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Ventricular Arrhythmias in Patients With Biventricular Assist Devices

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Running Title: Ventricular Arrhythmias Associated with Biventricular Assist Device

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ABSTRACT

Purpose:

Ventricular arrhythmias (VAs) are common in patients after left ventricular assist device (LVAD)n 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 to 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 had worse hemodynamics (mitral regurgitation and right-sided indices), 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.

Conclusion:

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.

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

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

Key words: Ventricular arrhythmia, ventricular tachycardia, biventricular assist device, heart failure

INTRODUCTION

Heart failure is estimated to affect 5.8 million people in the United States 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 – 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 to those without VAs. The purpose of our study is to assess the prevalence of clinically significant VAs after BIVAD placement in comparison to a propensity-matched LVAD population and assess adverse clinical outcomes in BIVAD patients with and without VA.

METHODS

Patient population and study design

This retrospective study consisted of 13 consecutive patients who received durable biventricular support between June 2014 to 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 seconds, requiring external defibrillation or appropriate ICD therapy (anti-tachycardic pacing (ATP) or shock), were recorded over time. VAs occurring in rapid succession were considered as 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.

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].

RESULTS

Patient population

A total of 13 patients received BIVADs as bridge-to-transplant. 10 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 to 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 nonischemic cardiomyopathy. Patients were followed for median of 263 [47 - 519] days.

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 (Figure 1). Median days to first VA event was 14 [2 – 28] days.

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 co-morbidities. 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 to 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) (Figure 2A).

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 Figure 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).

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 to BIVAD patients without VAs. Third, the presence of VA was associated with worse outcomes, irrespective of BIVAD or LVAD therapy.

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 to 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 to 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 arrythmia after BIVAD placement. The clinical significance and burden of atrial tachyarrythmias 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 play 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].

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

eight 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.

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 [31], a decrease in cardiac output during episodes of VA [32], , and a higher mortality in the presence of early postoperative VAs [3, 10, 21]. However, the clinical outcomes of patients with BIVADs who experience VAs is 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 [34-36].Similar to prior LVAD studies and our BIVAD cohort, LVAD patients with VA in our propensity-matched analysis also demonstrated worse composite outcomes compared to 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 raight 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 [37, 38] and LVAD placement [39]. 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 surgery, Residual mitral regurgitation after LVAD placement is not associated with higher risk of VA [30]. 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.

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 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 [41]. On the other hand, several studies have reported improved survival in patients with concurrent ICD and LVAD implants [22, 41]. In more recent studies involving patients with continuous LVADs, the survival benefit of an ICD is less certain [15, 23, 31]. 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) [42, 43]. 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.

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 [44], as has been shown in another case report [45]. There are also five small observational studies of successful VT ablation in patients with LVADs [24-27, 46]. 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 originating from the apical LVAD inflow cannula site [24, 25, 27, 46].

Since the presence of VAs after VAD implantation is associated with poor outcome, it raises the question of 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 [47]. 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.

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 this was a retrospective study, programming of ICDs was based on clinical judgement 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)C. 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.

CONCLUSION

Ventricular arrhythmias in patients with BIVADs are common but comparable to 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.

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.

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559 **Table 1.** Baseline characteristics of patients with BIVADs.

Baseline characteristics	VA Group (n = 6)	NonVA Group (n = 7)	P value
Age – yr.	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 – mo.	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 – %			
LVIDd – cm	15 [9 – 17]	15 [14 – 23]	0.657
LA diam – cm	7.7 [4.9 – 7.9]	6.9 [6.7 – 8.4]	0.945
LA vol – ml/m^2	5.0 [3.8 – 6.3]	5.3 [4.0 – 6.0]	1.000
RVSP – mmHg	43 [29 – 50]	56 [47 – 79]	0.138
TAPSE – cm	38 [31 – 44]	44 [19 – 56]	0.595
RV dilation ≥ moderate	1.3 [0.9 – 2.1]	1.6 [1.2 – 1.7]	0.876
Mitral regurgitation, ≥ moderate	0 (0)	3 (43)	0.192
Tricuspid regurgitation, ≥ moderate	2 (33)	7 (100)	**0.021**
Pre-operative support	2 (33)	6 (86)	0.103
IABP/Impella			
Intubated	3 (50)	1 (14)	0.266
Inotropes	1 (17)	2 (29)	1.000
	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
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 – 22727]	10198 [4432 – 14897]	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

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

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Table 3. Incidence of adverse events between the VA and NonVA group.

Adverse events	VA group (n = 6)		NonVA 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

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Table 4. Propensity score matched cohort baseline characteristics.

Baseline characteristics	BIVAD (n = 13)	LVAD (n = 13)	P value
Age – yr.	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 arrythmia	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

Figure 1. Monthly incidence of ventricular arrhythmia per patient-year.

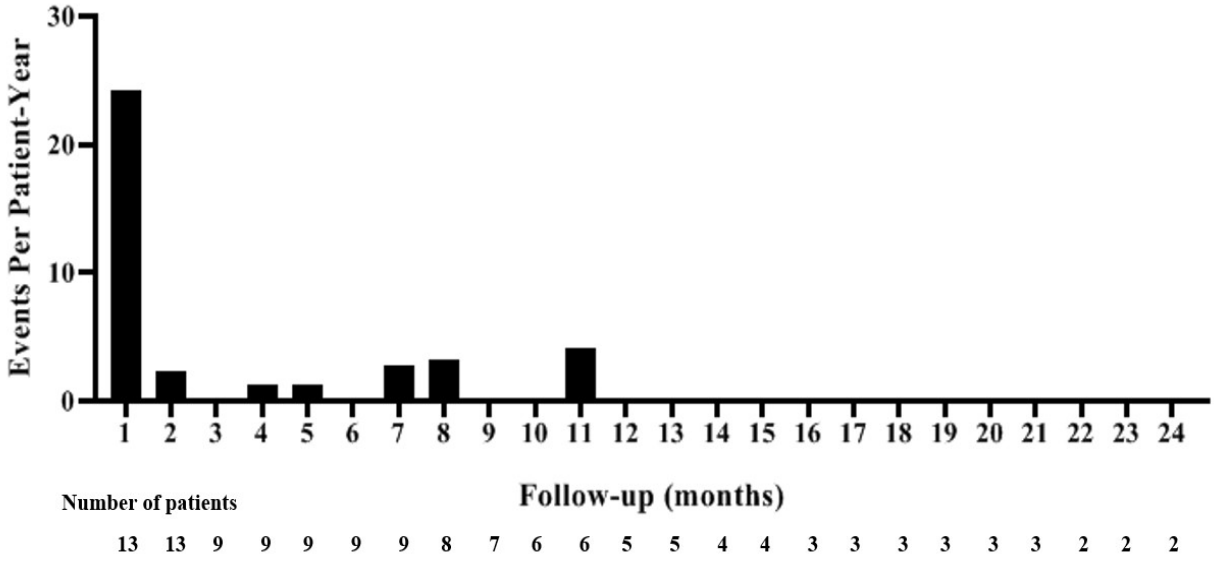

Figure 2. Kaplan Meier curve of composite outcome between groups, censored for transplant. A) Comparison of VA and non-VA patients with BIVADs. B) Comparison of VA and non-VA patients with LVADs. C) Comparison of VA group in BIVAD and VA group in LVAD patients.