Chapter

Arrhythmia Management in Pediatric Patients with Ventricular Assist Devices

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Abstract

Ventricular assist device therapy has emerged as an important approach in the management of advanced heart failure. Atrial and ventricular arrhythmias are commonly encountered in patients with heart failure. Patients requiring ventricular assist devices are at an increased risk of arrhythmia, which may cause symptoms and significant complications. There is recent focus on the prevalence and impact of atrial and ventricular arrhythmias in patients with durable ventricular assist devices. Ventricular arrhythmias in particular have been associated with significant symptoms and worse clinical outcomes. The goal of this chapter is to outline approaches to arrhythmia management in pediatric patients with ventricular assist devices.

Keywords: ventricular arrhythmia, ventricular assist device, supraventricular arrhythmia, mechanical support, pediatric, management

1. Introduction

Heart failure in children is a growing global public health concern. In the United States, approximately 14,000 children are hospitalized for heart failure annually [1]. Symptoms of heart failure may include poor feeding, poor growth, and exercise intolerance. Heart failure in pediatric patients has various etiologies including failing physiology in congenital heart disease, inflammatory disease such as myocarditis, arrhythmia, post chemotherapy exposure, primary cardiomyopathy, and cardiac transplant rejection. Patients with congenital heart disease are at increased risk for developing heart failure secondary to chronic volume overload, elevated atrial and ventricular pressure, inadequate myocardial perfusion, and persistent ventricular dysfunction following surgical intervention. It has been reported that approximately 70% of hospital admissions for pediatric heart failure involve patients with congenital heart disease [1]. The risk for heart failure in congenital heart disease increases with age, with nearly 25% of adult congenital heart disease patients experiencing heart failure by the age of 30 years [2]. The Fontan palliation has been associated with high risk of developing heart failure with independent predictors of single morphological right ventricle, higher right atrial pressure, and evidence of protein-losing enteropathy [3].

Heart failure in children is associated with high morbidity and mortality with 20-fold increased risk of death during hospitalization [4, 5]. Noncardiac complications may include sepsis, renal failure, and respiratory failure. Studies have demonstrated that factors associated with increased risk of hospital mortality include acute renal failure and hepatic injury [1]. Early intervention with appropriate medical therapy is important in the management of acute heart failure. In cases where conventional therapies are not sufficient, mechanical circulatory support may be necessary.

Ventricular assist device (VAD) therapy has emerged as an important tool in the management of severe and refractory heart failure. An increasing number of patients are supported by a VAD, improving survival of patients whether used as destination therapy, bridge to transplantation, or bridge to cardiac function recovery. Over 25,000 VADs have been implanted in the United States [6] and the number of devices implanted in pediatric patients has increased over the years [7–9]. Cardiomyopathy, congenital heart disease, and myocarditis are the most frequently encountered underlying conditions in pediatric heart failure patients requiring VAD therapy [10, 11]. As there is increased risk for atrial and ventricular tachyarrhythmias in patients with heart failure, it is not uncommon to encounter these arrhythmias following VAD implantation.

2. Ventricular assist devices

Mechanical circulatory support has become increasingly common in the management of heart failure. The initial objective of VAD therapy was a temporary form of mechanical circulatory support as a bridge to cardiac transplantation. Improved survival with VADs and deficient donor organ supply has since resulted in increased use as destination therapy. In modern practice, VADs are often used as chronic therapy or permanent circulatory support.

Device selection and timing of initiating VAD support are vital in optimizing cardiac function recovery and chance for survival. Anatomic variations secondary to congenital heart disease or surgical interventions pose technical challenges to VAD implantation [12]. Other factors including severe neurologic impairment, chromosomal or congenital anomalies with anticipated poor outcome and significant prematurity or low body weight should be taken into consideration prior to VAD implantation. Patient size, anticipated duration, type of support, and ultimate goal of therapy are important elements in device selection.

The EXCOR © (Berlin Heart) is specifically designed for infants and children, providing mechanical circulatory support via pulsatile membrane pumps. The system offers multiple pump and cannula sizes to accommodate different patient sizes. It is important to avoid mismatch between patient and device size as mismatch has been associated with poor outcome [12]. Unfortunately, early generation VADs utilizing pulsatile flow were characterized by high rates of complications including high incidence of device failure and poor survival. These early devices were preload-dependent and sensitive to changes in cardiac output including those related to arrhythmia. There has been notable improvement in patient survival and reduction in complications with transition to continuous flow VADs [8].

There are two subclassifications of continuous flow VAD design – axial and centrifugal. In general, axial flow is generated by a propeller in a pipe with filling completed by use of negative pressure while a bladed disk spinning in a cavity generates centrifugal flow [13]. The second-generation VAD HeartMate II © (Abbott) provides

short or long-term circulatory support for heart failure patients as a continuous flow system that funds via axial flow generated with mechanical bearings. It has a lower incidence of thromboembolic events compared to the first-generation VADs [12, 13]. The HVAD pump (HeartWare Inc) is a continuous-flow device with a centrifugal pump that is attached directly to the inflow cannula. It is smaller than the HeartMate II and, with adjustment in the implantation technique, has demonstrated utility in the pediatric heart failure population [14]. While output from continuous flow VADs is not immediately affected by arrhythmias, there may still be hemodynamic instability from deficient right ventricular support. Third generation VADs, HeartMate 3© (Abbott), generate continuous flow via a centrifugal flow pump utilizing a magnetically levitated rotor. The CentriMag/PediMag© (Abbott) is a centrifugal pump that is used for temporary support. The presence of arrhythmia may lead to a reduction in preload and subsequent decrease in device flow [15].

In select patients with severe biventricular systolic dysfunction, complete replacement of the ventricles may be warranted. This is achieved with temporary total artificial hearts (TAH, Syncardia). These devices provide global circulatory support through a pneumatic pulsatile pump with an external portable drive. The temporary total artificial heart is traditionally utilized as a bridge to transplantation.

The use of VADs in pediatric heart failure patients has increased in the past decade [7, 9, 16]. While the use of pulsatile-flow and continuous flow devices in pediatric patients have each increased over time, pulsatile-flow devices were more frequently utilized in younger, smaller patients and those with congenital heart disease [16]. In this population, the majority of VADs were implanted as bridge to transplant.

3. Pathophysiology of arrhythmias encountered in patients with ventricular assist devices

Pediatric patients with decompensated heart failure are at increased risk for tachyarrhythmias. Patients requiring VAD therapy are at high risk for atrial and ventricular arrhythmias. In one cohort, over 70% of children with VADs experienced an arrhythmia with nearly 20% developing new arrhythmia while on VAD therapy [11]. Ventricular tachycardia is consistently the most common arrhythmia reported post VAD implantation, with documentation of monomorphic and polymorphic ventricular tachycardia. The presence of ventricular arrhythmia prior to VAD therapy has been found to be predictive of ventricular arrhythmia post VAD implantation [17]. More than half of pediatric patients with arrhythmia prior to VAD therapy continue to experience arrhythmia while on VAD [11].

One main mechanism by which heart failure increases the risk of atrial fibrillation is through increased left atrial pressures [18]. Anisotropy and reduced atrial conduction velocity develop from scar secondary to the chronic increased left atrial pressure, promoting atrial tachyarrhythmia. Structural remodeling, atrial myopathy, and maladaptive gene expression are other mechanisms by which heart failure can facilitate the development of atrial fibrillation. Heart failure results in a proinflammatory state that leads to structural remodeling mediated by diffuse fibrosis, the consequence of which includes electrophysiologic heterogeneity and slowed conduction [19]. Associated left ventricular diastolic dysfunction transfers increased left ventricular filling pressure to the left atrium. Prolonged elevated left atrial pressure can result in dispersion of refractoriness. Studies have demonstrated prolongation in atrial refractoriness, P-wave duration, and conduction time in patients with atrial fibrillation [20]. Increased left

atrial pressure results in decrease in cardiac calcium ion channels, leading to calcium overload, increased diastolic calcium lead, and prolonged action potential duration. Increased calcium content has been demonstrated to portend afterdepolarizations from the pulmonary veins that serve as triggers for atrial fibrillation [21, 22].

There are several factors related to the underlying heart failure that may stimulate development of ventricular arrhythmia. Ventricular dysfunction has been found to be an independent risk factor for arrhythmia associated with VAD therapy [11, 23]. This is not unexpected as severe ventricular dysfunction itself can promote arrhythmia. The development of chamber enlargement, myocardial scar, and subendocardial ischemia can result in myocardial injury and become arrhythmogenic. Focal areas of scar result in a heterogenous area of healthy and infarcted myocardium with different conduction properties and refractoriness in close proximity [24]. This leads to anisotropy and areas of slow conduction, which is prime for reentry. Neurohormonal activation, enhanced catecholamines, electrolyte abnormalities, and altered calcium handling can also contribute to an environment prone to arrhythmia.

VAD implantation has been associated with electrophysiologic changes. Prolongation of the QT and corrected QT interval have been observed post VAD implantation and associated with tachyarrhythmia [25, 26]. Changes in channel regulation including upregulation of the Na+/Ca2+ exchange and downregulation of the voltage-gated K+ channel, may contribute to increase in action potential duration and development of delayed afterdepolarizations [27]. The VAD implantation process and presence of the device itself can prompt arrhythmia. Apical scar at the site of VAD inflow cannula insertion can contribute to reentrant ventricular tachyarrhythmias. Suction events where the VAD inflow cannula engages the ventricular wall result in decreased device output, reducing cardiac function support and increasing the risk for ventricular arrhythmia [28]. High VAD pump speed, VAD inflow cannula position, and low patient intravascular volume are contributing factors that increase the risk of suction events [13].

4. Arrhythmias encountered in patients with ventricular assist devices

4.1 Atrial tachyarrhythmia

Atrial arrhythmias are common on patients with heart failure. Atrial fibrillation is the most frequently encountered atrial arrhythmia. However, ectopic atrial tachycardia and atrial flutter are seen as well. Persistent atrial flutter can result in loss of AV synchrony and impaired ventricular filling. In certain patients with left VADs, atrial arrhythmias, particularly atrial flutter with rapid ventricular response, have been associated with hemodynamic compromise secondary to decompensated right heart failure [29, 30]. Improvement in right heart failure has been demonstrated after catheter ablation of the atrial flutter [29].

The pathophysiology of heart failure results in structural changes and electrical remodeling that encourage the development of atrial fibrillation. The frequency of atrial fibrillation increases with heart failure severity, reaching approximately 50% of patients with New York Heart Association (NYHA) Class IV classification [31]. In adult patients, atrial fibrillation may be encountered in over 40% of patients on VAD therapy [32]. There are conflicting results regarding the risk of thromboembolic events patients with atrial arrhythmia on VAD therapy; however, the presence of atrial fibrillation prior to VAD therapy has been shown to predict the occurrence of ventricular arrhythmia after VAD implantation [23].

It has been demonstrated that pediatric patients undergoing VAD therapy for cardiomyopathy or myocarditis have an increased risk of developing arrhythmia [10]. In a cohort of pediatric patients with VAD, 38% experienced an atrial arrhythmia [11]. The majority of the tachyarrhythmia episodes were non-sustained with a median rate of 150 bpm. There was no correlation between presence of arrhythmia and mortality [11]. In pediatric patients with VAD for primary diagnosis of arrhythmia, it has been demonstrated that nearly 70% have supraventricular tachycardia, of which nearly 40% are ectopic atrial tachycardia or atrial flutter [33].

4.2 Ventricular tachyarrhythmia

Before discussing the risks of ventricular arrhythmias in the context of pediatric VAD use, it is important to recognize the risks of these arrhythmias in patients with heart failure in general. Regardless of whether the reason for heart failure is secondary to cardiomyopathy or congenital heart disease, risks have been well described [24, 34]. Guidelines and consensus statements include recommendations for management, including the use of anti-arrhythmics as well as indications for implantation of implantable cardioverter-defibrillators (ICDs) [35, 36]. For this reason, many patients who present for VAD implant are already receiving anti-arrhythmics, have ICDs, or both. In fact, there are a handful of pediatric patients who have received VADs specifically for intractable ventricular arrhythmias [33, 37].

Early in the era of adult VAD use, it became clear that there was an association of new onset monomorphic ventricular tachycardia in the months following implant [38]. While the majority of arrhythmias tend to occur during the initial hospitalization at implant, later onset arrhythmias have also been documented [17]. In addition, given that most patients have significant heart failure, many will already have primary or secondary prevention ICDs with a history of ventricular arrhythmias [39]. Pediatric arrhythmia data in VADs are quite scarce. A 2015 study found over half of patients in a single center study developed ventricular arrhythmias [11]. A more recently published single center study found that patients with cardiomyopathy and myocarditis were more likely to have non-sustained and sustained ventricular tachycardia than those with congenital heart disease [10]. Additionally, those who had less left ventricular decompression were at a higher risk for having ventricular arrhythmias. Arrhythmia presence prior to VAD implant was associated with increased risk of ventricular arrhythmias and antiarrhythmic therapy was associated with decreased risk.

While isolated ventricular ectopy and often non-sustained ventricular tachycardia do not require significant intervention in patients with heart failure, once a VAD is implanted these will likely become even less hemodynamically significant given the additional support [40]. With more sustained arrhythmias, one would expect decreased flows given the loss of right ventricular contribution to cardiac output and if sustained enough, right ventricular failure. For this reason, those patients who receive VAD support specifically for intractable arrhythmias often are given biventricular support [41].

5. Management of Arrhythmias Encountered in patients with ventricular assist devices

It is important to note the potential for reversible causes of arrhythmia in pediatric patients with VAD. Electrolyte derangement, consequences of comorbidities, and drug–drug interactions with electrophysiologic effects should be considered. The

identification of reversible causes of atrial or ventricular arrhythmia may allow for management with conventional therapies. Limitation of known QT-prolonging medications and proarrhythmic agents is prudent.

Suction events where the VAD inflow cannula interacts with the ventricular wall can result in ventricular arrhythmia [28]. These events may be avoided by reducing high VAD pump speed and avoiding intravascular volume depletion. Recurrent suction events associated with ventricular arrhythmia may require fluid supplementation.

Studies have demonstrated that some adult patients with continuous-flow VAD remain hemodynamically stable while in ventricular tachyarrhythmia including ventricular fibrillation [40, 42–44]. While patients were symptomatic, there was no evidence of end-organ dysfunction as a result of the ventricular arrhythmia. After restoration of sinus rhythm, there was no recurrence of the ventricular arrhythmia [42]. This suggests that there can be hemodynamic stability with left VAD support during episodes of ventricular arrhythmia. However, prolonged ventricular fibrillation can result in right ventricular failure and subsequent sequela. As such, restoration of sinus rhythm would be prudent.

5.1 Medical management

5.1.1 Atrial arrhythmias

Beta blockers are standard first-line therapy for rate control in patients with heart failure. Rate control with beta blockers is usually sufficient for the management of atrial arrhythmias. Digoxin may be a useful adjunct to beta blocker therapy by slowing ventricular response to the atrial arrhythmia. Calcium channel blockers are not typically used in the setting of significant systolic dysfunction.

When rate control is insufficient, then restoration and maintenance of sinus rhythm may be required. Amiodarone and dofetilide are commonly utilized for conversion to sinus rhythm in adult patients. Amiodarone is the most commonly utilized antiarrhythmic as single-agent therapy in pediatric patients with VAD [33]. Refractory cases may require amiodarone in conjunction with beta blockers, certain sodium channel blockers, or digoxin.

5.1.2 Ventricular arrhythmias

Due to the underlying condition, most patients who have received a VAD likely have an indication for beta-blockade. However, it is unclear in the pediatric population if beta-blockade is adequate for prevention of ventricular arrhythmias. Adult studies are divergent with some studies demonstrating an association with beta-blocker nonuse and ventricular arrhythmias and others showing no differences [27, 45]. Amiodarone has been identified as protective against ventricular arrhythmias amongst non-LVAD patients with ICDs, however it comes with risks of adverse effects [46]. One adult study showed improved arrhythmia-free survival in LVAD patients with ventricular arrhythmias who were started on amiodarone as secondary prevention [17]. However, when baseline amiodarone use was studied in the LVAD population, there was an increased mortality associated with its use [47]. More data are needed to assess efficacy of antiarrhythmics in the adult LVAD population and there is a near-absence in data in the pediatric population. Therefore, decisions will continue to need to be patient-specific taking into account arrhythmia burden, substrate,

patient hemodynamics, drug–drug interactions, and type of VAD. Should an antiarrhythmic be initiated, as the first month post VAD implantation is reported as the highest risk [48], consideration could be made for discontinuation of antiarrhythmic medication over time in patients with longer-term VAD.

5.2 Catheter ablation

Catheter ablation of atrial arrhythmias in adult patients with heart failure has been proven to be feasible and effective [29, 49, 50]. Atrial fibrillation in setting of VAD therapy treated with catheter ablation has been associated with improved symptoms and cardiac function. Studies have demonstrated return to sinus rhythm, resolution of symptoms, and resolution of right heart failure with catheter ablation of atrial flutter in patients with VAD. No significant procedural complications or adverse events have been reported in this patient population, suggesting that radiofrequency catheter ablation of atrial arrhythmias in patients with VAD may be a reasonable first-line therapy. There are no similar data available in pediatric patients.

There have been no large studies investigating the role of catheter ablation in ventricular arrhythmias in pediatric patients with LVADs. There are a handful of adult case series and cohort studies documenting experience with 101 patients total [25]. These studies demonstrated relatively high procedural success (77–86%) with variable recurrence. One study demonstrated improved one year survival in the absence of arrhythmia recurrence [51]. It must be noted that there are specific considerations necessary for ablations in this patient population. They will require strict fluid management, invasive hemodynamic monitoring, and special care maneuvering in the vicinity of the cannula. Additionally, there may be effects on electroanatomic mapping and signal quality. Surgical ablation at the time of LVAD implant may be considered and is a class IIb indication in the 2017 guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death [35]. Again, there are no published pediatric studies examining ventricular catheter ablations in patients with VADs.

5.3 Implantable cardioverter-defibrillator

ICD therapy has been demonstrated to improve survival in patients with heart failure as well as those with cardiomyopathy with previous cardiac arrests [35]. Therefore, most patients with VADs have already received an ICD or meet criteria for having one implanted. There are currently no randomized control trials evaluating ICD use in patients with VADs in adults or children. Studies investigating the effects of ICD therapy in patients with VAD have had mixed results. Early reports in the era of pulsatile VADs suggested an improvement in mortality rates in patients with ICDs [27, 52]. With the publication of studies evaluating adults with continuous flow VADs, three meta-analyses were published, with overlapping data, all with the finding that ICD use conferred no benefit in mortality risk [53–55]. Based on this, there is a class IIa recommendation for implantation of an ICD in patients with LVADs who have had ventricular arrhythmias in the 2017 AHA/ACC/HRS guidelines on ventricular arrhythmias [35]. There is no mention of VADs in the 2021 pediatric device consensus statement [36].

It is important to keep in mind that with the support of a VAD, ventricular arrhythmias may no longer cause hemodynamic compromise and patients may not lose consciousness, therefore a shock from a device may be felt. Adverse events in

patients with ICDs and VADs are reported in up to 30% of patients and can include changes in thresholds, inappropriate shocks caused by oversensing, and increased defibrillation thresholds [56]. Most of these patients require an ICD modification. Programming changes should be considered in the patient with a VAD to minimize shocks in the awake patient. While studies have shown significant psychological effects of being shocked by a device versus no shock in adults, this has not been replicated in pediatrics, although limited data size may have affected the ability to detect this [57, 58]. Regardless, it is in everyone's best interest to minimize pain in our patients. A single center randomized study investigated whether lengthening detection zones and increasing the use of ATP differed from nominal settings [59]. This found no difference in time to first ICD shock, but there were no harmful effects in making these adjustments. Therefore, there have been recommendations to follow this strategy with a high rate for the VF cutoff zone and the maximum number of programmable intervals [25].

6. Conclusion

Pediatric heart failure is a complex clinical syndrome associated with high morbidity and mortality. While VAD therapy has emerged as an important tool in the management of severe or refractory heart failure, it is not uncommon to encounter arrhythmias in such patients, including during and after VAD therapy, due to the underlying pathology. To date, data on arrhythmias and arrhythmia management in the context of VADs in pediatric patients are lacking. While we have a baseline understanding of etiologies of arrhythmia substrates in patients with congenital heart disease and cardiomyopathy, the changes that occur with VAD implant are less well understood. Additionally, in pediatrics, there is evidence that new ventricular arrhythmias can present after VAD removal [11]. At this time, there is a scientific statement from the AHA that offers suggestions and recommendation for the adult population and can be a useful resource [25]. However, pediatric patients are unique and must be treated in a case-by-case basis. Maintaining sinus rhythm is clearly advantageous in the biventricular heart and can help avoid right heart failure [60]. However, in this era where fewer than 50% of pediatric patients are discharged with a VAD, one must ask how aggressively to treat these arrhythmias, especially when it comes to implanting an ICD [61]. With adult data suggesting no benefit to ICD implantation, there must be careful consideration before implanting one in a pediatric patient, especially if the patient will remain hospitalized. If an ICD is already in place, a multidisciplinary approach with the heart failure team, patient, and patient's family is necessary to determine what, if any, therapies should remain turned on when a VAD is implanted. Despite this, it is likely in the patient's best interest to avoid sustained arrhythmias and attempt to maintain appropriate heart rates to optimize VAD function, especially in single ventricle patients [41]. As technologies emerge and survival improves, the need for data to help direct management is greater than ever; however collaborative efforts will be absolutely necessary to gain the necessary knowledge.

Conflict of interest

The authors declare no conflict of interest.

Notes/thanks/other declarations

None.

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