

# Implantable Cardioverter Defibrillators in Patients With Continuous Flow Left Ventricular Assist Devices: Utilization Patterns, Related Procedures, and Complications

Paulino A. Alvarez, MD; Brett W. Sperry, MD; Antonio L. Pérez, MD, MBA; Dmitry M. Yaranov, MD; Varinder Randhawa, MD; Jacob Luthman, MD; Daniel J. Cantillon, MD; Randall C. Starling, MD, MPH

**Background**—The effect of implantable cardioverter defibrillators (ICD) in patients with continuous flow left ventricular assist devices (LVADs) on outcomes has not been evaluated in a randomized clinical trial.

**Methods and Results**—This is a retrospective single-center study that included patients who underwent continuous flow LVAD implantation at the Cleveland Clinic between October 2004 and March 2017. Patients were evaluated according to the presence or absence of ICD at the time of LVAD insertion. Among 486 patients in the study cohort, 387 (79.6%) had an ICD before LVAD insertion. Patients with ICD before LVAD were older and had lower use of pre-LVAD inotropes, extracorporeal membrane oxygenation, and mechanical ventilation. There were 81 patients (21.4% of patients with ICD) who required 93 procedures after LVAD: 74 generator exchanges, 12 lead revisions, and 7 complete system removals because of infection. Of the 99 patients without ICD, 52 (53%) underwent ICD implantation: 29 for primary prevention and 23 for secondary prevention. Patients were followed for a median of 401 (interquartile range 150–966) days. The presence of a pre-LVAD ICD was not associated with mortality in a multivariable model (hazard ratio 1.19, 95% CI 0.73–1.93,  $P=0.492$ ), nor was the presence of an ICD at any point when analyzed as a time-varying covariate (hazard ratio 1.05, 95% CI 0.50–2.20,  $P=0.907$ ).

**Conclusions**—There is no apparent mortality benefit associated with an ICD in a contemporary cohort of patients with continuous flow LVADs to balance considerable morbidity involving ICD-related procedures and complications. (*J Am Heart Assoc.* 2019;8:e011813. DOI: 10.1161/JAHA.118.011813.)

**Key Words:** implanted cardioverter defibrillator • infection • left ventricular assist device

Continuous flow left ventricular assist devices (LVADs) have become the standard of care in patients needing intracorporeal long-term mechanical circulatory support as a bridge to transplant or destination therapy. Implantable

cardioverter defibrillators (ICDs) are indicated for the prevention of sudden cardiac death in patients with heart failure with a left ventricular ejection fraction  $\leq 35\%$  who are more than 40 days post–myocardial infarction, on guideline-directed medical therapy, and expected to live  $>1$  year.<sup>1</sup>

Among the patients referred for LVAD therapy, the presence of an ICD is frequent and oscillated between 61% and 91% in most recent randomized controlled trials.<sup>2,3</sup> Ventricular arrhythmias are usually well tolerated in patients with LVADs, but this is variable and is related to the ability to withstand Fontan-type circulation.<sup>4</sup> The incidence of cardiac arrhythmia is lower with continuous flow LVADs when compared with pulsatile flow devices.<sup>5</sup> The possible mechanisms of ventricular arrhythmias and risk stratification schemes for active ICD in patients with LVAD have been reported previously.<sup>6,7</sup> Nevertheless, the burden of ICD procedures, complications, and benefits in this patient population is less clear.

Therefore, the objectives of our study were to evaluate (1) the frequency of ICD at baseline, (2) lead/device malfunction related to LVAD insertion procedure, (3) the frequency and

From the Department of Cardiovascular Medicine, Cleveland Clinic Foundation, Cleveland, OH (P.A.A., B.W.S., A.L.P., D.M.Y., V.R., J.L., D.J.C., R.C.S.); Department of Cardiovascular Medicine, University of Iowa, Iowa City, IA (P.A.A.); Mid America Heart Institute, Saint Luke's Hospital of Kansas City, Kansas City, MO (B.W.S.).

Accompanying Tables S1 and S2 are available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.118.011813>

This article was handled independently by N.A. Mark Estes III, MD as a guest editor. The editors had no role in the evaluation of the manuscript or in the decision about its acceptance.

**Correspondence to:** Paulino A. Alvarez, MD, E314-3GH, 200 Hawkins Dr, Iowa City, IA 52242. E-mail: paulino-alvarez@uiowa.edu

Received December 19, 2018; accepted June 14, 2019.

© 2019 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

## Clinical Perspective

### What Is New?

- Approximately 50% of the patients without implantable cardioverter defibrillator (ICD) before left ventricular assist devices will undergo ICD implantation.
- The burden of ICD-related procedures in patients with left ventricular assist devices is high, affecting 1 in 5 patients, and post left ventricular assist devices lead malfunction was seen in 4.6% of the patients.
- ICD associated infections was observed in 3% of our cohort, and the presence of a pre-left ventricular assist devices ICD or the presence of an ICD at any point in time was not associated with a decrease in mortality.

### What Are the Clinical Applications?

- Given the high burden of ICD procedures and potential complications with no evidence of survival benefit, a randomized trial of the use of ICD in this patient population is warranted.

reasons for ICD implantation after LVAD, (4) ICD-related procedures and associated complications, and (5) outcomes of patients according to ICD status.

## Methods

The data that support the findings of this study are available from the corresponding author (R.C.S.) upon reasonable request. Sharing patient data is subject to the limitations and approval by the Cleveland Clinic's institutional review board.

This was a retrospective single-center study that included patients who underwent continuous flow LVAD implantation at the Cleveland Clinic between October 2004 and March 2017. All patients >18 years of age were included in the analysis. Patients were grouped according to the presence or absence of ICD at the time of LVAD insertion. The type of ICD (single, dual, and biventricular) was recorded along with clinical characteristics, laboratory data, echocardiographic parameters, and hemodynamics at time of LVAD implantation. The last episode of sustained ventricular tachycardia or ventricular fibrillation before LVAD implantation was identified. This was based on medical notes, ICD available interrogations when available, and scanned medical records.

Outcomes after LVAD insertion were assessed including revisions of existing ICDs and subsequent implantation of ICDs in patients who did not initially have a device. Complications of procedures were systematically evaluated. Types of procedures included (1) new implant, (2) generator exchange, (3) lead revision, and (4) device upgrade.

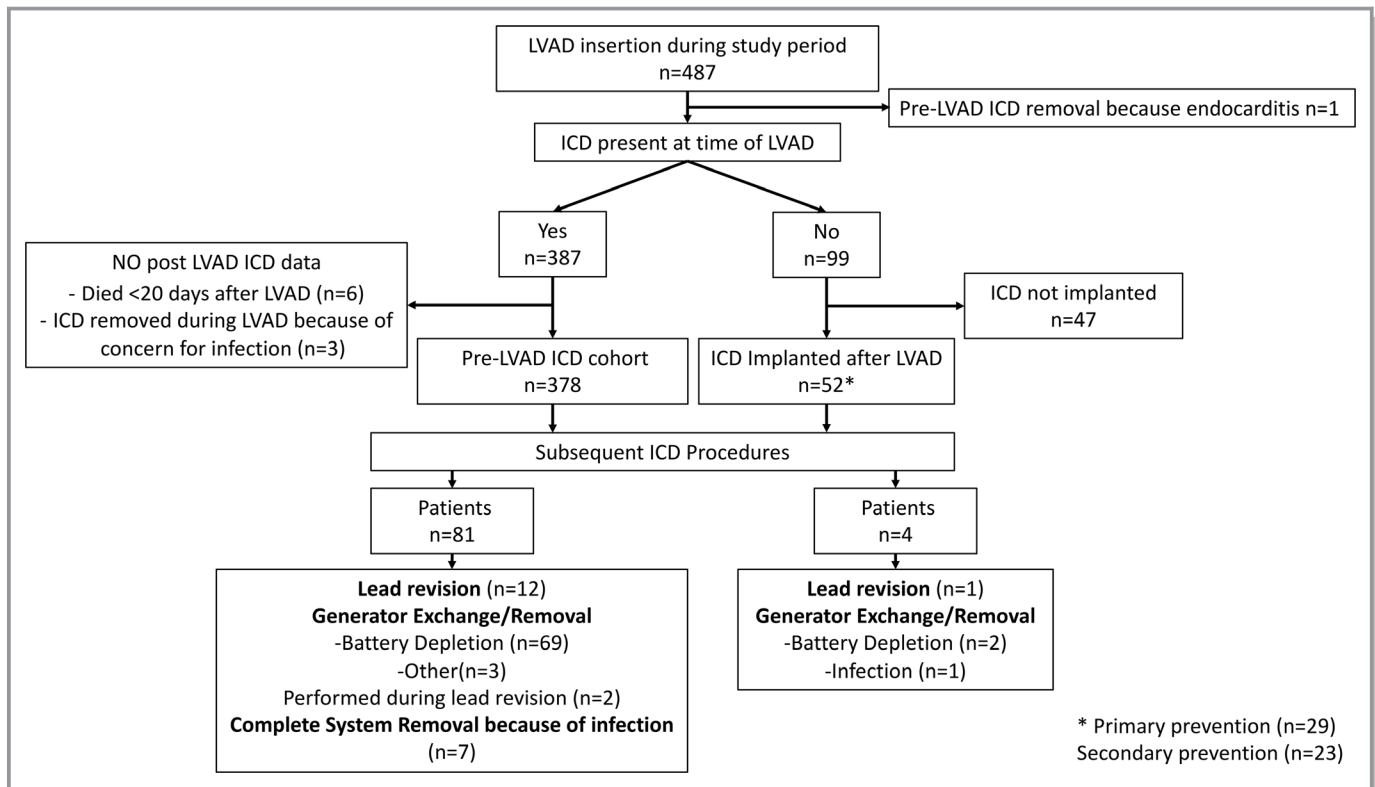
Complications were categorized into major and minor according to severity. All complications that required re-intervention were categorized as major complications because of their inherently higher risk of infection. Major complications included lead-related re-intervention, local infections requiring re-intervention, ICD-related systemic infections or endocarditis, pneumothorax requiring drainage, cardiac perforation, pocket revision, generator-lead interface problems requiring re-intervention, hematomas requiring re-intervention, procedure-related deaths, wound revisions, and stroke. Minor complications included wound infections treated with antibiotics, pneumothorax conservatively treated, and lead dislodgments without re-intervention. In order to evaluate the relationship between LVAD thrombosis/stroke, we analyzed the timing of those adverse events to the ICD intervention and classified them as procedural related if they occurred 7 days prior or within 14 days after the intervention and when an alternative cause was not detected. We analyzed the cause of death of the patients included in our cohort.

## Statistical Analysis

Continuous variables are presented as means±SD and are analyzed by Student *t* test. Categorical variables are presented as frequency and percentage and analyzed with Fisher exact test. Patient follow-up time was calculated as the time from LVAD implant until death or the last follow-up. Patients were censored at the time of heart transplantation. Overall survival was evaluated using a Cox model for death; variables included in the multivariable model were chosen a priori and included age, sex, bridge to transplant designation, hypertension, diabetes mellitus, chronic kidney disease, coronary artery disease, ventricular tachycardia/ventricular fibrillation (VT/VF), atrial fibrillation/flutter, and INTERMACS 1 (Interagency Registry for Mechanically Assisted Circulatory Support) status. Subsequently, the presence of an ICD was modeled as a time-varying covariate based upon if and when the ICD was implanted after LVAD. Statistical analyses were done using Stata (version 13, College Station, TX). The study was approved by the Institutional Review Board and informed consent was waived.

## Results

There were 487 patients who underwent LVAD implantation at the Cleveland Clinic during the study period; 1 patient had the ICD removed before LVAD implantation because of endocarditis and was excluded from the analysis (Figure 1). Of those, 387 (79.6%) had an ICD at the time of LVAD implantation. Characteristics of the patients with and without pre-LVAD ICD are shown in Table 1. Patients without a pre-LVAD ICD were younger, and had a higher frequency of pre-



**Figure 1.** A flow chart of the study cohort and subsequent ICD-related procedures is depicted. ICD indicates implantable cardioverter defibrillator; LVAD, left ventricular assist device.

LVAD inotropes, intra-aortic balloon pump, extracorporeal membrane oxygenation, and mechanical ventilation.

Pre-implantation VT/VF frequency was 59% in patients with pre-existing ICD and 26% in patients without ICD ( $P<0.001$ ). The median interval and associated interquartile range between documented VT/VF and LVAD implantation was 19 days (interquartile range 7328) and 8.5 days (415.2) in patients with and without pre-LVAD ICD, respectively ( $P<0.001$ ).

### Patients With Pre-LVAD ICD

In patients with a pre-LVAD ICD, cardiac resynchronization therapy defibrillator was present in 195 (50.4%), dual chamber in 102 (26.4%), and single-lead in 90 (23.3%) patients. The median time between ICD implant and LVAD insertion was 3.9 years (range 5 days–19 years).

After LVAD implant, 6 patients died within 20 days and 3 patients had the ICD removed at the time of the LVAD because of a concern for infection. There were 18 (4.6%) patients who had postoperative lead dysfunction with characteristics and mechanisms shown in Table 2. There were 93 procedures in 81 patients (20.9% of those with pre-LVAD ICD): generator exchange ( $n=74$ ), lead revision ( $n=12$ ), and complete system removal because of infection ( $n=7$ ). Among the patients who underwent generator exchange, battery depletion was the most

frequent indication ( $n=69$ ). The generator was exchanged in 2 patients during right ventricular lead replacement, 2 because of inability to interrogate/program the device, and 1 because of technical failure. The median time from LVAD implant to the first ICD procedure was 238.5 days. Timing and details of ICD infection are shown in Table 3.

There was 1 patient with pre LVAD ICD who had LVAD thrombosis requiring pump exchange 11 days after generator exchange for elective replacement interval. The international normalized ratio was 2 the day of the procedure and the patient had a history of an elevated lactic dehydrogenase 13 days prior.

### Patients Without Pre-LVAD ICD

Of the 99 patients without pre-LVAD ICD, 52 (52.5%) underwent ICD implantation during the follow-up period: 29 for primary prevention (44%, 13 with ischemic cardiomyopathy) and 23 for secondary prevention; of those, 9 had VT documented before LVAD implantation and 14 because of VT documented after LVAD implantation (6 occurred during the index hospitalization for LVAD implantation). Thirty-eight of 52 (73.1%) patients had a single-lead ICD implanted.

The median time from LVAD to ICD implantation was 28 days. There were 4 patients who required additional procedures after the initial ICD implantation. Two had a generator exchange because of end of life, 1 had a lead

**Table 1.** Characteristics of Patients With and Without ICD

	All (n=486)	ICD Pre-LVAD (n=387)	ICD Post-LVAD (n=52)	Never ICD (n=47)	P Value
<b>Demographics and comorbidities</b>					
Age, y	55.3±13.0	57.0±12.0	47.6±13.0	49.2±15.9	<0.001
BMI, kg/m <sup>2</sup>	28.2±5.5	28.5±5.4	26.9±5.4	27.5±6.2	0.098
Male	399 (82.1%)	329 (85.0%)	37 (71.2%)	33 (70.2%)	0.005
Hypertension	307 (63.2%)	264 (68.2%)	23 (44.2%)	20 (42.6%)	<0.001
Diabetes mellitus	187 (38.5%)	158 (40.8%)	11 (21.2%)	18 (38.3%)	0.020
Chronic obstructive pulmonary disease	61 (12.6%)	55 (14.2%)	5 (9.6%)	1 (2.1%)	0.037
Chronic kidney disease	113 (23.3%)	108 (27.9%)	4 (7.7%)	1 (2.1%)	<0.001
Cerebrovascular disease	74 (15.2%)	66 (17.1%)	4 (7.7%)	4 (8.5%)	0.093
Coronary artery bypass grafting	104 (21.4%)	92 (23.8%)	6 (11.5%)	6 (12.8%)	0.040
Ischemic cardiomyopathy	202 (41.6%)	154 (39.8%)	23 (44.2%)	25 (53.2%)	0.19
Peripheral vascular disease	20 (4.1%)	16 (4.1%)	2 (3.8%)	2 (4.3%)	1.00
Ventricular tachycardia or fibrillation	246 (51%)	220 (56.8%)	15 (28.8%)	11 (23.4%)	<0.001
Atrial fibrillation or flutter	244 (50.2%)	221 (57.1%)	13 (25.0%)	10 (21.3%)	<0.001
Left ventricular ejection fraction	15.2±5.75	15.3±5.54	14.5±5.7	14.8±7.2	0.355
<b>Implant index admission variables</b>					
Extracorporeal membrane oxygenation	29 (6.0%)	7 (1.8%)	9 (17.3%)	13 (27.7%)	<0.001
Invasive mechanical ventilation	51 (10.5%)	17 (4.4%)	18 (34.6%)	16 (34.0%)	<0.001
Inotropes	300 (61.7%)	226 (58.4%)	36 (69.2%)	38 (80.9%)	0.005
Intra-aortic balloon pump	117 (24.1%)	67 (17.3%)	26 (50.0%)	24 (51.1%)	<0.001
INTERMACS 1	96 (20%)	47 (12.1%)	23 (44.2%)	26 (55.3%)	<0.001
Axial flow LVAD	376 (77%)	291 (75.2%)	44 (84.6%)	41 (87.2%)	0.077
Bridge to transplant indication	281 (57.8%)	226 (58.4%)	31 (59.6%)	24 (51.1%)	0.62
Tricuspid valve intervention	133 (27.4%)	116 (30.0%)	5 (9.8%)	12 (25.5%)	0.005

BMI indicates body mass index; ICD, implantable cardioverter defibrillator; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVAD, left ventricular assist device.

revision, and 1 had system extraction because of *Pseudomonas* endocarditis (Table 3).

One patient died 11 days after ICD implantation. The cause of death was likely acute on chronic renal failure and hyperkalemic cardiac arrest (creatinine 4 mg/dL; K: 7.4 mEq/L). Another patient had an admission for septic shock 13 days after ICD implantation. Transesophageal echocardiogram showed a mobile echodensity in the ICD lead. Of note, blood cultures were negative but were obtained on empirical antibiotic therapy started at an outside facility. Infection was controlled on medical therapy and the patient was transplanted 6 months later.

## Outcomes

Patients were followed for a median of 401 (interquartile range 150–966) days. The unadjusted 30-day mortality was 5.2% and 10.1% in patients with and without pre-LVAD ICD,

respectively ( $P=0.097$ ). This early numerical difference is likely related to the difference in preoperative critical illness between groups as evidenced by baseline differences in advanced life support (Table 1). The main causes of death in our patients were sepsis (18.3%), ischemic stroke (14.6%), hemorrhagic stroke (14.0%), right ventricular failure (13.4%), pump thrombosis (12.2%), and multi-organ failure (7.3%). Details of the causes of death in our cohort are shown in Table 4. Overall, 131 (33.9%) patients with pre-LVAD ICD and 33 (33.3%) patients without pre-LVAD ICD died. Kaplan–Meier curves are seen in Figure 2. Presence of a pre-LVAD ICD was not associated with mortality in multivariable analysis (multivariable model hazard ratio 1.19, 95% CI 0.73–1.93,  $P=0.492$ ) (Tables S1 and S2). Additionally, presence of an ICD was used as a time-varying covariate to account for time post-LVAD with an ICD but was not associated with mortality in multivariable analyses (multivariable model hazard ratio 1.05, 95% CI 0.50–2.20,  $P=0.907$ ).

**Table 2.** Lead Dysfunction After LVAD Implantation in Patients With Pre-LVAD ICD

Patient	Age (y)	Sex	Lead	Revision	Mechanism
1	58	M	RV	Yes	Dislodgment
2	69	M	RV	Yes	Dislodgment
3	63	F	RV	Yes	Resected
4	68	M	RV	Yes	Cut TV repair
5	69	M	RV	Yes	Dislodgment
6	68	M	RV	Yes	Dislodgment
7	51	M	RA	Yes	Dislodgment
8	60	M	RV	Yes	Dislodgment
9	41	M	RA	Yes	Dislodgment
10	67	M	RV	Yes	Cut TV repair
11	53	M	LV	Yes	Dislodgment
12	65	M	RV	Yes	Dislodgment
13	31	F	RA & LV	No	Dislodgment
14	33	F	LV	No	Dislodgment
15	40	F	RV	No	Cut TV repair
16	65	M	LV	No	Dislodgment
17	57	M	RA	No	Dislodgment
18	66	M	LV	No	Dislodgment

F indicates female; ICD, implantable cardioverter defibrillator; LV, left ventricle; LVAD, left ventricular assist device; M, male; RA, right atrium; RV, right ventricle; TV, tricuspid valve.

There were a total of 119 (24.4%) bloodstream infections in the entire cohort: 95 (24.5%) in patients with a pre-LVAD ICD, 15 (28.8%) in patients who received a post-LVAD ICD, and 9 (19.1%) in a patient who never received an ICD ( $P=0.54$ ). There was no association between pre-LVAD ICD and time to bloodstream infection after censoring at heart transplant and using death as a competing risk (subhazard ratio 1.03, 95% CI 0.65–1.63,  $P=0.899$ ).

**Table 3.** Post LVAD ICD Infectious Complications

Patient	Pre-LVAD ICD	Age	Sex	Type of Infection	Microorganism	Days After LVAD
1	Yes	71	M	Pocket infection	Negative cultures	463
2	Yes	58	F	Pocket infection	Negative cultures	1248
3	Yes	24	F	Pocket infection	Negative cultures	38
4	Yes	72	M	Pocket infection with bacteremia	Coagulase negative <i>Staphylococcus</i> species	199
5	Yes	32	M	Pocket infection with bacteremia	<i>Staphylococcus lugdunensis</i>	268
6	Yes	51	M	Pocket infection with bacteremia	Coagulase negative <i>Staphylococcus</i> species	163
7	Yes	53	M	LVAD driveline infection with bacteremia	Methicillin sensitive <i>Staphylococcus aureus</i>	219
8	No	24	M	ICD-related endocarditis	<i>Pseudomonas aeruginosa</i>	271

F indicates female; ICD, implantable cardioverter defibrillator; LVAD, left ventricular assist device; M, male.

In the 387 patients with pre-LVAD ICD, there were 99 patients (25.5%) who received a total of 124 appropriate ICD shocks and 23 patients (5.9%) who received a total of 26 inappropriate shocks. Of the 220 patients without a history of VT/VF, 75 (34.1%) had an ICD shock while 24 of 167 (14.4%) patients without a history of VT/VF had an ICD shock in the follow-up period ( $P<0.001$ ). In the 52 patients implanted with an ICD after LVAD, 12 (23.0%) had a total of 22 appropriate ICD shocks and 2 (3.8%) had an inappropriate ICD shock. Of note, 7 of the 29 (24.1%) patients who had a post LVAD ICD for primary prevention had an appropriate ICD shock compared with 5 of the 23 (21.7%) of those who had a post LVAD ICD implantation for secondary prevention ( $P=0.8$ ).

## Discussion

In this study, the majority of patients (80%) with a continuous flow LVAD had an ICD at the time of LVAD implantation and another 11% had an ICD placed after LVAD. The principal findings of the present analysis are that ICD-related procedures are common among continuous flow LVAD patients and there was no demonstrable survival benefit conferred with an ICD. In addition to ICD-related procedures, morbidity was also common and included ICD shocks (31%) and complications related to leads (4%) and infection (2%).

In a seminal report from our institution, a significant survival benefit was observed in patients who had an ICD at the time of LVAD insertion, and this survival advantage was more significant among patients who had a history of VT.<sup>8</sup> However, the majority of these patients were supported with pulsatile flow LVAD devices (74.1%), patients without an isolated LVAD were included (13% with a right ventricular VAD only or biventricular VADs), and a minority had an ICD at the time of VAD placement (19%). In patients with a continuous flow LVAD, the benefits of an ICD have been more mixed. A systematic review and meta-analysis of 6 observational



**Table 4.** Causes of Death in Our Cohort

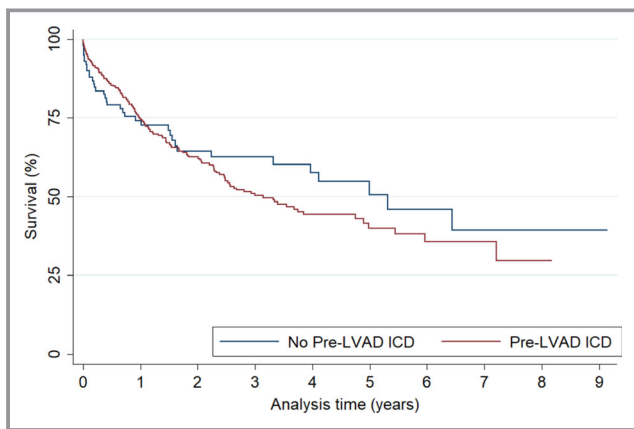
	All	Pre-LVAD ICD	Post-LVAD ICD	No ICD Post LVAD
	n=164 (%)	n=131 (%)	n=18 (%)	n=15 (%)
Sepsis	30 (18.3)	25 (19.1)	4 (22.2)	1 (6.7)
Ischemic stroke	24 (14.6)	15 (11.5)	4 (22.2)	5 (33.3)
Hemorrhagic stroke	23 (14.0)	18 (13.7)	3 (16.7)	2 (13.3)
Right ventricular failure	22 (13.4)	16 (12.2)	2 (11.1)	4 (26.7)
Pump thrombosis	20 (12.2)	17 (13.0)	3 (16.7)	
Multi-organ failure	13 (7.9)	11 (8.4)		2 (13.3)
Not able to determine	7 (4.3)	6 (4.6)	1 (5.6)	
Accidental power interruption	4 (2.4)	4 (3.1)		
Malignancy	4 (2.4)	3 (2.3)		1 (6.7)
Respiratory failure	3 (1.8)	2 (1.5)	1 (5.6)	
Hemorrhagic shock	3 (1.8)	3 (2.3)		
Vasoplegia	2 (1.2)	2 (1.5)		
Driveline malfunction	2 (1.2)	2 (1.5)		
Pulseless electrical activity	2 (1.2)	2 (1.5)		
Tamponade	1 (0.6)	1 (0.8)		
Subdural hematoma	1 (0.6)	1 (0.8)		
Device malfunction	1 (0.6)	1 (0.8)		
Acute renal failure	1 (0.6)	1 (0.8)		
Pulmonary hemorrhage	1 (0.6)	1 (0.8)		

ICD indicates implantable cardioverter defibrillator; LVAD, left ventricular assist device.

studies showed a significant interaction between type of LVAD and survival with respect to ICD, such that the benefit of ICD was negated when pulsatile LVADs were excluded.<sup>9</sup> An analysis of the United Network for Organ Sharing registry

showed improved survival with ICD in patients with and without LVAD waiting for heart transplantation.<sup>10</sup> However, a propensity-matched analysis of United Network for Organ Sharing concluded that an ICD in patients with continuous flow LVAD as bridge to transplant was not associated with a decrease in mortality.<sup>11</sup> However, this study did not account for patients with subsequently inserted ICDs. Our study adds to the body of evidence that an ICD was not associated with a decrease in mortality in the era of continuous flow LVAD devices.

The mechanisms of ventricular arrhythmias in LVAD patients include the severity of the underlying cardiomyopathy, the apical inflow cannula insertion site, inefficient left ventricular unloading, and excessive unloading (suction events). Patients with a ventricular arrhythmia before LVAD are more likely to have one after LVAD insertion, with the highest burden occurring within the first 30 days after LVAD implantation.<sup>6</sup> However, sustained ventricular arrhythmias can be tolerated without syncope or sudden death in LVAD patients, allowing for patients to survive these events and seek medical care.<sup>12</sup> In the HeartMate 2 destination therapy clinical trial, the continuous axial flow LVAD had significantly fewer arrhythmias than the pulsatile flow HeartMate XVE.<sup>5</sup>



**Figure 2.** Kaplan–Meier curves demonstrating the lack of association of pre-LVAD ICD with mortality ( $P=0.483$ ). ICD indicates implantable cardioverter defibrillator; LVAD, left ventricular assist device.

This decrease in arrhythmias coupled with improved LVAD function and device management has potentially led to the negation of ICD benefits in the current era.

The ICD-related procedures and complications in LVAD patients are not trivial. There were 18 (3%) lead dislodgments during the LVAD implantation, with 9 requiring revision. This is in accordance with what has been previously reported regarding common causes of lead revision after LVAD implantation.<sup>13</sup> There were an additional 3 cases of ICD lead removal during concomitant tricuspid valve repair in our cohort. Over half of the patients without a pre-LVAD ICD had one subsequently implanted. Approximately 20% of the patients were subjected to an ICD-related procedure, with generator replacement because of battery depletion being the most frequent. It is important to note that cardiac resynchronization therapy has not been shown to improve outcomes in patients with LVAD, but is associated with a higher number of generator changes.<sup>14</sup> Disabling LV lead pacing at the time of LVAD implantation may prolong battery life and reduce the number of required procedures, but further evaluation is needed in prospective studies. ICD-related procedures carry an inherent risk of lead- and pocket-related complications, which are mitigated by center volume.<sup>15</sup> ICD infection requiring system removal occurred in 1.8% and 1.9% of the patients with and without pre-LVAD ICD, respectively, in our study, which is in line with a prior report.<sup>16</sup>

The presence of ICD shocks has been reported to be associated with worse outcomes in patients with pulsatile and continuous flow LVAD.<sup>17,18</sup> In our cohort, ≈20% of the patients had an ICD shock. Further studies are needed to evaluate liberal or “monitor only” programming strategies in LVAD patients in order to minimize ICD shocks.<sup>19</sup> In addition, as there is some debate regarding the lack of benefit of ICDs in patients with a nonischemic cardiomyopathy,<sup>20</sup> further study is needed in the interaction of cardiomyopathy cause and LVAD with respect to ICD strategy.

## Limitations

The findings in this article should be evaluated in light of the following limitations. This is a single-center cohort and is retrospective in nature. While this is the largest experience of patients with a continuous flow LVAD published to date, a relatively small number of patients did not have a pre-LVAD ICD.

## Conclusion

ICD use is common in this contemporary cohort of patients with a continuous flow LVAD. There is no apparent mortality benefit in this population to balance considerable patient

morbidity, including ICD-related procedures in 1 in 5 and device shock in almost 1 in 3 patients. Further prospective studies are needed to better delineate optimal ICD implantation and programming strategies in patients in the current era with continuous flow devices.

## Disclosures

None.

## References

- Writing Committee M, Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH, Fonarow GC, Geraci SA, Horwich T, Januzzi JL, Johnson MR, Kasper EK, Levy WC, Masoudi FA, McBride PE, McMurray JJ, Mitchell JE, Peterson PN, Riegel B, Sam F, Stevenson LW, Tang WH, Tsai EJ, Wilkoff BL; American College of Cardiology Foundation/American Heart Association Task Force on Practice G. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. 2013;128:e240–e327.
- Rogers JG, Pagani FD, Tatroles AJ, Bhat G, Slaughter MS, Birks EJ, Boyce SW, Najjar SS, Jeevanandam V, Anderson AS, Gregoric ID, Mallidi H, Leadley K, Aaronson KD, Frazier OH, Milano CA. Intrapericardial left ventricular assist device for advanced heart failure. *N Engl J Med*. 2017;376:451–460.
- Mehra MR, Naka Y, Uriel N, Goldstein DJ, Cleveland JC Jr, Colombo PC, Walsh MN, Milano CA, Patel CB, Jorde UP, Pagani FD, Aaronson KD, Dean DA, McCants K, Itoh A, Ewald GA, Horstmannshof D, Long JW, Salerno C; Investigators M. A fully magnetically levitated circulatory pump for advanced heart failure. *N Engl J Med*. 2017;376:440–450.
- Kociol RD. Time for MADIT-VAD?: ICDs among LVAD patients. *JACC Heart Fail*. 2016;4:780–782.
- Slaughter MS, Rogers JG, Milano CA, Russell SD, Conte JV, Feldman D, Sun B, Tatroles AJ, Delgado RM III, Long JW, Wozniak TC, Ghumman W, Farrar DJ, Frazier OH; HeartMate III. Advanced heart failure treated with continuous-flow left ventricular assist device. *N Engl J Med*. 2009;361:2241–2251.
- Nakahara S, Chien C, Gelow J, Dalouk K, Henrikson CA, Mudd J, Stecker EC. Ventricular arrhythmias after left ventricular assist device. *Circ Arrhythm Electrophysiol*. 2013;6:648–654.
- Garan AR, Yuzefpolskaya M, Colombo PC, Morrow JP, Te-Frey R, Dano D, Takayama H, Naka Y, Garan H, Jorde UP, Uriel N. Ventricular arrhythmias and implantable cardioverter-defibrillator therapy in patients with continuous-flow left ventricular assist devices: need for primary prevention? *J Am Coll Cardiol*. 2013;61:2542–2550.
- Cantillon DJ, Tarakji KG, Kumbhani DJ, Smedira NG, Starling RC, Wilkoff BL. Improved survival among ventricular assist device recipients with a concomitant implantable cardioverter-defibrillator. *Heart Rhythm*. 2010;7:466–471.
- Vakil K, Kazmirczak F, Sathnur N, Adabag S, Cantillon DJ, Kiehl EL, Koene R, Cogswell R, Anand I, Roukoz H. Implantable cardioverter-defibrillator use in patients with left ventricular assist devices: a systematic review and meta-analysis. *JACC Heart Fail*. 2016;4:772–779.
- Vakil K, Duval S, Cogswell R, Eckman P, Levy WC, Anand I, Dardas T, Adabag S. Impact of implantable cardioverter-defibrillators on waitlist mortality among patients awaiting heart transplantation: an UNOS/OPTN analysis. *JACC Clin Electrophysiol*. 2017;3:33–40.
- Clerkin KJ, Topkara VK, Mancini DM, Yuzefpolskaya M, Demmer RT, Dizon JM, Takeda K, Takayama H, Naka Y, Colombo PC, Garan AR. The role of implantable cardioverter defibrillators in patients bridged to transplantation with a continuous-flow left ventricular assist device: a propensity score matched analysis. *J Heart Lung Transplant*. 2017;36:633–639.
- Oz MC, Rose EA, Slater J, Kuiper JJ, Catanese KA, Levin HR. Malignant ventricular arrhythmias are well tolerated in patients receiving long-term left ventricular assist devices. *J Am Coll Cardiol*. 1994;24:1688–1691.
- Ambardekar AV, Lowery CM, Allen LA, Cannon AP, Cleveland JC Jr, Lindenfeld J, Brieke A, Sauer WH. Effect of left ventricular assist device placement on preexisting implantable cardioverter-defibrillator leads. *J Card Fail*. 2010;16:327–331.
- Gopinathannair R, Roukoz H, Bhan A, Ravichandran A, Ahmed MM, Familtsev D, Bhat G, Cowger J, Abdullah M, Sandesara C, Dhawan R, Birks EJ, Trivedi JR, Slaughter MS. Cardiac resynchronization therapy and clinical outcomes in

- continuous flow left ventricular assist device recipients. *J Am Heart Assoc.* 2018;7:e009091. DOI: 10.1161/JAHA.118.009091.
15. Al-Khatib SM, Lucas FL, Jollis JG, Malenka DJ, Wennberg DE. The relation between patients' outcomes and the volume of cardioverter-defibrillator implantation procedures performed by physicians treating Medicare beneficiaries. *J Am Coll Cardiol.* 2005;46:1536–1540.
  16. Riaz T, Nienaber JJ, Baddour LM, Walker RC, Park SJ, Sohail MR. Cardiovascular implantable electronic device infections in left ventricular assist device recipients. *Pacing Clin Electrophysiol.* 2014;37:225–230.
  17. Ambardekar AV, Allen LA, Lindenfeld J, Lowery CM, Cannon AP, Cleveland JC Jr, Brieke A, Sauer WH. Implantable cardioverter-defibrillator shocks in patients with a left ventricular assist device. *J Heart Lung Transplant.* 2010;29:771–776.
  18. Omery B, Pedersen R, Sulemanjee N, Hastings TE, Cheema O, Roberts E, Downey FX, Crouch JD, Thohan V. Implication of appropriate ICD shock on mortality after continuous flow LVAD. *J Heart Lung Transplant.* 2018;37:S130.
  19. Richardson TD, Hale L, Arteaga C, Xu M, Keebler M, Schlendorf K, Danter M, Shah A, Lindenfeld J, Ellis CR. Prospective randomized evaluation of implantable cardioverter-defibrillator programming in patients with a left ventricular assist device. *J Am Heart Assoc.* 2018;7:e007748. DOI: 10.1161/JAHA.117.007748.
  20. Kober L, Thune JJ, Nielsen JC, Haarbo J, Videbaek L, Korup E, Jensen G, Hildebrandt P, Steffensen FH, Bruun NE, Eiskjaer H, Brandes A, Thogersen AM, Gustafsson F, Egstrup K, Videbaek R, Hassager C, Svendsen JH, Hofsten DE, Torp-Pedersen C, Pehrson S; DANISH Investigators. Defibrillator implantation in patients with nonischemic systolic heart failure. *N Engl J Med.* 2016;375:1221–1230.



# **SUPPLEMENTAL MATERIAL**

**Table S1. Multivariable model with respect to mortality.**

<b>Variable</b>	<b>Hazard ratio</b>	<b>95% confidence intervals</b>	<b>P value</b>
Pre-LVAD Implantable Cardioverter Defibrillator	1.19	0.73 -1.93	0.492
Age at LVAD implantation	1.02	1.00-1.04	0.006
Male	0.98	0.65-1.49	0.947
Bridge to Transplant	1.01	0.73-1.39	0.937
Hypertension	1.38	0.94-2.01	0.093
Diabetes	1.00	0.70-1.41	0.998
Chronic Kidney Disease	1.01	0.69-1.47	0.066
Coronary Artery Disease	0.99	0.71-1.40	0.994
Ventricular Fibrillation/Tachycardia	0.90	0.64-1.25	0.526
Atrial Fibrillation/Flutter	0.84	0.60-1.17	0.305
INTERMACS1	1.95	1.28-2.97	0.002

LVAD = left ventricular assist device.

**Table S2. Multivariable model with respect to mortality with time with ICD as time-varying covariate.**

<b>Variable</b>	<b>Hazard ratio</b>	<b>95% confidence intervals</b>	<b>P value</b>
Implantable Cardioverter Defibrillator	1.05	0.50-2.20	0.907
Age at LVAD implantation	1.02	1.00-1.03	0.022
Male	1.09	0.68-1.73	0.723
Bridge to Transplant	1.08	0.77-1.51	0.666
Hypertension	1.37	0.88-2.14	0.167
Diabetes	0.99	0.66-1.49	0.986
Chronic Kidney Disease	1.00	0.67-1.49	0.995
Coronary Artery Disease	0.98	0.69-1.41	0.931
Ventricular Fibrillation /Tachycardia	0.94	0.64-1.39	0.774
Atrial Fibrillation/ Flutter	0.89	0.61-1.28	0.524
INTERMACS1	2.16	1.30-3.58	0.003

LVAD = left ventricular assist device; ICD= Implantable Cardioverter Defibrillator.