Relation of Left Ventricular Assist Device Infections With Cardiac Transplant Outcomes

Aditya Parikh, MD[a,*], Michael Halista, MD[b], Samantha Raymond, MPH[c], Jason Feinman, MD[b], Donna Mancini, MD[a], Sumeet Mitter, MD[a], Maya Barghash, MD[a], Maria Trivieri, MD[a], Johanna Contreras, MD[a], Sarah Taimur, MD[a], Julie Roldan, AGACNP[a], Joseph Murphy, RN[a], Amit Pawale, MD[d], Anelechi Anyanwu, MD[d], Noah Moss, MD[a], Anuradha Lala, MD[a], and Sean Pinney, MD[a]

Left ventricular assist device (LVAD)−specific infections (LSIs) are common in patients on LVAD support awaiting heart transplant (HT), yet their impact on post-HT outcomes is not completely understood. We hypothesized that LSIs would result in vasoplegia and negatively affect post-HT 30-day and 1-year outcomes. LSI was defined as driveline, pump, or pocket infection. The short-term outcome was a composite of acute renal failure, allograft rejection, and mortality at 30 days after HT. The long-term outcome was a composite of allograft rejection and death within 1 year after HT. We performed a retrospective analysis of 111 HT recipients bridged with durable LVAD support at our institution from May 2012 to August 2019. Of these, 63 patients had LSIs, with 94% of the infections being driveline infections. Vasoplegia was more prevalent in the LSI group but not significantly (7 vs 2 persons, p = 0.3). There was no difference in the composite end point of acute renal failure, rejection, or death at 30 days (30% vs 25%, p = 0.55) or 1-year end point of rejection and death (38% vs 40%, p = 0.87) in patients with LSI versus those without LSI. In conclusion, LSIs were common in patients on LVAD who underwent HT in our single-center contemporary cohort. However, LSI was not associated with adverse outcomes at 30 days or at 1 year after HT. **(Am J Cardiol 2021;160:67−74)**

Left ventricular assist devices (LVADs) are frequently implanted as a bridge to transplantation for patients with end-stage heart failure awaiting heart transplant (HT).[1,2] From 2010 to 2018, approximately 43% of the nearly 37,000 worldwide HT recipients had a durable LVAD in place at the time of transplantation.[3] Although LVAD therapy has afforded improved quality of life and survival for patients on the waiting list, they are still limited by adverse events, the most common of which are LVAD-specific infections (LSIs). Data on the impact of LSI on post-HT outcomes come from reports limited by small numbers of patients with older-generation LVADs and show conflicting findings. Although LSIs are considered cured with the removal of hardware at the time of HT, the ensuing inflammatory response in the perioperative setting may adversely affect short-term outcomes. We hypothesized that LSIs would be associated with higher incidence of acute renal failure (ARF), allograft rejection, and mortality at 30 days after HT and allograft rejection and death at 1 year in HT patients bridged with contemporary LVAD therapy.

Methods

A retrospective analysis at our institution was conducted for patients who underwent HT from February 2012 to August 2019 bridged with a durable LVAD. Durable LVADs included the HeartMate II and HeartMate 3 LVAD (Abbott Laboratories, Abbott Park, Illinois) and the HeartWare HVAD (Medtronic, Minneapolis, Minnesota). The study was approved by the institutional review board at Icahn School of Medicine at Mount Sinai (New York, New York).

Patients were grouped by the presence or absence of an LSI while on LVAD support, further defined in accordance with the 2011 International Society for Heart and Lung Transplantation consensus statement, which states "infections that are specific to patients with ventricular assist devices, are related to the device hardware, and do not occur in non-ventricular assist device patients; (including) pump and cannula infections, pocket infections, and percutaneous driveline infections."[4] The presence of LSI was determined by chart review by 3 physicians (AP, MH, JF) and the microbiology of cultured organisms. Antibiotic regimen and route if given for this indication were recorded. Patient characteristics including demographics, co-morbid conditions, and clinical data were collected at the time of HT.

[a]The Zena and Michael A. Wiener Cardiovascular Institute; [b]Department of Internal Medicine; [c]Department of Population Health Science and Policy; and [d]Department of Cardiovascular Surgery, Icahn School of Medicine at Mount Sinai, New York, New York. Manuscript received May 1, 2021; revised manuscript received and accepted August 17, 2021.

Dr. Anuradha Lala and Dr. Sean Pinney contributed equally in preparation of the manuscript.

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*Corresponding author: Tel: +1 (212) 241-7300; fax: +1 (212) 289-5971.

E-mail address: aditya.parikh@mountsinai.org (A. Parikh).

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Intraoperative data were collected from anesthesia reports and corroborated with operative notes, including the severity of infection, ischemia time, cardiopulmonary bypass time, units of packed red blood cells received intraoperatively, and blood salvaged using Cell Saver (Haemonetics, Braintree, Massachusetts). Hemodynamic data, including cardiac output, cardiac index, and systemic vascular resistance, were collected postoperatively from documented Swan-Ganz pulmonary artery catheter measurements on arrival to the cardiothoracic intensive care unit (ICU), between 8 and 12 hours after arrival, and at 24 hours.

In all patients, we performed orthotopic HT by way of reoperative sternotomy using standard approaches. The entire LVAD was dissected out and mobilized before cardiectomy and the driveline transected as it exited the mediastinum. The recipient heart and the LVAD pump were then removed en bloc. If protective expanded polytetrafluorethylene sheets (Gore-Tex; W.L. Gore, Flagstaff, Arizona) had been placed, these were removed in entirety. If there was evidence of mediastinal infection, the pericardial well was washed out copiously with saline solution, and any potentially infected tissue was debrided before implantation of the allograft. The heart was then implanted. After weaning off bypass and securing of hemostasis, the LVAD driveline was explanted. The abdominal wall was debrided where necessary. For patients with infection, a drain was placed in the driveline tract. The driveline exit site was excised and debrided and was then either closed primarily or left to heal by secondary intention, depending on severity of infection. We removed all LVAD material at the time of transplantation.

The short-term primary outcome was a composite of ARF, allograft rejection, and mortality at 30 days after HT. The long-term outcome was a composite of allograft rejection and death within the first year after HT. Allograft rejection was defined as antibody-mediated rejection (pathologic antibody-mediated rejection $\geq$1), acute cellular rejection $\geq$2R as seen on endomyocardial biopsy specimen, or hemodynamic compromise with graft failure.[5,6] ARF was classified as (1) a threefold increase in creatinine from patient's baseline, (2) an increase in creatinine to $\geq$5.0 mg/100 ml for $\geq$48 hours after HT, or (3) new requirement for initiation of renal replacement therapy (continuous venovenous hemofiltration or hemodialysis) during index hospitalization.[7] Transplant rejection and mortality were assessed until 1 year after HT.

To explore potential mechanisms by which LSIs may have been associated with worse post-HT outcomes, the presence of perioperative vasoplegia was assessed. Vasoplegia was considered present if the following criteria were met: (1) vasopressor or inotropic support (epinephrine/norepinephrine $\geq$150 ng/kg/min, dopamine $\geq$10 μg/kg/min, or vasopressin $\geq$4 U/hour) at any time point within the first 24 hours of HT along with (2) systemic vascular resistance <800 dyne $\times$ s/cm^5 without hemodynamic right-sided heart failure or (3) any use of methylene blue or vitamin B_{12} complex within 24 hours of HT. Right-sided heart failure was considered if *central venous pressure* >15 mm Hg and cardiac index <2.2 L/min/m^2 or inotropic support >14 days.[8] This definition used here is consistently used at our institution and is based on directly obtained measurements to accurately describe the vasodilatory state. We also compared the outcomes based on this definition with vasoplegia determined by the vasoactive-inotropic score (VIS), which has recently gained recognition in measurement of hemodynamic cardiopulmonary derangements after cardiac surgery, and found similar results (data not shown). The VIS is dopamine + dobutamine + milrinone ($\times$ 10) + epinephrine ($\times$ 100) + norepinephrine ($\times$ 100) (all mg/kg/min) + vasopressin ($\times$ 10,000) (U/kg/min). Unfortunately, there is currently no consensus on a universally accepted definition of vasoplegia.

On the basis of our institutional protocol, all patients received standard immunosuppression, consisting of a calcineurin inhibitor, an antimetabolite, and corticosteroids. Induction immune suppression (polyclonal or monoclonal antibody) was not used. Immunosuppressive regimen was adjusted as needed by the advanced heart failure team. In particular, mycophenolate mofetil dosage was reduced or held based on the severity of the infection. Antimicrobial regimen and duration of treatment was determined based on guidance from the infectious disease specialists.

Demographics, clinical characteristics, and outcomes were compared between the 2 groups using two-sample *t* tests and Wilcoxon-Mann-Whitney tests for continuous measures and chi-square and Fisher's exact tests for categorical measures. Univariate (unadjusted) and multivariable (adjusted for age, gender, and United Network of Organ Sharing [UNOS] status) logistic regression models were estimated to assess the association of LSI with the primary outcome. The distribution of time to the short-term and long-term outcomes was estimated using the Kaplan-Meier method, and differences between the groups were assessed using a log-rank test. Cox regression models were estimated to assess the association of LSI association with time to the short-term and long-term outcomes. All analyses were conducted using *Statistical Analysis System* version 9.4 (SAS, Cary, North Carolina). The significance level was set at $\alpha = 0.05$, two sided.

Results

A total of 111 patients underwent HT from LVAD support between February 2012 and August 2019 at our institution (Figure 1). Most patients (n = 94, 85%) had LVADs implanted with a bridge to transplantation indication. However, 17 patients were implanted with bridge to decision or destination therapy indication before being accepted for transplant listing.

All patients were followed for at least 1 year after HT. Of the total cohort, 63 (57%) patients had a history of LSI. Patients with LSI were more likely to have a higher body surface area (2.05 vs 1.92 m^2, p = 0.018), have a history of tobacco use (62% vs 44%, p = 0.05), and have the highest urgency (UNOS 1A) status (95% vs 60%, p <0.001) compared with patients without LSI. Notably, there were no differences in gender, body mass index, device type, duration on LVAD support, or medical therapy (Table 1).

Among the 63 patients with LSI during LVAD support before HT, 59 (93.7%) had driveline infections, 2 (3%) had pump-pocket infections, and 1 (2%) had a sternal wound infection. There was an equal distribution of gram-positive

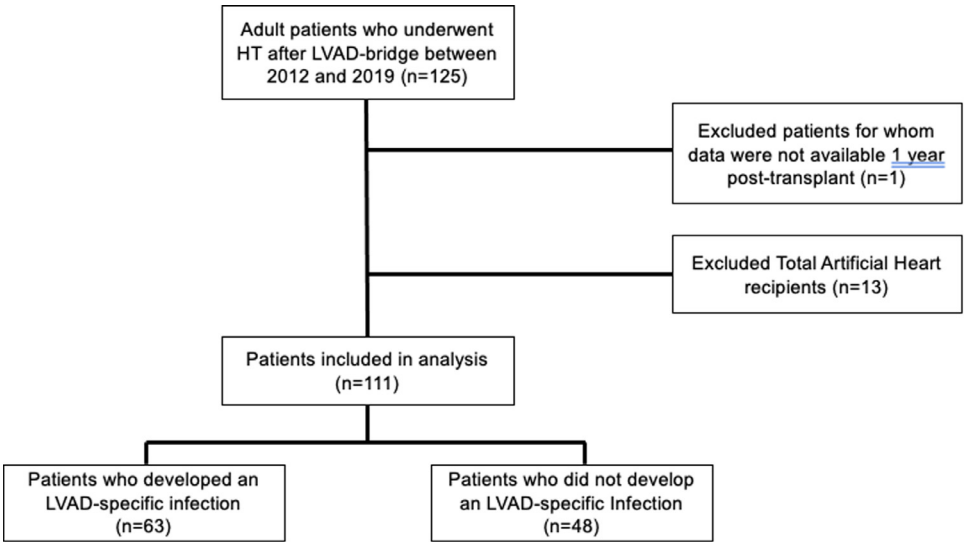


Figure 1. Study screening criteria and grouping criteria. Screening and final study enrollment. All patients who underwent heart transplant after LVAD bridge between 2012 and 2019 with follow-up data available for 1 year after heart transplant were included. Total artificial hearts were excluded. Patients were grouped by the presence or absence of an LVAD-specific infection.

(n = 26, 41.3%) and gram-negative (n = 27, 42.9%) organisms identified, with only 13% (n = 8) with polymicrobial infection and 3% (n = 2) where no organism was identified (Table 1). Nearly all patients with LSI (n = 61, 97%) were on antibiotics, with 57% (n = 36) on oral antibiotics and 40% (n = 25) on intravenous antibiotics at the time of HT.

In patients with LSI compared with those without LSI, no difference was found in median IT (164 vs 148 minutes, p = 0.9), median cardiopulmonary bypass time (164 vs 160 minutes, p = 0.68), packed red blood cells administered intraoperatively (3 vs 3 U, p = 0.28), or cell salvage product provided by way of the Cell Saver device (800 vs 1,000 ml, p = 0.37) (Table 2).

Of the 111 HT patients bridged with LVAD support, 28% (n = 31) experienced the 30-day outcome of a composite of ARF, allograft rejection, or death after HT; 39% (n = 43) experienced the 1-year composite outcome of allograft rejection and death (Table 3). There was no difference in the 30-day or 1-year composite end point between patients with LSI and those without LSI (30% vs 25%, p = 0.55 and 38% vs 40%, p = 0.87, respectively). A Kaplan-Meier analysis of the 30-day and 1-year outcomes are represented in Figures 2 and 3, respectively. Similarly, there was no difference in the individual components of the composite outcomes or in the secondary outcomes, including median ICU length of stay (7 vs 7 days, p = 0.79) and hospital length of stay (18 vs 20.5 days, p = 0.82). In a univariable linear regression model, LSI was not associated with the primary outcome (odds ratio 0.77, 95% confidence interval 0.33 to 1.8; Table 4). After adjusting for gender, age, and UNOS status, LSI remained unassociated with the primary outcome (odds ratio 0.75, 95% confidence interval 0.29 to 1.95).

The incidence of vasoplegia in the overall cohort was 8% (n = 9/111), with 11% (n = 7/63) in the LSI group and 4% (n = 2/42) in the group without LSI (p = 0.3). In addition, there was no difference in the median VIS calculated on arrival (20 vs 18.7, p = 0.24), at 8 hours (18 vs 18.85, p = 0.86), and at 24 hours (15 vs 14.13, p = 0.84) after arriving in the ICU.

Discussion

With approximately 40% of all patients awaiting heart transplantation bridged with LVAD support in the United States, a sizable proportion of patients are vulnerable to LVAD-associated adverse events before HT, namely LSI.[9] Yet, little data exist to inform the impact of LSI on post-HT outcomes. In this single-center retrospective study of more than 100 HT recipients bridged with LVAD support, more than one-half had LSI. However, its presence was neither associated with the short-term composite outcome of ARF, allograft rejection, or mortality at 30 days after HT nor associated with the 1-year composite end point of allograft rejection and death after HT. LSI was also not associated with prolonged ICU or hospital length of stay at the time of HT.

LVAD therapy has proved to be a remarkably effective provisional treatment for patients with end-stage heart failure awaiting HT. Despite advances in LVAD device design and the overall success of this therapy, infectious complications continue to be among the most serious threats to long-term survival of patients.[9] Conservative therapy with antibiotics and local incision and drainage provide short-term treatment; however, they are rarely curative. Cardiac transplantation offers the best long-term solution for LSI in cases when all of the infected hardware source can be removed. The presence of LSI afforded a higher status on the transplant waiting list when appropriate, but the recent revision to the UNOS heart allocation policy in the United States not only moved stable patients on LVAD support to a lower tier but also eliminated priority to patients with infectious complications associated with the device. The question of whether LSI might be associated with adverse events after HT is unknown but will be crucial in management of this growing population.

Table 1
Patient and clinical characteristics pretransplant of LVAD-specific infection and no LVAD-specific infection groups

Variables	All patients (n = 111)	LVAD-specific infection (n = 63)	No LVAD-specific infection (n = 48)	p value*
Male	89 (80%)	54 (86%)	35 (73%)	0.09
Age (years), median (IQR)	56.00 (47.00, 65.00)	55.00 (46.00, 64.00)	58.00 (48.00, 67.00)	0.369
Weight (kg), mean (SD)	83.49 (19.37)	86.65 (19.20)	79.34 (18.99)	0.048†
BSA, mean (SD)	1.99 (0.28)	2.05 (0.27)	1.92 (0.28)	0.018†
BMI, mean (SD)	27.62 (4.99)	27.85 (4.88)	27.33 (5.16)	0.592†
Race, n				0.182
Asian	13 (12%)	6 (10%)	7 (15%)	
Black	35 (32%)	25 (40%)	10 (21%)	
Hispanic	24 (22%)	11 (18%)	13 (27%)	
White	38 (34%)	21 (33%)	17 (35%)	
Missing	1 (1%)	0 (0%)	1 (2%)	
Hypertension	72 (65%)	40 (64%)	32 (67%)	0.729
Diabetes mellitus	51 (46%)	29 (46%)	22 (46%)	0.983
Smoker	60 (54%)	39 (62%)	21 (44%)	0.05
UNOS status				<0.001
1A	89 (80%)	60 (95%)	29 (60%)	
1B	22 (20%)	3 (5%)	19 (40%)	
EGFR				0.172‡
≥60	67 (60%)	39 (62%)	28 (58%)	
31-59	41 (37%)	24 (38%)	17 (35%)	
≤30	3 (3%)	0 (0%)	3 (6%)	
Albumin, median (IQR)	3.90 (3.60, 4.20)	3.90 (3.60, 4.40)	3.90 (3.65, 4.20)	0.542
Etiology of cardiomyopathy				0.335
Ischemic	26 (23%)	13 (20%)	13 (27%)	
Nonischemic	79 (71%)	48 (76%)	31 (65%)	
Missing	6 (5%)	2 (3%)	4 (8%)	
Repeat sternotomy,§	103 (93%)	59 (94%)	44 (92%)	0.725‡
Device				0.433‡
HM3	10 (9%)	5 (8%)	5 (10%)	
HMII	93 (84%)	55 (87%)	38 (79%)	
HVAD	8 (7%)	3 (5%)	5 (10%)	
Duration on LVAD in days, median (IQR)	425.00 (234.00, 596.00)	429.00 (259.00, 596.00)	370.50 (197.00, 643.00)	0.547
Use of ACEI, ARB, or ARNI	50 (45%)	27 (43%)	23 (48%)	0.596
Use of BB	66 (60%)	37 (59%)	29 (60%)	0.858
Microbiology of organism				
None	47 (42%)	2 (3%)	45 (94%)	<0.001‡
Gram-positive	29 (26%)	26 (41%)	3 (6%)	
Gram-negative	27 (24%)	27 (43%)	0 (0%)	
Polymicrobial	8 (7%)	8 (13%)	0 (0%)	
Antibiotics				<0.001
None	45 (41%)	2 (3%)	43 (90%)	
Oral	37 (33%)	36 (57%)	1 (2%)	
Intravenous	29 (26%)	25 (40%)	4 (8%)	
Driveline infection	59 (53%)	59 (94%)	0 (0%)	

* p values do not include missing values. Chi-square tests were used for categorical variables unless otherwise noted and Wilcoxon-Mann-Whitney tests for continuous variables unless otherwise noted.

† Two-sample *t* test used.

‡ Fisher's exact test used.

§ Some had LVAD placed using a sternum-sparing, less invasive implant technique.

ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; ACEI = ACE inhibitor; BB = beta blocker; BMI = body mass index; BSA = body surface area; EGFR = estimated glomerular filtration rate; HM3 = HeartMate 3; HMII = HeartMate II; HVAD = heart ventricular assist device; HTN = hypertension; IQR = interquartile range; LVAD = left ventricular assist device; SD = standard deviation; UNOS = United Network for Organ Sharing.

Studies that have explored this question have yielded discrepant findings.[10–13] Specifically, 3 studies showed no correlation with outcomes but had a lower proportion of patients with LSI, ranging from 20% to 60% compared with the 57% seen in our cohort.[10–12] In the first of these, the Cleveland Clinic experience reported on 21 patients with LSI who underwent HT, and their post-HT outcomes were similar to nonmatched patients without LSI.[10] Shulman et al in 2009 showed no difference in post-transplant survival in 110 patients with and without LVAD-related infection; however, there were little data on patient demographics or source of infection.[11]

Three large UNOS registry analyses investigating the impact of all LVAD-related complications on post-HT

Table 2
Perioperative and transplant characteristics of LVAD-specific infection and no LVAD-specific infection groups

Variable	All patients (n = 111)	LVAD-specific infection (n = 63)	No LVAD-specific infection (n = 48)	p value*
Ischemia time in minutes, median (IQR)	153.00 (108.00, 212.00)	164.00 (106.00, 212.00)	148.00 (109.50, 216.00)	0.898
CPB time in minutes, median (IQR)	161.00 (145.00, 188.00)	164.00 (145.00, 201.00)	159.50 (145.00, 179.00)	0.684
pRBC in units, median (IQR)	3.00 (1.00, 5.00)	3.00 (2.00, 5.00)	3.00 (1.00, 4.00)	0.283
Cell saver in milliliters, median (IQR)	950.00 (500.00, 1500.00)	800.00 (500.00, 1500.00)	1000.00 (500.00, 1554.50)	0.366

* Wilcoxon-Mann-Whitney tests were used for all p values.
CBP = cardiopulmonary bypass; IQR = interquartile range; LVAD = left ventricular assist device; pRBC = packed red blood cell.

Table 3
Outcomes of LVAD-specific infection and no LVAD-specific infection groups

Variables	All patients (n = 111)	LVAD-specific infection (n = 63)	No LVAD-specific infection (n = 48)	p value*
Short-term composite outcome	31 (28%)	19 (30%)	12 (25%)	0.549
Death at 30 days	9 (8%)	4 (6%)	5 (10%)	
Graft rejection at 30 days	19 (17%)	11 (18%)	8 (17%)	
ARF at 30 days	17 (15%)	11 (18%)	6 (13%)	
Long-term composite outcome	43 (39%)	24 (38%)	19 (40%)	0.873
Death at 1 year	14 (13%)	8 (13%)	6 (13%)	
Graft rejection at 1 year, n (%)	34 (31%)	19 (30%)	15 (31%)	
ICU length of stay in days, median (IQR)	7.00 (4.00, 16.00)	7.00 (4.00, 15.00)	7.00 (4.00, 17.00)	0.793
Hospital length of stay in days, median (IQR)	19.00 (13.00, 30.00)	18.00 (13.00, 31.00)	20.50 (13.00, 29.50)	0.819
Vasoplegia	9 (8%)	7 (11%)	2 (4%)	0.295†
VIS score on arrival, median (IQR)	19.40 (11.50, 25.50)	20.00 (13.00, 26.60)	18.73 (10.50, 24.77)	0.243
VIS score at hour 8	18.30 (13.00, 26.25)	18.00 (14.44, 26.00)	18.85 (12.50, 26.70)	0.861
VIS score at hour 24	15.00 (9.50, 20.75)	15.00 (9.50, 21.44)	14.13 (9.75, 20.57)	0.838

* p Values do not include missing or N/A values. Chi-square tests were used for categorical variables and Wilcoxon-Mann-Whitney tests for continuous variables unless otherwise noted.
† Fisher's exact test used.

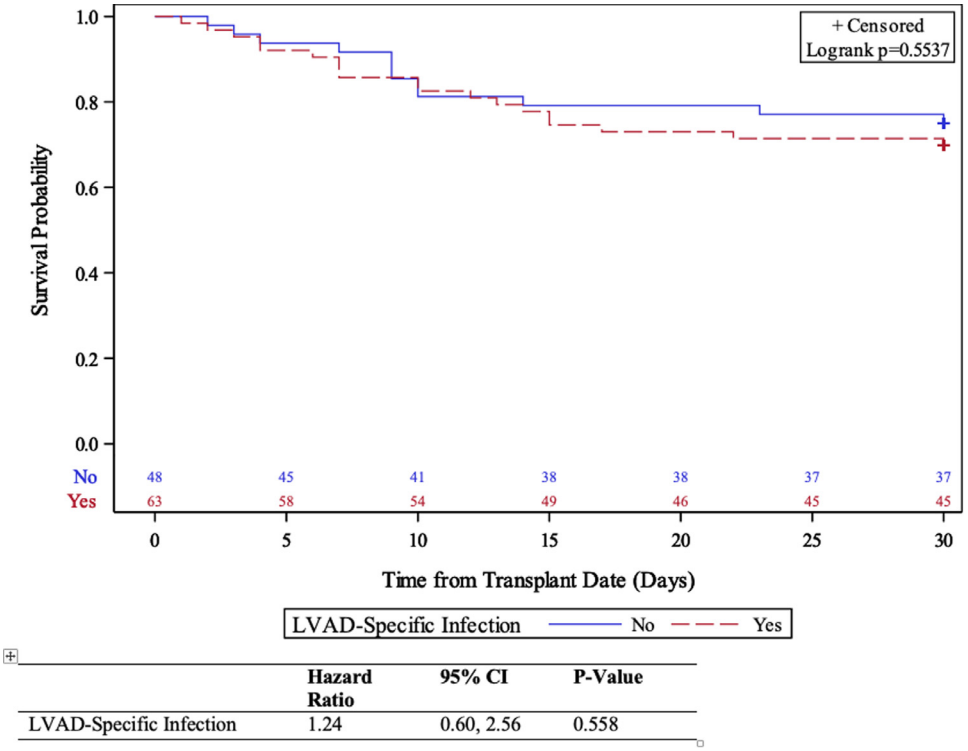
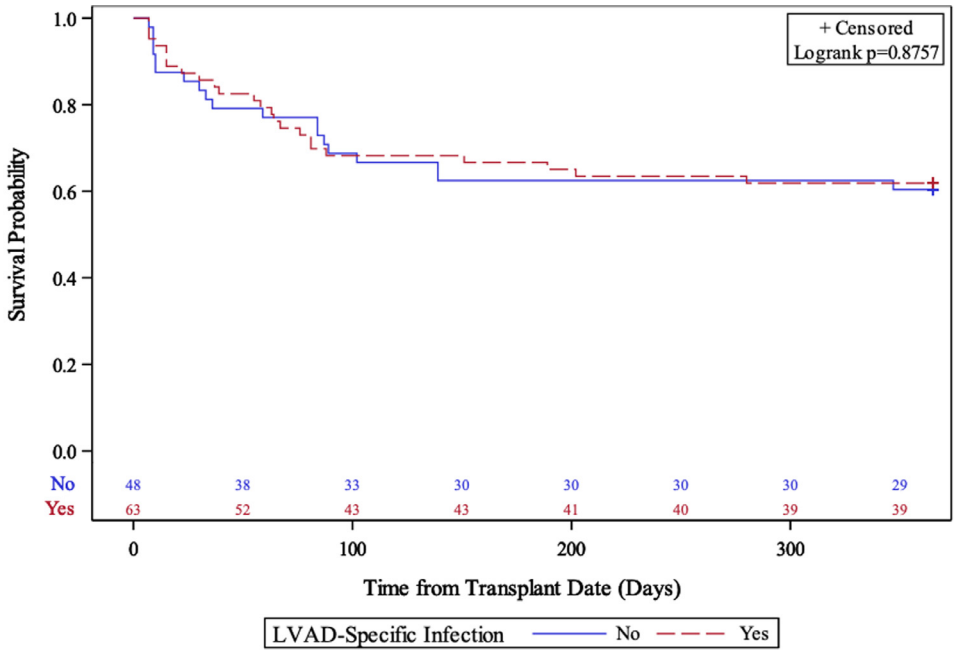


Figure 2. Impact of LSI on short-term outcome of acute renal failure, allograft rejection, and death at 30 days after HT. CI = confidence interval.



	Hazard Ratio	95% CI	P-Value
LVAD-Specific Infection	0.95	0.52, 1.74	0.876

Figure 3. Impact of LSI on long-term outcome of allograft rejection and death within 1 year after HT. CI = confidence interval.

outcomes have yielded disparate results. The earliest of these by Healy et al included 2,407 patients and showed a greater risk of death at 1 year after an LVAD bridge to HT in patients with device infection compared with patients using a 30-day time for UNOS status 1A indication without complication.[14] Another UNOS registry analysis performed by Quader et al[13] found inferior survival in patients with LVAD-related complications. The most recent analysis by Chauhan et al included patients on continuous-flow LVAD support between 2005 and 2015 and showed that although episodes of rejection may be increased with prolonged support, there was no difference in post-HT survival based on LVAD infection.[12]

Finally, a systematic review summarizing the previously mentioned studies and earlier noncontemporary cohorts concluded that LSI did not affect mortality after HT.[15] With a lack of standardized definition for LSI across studies and the absence of demographic data and information regarding the type of infection, these data should be interpreted with caution.

To our knowledge, our study represents one of the largest single-center contemporary cohorts studying the impact of LSI on post-HT outcomes, including patients supported on the most commonly used Heartmate 3 LVAD. The definition of LSI was standardized based on the criteria provided by the *International Journal of Heart and Lung Transplantation Consensus* document.[4] In our cohort, LSIs were common, occurring in approximately 57% of the patients. The vast majority of LSIs were attributed to driveline infections, and there was an equal distribution of gram-positive and gram-negative organisms. Of the studies investigating the impact of infectious complications in patients supported with LVAD who underwent HT, only Tong et al[10] reported microbiology information and similarly showed equal distribution between gram-positive and gram-negative organisms.

The composite end point of ARF, rejection, and mortality at 30 days after HT was selected based on the postulation that the presence of infection, in particular with gram-negative organisms, would exacerbate even more a cytokine-mediated inflammatory response in the perioperative setting, resulting in vasoplegia.[16,17] Vasoplegia tends to portend a worse prognosis and has been associated with increased hospital length of stay, in-hospital mortality, and overall outcome. The development of postoperative vasoplegia can lead to adverse outcomes such as respiratory failure, bleeding complications, and longer ICU stays regardless of the inciting cause.[8,19,18,20,21] In addition, the use of high-dose vasoconstrictors can lead to worsening

Table 4
Logistic regression model of short-term composite outcome, n = 111

Variables	Univariate			Multivariable		
	OR	95% CI	p value	OR	95% CI	p value
Age in years	1.00	0.97-1.03	0.907	1.00	0.96-1.03	0.839
Sex (female vs male)	0.71	0.24-2.13	0.545	0.72	0.23-2.22	0.563
LVAD-specific infection (yes vs no)	0.77	0.33-1.80	0.549	0.75	0.29-1.95	0.560
UNOS status (1A vs 1B)	1.04	0.37-2.96	0.939	0.82	0.25-2.74	0.746

end-organ function such as renal failure, which in turn may lead to adverse longer-term outcomes.

We demonstrated that 11% of patients had perioperative vasoplegia. Although vasoplegia occurred more frequently in patients with LSI, the difference was not statistically significant. This finding was further validated by the absence of difference in the calculated VIS, which has been increasingly used to calculate hemodynamic cardiopulmonary derangements after cardiac surgery.[21−24] The presence of LSI did not affect the rate of perioperative renal failure or ICU or hospital length of stay, and it did not influence the rate of allograft rejection or mortality within 1 year of HT. In our cohort, LSI was more common in men and was associated with higher body surface area but not with body mass index as described in previous studies. Reoperative sternotomy status and the duration of LVAD support did not affect the incidence of LSI.

Our findings suggest that LSIs do not appear to negatively affect post-transplant outcomes. However, LSIs continue to contribute significantly to morbidity for patients on LVAD support. LSIs result in increased health care utilization, are the leading cause of readmission, and increase hospital length of stay for patients supported on LVAD.[25,26] Ongoing clinical care and research efforts are needed to further elucidate the most effective methods to prevent and treat LSIs.

This study has few notable limitations. The first is that it is a retrospective, single-center nonrandomized study that is subject to selection bias and confounding. In addition, the relatively small number of patients in the cohort may limit the power to detect small differences. On the basis of the single-center experience, patients may have been selected for device implantation and cardiac transplantation in a biased manner, and this bias may have influenced the results.

Conclusions

In summary, in this contemporary cohort of patients on LVAD support, the presence of infection neither influenced the short-term outcome of ARF, allograft rejection, or death at 30 days after HT nor affected post-HT rejection or survival at 1 year.

Authors' Contributions

Aditya Parikh: Conceptualization, Methodology, Investigation, Data Curation, Writing − Original Draft Preparation; Michael Halista: Investigation, Data Curation, Writing − Original Draft Preparation; Samantha Raymond: Formal Analysis; Jason Feinman: Investigation, Data Curation; Donna Mancini: Writing − Reviewing and Editing, Supervision; Sumeet Mitter: Writing − Reviewing and Editing, Supervision; Maya Barghash: Writing − Reviewing and Editing, Supervision; Maria Trivieri: Writing − Reviewing and Editing, Supervision; Johanna Contreras: Writing − Reviewing and Editing, Supervision; Sarah Taimur: Writing − Reviewing and Editing, Supervision; Julie Roldan: Writing − Reviewing and Editing, Supervision; Joseph Murphy: Writing − Reviewing and Editing, Supervision; Amit Pawale: Writing − Reviewing and Editing, Supervision; Anelechi Anyanwu: Writing − Reviewing and Editing, Supervision; Noah Moss: Writing − Reviewing and Editing, Supervision; Anuradha Lala: Conceptualization, Methodology, Writing − Reviewing and Editing, Supervision; Sean Pinney: Conceptualization, Methodology, Writing − Reviewing and Editing, Supervision.

Disclosures

Dr. Sean Pinney reports serving on the advisory board or receiving consulting fees from Abbott, CareDx Inc, Medtronic, and Procyrion. The remaining authors have no conflicts of interest to disclose.

1. Stehlik J, Edwards LB, Kucheryavaya AY, Aurora P, Christie JD, Kirk R, Dobbels F, Rahmel AO, Hertz MI. The registry of the international society for heart and lung transplantation: twenty-seventh official adult heart transplant report−2010. *J Heart Lung Transplant* 2010;29:1089–1103.
2. Ehsan A, Zeymo A, McDermott J, Shara NM, Sellke FW, Yousefzai R, Al-Refaie WB. Utilization of left ventricular assist devices in vulnerable adults across Medicaid expansion [published correction appears in *J Surg Res* 2020;256:704]. *J Surg Res* 2019;243:503–508.
3. The International Society for Heart and Lung Transplantation. International Thoracic Organ Transplant (TTX) registry data slides: adult heart transplantation statistics, 2019. Available at: https://ishltregistries.org/registries/slides.asp. Accessed on November 4, 2019.
4. Hannan MM, Husain S, Mattner F, Danziger-Isakov L, Drew RJ, Corey GR, Schueler S, Holman WL, Lawler LP, Gordon SM, Mahon NG, Herre JM, Gould K, Montoya JG, Padera RF, Kormos RL, Conte JV, Mooney ML, International Society for Heart and Lung Transplantation. Working formulation for the standardization of definitions of infections in patients using ventricular assist devices. *J Heart Lung Transplant* 2011;30:375–384.
5. Stewart S, Winters GL, Fishbein MC, Tazelaar HD, Kobashigawa J, Abrams J, Andersen CB, Angelini A, Berry GJ, Burke MM, Demetris AJ, Hammond E, Itescu S, Marboe CC, McManus B, Reed EF, Reinsmoen NL, Rodriguez ER, Rose AG, Rose M, Suciu-Focia N, Zeevi A, Billingham ME. Revision of the 1990 working formulation for the standardization of nomenclature in the diagnosis of heart rejection. *J Heart Lung Transplant* 2005;24:1710–1720.
6. Colvin MM, Cook JL, Chang P, Francis G, Hsu DT, Kiernan MS, Kobashigawa JA, Lindenfeld JA, Masri SC, Miller D, O'Connell J, Rodriguez ER, Rosengard B, Self S, White-Williams C, Zeevi A. American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology. American Heart Association Heart Failure and Transplantation Committee of the Council on Cardiopulmonary Critical Care, Perioperative and Resuscitation. American Heart Association Heart Failure and Transplantation Committee of the Council on Cardiovascular Disease in the Young. American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology, Council on Cardiovascular and Stroke Nursing. American Heart Association Heart Failure and Transplantation Committee of the Council on Cardiovascular Radiology and Intervention. American Heart Association Heart Failure and Transplantation Committee of the Council on Cardiovascular Surgery and Anesthesia. Antibody-mediated rejection in cardiac transplantation: emerging knowledge in diagnosis and management: a scientific statement from the American Heart Association. *Circulation* 2015;131:1608–1639.
7. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, Levin A, Acute Kidney Injury Network. Acute kidney injury network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care* 2007;11:R31.
8. Levin MA, Lin HM, Castillo JG, Adams DH, Reich DL, Fischer GW. Early on-cardiopulmonary bypass hypotension and other factors associated with vasoplegic syndrome. *Circulation* 2009;120:1664–1671.
9. Mehra MR, Uriel N, Naka Y, Cleveland JC Jr, Yuzefpolskaya M, Salerno CT, Walsh MN, Milano CA, Patel CB, Hutchins SW, Ransom J, Ewald GA, Itoh A, Raval NY, Silvestry SC, Cogswell R, John R, Bhimaraj A, Bruckner BA, Lowes BD, Um JY, Jeevanandam V, Sayer G,

Mangi AA, Molina EJ, Sheikh F, Aaronson K, Pagani FD, Cotts WG, Tatooles AJ, Babu A, Chomsky D, Katz JN, Tessmann PB, Dean D, Krishnamoorthy A, Chuang J, Topuria I, Sood P, Goldstein DJ, MOMENTUM 3 Investigators. A fully magnetically levitated left ventricular assist device — final report. *N Engl J Med* 2019;380:1618–1627.
10. Tong MZ, Smedira NG, Soltesz EG, Starling RC, Koval CE, Porepa L, Moazami N. Outcomes of heart transplant after left ventricular assist device specific and related infection. *Ann Thorac Surg* 2015; 100:1292–1297.
11. Schulman AR, Martens TP, Russo MJ, Christos PJ, Gordon RJ, Lowy FD, Oz MC, Naka Y. Effect of left ventricular assist device infection on post-transplant outcomes. *J Heart Lung Transplant* 2009;28:237–242.
12. Healy AH, Baird BC, Drakos SG, Stehlik J, Selzman CH. Impact of ventricular assist device complications on posttransplant survival: an analysis of the united network of organ sharing database. *Ann Thorac Surg* 2013;95:870–875.
13. Quader MA, Wolfe LG, Kasirajan V. Heart transplantation outcomes in patients with continuous-flow left ventricular assist device-related complications. *J Heart Lung Transplant* 2015; 34:75–81.
14. Chauhan D, Okoh AK, Fugar S, Karanam R, Baran D, Zucker M, Camacho M, Russo MJ. Impact of left-ventricular assist device −related complications on posttransplant graft survival. *Ann Thorac Surg* 2017;104:1947–1952.
15. Chahal D, Sepehry AA, Nazzari H, Wright AJ, Toma M. The impact of left ventricular assist device infections on postcardiac transplant outcomes: a systematic review and meta-analysis. *ASAIO J* 2019;65:827–836.
16. Caruso R, Trunfio S, Milazzo F, Campolo J, De Maria R, Colombo T, Parolini M, Cannata A, Russo C, Paino R, Frigerio M, Martinelli L, Parodi O. Early expression of pro- and anti-inflammatory cytokines in left ventricular assist device recipients with multiple organ failure syndrome. *ASAIO J* 2010;56:313–318.
17. Haeffner-Cavaillon N, Roussellier N, Ponzio O, Carreno MP, Laude M, Carpentier A, Kazatchkine MD. Induction of interleukin-1 production in patients undergoing cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 1989;98:1100–1106.
18. Carrel T, Englberger L, Mohacsi P, Neidhart P, Schmidli J. Low systemic vascular resistance after cardiopulmonary bypass: incidence, etiology, and clinical importance. *J Cardiovasc Surg* 2000;15:347–353.
19. Gomes WJ, Carvalho AC, Palma JH, Teles CA, Branco JNR, Silas MG, Buffolo E. Vasoplegic syndrome after open heart surgery. *J Cardiovasc Surg (Torino)* 1998;39:619–623.
20. Byrne JG, Leacche M, Paul S, Mihaljevic T, Rawn JD, Shernan SK, Mudge GH, Stevenson LW. Risk factors and outcomes for "vasoplegia syndrome" following cardiac transplantation. *Eur J Cardiothorac Surg* 2004;25:327–332.
21. Gaies MG, Gurney JG, Yen AH, Napoli ML, Gajarski RJ, Ohye RG, Charpie JR, Hirsch JC. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. *Pediatr Crit Care Med* 2010;11:234–238.
22. Sanil Y, Aggarwal S. Vasoactive-inotropic score after pediatric heart transplant: a marker of adverse outcome. *Pediatr Transplant* 2013;17:567–572.
23. Yamazaki Y, Oba K, Matsui Y, Morimoto Y. Vasoactive-inotropic score as a predictor of morbidity and mortality in adults after cardiac surgery with cardiopulmonary bypass. *J Anesth* 2018;32:167–173.
24. Han J, Pinsino A, Sanchez J, Takayama H, Garan AR, Topkara VK, Naka Y, Demmer RT, Kurlansky PA, Colombo PC, Takeda K, Yuzefpolskaya M. Prognostic value of vasoactive-inotropic score following continuous flow left ventricular assist device implantation. *J Heart Lung Transplant* 2019;38:930–938.
25. Slaughter MS, Bostic R, Tong K, Russo M, Rogers JG. Temporal changes in hospital costs for left ventricular assist device implantation. *J Card Surg* 2011;26:535–541.
26. O'Horo JC, Abu Saleh OM, Stulak JM, Wilhelm MP, Baddour LM, Rizwan Sohail M. Left ventricular assist device infections: a systematic review. *ASAIO J* 2018;64:287–294.