but used more BiVAD support then other groups. Very-low volume centers had the lowest percentage of patients on BiVAD support and the longest cardiopulmonary bypass times.

There were 459 early (within 90 days) deaths overall in profile 1 and 2 patients. No significant differences in 90-day mortality were observed among very low (15%, n = 42), low (11%, n = 144), medium (12%, n = 140), or high volume (15%, n = 133) centers (p = 0.057). A significant difference existed in overall survival of profile 1 and 2 patients based on center volume (p = 0.037) (Figure 2). On pairwise comparison between groups, there were no differences between survival in very-low volume centers (HR: 1.20 [95% CI: 0.95 to 1.54]) and that of medium volume centers. However, patients who received implants at higher volume centers had higher unadjusted mortality than patients who received theirs at medium (HR: 1.2 [95% CI: 1.1 to 1.5]) volume centers. After accounting for known correlates of risk, center volume was not predictive of mortality in INTERMACS profile 1 and 2 patients (p = 0.25). The adjusted hazard ratios for mortality in high-volume (HR: 1.17 [95% CI: 0.99 to 1.38]; p = 0.06) and very-low volume centers (HR: 1.17 [95% CI: 0.92 to 1.50]; p = 0.21) were not significantly higher than that of medium volume centers.

CAUSES OF DEATH BY CENTER VOLUME. Table 4 shows the causes of death in the INTERMACS sample according to center volume (Pearson p > 0.05). Very-low volume centers had higher frequencies of death from infection and from pulmonary and noncardiac causes. High volume centers had more multisystem organ failure and few reported deaths due to right ventricular failure.

DISCUSSION

Although several studies have identified pre-operative risk factors for mortality after LVAD implantation, the impact of center surgical experience on overall patient survival has not been thoroughly examined. In this analysis of 7,416 patients enrolled in INTERMACS, we found a bimodal risk of adverse outcomes associated with center volume: very low and high volume centers have lower average survivals than centers that perform 30 to 50 VADs a year. The increased mortality association persisted even after adjusting for known correlates of LVAD candidate operative risk.

Surgical volume has been associated with patient outcomes in several studies, including that of patients undergoing general cardiac procedures. In a study by Birkmeyer et al. (1), patients undergoing cardiac bypass surgery at high volume centers had an operative mortality of 4.8% compared with 6.1% at very-low volume centers. In a separate analysis by Gonzalez et al. (4), patients undergoing aortic valve replacement at very-low volume centers were 12% more likely to have a major complication than those at high volume hospitals, and patients were 57% more likely to die if a complication occurred. Similar to these prior studies, yet from a different patient population, we found an increase in mortality in patients undergoing LVAD implant at centers performing <10 implants per year. Aside from advanced age, patients implanted at very-low volume centers did not present with a greater frequency of high risk features. After controlling for known correlates of LVAD mortality (8,11), adjusted mortality remained 32% higher at very-low volume LVAD centers than at medium volume centers.

This study was not designed to determine why outcomes are worse at very-low volume VAD centers,

but the data from this analysis and others foster hypotheses. Ninety-day mortality in very-low volume INTERMACS centers was 35% higher than medium volume centers. The data herein support findings from Shah et al. (6), who showed that U.S. centers performing <23 LVADs/year had 50% higher inpatient mortality than higher volume centers. Very-low volume centers in INTERMACS increased the overall period of operative risk with the addition of concomitant procedures (42%) and with extended times on cardiopulmonary bypass. Other studies have shown that concomitant procedures increase LVAD operative mortality (11,14–16). Aside from addressing mechanical aortic valves, data demonstrating consistent benefit from mitral and tricuspid valve interventions and concomitant coronary bypass are lacking (14,15,17,18). At low volume centers, omitting additional procedures, thereby reducing procedural complexity, may be one means of improving operative outcomes.

Unmeasured factors, such as surgical experience, perioperative management, quality and frequency of outpatient follow-up, identification and management of LVAD-related complications, and variations in patient management protocols (e.g., anticoagulation and blood pressure) could also be hypothesized to play a role in the increased incidence of death at very-low volume LVAD centers. Certainly, more studies are needed to better understand the causes of increased mortality at low volume centers. Until then, it begs the question whether stricter center volume minimums are necessary for ensuring good patient outcomes after LVAD. In the United States, the Centers for Medical and Medicaid Services (CMS) center volume standards are currently set at 10 VADs or total artificial hearts over a 3-year period (19). These INTERMACS data and data from Shah et al. (6) would suggest that CMS VAD volume minimums are set too low.

An unexpected finding from this analysis was the higher risk-adjusted mortality among patients receiving implants at high volume centers than at medium volume centers. In fact, survival in the high volume cohort was no better than that observed in the very-low volume cohort. The reasons for this are not entirely clear. Hypothetically, referral bias may play a role in mortality differences, with larger volume institutions having a sicker mixture of patients, some of whom may have already been declined for surgery at lower volume centers. This hypothesis is supported by the greater proportion of patients categorized as INTERMACS profile 1 or 2, those on BiVAD support, and/or those with pre-operative renal dysfunction in the high center volume group, with a high percentage of deaths from multisystem organ failure and/or progressive heart failure. Within the INTERMACS profile 1 and 2 sample, patients at high volume centers were older, had more pre-operative cardiac arrests, and worse renal function than other groups. These factors could account for the increased operative mortality (HR: 1.28) observed in high volume INTERMACS centers. After adjusting for known LVAD mortality risk correlates, overall mortality remained 17% higher in high volume centers compared with centers implanting 31 to 50 VADs a year. Although trends were noted, high volume centers did not demonstrate a significantly higher operative and/or adjusted overall mortality in the sickest of VAD patients, the INTERMACS profile 1 and 2 group.

Although many risk models and risk factors for LVAD mortality have been devised, predicting mortality after LVAD implantation remains imperfect (7,8,11–13). Thus, it remains possible that, despite

TABLE 4 Causes of Death by Center Volume

	Center Volume			
	≤10 (n = 195)	11–30 (n = 630)	31–50 (n = 603)	>50 (n = 469)
Device malfunction	4 (2.1)	20 (3.2)	18 (3.0)	11 (2.3)
Hemolysis	2 (1.0)	3 (0.5)	4 (0.7)	2 (0.4)
Neurological dysfunction	31 (16)	97 (15)	128 (21)	97 (21)
Major bleed event	4 (2.1)	19 (3.0)	18 (3.0)	8 (1.7)
Infection	15 (7.7)	37 (5.9)	30 (5.0)	21 (4.5)
RV failure	8 (4.1)	25 (4.0)	20 (3.3)	8 (1.7)
MSOF	27 (14)	110 (18)	119 (20)	101 (22)
Myocardial infarction	0 (0)	4 (0.6)	3 (0.5)	2 (0.4)
End-stage heart failure	12 (6.2)	31 (4.9)	36 (6.0)	42 (9.0)
Cardiovascular: other	9 (4.6)	26 (4.1)	19 (3.2)	19 (4.1)
Arrhythmia	3 (1.5)	15 (2.4)	13 (2.2)	14 (0.7)
Sudden cardiac death	5 (2.6)	24 (3.8)	23 (3.8)	21 (4.5)
Non-CNS embolism	2 (1.0)	5 (0.8)	1 (0.2)	1 (0.2)
Pulmonary failure	19 (9.7)	42 (6.7)	38 (6.3)	29 (6.2)
Renal failure	1 (0.5)	2 (0.3)	2 (0.3)	4 (0.9)
Hepatic failure	0 (0)	3 (0.5)	3 (0.5)	2 (0.4)
GI dysfunction	0 (0)	8 (1.3)	1 (0.2)	4 (0.9)
Cancer	2 (1.0)	11 (1.7)	4 (0.7)	5 (1.1)
Psychiatric	0 (0)	1 (0.2)	2 (0.3)	2 (0.4)
Noncardiovascular, other	19 (9.7)	46 (7.3)	29 (4.8)	27 (5.8)
Trauma/accident	3 (1.5)	5 (0.8)	3 (0.2)	2 (0.4)
Withdrawal care	29 (15)	96 (15)	89 (15)	47 (10)

Values are n (%). Overall p value >0.05.

CNS = central nervous system; GI = gastrointestinal; MSOF = multisystem organ failure; RV = right ventricle.

multivariate adjustments, high patient urgency due to referral bias may be the basis for the inferior outcomes at high volume centers. However, as the survival curves continue to separate after the peri-operative period, it is also important to consider other causes for the increased mortality seen at higher volume centers. Perhaps volumes of patients on LVAD support are so large at these centers that differences exist in the quality of outpatient management and/or the management of device complications. Alternatively, patient selection may play a role, and mortality at high volume centers could be the result of the progression of other medical comorbidities during long-term support. These questions cannot be answered from the study herein but warrant investigation. Although simultaneously acknowledging the presence of unmeasured factors possibly leading to a higher risk LVAD candidate phenotype at higher volume centers, one could still argue that measures to improve outcomes at any VAD center with higher than risk-predicted mortality are warranted.

STUDY LIMITATIONS. We were only given center volumes for the years 2012 to 2014. Although the 2012 to 2014 cohort was similar to the entire INTERMACS sample, this represents a limited INTERMACS analysis. Furthermore, we were unable to investigate if fluctuations in center LVAD volume impacted patient outcomes or if outcomes varied based on the presence or absence of transplantation capabilities or an academic affiliation. Surgeon volume has been shown to be inversely related to operative mortality for cardiac (including LVAD) and vascular procedures (3,5). Many LVAD centers have more than one LVAD surgeon, and the impact of individual surgeon experience, rather than overall center volume, was not analyzed. This is particularly true for larger volume centers, which may have more surgeons (inclusive of trainees) who have individually less surgical experience. It is possible that an individual very low or high-volume center had disproportionately high mortality, skewing group results. In the spirit of INTERMACS and collaborative research, these data are not provided for analysis. Finally, multiple comparisons were performed in several analyses herein, increasing the possibility of false positive covariate correlations with VAD outcomes.

CONCLUSIONS

Patients undergoing LVAD implant at very low (<10 implants per year) and high volume U.S. centers (>50 implants per year) have inferior outcomes to patients having surgery at centers performing 31 to 50 VADs a year. While the higher mortality observed at higher volume centers may be due to referral bias, these findings support the need for regular performance improvement evaluations, comparing individual center outcomes to risk-adjusted national averages. Coincidently, strategies enacted to improve average LVAD patient survival in those centers that underperform are warranted. Finally, INTERMACS data would suggest that current U.S. VAD center standards (10 VAD/total artificial hearts over 3 years) imposed by CMS are too lenient and warrant reconsideration (19).

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Center surgical experience has been shown to impact patient outcome for many cardiac and noncardiac surgeries. Using a large national database of LVAD patients, we show that patients undergoing LVAD implant at very-low volume centers (≤10 LVADs a year) have inferior outcome to those implanted at centers performing 30 to 50 LVADs a year. In addition, patients implanted at high volume centers (>50 VADs a year) have similar operative mortality but worse long term survival then patients implanted at lower volume centers. These results highlight the need for development of national performance evaluations for LVAD centers and reconsideration of current U.S. LVAD center implant minimums.

TRANSLATIONAL OUTLOOK: These data identify another facet impacting variability in patient outcomes after LVAD implant with important implications for U.S. health care expenditures. The findings may provide data for devising healthcare performance reimbursement goals and for guiding targeted improvements in individual LVAD center outcomes.

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KEY WORDS LVAD, mortality, risks, volume

APPENDIX For a supplemental table, please see the online version of this paper.