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## Atrial arrhythmias in patients with left ventricular assist devices

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### Abstract

**Purpose of review**—Atrial arrhythmias commonly occur in patients with advanced heart failure with reduced ejection fraction (HFrEF) who require left ventricular assist devices (LVADs) implantation. This review summarizes the current literature regarding the incidence, prevalence, and predictors of atrial arrhythmias in LVAD patients and its impact on the clinical outcomes. Moreover, we review the mechanisms and management strategies of atrial arrhythmias in this population.

**Recent findings**—Atrial arrhythmias including atrial fibrillation, atrial flutter, and atrial tachycardia are highly prevalent in patients with advanced HFrEF before or after the LVAD implantation. Atrial arrhythmias have a significant impact on overall clinical outcome including survival, heart failure hospitalization, quality of life, thromboembolic events and resource utilization. Atrial fibrillation and other atrial arrhythmias frequently coexist in this population. In patients with atrial arrhythmias and LVAD, anticoagulation and cardiovascular implantable electronic devices should be closely monitored and managed to prevent thromboembolic events or inappropriate shocks. Rhythm and rate control strategies are comparable regarding overall clinical outcomes in this population. LVADs induce favorable atrial remodeling in patients with HFrEF.

**Summary**—Atrial arrhythmias are highly common in LVAD patients and have significant impact on overall clinical outcomes. Further studies are needed to determine optimal management and prevention of atrial arrhythmias in LVAD population.

#### Keywords

atrial arrhythmias; atrial fibrillation; heart failure; left ventricular assist devices

## INTRODUCTION

Left ventricular assist devices (LVADs) are commonly used for patients with advanced heart failure with reduced ejection fraction (HFrEF), as both a bridge to transplantation or as

Conflicts of interest

There are no conflicts of interest.

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destination therapy  $[1,2^{\bullet\bullet}]$ . It is expected that number of patients who require LVAD will increase over time because of the increasing prevalence of HFrEF and the limited availability of transplant hearts. Understanding the relationship between LVADs and atrial arrhythmias is required to develop evidence-based strategies for the management of these patients. It is important to define the clinical characteristic, predictors, and treatment outcome in this population. Recent studies have shown that atrial arrhythmias, particularly atrial fibrillation, are highly prevalent in patients with advanced HFrEF before or after the LVAD implantation  $[1,2^{\bullet\bullet},3-6,7^{\bullet},8,9]$ . Atrial arrhythmias have significant clinical and therapeutic implications in this population. We review the literature on atrial arrhythmias in the LVAD population with a focus on epidemiology, predictors, outcomes, and management strategies including the rhythm versus rate control.

## EPIDEMIOLOGY AND PREDICTORS OF ATRIAL ARRHYTHMIAS IN THE LEFT VENTRICULAR ASSIST DEVICE POPULATION

Atrial fibrillation and HFrEF commonly coexist and this combination is associated with an increased risk of all-cause mortality and morbidity relative to either condition in isolation [1,2<sup>40</sup>,3,4], Although specific data about other atrial arrhythmias are limited, the coexistence of atrial fibrillation and HFrEF causes a higher risk of stroke, hospitalization, dementia, kidney failure, myocardial infarction, and death than in those with heart failure or atrial fibrillation alone [1,2<sup>40</sup>,3,4], In addition to atrial fibrillation, the incidence and prevalence of other atrial arrhythmias including atrial flutter (AFL) and atrial tachycardia are high in patients with HFrEF with or without LVAD implantation [2<sup>40</sup>,5,6], Atrial arrhythmias in HFrEF without LVAD are summarized elsewhere in this issue of the Journal. Here, we focus on atrial arrhythmias in patients with advanced HFrEF who require LVAD.

#### Preleft ventricular assist devices prevalence of atrial arrhythmias

Several investigators have demonstrated that atrial fibrillation is the most common sustained arrhythmia in pre-LVAD or post-LVAD patients with advanced HFrEF [5,6,7<sup>••</sup>,8–10]. A history of atrial fibrillation is present in 21–54% of patients with advanced HFrEF who are receiving LVADs [2<sup>•••</sup>,5,6,7<sup>••</sup>,8]. Atrial fibrillation is found to be predominantly paroxysmal. Atrial tachycardia and AFL are reported in 15–22% of this population. AFL is the second most common atrial arrhythmia that experienced by 14% in pre-LVAD patients. The prevalence of atrial tachycardia is about 7% and atrioventricular nodal reentrant tachycardia 1%. AFL and atrial tachycardia are often concomitantly existing with atrial fibrillation in these patients.

#### Postleft ventricular assist devices incidence of atrial arrhythmias

Patients with HFrEF who undergo LVAD implantation have an increased incidence of atrial arrhythmias, particularly atrial fibrillation [2<sup>46</sup>,5,6,7<sup>46</sup>,8]. The incidence of new onset atrial arrhythmias after LVAD is high in both the early postoperative period and afterward. Atrial fibrillation is documented in about 8% of patients after the first 30 days of LVAD [6,9,10]. Approximately 10–20% of patients develop new onset atrial fibrillation in the year following LVAD implant [5,6,7<sup>46</sup>,8]. In other cardiac surgery populations, postoperative atrial fibrillation occurs in 15–20% of patients. Overall, incidence of de-novo post-LVAD atrial

fibrillation is about 20–30% during long-term follow-up. Finally, in a significant minority of patients with atrial fibrillation prior to LVAD implantation (15–25%), no atrial fibrillation detected in follow-up including on implantable device monitoring which may be due to favorable left atrial remodeling [5]. Atrial tachycardia is second most common new onset atrial arrhythmia after LVAD [6]. New onset AFL and atrioventricular nodal reentrant tachycardia are also documented [6]. In patients with paroxysmal atrial fibrillation, either de-novo or recurrent, about 9% progress to persistent atrial fibrillation after LVAD implantation in long-term follow-up [6].

#### Predictors or atrial arrhythmias in left ventricular assist devices patients

The risk of new onset atrial fibrillation in HFrEF without LVAD is higher with increasing age, decreased LV diastolic elastance, diabetes, hypertension, increased diuretic use, and renal impairment [2<sup>10</sup>,6]. Similarly, older age, renal insufficiency, and lung disease are predictors of new onset atrial fibrillation after LVAD. In addition to those, ischemic cardiomyopathy, prior coronary artery bypass grafting, thyroid disease, and prolonged partial response interval (>200 ms) are associated with atrial fibrillation recurrence in post-LVAD patients [6]. Male sex is more common in atrial fibrillation and AFL patients. But, there is no significant sex-based difference in overall clinical outcome.

#### Pathophysiology of atrial arrhythmias in left ventricular assist devices patients

The pathophysiology of atrial arrhythmias in HFrEF is complex and involves multiple interacting factors [1,2<sup>44</sup>,3–6,7<sup>4</sup>,8–17]. LVAD alters the relation between atrial arrhythmias and HFrEF by reducing left sided pressures with resulting left atrial remodeling [5,6,7<sup>III</sup>,8– 16]. Atrial arrhythmias in HFrEF with or without LVAD is associated with complex atrial electroanatomical remodeling that is triggered by stretch, neurohormonal activation, and oxidative stress [5.6,7<sup>44</sup>,8–16]. Overall, LVADs induce favorable atrial structural and electrical remodeling by improving left atrial size and volume index. Unloading of the LV with LVAD generally reduces atrial pressures, valvular regurgitation, and atrial dimensions. This can reduce atrial fibrillation in long-term in some LVAD patients. Despite other improvements in left atrial parameters, preliminary evidence suggests that the left atrial appendage continues to have contractile dysfunction and may be a site of thrombosis despite mechanical unloading and anticoagulation with LVAD implantation [17-24]. Significant valvular disease can also persist in some patients and is associated with higher atrial pressures, atrial dilation, and early hospitalization and death [11,12]. However, no studies have directly correlated chronic valvular dysfunction or suboptimal hemodynamic assessments with incident atrial fibrillation or atrial arrhythmias in LVAD patients [6,7<sup>III</sup>]. In the acute postoperative setting, atrial arrhythmias have been associated right ventricle (RV) failure suggesting that postoperative atrial arrhythmias may be due to elevated right atrial pressures [10]. Conversely, atrial fibrillation and atrial arrhythmias with rapid ventricular rates can cause RV failure [13–15]. At the molecular and cellular level, atrial fibrillation in HFrEF is associated with atrial energy deficit, oxidative, and metabolic stress [16]. This occurs with mitochondrial dysfunction [16]. Atrial tissue fibrosis, inflammation/infiltration, and cardiomyocyte loss have been shown as part of atrial remodeling with HFrEF, atrial arrhythmias, and LVAD. However, further mechanistic studies are warranted for understanding the molecular mechanism of the disease to develop preventive strategies.

#### Impact of atrial arrhythmias on clinical outcomes in left ventricular assist devices patients

Atrial arrhythmias have significant effect on overall clinical outcomes in LVAD recipients  $[2^{\bullet\bullet}, 5, 15-27]$ . A preoperative history of persistent or permanent atrial fibrillation and atrial tachycardia has been associated with earlier heart failure hospitalization and mortality after LVAD placement [5,6,15,20,21]. This finding has not been uniformly replicated in all studies and paroxysmal atrial fibrillation without further classification have not been associated with increased mortality [7<sup>•</sup>,8,22-24]. Though these series control for confounding patient factors, it is unclear whether persistent atrial fibrillation identifies patients with more comorbidities or whether persistent atrial arrhythmias independently impact outcomes. The latter possibility is suggested by evidence that atrial fibrillation is associated with right ventricular failure and ventricular arrhythmias after LVAD [10,15,25-27]. LVAD patients with atrial fibrillation also have a higher risk of ventricular arrhythmia. Finally, the development of atrial fibrillation episodes after LVAD has also been associated with increased mortality [2<sup>•••</sup>,5,6].

In addition to mortality and hospitalization for heart failure, atrial fibrillation has been associated with other morbidity in LVAD patients including lower quality of life scores, 6-min walk distance, and peak VO<sub>2</sub> consumption [5,14]. As with other cardiac surgery populations, postoperative atrial fibrillation is associated with morbidity and resource utilization including prolonged mechanical ventilation, unanticipated right ventricular assist device use, discharge to facility, and prolonged ICU and hospital stay [10].

Although initial studies suggested that a history of atrial fibrillation was associated with increased risk of thromboembolism after LVAD, the majority of subsequent studies have demonstrated no increased risk of thromboembolic or bleeding events  $[2^{\blacksquare,5,6,7^{\blacksquare},8,9,17-20]$ . Though this data is heterogeneous with variable definitions of atrial fibrillation, differing anticoagulation and antiplatelet practices, and inclusion of different LVAD pump types, in totality it implies that the inherent thrombogenicity of LVAD therapy makes the contribution of atrial fibrillation to thromboembolic risk marginal. However, with new LVAD pump designs that carry a lower risk of hemocompatibility related events, atrial fibrillation does not appear to be associated with increased thromboembolic or bleeding outcomes [28].

#### Management of atrial arrhythmias in left ventricular assist devices patients

The management of atrial arrhythmias in LVAD patient is complex and similar to non-LVAD patient. There is insufficient data to change the current practice for particular therapeutic strategies in management of atrial arrhythmias in this population. In general, atrial arrhythmias in patients with LVAD are well tolerated. Yet, atrial arrhythmias may have significant hemodynamic impact in some LVAD patients. The management of these patients should be individualized regarding rhythm versus rate control or antiarrhythmic drug versus catheter ablation strategies for atrial arrhythmias [1,2<sup>•••</sup>,3]. Also, anticoagulation and cardiovascular implantable electronic devices (CIED) should be closely monitored and adjusted.

#### Rhythm versus rate control

In retrospective series, there is no clear benefit or harm of pharmacologic rhythm control agents in LVAD patients with atrial fibrillation [2<sup>44</sup>,7<sup>4</sup>]. Rhythm control can be achieved by using class III antiarrhythmic drugs, amiodarone or dofetilide or sotalol, in this population [1,3]. Even though there is no reported negative impact of those agents on survival in patients with LVAD, antiarrhythmic agents should be administered with caution due to drug metabolism and potential side effects. Though rhythm control with catheter ablation has demonstrated morbidity and mortality benefit in patients with atrial fibrillation and heart failure without LVAD, similar data does not exist for patients with LVAD [29-31]. There is a paucity of data regarding catheter ablation of atrial fibrillation and other atrial arrhythmias in LVAD patients. In the largest series, eight patients with AFL, rapid ventricular response, and evidence of right ventricular failure underwent AFL ablation with improvement of right ventricle failure and resolution of inappropriate implantable cardioverter defibrillator shocks [13]. Outside of this report, two case reports describe ablation of AFL and pulmonary vein isolation for management of atrial arrhythmias causing rapid ventricular rates and decompensated heart failure [32,33]. Therefore, while ablation of AFL may be reasonable when rapid ventricular rates cause clear symptomatic or hemodynamic decompensation, there is no evidence that broader attempts at rhythm control therapy are beneficial. If atrial arrhythmias with rapid ventricular response compromise LVAD flows and performance, cardioversion should be considered to restore and maintain sinus rhythm in these patients. Rhythm control measures (antiarrhythmic drugs and electrical cardioversion) are not found to be associated with reduced mortality, thromboembolism, or bleeding in patients with atrial fibrillation.

#### Medical management of rate control

An effective for rate control strategy can be achieved by using  $\beta$ -blockers, with or without combination with digoxin. Target ventricular rate needs to be individualized based on patient's symptoms, hemodynamic status, and comorbidities. Also, digoxin is show to reduce the rate of heart failure-related hospitalizations in patients with HFrEF after LVAD implantation [34]. If  $\beta$ -blocker and digoxin combination is not sufficient to control ventricular rate, antiarrhythmic, particularly amiodarone can be considered as rate control agent in these patients. If atrial arrhythmias are drug-resistant or the patient is drug-intolerant, it is reasonable to consider catheter ablation including atrioventricular nodal ablation [35].

#### Cardiovascular implantable electronic devices and anticoagulation

Majority of LVAD patients have CIED for the primary or secondary prevention of sudden cardiac death due to HFrEF or ventricular arrhythmias [1,2<sup>11</sup>]. In the MOMENTUM clinical trial, 68% of HeartMate 3 recipients had CIED at the time of LVAD implantation [36]. Dynamic management of CIED after LVAD implantation is critical in patients with atrial arrhythmias to prevent inappropriate detection and therapies. Inappropriate shocks are common in LVAD patients with atrial arrhythmias, optimal and timely device programming must be done after LVAD implantation. Anticoagulation is critical in patients with atrial arrhythmias, and LVAD which requires close follow-up and management to diminish the

risk of thromboembolic events and LVAD thrombus. However, left atrial appendage occlusion during LVAD implantation surgery decreases thromboembolic events and therefore, can be considered in patient who has pre-LVAD atrial fibrillation or AFL [18–20]. However, there are several areas that need to be investigated for better evidenced base management decisions. Those include subclinical incidental atrial fibrillation/AFL/atrial tachycardia detection on CIEDs, prevention of inappropriate shocks or thromboembolic events.

Regarding management of atrial arrhythmias in patients with LVAD, our recommendations based on current literature incorporated to recent consensus statement in Table 1 [2<sup>11</sup>]. Current studies are limited by their retrospective and single-center nature, and therefore, the variability in results is inevitable.

#### CONCLUSION

Based on the evidence to date, atrial arrhythmias are prevalent in LVAD patients and have significant impact in overall clinical outcome in this population. Despite current efforts for medical or catheter-based treatment, atrial arrhythmias remain an important determinant of morbidity and mortality in LVAD population in addition to the patients' underlying clinical characteristics. Thus, prospective multicenter studies are needed to explore impact of atrial arrhythmias in LVAD patient and also to determine optimal management strategy to improve clinical outcome in this population. Prevention of atrial arrhythmias in LVAD patients should be the ultimate goal.

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#### **KEY POINTS**

- Atrial arrhythmias, particularly atrial fibrillation, are highly prevalent in patients with LVADs.
- Atrial arrhythmias are important determining factor of overall clinical outcome in LVAD patients.
- Rhythm versus rate control strategies in management of atrial arrhythmias in LVAD patients provide similar outcome.
- Anticoagulation and cardiovascular implantable electronic devices should be closely monitored and optimized in LVAD patients with atrial arrhythmias.
- Further studies are warranted to determine optimal management strategies and prevention of atrial arrhythmias in LVAD population.

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# Table 1.

The management of atrial arrhythmias in left ventricular assist devices patients

- The management of AAs in LVAD patients should be individualized regarding rhythm versus rate control or antiarrhythmic drugs versus catheter ablation strategies
- Current guideline recommendations for the treatment of AAs by using pharmacological or nonpharmacological approaches in non-LVAD population can be followed in LVAD patients

2

- AAs with rapid ventricular response compromising LVAD flows and performance should undergo electrical or chemical cardioversion, and rhythm control should be considered in these 3
  - If there is a clear hemodynamic and functional compromise from the AFL, ablation therapy should be considered as a first-line therapy for typical AFL in patients with an LVAD patients 4
- Since inappropriate shocks can occur in LYAD patients with AAs, close monitoring of CIED with optimal and timely programming should be performed after LYAD implantation
  - n 9
    - Close monitoring and optimization of anticoagulation are particularly important in patients with AF/AFL and LVAD in order to prevent thromboembolic events
      - Left atrial appendage occlusion with LVAD implantation can be considered in selected patient population since this may help to decrease thromboembolic events

AAs, atrial arrhythmias; AF, atrial fibrillation; AFL, atrial flutter; CIED, cardiovascular implantable electronic devices; LVADs, left ventricular assist devices.