Published in final edited form as:

ASAIO J. 2014 ; 60(1): 44–48. doi:10.1097/MAT.000000000000011.

Outcomes After Implantable Left Ventricular Assist Device Replacement Procedures

Matthew A. Schechter*, Mani A. Daneshmand*, Chetan B. Patel†, Laura J. Blue*, Joseph G. Rogers†, and Carmelo A. Milano*

*Department of Surgery, Duke University Medical Center, Durham, North Carolina

†Department of Medicine, Duke University Medical Center, Durham, North Carolina

Abstract

As the duration of support increases for patients with continuous flow left ventricular assist devices (LVADs), device replacement may still be necessary for a variety of indications. Outcomes after replacement LVAD surgeries have not been extensively described, and whether these patients experience outcomes similar to primary LVAD implant patients remains unclear. From 2003 to 2012, 342 consecutive implantable LVAD procedures took place at a single institution, of which 201 were considered destination therapy. Within this larger group, 30 patients underwent 35 replacement procedures. The three major indications for replacement LVAD procedures were mechanical/electrical failure (57%), hemolysis/thrombosis (29%), and infection (14%). Propensity matching using preoperative characteristics was used to generate a primary implant control group to determine the impact of the replacement status on outcomes. Thirty-day and 1-year survival after LVAD replacement was 90% and 48%, respectively. Survival outcomes were worse for patients undergoing device replacement compared with the matched primary cohort ($p = 0.03$). The need for transfusion and the incidence of postoperative right ventricular and renal dysfunction were similar between the two groups, as was length of hospitalization. There was no difference between the rates of postoperative infection or stroke. Emergent replacement procedures had a higher mortality than those done nonemergently. Given these findings, earlier timing for replacement, temporary stabilization with an extracorporeal device, and use of a nonsternotomy surgical approach should be investigated as strategies to improve outcomes.

Keywords

circulatory assist devices; reoperation; circulatory assist device; outcomes; statistics; survival analysis

Implantable continuous flow left ventricular assist device (LVAD) pumps have gained increased usage for bridge to cardiac transplantation (BTT) and particularly for permanent

Copyright © 2013 by the American Society for Artificial Internal Organs

Reprint Requests: Carmelo A. Milano, MD, Division of Cardiac and Thoracic Surgery, Duke University Medical Center, Box 3043, Durham, NC 27710. milan002@mc.duke.edu.

Disclosure: Dr. Milano and Mrs. Blue have served as consultants for Thoratec Inc. and HeartWare Inc. Dr. Rogers has served as a consultant for Thoratec Inc. Dr. Patel has served as a consultant for HeartWare Inc. Drs. Schechter and Daneshmand have nothing to disclose with regard to commercial support.

implantation (known as destination therapy or DT). Some of this increased utilization has resulted from improved durability and reduced need for device replacement because of mechanical failure.¹ Nevertheless, even with rotary LVADs, device replacement may be necessary. Potential indications for rotary LVAD replacement fall into three broad categories: hemolysis or pump thrombosis, electrical failure (such as damage to the internal power cord), and device infections.

The decision to proceed with device replacement has many implications, not only with respect to the risk of surgical replacement, but also the continued risks associated with ongoing device support. In many instances, these replacement cases may be undertaken in patients who have undergone more than one prior sternotomy. In addition, patients may have end-organ dysfunction related to the pump-related complication, such as renal dysfunction related to hemolysis, infection/sepsis, or worsening heart failure. Procedures for device replacement may be emergent in nature, further adding to the procedural risk. Therefore, replacement LVAD procedures may represent cases with increased procedural mortality and morbidity risk. On the contrary, the modular design of some of these devices may enable less invasive surgical approaches with retention of the outflow graft from the original device.² Such strategies may result in safer exchanges and reduced recovery time.

Several publications have described successful case series of LVAD replacement.^{3–7} These reports have not presented primary implant control cohorts for comparison and have not sought to define risk factors for negative outcomes after replacement. In this report, we examine outcomes from replacement LVAD procedures and compare these with primary implants with matched risk factors. Given the greater risk of these procedures and the increased cost, further investigation on survival and other important outcomes is warranted. Currently, there are no published guidelines on indications or timing for replacement procedures. Examination of these outcomes will hopefully help determine how to optimize patients and when to forego what may be futile use of significant resources.

Methods

The Duke University Institutional Review Board approved the study protocol, and the requirement for patient consent was waived. The medical records of all patients who received an implantable LVAD at Duke University Medical Center from January 2003 to November 2012 were reviewed. The replacement group consisted of all consecutive patients during this time period who underwent an LVAD replacement procedure, defined as removal of an implanted LVAD system and insertion of another implantable system. Patients who were transitioned from an extracorporeal LVAD to an implanted system were specifically excluded. Baseline patient characteristics were collected, including age, gender, race, heart failure etiology, the presence of concurrent diabetes, hypertension, peripheral vascular disease, pulmonary disease (decreased pulmonary function requiring medication), preprocedural hemodynamics, albumin, renal function, presence of anemia or coagulopathy, and need for preprocedural inotropic support, intra-aortic balloon support, or mechanical ventilation. Indication for LVAD (BTT or DT), need for repeat sternotomy, and type of device were also obtained from medical records. The indication for device replacement was determined from the operative note and divided into three categories: 1) mechanical/

electrical failure; 2) pump thrombosis/hemolysis; and 3) device infection. Finally, the medical records were reviewed to determine and categorize cases as emergent or nonemergent. An emergent procedure was defined as one which was performed during nonelective operative time or the patient's American Society of Anesthesiologist physical status class was designated as "E."

All replacement procedures were examined to determine early survival outcomes, but only the first replacement was included in the matched analyses. In addition to survival, postoperative adverse events were examined and compared, including incidence of postoperative right ventricular dysfunction, postoperative renal failure, transfusion requirement in the first 72 hours postoperation, length of hospital stay, incidence of stroke, and incidence of driveline infection. Postoperative right ventricular dysfunction was defined as the need for a right ventricular assist device or use of intravenous inotropes for 14 continuous days postoperatively. Postoperative renal failure was defined as a doubling of the patient's preoperative creatinine. Driveline infection was defined as any driveline infection that required initiation of antibiotics. Stroke was defined as focal neurologic deficits that persist past 24 hours or lasts <24 hours but is associated with changes on brain imaging.

To better understand how outcomes of replacement procedures compare with primary implantation procedures, a subgroup of patients who underwent primary LVAD implantation was identified from the larger LVAD DT population based on their propensity for undergoing a replacement procedure. A multivariate logistic regression model, using all the previously described preoperative variables (including emergent status), was used to estimate the likelihood of requiring a replacement procedure for all patients who underwent LVAD implantation. These propensity scores were then used to match a subset of primary LVAD implant recipients to the LVAD replacement patients. Again, for those patients who had multiple replacement procedures, only the first replacement procedure was used in the matching and subsequent comparison. All patients who received an implantable LVAD as DT between 2003 and 2012 were included as a third group for further comparison of survival outcomes. Comparison of the preoperative characteristics and outcomes of the matched cohort was performed using Fisher's exact test for categorical variables and Wilcoxon rank sum test for continuous variables. Survival for all groups was displayed using Kaplan-Meier analysis and was compared by the log-rank test.

Results

From January 2003 to November 2012, 342 patients received an implantable LVAD at Duke University Medical Center, of which 201 were for DT (58.8%). Within this larger cohort, 30 patients underwent a total of 35 LVAD replacement procedures. Indication for initial LVAD implantation in these patients was DT in 25 patients and BTT in five patients (16.7%). The median time to initial LVAD replacement in the entire cohort was 439 (range: 19–1,161) days. For patients with a HeartMate XVE, the median time was 413 (range: 301–628) days, and for HeartMate II patients, the median time to LVAD replacement was 601 (range: 19–1,161) days. The time to device failure was not different based on device type ($p = 0.19$). The indications for replacement and type of devices exchanged for the 35 replacement procedures are listed in Table 1. Most replacement procedures were due to mechanical/

electrical failure ($n = 20$, 57%). Thrombosis/hemolysis was the indication for half of the HeartMate II exchanges ($n = 8$), whereas five patients with a HeartMate II (36%) underwent exchange due to mechanical/electrical issues, which consisted of internal power cord disruptions in all cases. Infection was the indication for two HeartMate II exchanges and three XVE exchanges, whereas the single HeartWare to HeartMate II exchange was due to thrombosis. The most common replacement device was the HeartMate II (26/35, 74%).

Table 2 lists the preimplantation characteristics of the LVAD replacement group, the matched primary implant group, and the entire DT group during this time period. There were no statistically significant differences between the replacement group and the matched primary group. The number of patients who received a pulsatile LVAD was similar in each group (seven in the replacement group, eight in the matched primary group).

Three patients required multiple pump replacements. Two patients required only a second replacement procedure. Both patients had the same device implanted as their first replacement (HeartMate II) and for the same indication (mechanical failure in one, thrombosis/hemolysis in the other). These repeat exchanges occurred at 36 days (mechanical failure) and 182 days (thrombosis/hemolysis) after the first replacement procedure. The third patient underwent four separate device replacements, all due to mechanical failure. This patient received the same device for the first three replacements (HeartMate XVE), with a HeartMate II being used for his fourth replacement procedure. All these multiple replacement procedures were considered nonemergent. There were no early postoperative deaths from these procedures, and all patients survived over a year after these repeat replacements.

Overall, nine LVAD replacements were done emergently, four due to mechanical/electrical issues and five due to thrombosis/hemolysis. Of the nine patients who had an emergent replacement procedure, five (55%) died within the first 6 months. This compares with only three deaths within the same time period for the patients done nonemergently ($n = 26$, 11.5%). Overall survival was worse for patients undergoing emergent replacement than those who had a nonemergent replacement ($p = 0.04$).

Survival curves for the LVAD replacements, matched primary group, and all DT LVADs are shown in Figure 1. Replacement procedures had a significant reduction in survival compared with the matched cohort ($p = 0.03$). The 30-day survival for the initial replacement procedures was 90.0% (overall 91.4%) compared with 100% for the matched group. All three early deaths in the replacement group were patients who underwent emergent exchanges due to thrombosis/hemolysis. One of the three patients experienced LVAD pump thrombosis during a tracheostomy, resulting in prolonged cardiac arrest before device replacement. This patient developed severe coagulopathy and worsening hypoxia, and died the day of the procedure. The other two patients, undergoing emergent exchanges after 41 and 397 days of support (respectively), developed right ventricle (RV) dysfunction during their procedures and died of multiorgan system failure. One-year Kaplan-Meier survival for the replacement group and matched primary implant group was 50.8% and 83.3%, respectively. Within the replacement group, survival was not significantly different between patients who initially had a pulsatile LVAD *versus* those with a rotary LVAD or

was there a survival difference based on type of replacement LVAD ($p = 0.4$ for both). For all DT LVAD recipients, the 30 day survival was 94.0%, and 1 year survival was 81.0%.

The complication rates for these two groups are shown in Table 3. Compared with the matched cohort, patients who underwent a replacement procedure had a similar incidence of RV dysfunction, acute renal failure, and early postoperative transfusion requirement. The length of hospitalization after the replacement procedures was significantly shorter than the matched cohort ($p = 0.04$). Neither the driveline infection rate nor the postoperative stroke rates differed between the two groups.

Comment

Despite the adoption of more durable continuous flow designs, implantable LVAD replacement procedures are still required for three broad indications: mechanical/electrical failure, hemolysis/thrombosis, and infection. In this report, we present a single institutional experience with device replacement and compare outcomes with a propensity-matched primary implant group. Overall, our survival outcomes are similar to those reported by other groups for LVAD replacement procedures (Table 4). Our analysis suggests that the replacement cohort has worse survival than a matched group of primary implants. Thus, the replacement procedure itself provides an increased risk to the patient independent of baseline patient characteristics.

In this report, there were three early deaths of 35 replacements, and all three were highly unstable before the replacement procedure, with threatened end-organ perfusion and in one case cardiac arrest. Overall, emergent replacement procedures had a worse survival. The preoperative instability of these patients undoubtedly impacted their outcome, and some of the emergent replacements may have been futile. Another option for these very unstable patients may have been temporary mechanical support with either an extracorporeal membrane oxygenation or an extracorporeal VAD system. This strategy was used on two occasions at our institution with successful results. One patient required the emergent explantation of a VentrAssist implantable LVAD due to severe pump thrombosis. The patient was placed on a paracorporeal device (Thoratec PVAD), and eventually received a HeartMate II device when deemed more stable. This patient is alive 3 years after this replacement. The second patient, who presented with severe infection of their HeartMate XVE, also had a Thoratec PVAD replacement. Once the patient cleared the bacteremia, a HeartMate II was placed, and the patient survived for over 5 years. As these two patients had replacements with extracorporeal devices, they were not included in this series. However, these cases suggest that for LVAD recipients in need of emergent device replacement, temporary stabilization with an extracorporeal support system should be considered.

Adverse events for replacement procedures remain substantial. The significant transfusion requirement and incidence of RV dysfunction may relate to the need for a difficult redo median sternotomy in most of the replacements. Five patients with HeartMate II devices underwent replacements *via* a subcostal approach. In these cases, preoperative imaging was obtained to examine the inflow cannula and the outflow graft, and these components were

not replaced but rather were retained from the primary device. If there were concerns regarding the inflow cannula or outflow graft, the subcostal approach was not used. The modular HeartMate II design enables this strategy as previously described.² For these patients, peripheral cardiopulmonary bypass was established and a peripherally inserted ascending aortic catheter was used for deairing. Although the subcostal approach was used for patients who were more stable and more carefully selected, all the subcostal patients survived the procedure and were discharged home with a shorter postprocedure hospitalization. The use of the subcostal approach for several replacements could account for some of the decreased length of hospitalization of the replacement group. This less invasive approach may also enable reduced adverse events associated with replacement.

The ability to define a matched control group for the replacement procedures represents one of the limitations of this study. The propensity-matched group underwent primary LVAD implants, and the indication for this procedure is class IV heart failure that has failed medical management. Conversely, the replacement cohort had the indications of device malfunction, thrombosis/hemolysis, or infection but may have been relatively functional in terms of heart failure class. Furthermore, although the matched control group may have had chronic end-organ hypoperfusion from heart failure, the replacement group generally presented more acutely with device alarms, device stoppage, or acute malfunction due to thrombus. This acuity cannot currently be defined using the INTERMACS profiling system but likely influences outcomes after replacement procedures. Inotropic or intraortic balloon pump support was common in patients before the primary implants but generally not indicated for the replacement group. Risk factors for negative outcomes after replacement procedures have not been defined and may be different than risk factors for primary LVAD implants. For these reasons, there are trends toward differences between some of the variables in the control primary *versus* the replacement cohorts. Furthermore, some key variables in determining outcomes after replacement LVAD placement may have been missed.

A number of patients within our replacement cohort initially had first-generation LVADs. Although these devices are no longer used for DT, the technical aspects of the replacement procedure do not differ from replacement procedures involving more modern devices. Device type also had no effect on survival outcomes within our replacement group.

Although permanent implanted LVAD therapy has achieved an impressive survival advantage compared with continuous inotropic support for the most advanced heart failure patients, the morbidity and cost of this therapy have limited its broader application. These device replacements may enable improved survival, but at significant additional risk and cost. All replacement procedures, even those conducted *via* a subcostal approach, required cardiopulmonary bypass and a substantial postprocedure hospitalization. One patient in this report underwent four replacement procedures, receiving a total of five devices. Given these issues, guidelines for device replacement, which are currently not available, need to be carefully developed by experts in the field. They should address how to monitor and treat patients who develop early signs of device failure, infection, or thrombosis, so as to intervene before these patients require an emergent exchange. Outcomes such as freedom from reinfection when the indication for replacement is infection warrant investigation.

Furthermore, industry and clinical investigators should continue to focus studies and device designs to reduce the need for replacement. Future clinical trials of new products should maintain the need for device replacement as an important end-point. Although this report and previous similar reports provide a snapshot of outcomes at highly experienced centers, as the therapy expands, many less experienced centers may consider replacement procedures. More comprehensive reviews of replacement procedures at all DT centers should be analyzed through INTERMACS.

References

1. Slaughter MS, Rogers JG, Milano CA, et al. HeartMate II Investigators: Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med*. 2009; 361:2241–2251. [PubMed: 19920051]
2. Rogers JG, Jollis JG, Milano CA. Replacement of continuous-flow left ventricular assist device via left subcostal incision. *J Thorac Cardiovasc Surg*. 2012; 143:975–976. [PubMed: 22035962]
3. Dembitsky WP, Tector AJ, Park S, et al. Left ventricular assist device performance with long-term circulatory support: lessons from the REMATCH trial. *Ann Thorac Surg*. 2004; 78:2123–2129. discussion 2129. [PubMed: 15561049]
4. Gregoric ID. Exchange techniques for implantable ventricular assist devices. *ASAIO J*. 2008; 54:14–19. [PubMed: 18204310]
5. Adamson RM, Dembitsky WP, Baradarian S, et al. HeartMate left ventricular assist system exchange: results and technical considerations. *ASAIO J*. 2009; 55:598–601. [PubMed: 19779301]
6. Stulak JM, Cowger J, Haft JW, Romano MA, Aaronson KD, Pagani FD. Device exchange after primary left ventricular assist device implantation: indications and outcomes. *Ann Thorac Surg*. 2013; 95:1262–1267. discussion 1267. [PubMed: 23063192]
7. Moazami N, Milano CA, John R, et al. HeartMate II Investigators: Pump replacement for left ventricular assist device failure can be done safely and is associated with low mortality. *Ann Thorac Surg*. 2013; 95:500–505. [PubMed: 23261114]

Figure 1.
Kaplan-Meier survival curves. DT, destination therapy; LVAD, left ventricular assist device.

Table 1

Indications for LVAD Replacement and Types of Devices Exchanged

Indication	Device Types		Surgical Incision	
Mechanical/electrical failure	20	HeartMate II → HeartMate II	16	Redo sternotomy
	10	HeartMate XVE → HeartMate XVE	9	Left subcostal
Thrombosis/hemolysis	5	HeartMate XVE → HeartMate II	9	
Infection		HeartWare → HeartMate II	1	

LVAD, left ventricular assist device.

Table 2**Preimplant Characteristics for LVAD Patients**

Characteristic	Replacement (n = 30)	Matched (n = 30)	p Value	DT LVAD Recipients (n = 201)
Age (years)	58.0 (47, 67)	67.5 (53, 73)	0.07	65 (53, 71)
Sex (% male)	66.7	80.0	0.38	73.6
BMI	30.3 (25.8, 35.3)	28.8 (25.5, 33.2)	0.93	28.5 (25.0, 33.7)
Heart failure etiology (% NICM)	36.6	56.7	0.19	42.3
Diabetes (%)	43.3	43.3	0.99	49.8
Hypertension (%)	60.0	56.7	0.99	52.2
Peripheral vascular disease (%)	6.7	13.3	0.67	9.45
Pulmonary disease (%)	20.0	23.3	0.99	22.9
Albumin (g/dl)	3.25 (2.8, 3.8)	3.45 (2.9, 3.7)	0.95	3.20 (2.6, 3.6)
Creatinine (mg/dl)	1.4 (1.2, 1.7)	1.7 (1.2, 2.0)	0.34	1.5 (1.1, 1.9)
Hematocrit (%)	32.0 (28, 37)	33.0 (31, 37)	0.28	34.0 (30, 38)
Prothombin time (second)	14.8 (12.8, 16)	14.2 (12.9, 16)	0.99	14.20 (13.2, 15.9)
Central venous pressure	11 (4, 17)	12 (8, 18)	0.38	12.00 (8, 18)
Preoperative support (%)				
Inotropes	30.0	40.0	0.59	79.1
IABP	6.6	13.3	0.67	33.4
Mechanical ventilation	10.0	13.3	0.99	7.0
Previous sternotomy (%)	100	100	0.99	44.8
Emergent case (%)	30.0	20.0	0.55	12.4

Continuous variables are expressed as median (25th, 75th percentile).

BMI, body mass index; IABP, intra-aortic balloon pump; LVAD, left ventricular assist device; NICM, nonischemic cardiomyopathy.

Table 3

Complication Rate

Complication	Replacement (n = 30)	Matched (n = 30)	p Value
RV dysfunction (% , n)	16.6% (5)	30.0% (9)	NS
Acute renal failure (% , n)	30.0% (9)	10.0% (3)	NS
Total 72-hour transfusion requirement (units)	7 (3, 16.5)	8 (3.25, 19)	NS
Length of postoperative stay (days)	13 (8, 20)	20 (10.5, 32)	0.04
Stroke rate (per 100 patient-years)	19.4	12.8	NS
Infection rate (per 100 patient-years)	16.6	17.0	NS

Continuous variables are expressed as median (25th, 75th percentile).

RV, right ventricle.

Table 4

Other LVAD Pump Exchange Series

Author (Year)	Patients (Procedures)	Type of Device (% Continuous Flow)	Indications (% Mechanical/Electrical Failure)	30-day Mortality
Dembitsky <i>et al.</i> (2004) ³	23 (29)	Initial: 0% Replacement: 0%	89.7%	NR
Gregoric (2008) ⁴	16 (19)	Initial: 26.3% Replacement: 78.9%	68.4%	10.5%
Adamson <i>et al.</i> (2009) ⁵	15 (19)	Initial: 0% Replacement: 26.3%	89.5%	NR
Stulak <i>et al.</i> (2012) ⁶	44 (56)	Initial: 57.1% Replacement: 73.2%	45.6%	3.5%
Moazami <i>et al.</i> (2012) ⁷ (multicenter)	72 (77)	Initial: 97.3% Replacement: 100%	55.6%	6.5%
Schechter (2013)	30 (35)	Initial: 51.4% Replacement: 74.3%	57.1%	8.6%

LVAD, left ventricular assist device; NR, not recorded.