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Review

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Atrial fibrillation in mechanical circulatory support patients

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Abstract

Atrial fibrillation (AF) is known to be one of the most common arrhythmias noted in cardiac procedures and is frequently associated with heart failure. As frequent interventions for patients with heart failure involve implantation of mechanical circulatory assist devices (e.g., left ventricular assist devices), it is timely to review the role this arrhythmia has on adverse clinical outcomes. A comprehensive literature search was conducted for PubMed. Relevant medical subject heading (MeSH) terms used in the initial literature search include "Heart-Assist Devices", "Extracorporeal Membrane Oxygenation", "Atrial Fibrillation", "Heart Failure", "Mortality", "Hospital Readmission", "stroke", "Postoperative Complications". In this review, the relevant literature was highlighted to identify the incidence, clinical impacts, and management of AF surrounding mechanical circulatory support implantation. The incidence of AF in this mechanical circulatory support device population was similar to that of patients with other cardiac procedures (10%-40%). Moreover, in most studies, preoperative AF was not significantly associated with adverse outcomes. In contrast, however, it appears that postoperative atrial fibrillation may predispose patients to increased risk for thromboembolic events and adverse long-term outcomes.

Keywords: Atrial fibrillation, mechanical circulatory support, left ventricular assist device, extracorporeal membrane oxygenation, impella

INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia, and its pathophysiology appears to be intertwined with that of heart failure (HF)[1], as one diagnosis may predispose to the other diagnosis[2]. AF affects about 50% of New York Heart Association (NYHA) class IV patients with HF; its prevalence in HF patients increases with increasing HF disease severity[3]. Increased distention and remodeling of the HF patients' atria disrupt the myocardial conduction pathways and may lead to subsequent AF[4].

Approximately 6.2 million adults in the United States (US) have been diagnosed with HF, according to the Centers for Disease Control. Advanced HF patients not responding to maximal medical therapy ultimately require heart transplantation. Due to a shortage of donor hearts (i.e., only 3597 heart transplants performed with 4086 newly listed US-based candidates during 2019[5]), over 5000 HF patients were placed on ventricular assist devices in 2000.

In general, HF patients' survival has been continuously improving. For the patients ineligible to receive a heart transplant, destination therapy using left ventricular assist devices (LVADs) has been used since the 1990s to improve end-stage HF patients' outcomes[6]. Further improvement in these LVAD patients' outcomes was achieved with increased patient management experience, improved patient selection and coordination of intensive post-discharge follow-up programs; additionally, there have been substantial technological LVAD advancements since the early 2000s[7-10].

To provide temporary assistance or to avoid cardiopulmonary deficit, intra-aortic balloon pumps, percutaneous ventricular assist devices/Impella (Abiomed, Danvers, Massachusetts), or veno-arterial extracorporeal membrane oxygenation (ECMO) have been used to treat patients with life-threatening medically refractory cardiogenic shock in an acute care setting. Patients treated with ECMO had improved 30-day survival by 33% compared to patients treated with intra-aortic balloon pumps[11]. However, during the past decade, from 2003 to 2014, ECMO patients' outcomes have remained grim, with survival to discharge estimated at 50%[12,13].

Within the LVAD population, AF has been reported with divergent results regarding its effect on patient outcomes. Based on the very limited literature to date, AF appears in 30%-50% of patients undergoing LVAD placement[14-16]. However, it is unclear whether AF is a pre-LVAD risk factor or a post-LVAD complication leading to the cascade for worse post-LVAD outcomes. To date, AF in LVAD patients has not been well characterized. For ECMO patients, similarly, AF as an impediment to myocardial recovery has not been evaluated. Given this "gap" in AF knowledge, this review raises crucial questions intended to target future investigations, as well as to identify novel opportunities to improve mechanical circulatory assist device patients' quality of care.

METHODS

Exposing key areas of uncertainty and identifying opportunities for future research, the available literature related to AF in patients with mechanical circulatory support has been summarized. Two reviewers (Yaligar A and Obeid JM) conducted a rigorous literature search of indexed articles in PubMed from inception through August 2021. The search strategy included relevant MeSH terms and keywords, including mechanical circulatory support devices, clinical risk factors, and adverse outcomes. A detailed search strategy is available in the online Supplementary Table 1. Further, Web of Science was used to perform a "backwards" citation search to capture additional relevant references. Following our detailed search strategy, we obtained 333 articles; of these, 298 were excluded due to a lack of AF incidence rates or multivariable model results.

RESULTS

Incidence of AF prior to LVAD

In the published literature, the incidence of AF prior to LVAD implantation ranged between 12.1% to 57.6%. Across these studies, the cumulative AF incidence rate was estimated at 36.2%. The reported incidence of other preoperative cardiac arrythmias ranged from 1.2% to 72.0%, with the cumulative incidence for preoperative cardiac arrythmias estimated at 16.5% [Table 1]. Not surprisingly, AF was the most frequent preoperative arrythmia reported for LVAD patients.

Post-LVAD predisposing factors and incidence of postoperative AF

Across the reviewed literature, a wide variety of risk factors were associated with postoperative AF (POAF) for patients following LVAD implantation. Several studies documented that chronic obstructive pulmonary disease (COPD) was a multivariable predictor of LVAD patients' POAF. Additional predictors included increasing age and renal insufficiency (OR 1.5, CI: 1.0-2.2)[17]. Notably, female gender was found to be significantly associated with POAF (OR 4.0, CI: 1.6-10.2)[16]. For recurrent AF post-LVAD implantation, the most important significant multivariable predictors included pre-LVAD AF (OR 18.5, CI: 6.6-51.8)[16] as well as increasing age (OR 1.04, CI: 1.01-1.07) and first-degree heart block based on pre-LVAD electrocardiogram readings (OR 2.4, CI: 1.1-5.4)[17].

The post-LVAD patients' new-onset and overall POAF rates were reported to vary greatly, ranging from 2.1% to 27.7% and 11.7% to 57.9%, respectively [Table 1]. Moreover, Deshmukh *et al*. indicated an increased proportion of patients with POAF greater than 30 days post-LVAD implant (7.8% *vs.* 20.6%)[17]. This range of incidence rates is similar to that of AF following other cardiac interventions, which range from 10%-40%.

Most common clinical outcomes following LVAD implantation in the literature reporting preoperative AF or POAF

From the included articles, the most common clinical outcomes following LVAD implantation in studies that reported preoperative/postoperative AF were compiled [Table 2]. The most frequently reported clinical outcomes included mortality, stroke (either ischemic or hemorrhagic), and bleeding events.

Literature risk factors associated with adverse outcomes following LVAD implantation

The most common clinical risk factors associated with adverse outcomes (mortality, stroke, bleeding events, and thromboembolic events) have been catalogued in Tables 3-6. Across the literature reviewed, AF was not found to be a univariate, multivariable, or Cox proportional hazards model predictor of bleeding or stroke-related events. However, AF was occasionally noted to be a predictor of mortality and thromboembolic events.

Effect of pre-OP AF on LVAD outcomes

AF induces turbulent flow and, consequently, hypercoagulability in the atria that can lead to thromboembolic (TE) events. When AF is coupled with mechanical circulatory support, the inherent risk of device thrombosis increases. If thrombosis occurs, this may subsequently lead to imminent life-threatening circulatory arrest. Thus, early studies raised concerns for worse adverse outcomes in AF patients undergoing LVAD implantation.

For AF patients, increased rates of TE events have been reported, including device thrombosis[15], increased recurrence of ventricular arrhythmias[27], as well as increased adverse events and mortality despite anticoagulation[14]. To date, these limited reports for a pre-op AF impact have been based upon retrospective cohort studies. For preoperative AF, however, prospective LVAD investigations may reveal a lower impact for pre-op AF patients.

Table 1. Summary of preoperative cardiac arrhythmia, preoperative AF, postoperative arrhythmia, and POAF rates

Author	Preoperative arrhythmia (%)	Postoperative arrhythmia (%)	Preoperative AF (%)	POAF (%)
Colombo *et al.* 2019[18]			162/361 (44.9)	
Cho *et al.* 2020[19]	Hx of VA: 282/642 (43.9)		334/642 (52.0)	
Chiang *et al.* 2020[20]			109/247 (44.1)	
Galand *et al.* 2019[21]		162/652 (24.8)		267/652 (41.0) does not specify AF definition
Blumer *et al.* 2020[22]			7667/18378 (41.7)	
Tahsili-Fahadan *et al.* 2018[23]			332/744 (44.6)	
Parikh *et al.* 2016[24]			805/1813 (44.4)	
Sherazi *et al.* 2018[25]			10/30 (30.0)	
Papathanisious *et al.* 2019[26]			62/139 (44.6)	
Hickey *et al.* 2020[27]		38/92 (41)	53/92 (57.6)	
Deshmukh *et al.* 2017[17]	178/331 (53.8)	104/331 (31.4) new-onset AA	152/331 (45.9)	37/179 (20.7) new-onset POAF
Brenyo *et al.* 2012[28]	Hx of VA: 26/61 (42.6)	Post-Op VA: 19/43 (44.2)	31/61 (50.8)	
Iwasaki *et al.* 2020[29]			45/147 (30.6)	
Deshmukh *et al.* 2018[30]				13/47 (27.7) new-onset POAF
Hickey *et al.* 2016[16]			67/249 (26.9)	90/249 (36.1) overall POAF 33/182 (18.1) new-onset POAF
Noll *et al.* 2019[31]			199/418 (47.6)	242/418 (57.9) overall POAF
Gonuguntla *et al.* 2020[32]			932/2359 (39.51)	
Imamura *et al.* 2019[33]			23/190 (12.1)	19/162 (11.7) overall POAF 3/140 (2.1) new-onset POAF
Joy *et al.* 2016[34]			2119/8879 (23.9)	
Morgan *et al.* 2016[35]			79/140 (32.9)	
Xuereb *et al.* 2016[36]			78/240 (32.5)	
Acharya *et al.* 2017[37]	86/7112 (1.2)			
Hui *et al.* 2019[38]			110/126 (41.4)	
Hawkins *et al.* 2018[39]			375/1064 (35.2)	121/689 (17.6) new-onset POAF
Teuteberg *et al.* 2015[40]	275/382 (72.0)			
Xia *et al.* 2016[41]			831/3909 (21.4)	
Martins *et al.* 2019[42]	Hx of VA: 223/652 (34.2) Hx of SVT: 302/652 (46.3)	61/652 (9.4)		
Kurihara *et al.* 2018[43]			229/526 (43.5)	
Enriquez *et al.* 2014[14]			50/146 (47.2)	5/51 (9.8) new-onset POAF
Nassif *et al.* 2016[44]			105/249 (42)	
Izzy *et al.* 2018[45]			124/183 (68)	
Brisco *et al.* 2014[46]	373/755 (49.4)	231/755 (30.6)		
Morris *et al.* 2015[47]			44/110 (40.0)	
Dang *et al.* 2005[48]	61/119 (51.3)			
Stulak *et al.* 2013[15]			120/389 (30.8)	

VA: Ventricular arrhythmias; SVT: supraventricular tachycardia; POAF: postoperative atrial fibrillation.

Table 2. Most common clinical endpoints in articles reporting preoperative AF or POAF

Author	Mortality	TE events	Bleeding events	Stroke (ischemic, hemorrhagic, both)	Arrythmia	Prolonged mechanical ventilation
Colombo *et al.* 2019[18]	X			X		
Cho *et al.* 2020[19]		X	X	X	X	
Chiang *et al.* 2020[20]	X			X		
Galand *et al.* 2019[21]	X				X	
Tahsili-Fahadan *et al.* 2018[23]	X			X		
Parikh *et al.* 2016[24]	X	X		X		
Sherazi *et al.* 2018[25]			X			
Papathanisious *et al.* 2019[26]	X		X			X
Hickey *et al.* 2020[27]	X				X	
Deshmukh *et al.* 2017[17]	X				X	
Brenyo *et al.* 2012) [28]	X				X	
Iwasaki *et al.* 2020[29]	X		X	X		
Deshmukh *et al.* 2018[30]	X	X		X	X	
Hickey *et al.* 2016[16]	X				X	
Noll *et al.* 2019[31]	X	X	X	X		
Gonuguntla *et al.* 2020[32]	X		X			
Imamura *et al.* 2019[33]	X	X	X	X		
Joy *et al.* 2016[34]	X		X			
Morgan *et al.* 2016[35]	X		X	X		
Xuereb *et al.* 2016[36]	X	X	X	X	X	
Hui *et al.* 2018[38]	X					
Hawkins *et al.* 2018[39]	X			X		X
Xia *et al.* 2016[41]	X	X		X		
Kurihara *et al.* 2018[43]	X			X		
Enriquez *et al.* 2014[14]	X	X	X	X		
Nassif *et al.* 2016[44]		X	X	X		
Izzy *et al.* 2018[45]	X			X		
Stulak *et al.* 2013[15]	X	X		X		
Morris *et al.* 2015[47]	X			X		
Blumer *et al.* 2020[22]	X	X	X	X		
Total count	**27**	**11**	**13**	**20**	**8**	**2**

Given the paucity of individual investigations examining pre-op AF, the first systematic reviews were published recently in 2018. The first LVAD meta-analysis included 11 studies with 6351 patients with continuous-flow LVAD devices and did not find differences in TE events, device thrombosis or stroke in patient with and without AF[49]. This finding was reiterated by two different meta-analyses of seven retrospective studies. There was no difference in TE events, stroke, or device thrombosis between the preoperative AF and no AF groups[50,51]. Although no TE rate differences were found for AF versus no AF patients, one study reported a significant increase in mortality in the pre-op AF LVAD population with a relative risk (RR) of 1.16 with a 95% confidence interval (CI) ranging from 1.05 to 1.28[50]. However, Tantrachoti *et al.* raised the question as to whether these pre-op AF differences may have been due to a sicker pre-op AF population, as the pre-op AF population was older and had increased rates of other comorbidities, including diabetes and advanced kidney disease[50].

Table 3. Comparison of literature models- risk factors affecting mortality

	Galand *et al.* 2019[21]	Deshmukh *et al.* 2017[17]	Brenyo *et al.* 2012[28]	Hickey *et al.* 2016[16]	Noll *et al.* 2019[31]	Morgan *et al.* 2016[35]	Hawkins *et al.* 2018[39]	Xia *et al.* 2016[41]	Kurihara *et al.* 2018[43]	Izzy *et al.* 2018[45]	Morris *et al.* 2015[47]
Age							X	X	X		
Gender				X				X			
Hx of AF		X	X*	*	**	*		**	**	*	*
POAF	X			*			**				
Intermacs registry								X			
Heart failure duration	X										
Implantable cardiac defibrillator	X		X								
Any surgery combined with LVAD	X										
Early ventricular arrhythmias	X										
Amiodarone	X										
Albumin		X									
Atrial tachycardia		X									
CABG		X									
Hx of ventricular arrhythmias		X	X*								
Peripheral vascular disease			X								
LVAD complication			X								
Prior valve/cardiac surgery					X				X		
Liver biopsy						X					
Mechanical circulatory support at time of VAD						X					
Aspartate transaminase						X					
Alanine aminotransferase						X					
Hematocrit							X				
Ischemic cardiopathy								X			
Chronic kidney diseases								X			
Severe tricuspid regurgitation									X		
Preoperative inotropes									X		
Body mass index									X		
Body surface area									X		
Ischemic stroke										X	
Hemorrhagic stroke										X	
Diabetes mellitus										X	
Platelets											X

X*Significant association has been ventricular arrhythmias and mortality; *AF evaluated, not significant univariate predictor; **AF evaluated in MV or Cox proportional hazards model, not a significant predictor; AF: atrial fibrillation; POAF: postoperative atrial fibrillation; LVAD: left ventricular assist device; CABG: coronary artery bypass graft.

Table 4. Comparison of literature models-risk factors affecting thromboembolic events

	Chiang *et al.* 2020[20]	Deshmukh *et al.* 2018[30]	Teuteberg *et al.* 2015[40]	Xia *et al.* 2016[41]	Nassif *et al.* 2016[44]	Stulak *et al.* 2013[15]	Imamura *et al.* 2019[33]
Age							X
Gender				X			
Hx of AF	*		X	**	**	X	**
POAF		X					
INTERMACS				X			
Device type	X						
Hx of cerebrovascular disease or transient Ischemic attacks							
Hx of deep vein thrombosis or pulmonary embolus							
LVAD indication	X						
Aspirin			X				X
Hx of peripheral vascular disease				X			
Body mass index				X			
Ischemic cardiomyopathy				X			
Pulmonary disease				X			
International normalized ratio					X		

*AF evaluated, not significant univariate predictor; **AF evaluated in multivariable model, but not a significant predictor; AF: atrial fibrillation; POAF: postoperative atrial fibrillation; LVAD: left ventricular assist device.

Similarly, Usman *et al.* found an increased risk of gastrointestinal bleeding for their pre-op AF LVAD patients (RR 1.27; 95%CI: 1.05-1.55) without any other increased bleeding-related risks[51]. Again, this study raised the possibility that other differences may be confounding this association, in addition to patient age as a possible contributor to increased bleeding risk. Also, this study's patients with preoperative AF were more aggressively anticoagulated. In combination with risk-adjustment techniques, future database research may need to employ more complex analytical approaches (e.g., propensity scores to adjust for the differential likelihood of treatments received) to mitigate the fact that patients with AF are generally sicker at baseline than non-AF patients.

Outcomes associated with POAF

Postoperative AF is a known risk factor for adverse clinical outcomes, including readmission, operative mortality, and long-term survival in cardiac surgery patients. Specifically, for LVAD patients with postoperative AF, various short-term and long-term outcome measures may be dramatically impacted by the patients' severity of cardiac disease and the complexity of their comorbidities, as well as their status upon presentation.

For short-term LVAD outcomes, postoperative AF was found to not have significant adverse impacts on 30-day mortality, increased length of stay, and 30-day TE events[30]. However, risk-adjusted models show major morbidity (OR 2.5), unplanned RVAD (OR 2.9), cardiac arrest (OR 3.4), prolonged ventilation (OR 2.7), reoperation (OR 1.8), discharge to facility (OR 2.2), and an increased postoperative and ICU length of stay

Table 5. Comparison of literature models-risk factors affecting bleeding events

	Cho *et al.* 2020[19]	Tahsili-Fahadan *et al.* 2018[23]	Gonuguntula *et al.* 2020[32]	Joy *et al.* 2016[34]	Nassif *et al.* 2016[44]	Teuteberg *et al.* 2015[40]
Age				X	X	
Gender						
Hx of AF	**	**	*	**	**	*
POAF						
Intermacs						
Hx of cerebrovascular disease or transient ischemic attacks	X					
International normalized ratio	X				X	X
Aspirin	X					X
Mean arterial pressure						X
Diabetes mellitus		X				
Body mass index			X			
Acute kidney injury			X			
Peripheral vascular disease			X			
Hemiplegia/paraplegia			X			
Moderate/severe liver disease			X			
Peptic ulcer disease			X	X		
Aortic valve procedure			X			
Venous thromboembolism			X			
Mechanical ventilation				X		
Coronary artery disease				X		
LVAD implant year				X		

*AF evaluated, not significant univariate predictor; **AF evaluated in MV or Cox proportional hazards model, not a significant predictor; AF: atrial fibrillation; POAF: postoperative atrial fibrillation; LVAD: left ventricular assist device.

all significantly associated with POAF in LVAD implant patients[39]. Also, for long-term outcomes, TE events (device thrombosis and ischemic stroke) were significantly increased with POAF (OR 5.5, CI: 1.4-21.7)[30]. Across publications, however, there was not a consistent association between POAF and long-term mortality.

Paroxysmal AF

A study by Enriquez *et al.* categorized persistent AF and paroxysmal AF separately in 106 LVAD patients, 55 of which had AF; this included 36 patients with paroxysmal AF *vs.* 19 with persistent AF[14]. Of note, the AF population for this study included both preoperative AF patients and those who developed AF post-LVAD following the perioperative period (> 30 days), (50 with AF pre-op and 5 post LVAD implantation). Comparing AF patients *vs.* non-AF patients, the heart failure hospitalization rates increased post LVAD implantation ($P < 0.01$); however, these AF patients were also older. Moreover, there was a significant trend for an increased rate of death ($P = 0.06$) in patients with persistent AF; but there was no difference in heart failure hospitalization rates for paroxysmal AF patients.

In a large 330 LVAD patient cohort study, patients were followed for 330 days to evaluate their clinical outcomes. Within the first 30 days post-LVAD, POAF was found in 14% of patients, including 7.8% of patients without pre-LVAD AF. New-onset AF was associated with increasing age, renal insufficiency, and lung disease. Of the patients with pre-LVAD paroxysmal AF, 43% had no post-LVAD AF[28].

Table 6. Comparison of literature models-risk factors affecting stroke (ischemic, hemorrhagic, or either)

	Colombo *et al.* 2020[18]	Cho *et al.* 2020[19]	Tahsili-Fahadan *et al.* 2018[23]	Parikh *et al.* 2020[24]	Morris *et al.* 2015[47]	Izzy *et al.* 2018[45]	Iwasaki *et al.* 2020[29]
Age							
Gender			X	X	X		
Hx of AF	*	**	**	**	*	*	*
POAF							
Intermacs							
Device type	X						
Peripheral vascular disease		X					
International normalized ratio		X					
Left ventricular thrombus		X					
Coronary artery disease			X				
Hx of cerebrovascular disease or transient ischemic attach						X	
Right ventricular failure						X	
Albumin					X	X	
Pulmonary disease						X	
Low cardiac index							X
Body mass index							X
Time in the therapeutic range					X		

*AF evaluated, not significant univariate predictor; **AF evaluated in MV or Cox proportional hazards model, not a significant predictor; AF: atrial fibrillation; POAF: postoperative atrial fibrillation.

Associations with ventricular arrhythmias

One prospective observational study examined ventricular tachycardia events in pre- and post-LVAD patients (n = 98), of which 75% had AF pre-LVAD implantation. Preoperative AF was found to be a predisposing factor to the development of post-op ventricular arrhythmia events, along with a history of pre-op ventricular arrhythmia and larger left ventricular end-diastolic diameters. This study did not find effects on mortality in patients with a history of AF or in patients with post-op ventricular arrhythmias[52]. Another retrospective study did find an association between AF and ventricular arrhythmias in which recurrent ventricular arrhythmias were associated with increased mortality[16].

Other mechanical life support (ECMO and Impella^{R})

Postoperative AF has been briefly studied in patients with cardiogenic shock in the acute setting requiring mechanical circulatory support. Two observational cohort studies investigating predisposing factors for survival and adverse outcomes in patients on ECMO studied AF in this population without finding any significant effect on either survival or mortality[53,54]. The effect of AF on outcomes in patients with acute myocardial infarction requiring Impella^{R} support was examined in a large database study[55]. It found that AF was associated with increased respiratory complications and increased healthcare expenses in the form of longer length of stay, more frequent transfer to facilities upon discharge and higher hospital charges. However, all-cause in-hospital mortality was similar in the AF and no AF groups. This study did not differentiate between pre-procedure and post-procedure AF due to the nature of data collection using ICD-9 codes extracted from an administrative database. Another study investigated the effect of arrhythmias on 109 consecutive survivors of sudden cardiac death requiring Impella^{R} support[56]. It did not find associations with either ventricular or supraventricular arrhythmias, including pre-procedure and post-procedure AF on mortality, suggesting that the Impella^{R} device may compensate for the hemodynamic imbalances caused by arrhythmias in the acute setting. The same may be applicable in the ECMO population. Furthermore, the acuity of these patients and high early mortality rates obfuscate any long-term adverse effects AF may have.

Hemocompatibility related adverse events and management of anticoagulation in LVAD patients

Hemocompatibility or the interaction of mechanical surface and blood products lead to the activation/destruction of circulating blood elements[57], including bleeding and TE events. Imamura *et al.* studied hemocompatibility related adverse events in 190 LVAD patients with a goal INR 2 to 2.5 regardless of AF status, and found comparable hemocompatibility adverse events in an AF *vs.* no AF Japanese LVAD population within 1 year (17% *vs.* 24%; $P = 0.5$) using propensity score matching; their propensity score-adjusted for age, aspirin use, INR and angiotensin-converting enzyme inhibitors[33]. Worse outcomes were documented for patients of advanced age and patients not placed on aspirin therapy.

In LVAD patients with pre-op AF, the predisposition to TE events is conflicting in the literature. Certain studies have indicated no differences in postoperative TE between patients with pre-op AF and no pre-op AF[43,58,59]. Enriquez *et al.* found similar rates of TE events in LVAD patients with and without AF (17% incidence), although AF patients had higher INR levels (INR 2.3 *vs.* 1.5 in the four weeks leading to the TE events)[14]. Another study noted pre-op AF to be significantly associated with increased TE event rates (38% *vs.* 21% TE events at 1 year, $P < 0.001$)[15]. Interestingly, Noll *et al.* found TE to be decreased in patients with preoperative AF, which appears likely to be attributed to differences in anticoagulation treatment regimens[31]. All current pooled analyses of population-based studies have indicated that preoperative AF does not increase the risk of TE events post-LVAD implantation[49-51]. On the other hand, as previously discussed, TE events are more common in postoperative AF patients.

The current anticoagulation management recommendations for HeartMate II LVAD patients include anticoagulation with warfarin to a target INR between 2.0-3.2 with a goal of 2.6, as well as treatment with aspirin[44,60]. Some authors have used higher INR goals for AF patients[14,51]. Further optimization of the surface coating of LVAD devices may reduce TE events[61]. In fact, a lower INR goal of 1.5-1.9 is recommended in HeartMate III devices[62].

Resolution of AF post LVAD implantation

Heart failure may improve after LVAD implantation due to cardiac remodeling. In fact, 1.4% to 5% of LVAD patients have sufficient cardiac recovery for successful device explantation[14,63-66]. Purportedly, left ventricular diameter decreases and wall thickness increases due to decreased stretching of the left ventricle from LVAD unloading[67]. Biopsies from pre-LVAD and post-LVAD explants showed a decrease in collagen deposition and decreased myocardial TNF-alfa content[68]. Electrical remodeling was also found after LVAD implantation with decreased QRS[69]. Ventricular unloading and decreased pre-load after LVAD implantation result in decreased atrial stretching. Left atrial size and volume index were found to be significantly decreased post-LVAD implantation as seen on echocardiogram[17]. Patients with AF present pre-LVAD may recover from AF after implantation due to cardiac remodeling. Rates of AF recovery post-LVAD implantation range from 18%[13] to 26%[16,33] and 43% from paroxysmal AF[17].

CONCLUSION

Although AF may be associated with worse outcomes in the majority of cardiac surgery patients, AF is a marker for a more severely ill mechanical circulatory support patient population which may predispose to increased TE events and bleeding-related events. For mechanical circulatory support patients, at least so far, there has been no clear association documented between either preoperative or postoperative AF with post-procedural mortality. This lack of an AF-related impact may be due to the more complex treatment course and inherently shorter longevity of this unique cardiac surgical patient population. Given that AF and HF are so intimately associated, moreover, it is difficult to assess the effect of either preoperative or postoperative AF separately upon patient outcomes.

Until now, only retrospective observational reports have been occasionally included in meta-analysis (Class III evidence). As a critical "gap" in knowledge identified by this review, this field lacks the advantage of any prospective database analyses - where data have been captured for mechanical support patients to address this question directly. Additionally, it was surprising to learn that there are no randomized trials on this specific topic, as other atrial fibrillation rate and rhythm control strategies have not been targeted for evaluation in this higher-risk patient subpopulation, treating AF by trans-catheter ablation or left atrial appendage clipping at the time of LVAD implantation are known strategies that lack data in this population. Beyond the LVAD studies identified, moreover, there have been no studies published evaluating preoperative AF in mechanical circulatory support patients, or the impact of mechanical circulatory post-procedural AF rates on these patients' outcomes. Of the patients experiencing post-procedural AF, it is unknown as to what interventions may be life-prolonging. Additional research now appears warranted to provide evidence-based, data-driven mechanical circulatory support procedural guidelines for preoperative AF and postoperative AF treatments for this unique patient population.

To summarize, preoperative AF, as opposed to POAF, seems to have a little discernable effect on outcomes in HF patients requiring mechanical circulatory support. Despite the major registries for LVAD and ECMO [i.e., the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) and Extracorporeal Life Support Organization (ELSO) registries] reporting cardiac arrythmia in their postoperative data collection form, preoperative AF and POAF have not been specifically evaluated. Given these database monitoring programs have been initiated to improve mechanical circulatory support patients' quality of care, high integrity preoperative AF and postoperative AF data should be gathered and analyzed in the future.

DECLARATIONS

Authors' contributions

Concept, drafting, analysis, critical revision, final approval: Obeid JM, Yaligar A, McLarty AJ, Bilfinger TV, Tannous HJ, Shroyer ALW
Data collection: Obeid JM, Yaligar A

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All authors declared that there are no conflicts of interest.

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Consent for publication

Not applicable.

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