Journal of Interventional Cardiac Electrophysiology (2020) 58:243–252
https://doi.org/10.1007/s10840-019-00682-0

ORIGINAL RESEARCH

Ventricular arrhythmias in patients with biventricular assist devices

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Received: 5 September 2019 / Accepted: 2 December 2019 / Published online: 14 December 2019

Abstract

Purpose Ventricular arrhythmias (VAs) are common in patients after left ventricular assist device (LVAD) implant and are associated with worse outcomes. However, the prevalence and impact of VA in patients with durable biventricular assist device (BIVAD) is unknown. We performed a retrospective cohort study of patients with BIVADs to evaluate the prevalence of VA and their clinical outcomes.

Methods Consecutive patients who received a BIVAD between June 2014 and July 2017 at our medical center were included. The prevalence of VA, defined as sustained ventricular tachycardia or fibrillation requiring defibrillation or ICD therapy, was compared between BIVAD patients and a propensity-matched population of patients with LVAD from our center. The occurrence of adverse clinical events was compared between BIVAD patients with and without VA.

Results Of the 13 patients with BIVADs, 6 patients (46%) experienced clinically significant VA, similar to a propensity-matched LVAD population (38%, $p = 1.00$). There were no differences in baseline characteristics between the two cohorts, except patients in the non-VA group who had worse hemodynamics (mitral regurgitation and right-sided indices), had less history of VA, and were younger. BIVAD patients with VA had a higher incidence of major bleeding (MR 3.05 (1.07–8.66), $p = 0.036$) and worse composite outcomes (log-rank test, $p = 0.046$). The presence of VA was associated with worse outcomes in both LVAD and BIVAD groups.

Conclusions Ventricular arrhythmias are common in patients with BIVADs and are associated with worse outcomes. Future work should assess whether therapies such as ablation improve the outcome of BIVAD patients with VA.

Keywords Ventricular arrhythmia · Ventricular tachycardia · Biventricular assist device · Heart failure

Abbreviations

AF	Atrial fibrillation
ATP	Anti-tachycardia pacing
BIVAD	Biventricular assist device
CVA	Cerebrovascular accident
EF	Ejection fraction
EPPY	Events per patient year
GFR	Glomerular filtration rate
GI	Gastrointestinal
HF	Heart failure
IABP	Intra-aortic balloon pump
ICD	Implanted cardioverter-defibrillator
INTERMACS	Interagency Registry for Mechanically Assisted Circulatory Support
LA	Left atrium
LVAD	Left ventricular assist device
LV-HVAD	Left ventricular HeartWare ventricular assist device
RA-HVAD	Right atrial HeartWare ventricular assist device
LVIDd	Left ventricle internal diameter diastole
PAPI	Pulmonary artery pulsatility index
PASP	Pulmonary artery systolic pressure
PCWP	Pulmonary capillary wedge pressure
PVR	Pulmonary vascular resistance
RAP	Right atrial pressure
RV	Right ventricle

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RVSP	Right ventricular systolic pressure
RVSWI	Right ventricular stroke work index
RVAD	Right ventricular assist device
TAPSE	Tricuspid annular plane systolic excursion
VA	Ventricular arrhythmia
VT	Ventricular tachycardia

1 Introduction

Heart failure is estimated to affect 5.8 million people in the USA and is expected to increase [1]. Despite advances in guideline-directed medical and electronic device therapies, mortality and morbidity remain high in patients with advanced heart failure. Given the shortage of donors available for transplant, the use of ventricular assist devices (VADs) has grown substantially over the years [2].

Ventricular arrhythmias (VAs) are common comorbidities in patients with left ventricular assist devices (LVADs), with rates ranging from 20 to 50% [3–7]. These events have been reported to occur more frequently within the first 30 days of left ventricular assist device (LVAD) placement [8, 9], and early occurrences of VA have been associated with higher mortality [3, 10]. In patients with concomitant right ventricular failure, durable biventricular assist devices (BIVADs) are increasingly implanted with promising results [11–13]. There are currently limited data on the prevalence and outcomes of VAs in patients with BIVADs. Although VAs may be tolerated over the short term due to hemodynamic support provided by the BIVAD, we hypothesize that patients with clinically significant VAs after BIVAD placement may have worse outcomes compared with those without VAs. The purpose of our study is to assess the prevalence of clinically significant VAs after BIVAD placement in comparison with a propensity-matched LVAD population and assess adverse clinical outcomes in BIVAD patients with and without VA.

2 Methods

2.1 Patient population and study design

This retrospective study consisted of 13 consecutive patients who received durable biventricular support between June 2014 and July 2017 at University of California, San Diego. Twelve patients underwent implantation of HeartWare device (HVAD, Medtronic, Minnesota, MN) in a left ventricular (LV-HVAD) and right atrial (RA-HVAD) configuration. One patient received a HeartMate II (HM2, Abbott, Pleasanton, CA) LVAD and a RA-HVAD. In all patients, the right ventricular assist device (RVAD) cannula was placed in the anterior wall of the right atrium to improve flow dynamics and reduce the incidence of suction events, as described previously [12, 13]. The occurrence of clinically significant VA, defined as sustained ventricular tachycardia (VT) or ventricular fibrillation lasting ≥ 30 s, requiring external defibrillation or appropriate ICD therapy (anti-tachycardic pacing (ATP) or shock), were recorded over time. VAs occurring in rapid succession were considered a single event.

Patients were divided into two groups, those with clinically significant VAs after BIVAD placement (VA group) and those without (non-VA group). Relevant baseline characteristics prior to biventricular support including age, gender, duration of heart failure, medical comorbidities, echocardiogram, right heart catheterization, and laboratory data were compared between the two groups. VA and ICD events were obtained via ICD interrogation reports and thorough chart review of telemetry and ECG criteria. Patients were followed until occurrence of death, transplant, or RVAD decommissioning. Adverse events defined by the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) criteria [14] were recorded, including death, heart failure hospitalization, total hospitalization, RVAD thrombosis, major bleeding, infection, renal failure, respiratory, and neurologic dysfunction. Additionally, propensity score analysis was performed to compare prevalence of VA and composite outcome between LVAD and BIVAD patients.

2.2 Statistical analysis

Categorical baseline variables were presented as numbers with proportions and compared using Fisher's exact test. Continuous variables were presented as median with interquartile range (Q1-Q3) and compared with the Mann-Whitney test. Poisson regression analysis was used to compare incidence rates of adverse events, presented as mean ratios (MR). The Poisson model was adjusted for patient age at the time of BIVAD placement, with the logarithm of follow up time (one-patient year) used as an offset. The Poisson over-dispersion model was used in the presence of over-dispersion. Kaplan-Meier estimate of composite outcome (death, heart failure hospitalization, major bleeding, and RVAD thrombosis) was performed for both groups, censoring for transplant. Survival curves were compared using the log-rank test. Statistical analysis was performed using SPSS for Windows Version 25 (SPSS Inc. Chicago, IL, USA). For all analyses, $p < 0.05$ (two tailed) was considered statistically significant.

Propensity score analysis was performed using a logistic regression model in patients who had LVAD placement at our medical center from August 2011 to August 2018 ($n = 181$). Covariates included in propensity score calculation were selected based on prior studies [15] and included demographic (age, sex, ethnicity) and clinical (body mass index, bridge to transplant, HVAD, INTERMACS profile, non-ischemic heart failure, prior history of VA, hypertension, diabetes, atrial fibrillation, renal function, platelet count, international normalized ratio, ejection fraction, use of class three anti-arrhythmic drugs, and angiotensin-converting enzyme inhibitors) characteristics. BIVAD and LVAD patients were matched in a 1 : 1 manner based on the propensity score of each patient. A caliper width of 20% of the standard deviation of the logit of the propensity score was used, which eliminates 99% of the bias owing to measured confounding variables [16].

3 Results

3.1 Patient population

A total of 13 patients received BIVADs as bridge-to-transplant. Ten patients (77%) had contemporaneous BIVAD placement and 3 patients had conversion from LVAD alone to BIVAD due to progressive right ventricular failure and hemodynamic instability at post-LVAD day 1, 4, and 13, respectively. Baseline characteristics of all patients are presented in Table 1. Notable differences between the VA and non-VA groups were observed in age (53.5 [47–57] vs 29 [20–49], $p = 0.035$), presence of moderate or severe mitral regurgitation (33% vs 100%, $p = 0.021$), right atrial pressure (13 [11–19] vs 21 [20–23], $p = 0.04$), and pulmonary artery pulsatility index (1.8 [1.6–2.2] vs 1.0 [0.8–1.3], $p = 0.016$). Additionally, all 6 patients in the VA group had a history of VAs prior to BIVAD placement, compared with 2 patients in the non-VA group (100.0% vs 29%, $p = 0.021$). Etiology of heart failure is listed in Table 2. Of the 13 patients, 2 (15%) had ischemic cardiomyopathy and the remaining 11 patients (85%) had non-ischemic cardiomyopathy. Patients were followed for median of 263 (47–519) days.

3.2 Prevalence of VA after BIVAD placement

Overall, 6 of the 13 patients (46%) experienced clinically significant VAs after BIVAD placement. A total of 62 interventions (33 ICD shocks, 3 ATP, 26 external defibrillations) were delivered for 41 episodes of VA. Among the 41 episodes of VA, 56% were associated with inotrope use ($n = 23$), 12% were associated with suction event ($n = 5$), 7% were associated with electrolyte derangement ($n = 3$; serum potassium ≤ 3.0 mmol/l), and 5% were associated with RVAD thrombosis ($n = 2$). Twenty percent ($n = 8$) of the VA episodes were not associated with any clear identifiable triggers. VAs more commonly occurred in the first month after BIVAD placement (Fig. 1). Median days to first VA event were 14 (2–28) days.

3.3 Outcomes of patients with VA after BIVAD placement

Of the six patients in the VA group, one expired while on BIVAD support and two received transplant. Three patients experienced recurrent RVAD thrombosis, two of whom had their RVADs decommissioned and later expired, and one was transitioned to destination therapy due to his comorbidities. In comparison, six of the seven patients in the non-VA group received transplant. One patient experienced recurrent RVAD thrombosis leading to RVAD decommissioning.

The most common adverse events after BIVAD placement were major bleeding and hospital readmission (Table 3). Poisson regression analysis, adjusting for age, was used to compare the incidence of adverse events (events per patient–year). The VA group had a higher rate of major bleeding compared with the non-VA group (MR 3.049, 95% CI [1.073–8.664], $p = 0.036$), but there was no difference in incidence of heart failure hospitalization, total hospitalization, RVAD thrombosis, driveline or VAD infection, renal failure, respiratory failure, and cerebrovascular accidents when analyzed individually. Kaplan-Meier curve of composite outcome revealed rapid separation of the curves for event-free survival favoring the non-VA group ($p = 0.046$) (Fig. 2a).

3.4 Comparison between patients with BIVADs and LVADs

There was no difference in baseline characteristics between patients with BIVADs and LVADs after propensity score matching (Table 4). Prevalence of VA was similar between the two groups (46% vs 38%, $p = 1.00$). Kaplan-Meier analysis of composite outcomes is shown in Fig. 2. Event-free survival favored the non-VA group in both BIVAD ($p = 0.046$) and LVAD patients ($p = 0.009$). However, there was no statistical difference in composite outcomes of the VA groups when comparing BIVAD vs LVAD patients (log-rank $p = 0.470$).

4 Discussion

There are three key findings in this study. First, the prevalence of VAs during BIVAD therapy was high, but similar to a propensity-matched LVAD population. Second, BIVAD patients with VAs experienced more major bleeding and had worse composite post-operative cardiovascular morbidity compared with BIVAD patients without VAs. Third, the presence of VA was associated with worse outcomes, irrespective of BIVAD or LVAD therapy.

Table 1 Baseline characteristics of patients with BIVADs

Baseline characteristics	VA group ($n = 6$)	Non-VA group ($n = 7$)	p value
Age (year)	54 (47–57)	29 (20–49)	0.035
Male sex	6 (100)	5 (71)	0.462
Ethnicity			0.629
White	2 (33)	2 (29)	
Black	2 (33)	1 (14)	
Other	2 (33)	4 (57)	
Body mass index (kg/m$^{2)}$	29.7 (26.0–33.9)	23.5 (19.6–34.2)	0.313
Indication			
Bridge to transplant	6 (100)	7 (100)	1.000
HF etiology			
Non-ischemic	4 (67)	7 (100)	0.192
INTERMACS profile			0.724
1	4 (67)	4 (57)	
2	2 (33)	3 (43)	
Home inotrope use	1 (17)	3 (43)	0.559
ICD present	4 (67)	6 (86)	0.559
HF duration (months)	35 (8–120)	66 (5–96)	1.000
HF hospitalizations pre-BIVAD (no.)	6 (1–7)	4 (2–6)	0.914
Comorbidities			
History of ventricular arrhythmia	6 (100)	2 (29)	0.021
Diabetes	3 (50)	2 (29)	0.592
Hypertension	3 (50)	3 (43)	1.000
Hyperlipidemia	5 (83)	0 (0)	0.005
Atrial fibrillation	3 (50)	5 (71)	0.592
Chronic kidney disease ≥ stage 3	2 (33)	1 (14)	0.559
End-stage renal disease	0 (0)	0 (0)	–
Echocardiogram			
EF (%)	15 (9–17)	15 (14–23)	0.657
LVIDd (cm)	7.7 (4.9–7.9)	6.9 (6.7–8.4)	0.945
LA diam (cm)	5.0 (3.8–6.3)	5.3 (4.0–6.0)	1.000
LA vol (ml/m^2)	43 (29–50)	56 (47–79)	0.138
RVSP (mmHg)	38 (31–44)	44 (19–56)	0.595
TAPSE (cm)	1.3 (0.9–2.1)	1.6 (1.2–1.7)	0.876
RV dilation ≥ moderate	0 (0)	3 (43)	0.192
Mitral regurgitation, ≥ moderate	2 (33)	7 (100)	0.021
Tricuspid regurgitation, ≥ moderate	2 (33)	6 (86)	0.103
Pre-operative support			
IABP/impella	3 (50)	1 (14)	0.266
Intubated	1 (17)	2 (29)	1.000
Inotropes	6 (100)	7 (100)	–
> 1 Inotrope	3 (50)	5 (71)	0.592
Vasopressors	2 (33)	1 (14)	0.559
Hemodialysis	1 (17)	1 (14)	1.000
Length of stay pre-implant (days)	11 (6–15)	13 (7–37)	0.628
Hemodynamic parameters			
Heart rate (beats/min)	96 (71–110)	111 (89–118)	0.276
Systolic blood pressure (mmHg)	96 (93–97)	100 (80–110)	0.509
RAP (mmHg)	13 (11–19)	21 (20–23)	0.040
PASP (mmHg)	56 (49–68)	50 (47–53)	0.465

Table 1 (continued)

Baseline characteristics	VA group ($n = 6$)	Non-VA group ($n = 7$)	p value
PCWP (mmHg)	29 (26–31)	31 (30–35)	0.466
Pulmonary artery saturation (%)	48.5 (37–51)	34 (30–38)	0.110
Cardiac output (l/min)	3.8 (3.2–4.7)	2.6 (2.2–3.3)	0.277
Cardiac index (l/min/m^2)	1.6 (1.3–2.2)	1.3 (1.2–1.7)	0.558
PVR (wood unit)	4.4 (2.4–5.2)	3.0 (1.8–5.6)	0.755
RAP/PCWP	0.5 (0.4–0.6)	0.6 (0.5–0.8)	0.159
PAPI	1.8 (1.6–2.2)	1.0 (0.8–1.3)	0.016
RVSWI (mmHg*ml/m^2)	5.2 (3.0–6.3)	2.5 (2.1–3.6)	0.286
Laboratory parameters			
White blood cells (10^3/ul)	7.7 (7.0–10.3)	9.4 (7.9–10.6)	0.508
Hemoglobin (g/dl)	10.9 (10.5–12.0)	9.2 (7.8–11.0)	0.181
Platelets (10^3/mm^3)	161 (121–224)	150 (130–197)	1.000
Sodium (mmol/l)	129 (126–133)	124 (121–128)	0.149
Blood urea nitrogen (mg/dl)	26 (16–43)	29 (27–34)	0.510
Creatinine (mg/dl)	1.5 (1.3–1.7)	1.4 (1.3–1.8)	0.342
GFR (ml/min/m^2)	49 (41–53)	50 (47–53)	0.557
Alanine aminotransferase (U/l)	26 (16–42)	25 (14–149)	0.916
Aspartate aminotransferase (U/l)	31 (21–49)	31 (20–71)	0.945
Albumin (g/dl)	3.3 (3.1–3.6)	3.6 (3.5–3.8)	0.119
Total bilirubin (mg/dl)	2.2 (0.5–3.4)	1.7 (1.4–2.2)	0.731
International normalized ratio	1.4 (1.3–1.7)	1.7 (1.3–1.9)	0.534
Pro-brain natriuretic peptide	7412 (4006–22,727)	10,198 (4432–14,897)	0.937
Anti-arrhythmic therapy			
Mexiletine	1 (17)	0 (0)	0.462
Beta-blocker	0 (0)	0 (0)	–
Amiodarone	4 (67)	4 (57)	1.000
Prior ablation procedure	0 (0)	0 (0)	–

Values are presented as median (interquartile range) for continuous variables and number (percentage) for categorical variables

BIVAD, biventricular assist device; *EF*, ejection fraction; *GFR*, glomerular filtration rate; *HF*, heart failure; *IABP*, intra-aortic balloon pump; *ICD*, implanted cardioverter-defibrillator; *INTERMACS*, Interagency Registry for Mechanically Assisted Circulatory Support; *LA*, left atrial; *LVIDd*, left ventricle internal diameter diastole; *PAPI*, pulmonary artery pulsatility index; *PASP*, pulmonary artery systolic pressure; *PCWP*, pulmonary capillary wedge pressure; *PVR*, pulmonary vascular resistance; *RAP*, right atrial pressure; *RV*, right ventricle; *RVSP*, right ventricular systolic pressure; *RVSWI*, right ventricular stroke work index; *TAPSE*, tricuspid annular plane systolic excursion

4.1 Prevalence of VA in patients with BIVADs

To our knowledge, this was the first study to specifically evaluate the prevalence and outcomes of VAs in patients with BIVADs with right-sided inflow cannula placed in the right atrial position. In our study, 46% of patients experienced clinically significant VAs after BIVAD placement. Although this is high, this is comparable with prior studies reported in the LVAD population [3, 4, 17] and not significantly different from our propensity-matched LVAD group. One explanation may be that RA placement of the RVAD is more favorable hemodynamically compared with RV placement. Prior studies have suggested RV placement of RVAD is associated with increased suction events and RVAD thrombosis [12, 18], both of which could precipitate VAs. In addition, RA placement avoids scarring of the RV, further decreasing the risk of VA by preventing scar formation. While RA-HVAD does carry the theoretical risk of increased atrial arrhythmias due to scarring, none of our patients developed new onset atrial arrhythmia after BIVAD placement. The clinical significance and burden of atrial tachyarrhythmias after BIVAD placement was beyond the scope of this study and is an area for future research.

Similar to prior LVAD studies [19–23], we found that a prior history of VAs was associated with development of clinically significant VAs after BIVAD placement. This supports the theory that pre-existing substrate due to underlying cardiomyopathy plays an important role in arrhythmogenesis. Multiple studies of LVAD patients who underwent VT ablation showed that the majority of VTs originate in previously diseased substrate distributed throughout the left ventricle [24–27].

Table 2 Etiology of heart failure

Patient	Etiology of heart failure
1	Ischemic
2	Idiopathic
3	Hypertrophic cardiomyopathy
4	Idiopathic
5	Ischemic
6	Rheumatic heart disease
7	Anabolic steroid abuse
8	Sarcoidosis
9	Idiopathic
10	Myocarditis
11	Idiopathic
12	Idiopathic
13	Myocarditis

The majority of VAs occurred within the first month after BIVAD placement, as has been observed in previous LVAD studies [7, 8]. This was not unexpected, as patients are more likely to require inotropic agents post-operatively and are more prone to large fluid shifts, which can cause electrolyte derangement, suction events, or ventricular distension. Interestingly, there was significant variation in the time to first VA event in our patient cohort and two patients experienced occurrence of VAs throughout ventricular support. One explanation is that the timing of these VAs is dependent on their underlying mechanism. In a study by Sacher et al., VAs originating from prior diseased substrates occurred a median of 8 days after LVAD placement, whereas VAs originating from the LVAD cannula site can occur as many as 187 days post-procedure [24]. In addition, several studies have demonstrated changes in gene expression involved in arrhythmogenesis with prolonged VAD therapy [5, 28, 29]. Cardiac remodeling may play a role in continued VAs during mechanical support.

4.2 Sustained VA associated with adverse outcomes

It has been shown in prior work that patients with VAs after LVAD placement have higher rates of right ventricular failure [30], a decrease in cardiac output during episodes of VA [31],, and a higher mortality in the presence of early post-operative VAs [3, 10, 21]. However, the clinical outcomes of patients with BIVADs who experience VAs are less clear. In our study, we found that BIVAD patients with post-operative VAs had worse composite outcomes and a higher incidence of major bleeding after adjusting for age. This may be partly attributed to the larger number of patients in the VA group treated with amiodarone, which is an inhibitor of warfarin metabolism. Although not statistically significant, more patients in the VA group experienced recurrent RVAD thrombosis which causes elevated right heart pressure, a known association with GI bleeding [32–34].Similar to prior LVAD studies and our BIVAD cohort, LVAD patients with VA in our propensity-matched analysis also demonstrated worse composite outcomes compared with patients without VA. However, there was no difference in composite outcomes between BIVAD and LVAD patients experiencing VA, suggesting that the presence of VA is an important risk factor associated with worse outcomes.

It is worth noting that there were a few differences in baseline comorbidities between the two groups, without favoring a specific group. The non-VA cohort were younger but had worse hemodynamics on pre-VAD right heart catherization and echocardiogram (more moderate-severe mitral regurgitation, higher right atrial pressures, and worse pulmonary artery pulsatility). This is likely reflective of the severity and complexity of illness in the BIVAD patient population. Previous studies have shown varying effects of age on outcome after BIVAD [35, 36] and LVAD placement [37]. In the patients with moderate-severe mitral regurgitation, all patients improved to mild regurgitation, except one patient who improved from severe to moderate disease on follow-up echocardiogram. None of these patients underwent concomitant mitral valve repair or replacement during their BIVAD

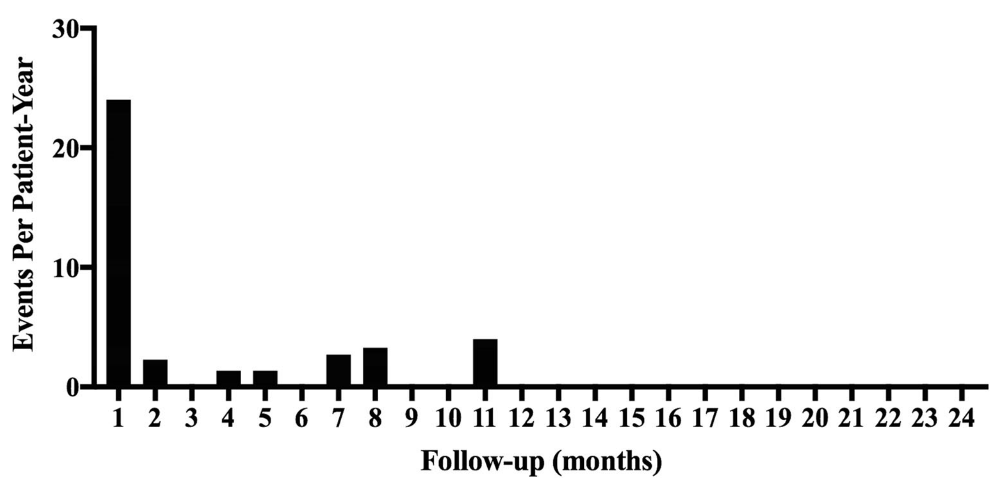

Fig. 1 Monthly incidence of ventricular arrhythmia per patient year

Table 3 Incidence of adverse events between the VA and non-VA group

Adverse events	VA group ($n = 6$)		Non-VA group ($n = 7$)		Mean ratio (MR) (95% CI)	p value
	Events	EPPY	Events	EPPY		
HF hospitalization	2	0.604	3	0.690	1.246 (0.174–8.903)	0.827
Total hospitalization	9	3.019	12	2.762	1.313 (0.543–3.177)	0.546
Major bleeding	18	3.175	6	1.198	3.049 (1.073–8.664)	0.036
RVAD thrombosis	5	0.882	4	0.798	2.089 (0.394–11.084	0.387
Infection	8	1.411	7	1.397	0.823 (0.278–2.440)	0.823
Renal failure	3	0.705	1	0.200	2.205 (0.225–21.600)	0.497
Respiratory failure	6	1.235	4	0.798	1.916 (0.226–16.258)	0.551
CVA	1	0.353	1	0.200	1.836 (0.170–191.785)	0.616

Mean ratio is adjusted for age. *CVA*, cerebrovascular accident; *EPPY*, events per patient year; *HF*, heart failure; *RVAD*, right ventricular assist device

surgery. Residual mitral regurgitation after LVAD placement is not associated with higher risk of VA [38]. Finally, more patients in the VA group had a prior history of VA, which is a known predictor of worse outcomes in LVAD patients, likely due to its close association with development of VA after VAD implantation. We cannot conclude that prior history of VA is an independent risk factor for worse outcome in BIVAD patients, given all patients with prior history of VA in the VA group had occurrence of VA after BIVAD placement.

4.3 Role of ICD in patients with BIVADs

There was no statistical difference in the prevalence of implanted ICDs between the two groups in this study population (67% vs 86%, $p = 0.56$) and it was similar to the prevalence reported in studies of VAD patients. However, only one study to date has assessed the survival of these patients with BIVADs [39]. On the other hand, several studies have reported improved survival in patients with concurrent ICD and LVAD implants [22, 39]. In more recent studies involving patients with continuous LVADs, the survival benefit of an ICD is less certain [15, 23, 30]. Regardless, both 2017 ACC/AHA/HRS and 2013 International Society for Heart and Lung Transplant (ISHLT) guidelines recommend ICD placement in patients with LVADs who experience sustained VAs (Class IIA) [40, 41]. Further research is required to assess survival benefit of an ICD in patients with BIVADs. Based on this study, it is possible that patients with VAs may benefit from ICD implantation, but most of these patients are bridge to transplant.

4.4 Ablation of VA in patients with BIVADs

Catheter ablation of VAs may be effective in patients who experience refractory VT despite medical treatment. We had previously reported a case of refractory unstable VT in a patient with a BIVAD who was successfully treated with catheter ablation [42], as has been shown in another case report [43]. There are also five small observational studies of successful VT ablation in patients with LVADs [24–27, 44]. These studies suggest that ablation is feasible and decreases VA burden. The majority of VTs originated from previous intrinsic myocardial scar, while approximately 30% of VTs originate from the apical LVAD inflow cannula site [24, 25, 27, 44].

Since the presence of VAs after VAD implantation is associated with poor outcome, it raises the question of

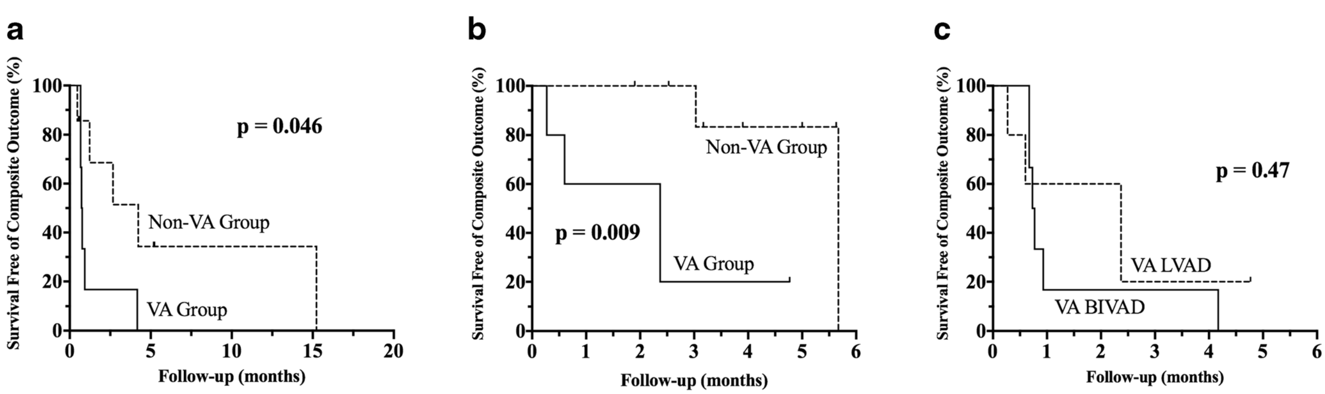

Fig. 2 Kaplan-Meier curve of composite outcome between groups, censored for transplant. **a** Comparison of VA and non-VA patients with BIVADs. **b** Comparison of VA and non-VA patients with LVADs. **c** Comparison of VA group in BIVAD and VA group in LVAD patients

Table 4 Propensity score–matched cohort baseline characteristics

Baseline characteristics	BIVAD ($n = 13$)	LVAD ($n = 13$)	p value
Age (year)	47 (28–54)	52 (41–59)	0.304
Male sex	11 (85)	10 (77)	1.000
Ethnicity			1.000
White	4 (31)	4 (31)	
Non-white	9 (69)	9 (69)	
Body mass index (kg/m^2)	26.5 (21.6–34.1)	26.9 (25.7–29.8)	0.990
Indication			1.000
Bridge to transplant	13 (100)	13 (100)	
VAD type	HeartWare*	HeartWare	–
INTERMACS profile			1.000
1	8 (62)	8 (62)	
2	5 (38)	4 (31)	
3	0 (0)	1 (7)	
HF etiology			1.000
Non-ischemic	11 (85)	11 (85)	
History of ventricular arrhythmia	8 (62)	9 (69)	1.000
Diabetes	5 (38)	4 (31)	1.000
Hypertension	6 (46)	6 (46)	1.000
Atrial fibrillation	8 (62)	8 (62)	1.000
Creatinine (mg/dl)	1.39 (1.34–1.72)	1.29 (1.04–2.06)	0.553
GFR (ml/min/m^2)	50 (45–53)	61 (31–75)	0.787
Platelet (10^3/mm^3)	150 (127–210)	199 (130–218)	0.830
International normalized ratio	1.5 (1.3–1.8)	1.3 (1.2–1.6)	0.110
Ejection fraction (%)	15 (14–21)	15 (11–20)	0.712

Values are presented as median (interquartile range) for continuous variables and number (percentage) for categorical variables

HF, heart failure; *INTERMACS*, Interagency Registry for Mechanically Assisted Circulatory Support; *VAD*, ventricular assist device

*One patient had a HeartMate II left ventricular assist device

whether VT ablation will have an effect on improved survival. In a retrospective study involving 34 LVAD patients who underwent VT ablation, 10 (29%) expired at a mean follow-up of 25 months [24]. In another work involving 7 LVAD patients who underwent VT ablation, 3 (43%) expired [27]. In a study involving 5 patients who received prophylactic epicardial ablation during LVAD placement, 3 had acute procedural success, but only 1 survived at the end of 1-year follow-up [45]. Despite the high mortality rates reported in the above studies, their sample sizes were small which limits generalizability, and survival was not the primary endpoint. The mortality benefit of VT ablation for patients with BIVADs is still unclear and is a subject of ongoing investigation.

4.5 Limitations

We acknowledge several limitations to our study. First, this was a small study which may limit the generalizability and may appear to be underpowered to detect difference in individual adverse outcomes and prevalence of VA between BIVAD and LVAD groups. However, propensity matching was performed to control for confounding covariates to improve the sensitivity of this analysis. Additionally, the sample sizes for both groups were sufficient to detect differences in adverse outcomes. Second, given that this was a retrospective study, programming of ICDs was based on clinical judgment of the attending physicians as opposed to a defined protocol (e.g., patients who have more aggressive ATP and shock protocols may have more ICD therapies as a result). However, practice variations are minimized given this is a single center study. Third, ICD interrogation data may not be complete, and three patients did not have ICDs implanted. We attempted to overcome this by reviewing all inpatient documentation, outside hospital records, ECGs, and telemetry tracings. Finally, ventricular origin of VA was not able to be performed for all patients due to lack of 12 lead ECG for most VA events. Despite these limitations, our study provides important findings in an area with very limited data.

5 Conclusion

Ventricular arrhythmias in patients with BIVADs are common but comparable with a similar LVAD population and are associated with worse outcomes despite RV support. Future work should assess whether therapies such as ablation improve the outcome of BIVAD patients with VA.

Funding information This work was partially supported by a research grant from the American Heart Association (19CDA34760021).

Compliance with ethical standards

The study protocol was approved by the institutional review board at University of California San Diego and adhered to the principles of the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study.

Conflict of interest Drs. Lin, Tran, Brambatti, Pretorius, Pollema, Hoffmayer, and Han have no disclosures. Dr. Adler is a consultant for Medtronic and Abbott. Dr. Feld is Director of the Cardiac Electrophysiology Fellowship Training Program whom receives fellowship stipend support from Medtronic, Abbott, Boston Scientific, Biosense Webster, and Biotronik. Dr. Krummen reports fellowship support from Medtronic, Boston Scientific, Abbott, and Biotronik. Dr. Ho has received research grants from the National Institutes of Health (1KL2TR001444) and the American Heart Association (19CDA34760021) for work related to this project, grant support from Abbott for work unrelated to this project, fellowship support from Medtronic, Boston Scientific, Abbott, and Biotronik, and has equity in Vektor Medical Inc. which is unrelated to this project.

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