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Review

Implantable cardioverter defibrillators and biventricular pacing in pediatric dilated cardiomyopathy: Preventing death and delaying heart transplant

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ABSTRACT

Dilated cardiomyopathy (DCM) is a frequent cause of mortality and heart transplantation in pediatric patients. Device therapy has been shown to improve mortality and transplantation rates in adult patients with dilated cardiomyopathy. However, the criteria that are used to guide implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy (CRT) devices in adult patients cannot be directly applied to pediatric patients. ICDs are a proven treatment for the prevention of sudden cardiac death (SCD), but it is difficult to quantify SCD in the pediatric DCM population. CRT has been proven to improve hemodynamic function, quality of life, and survival in adult patients with cardiomyopathy, but similar data in pediatric patients in not available. Currently, providers have to extrapolate adult criteria for CRT initiation for pediatric patients while tailoring the approach specifically for each patient due to the heterogeneity of disease and the range of ages. To create evidence-based guidelines for device therapy in pediatric patients with DCM, additional studies need to be done to quantify the risks factors for SCD as well as to understand the relationship between mechanical and electrical dyssynchrony. Additionally, there are no devices that are specifically designed for pediatric use, which can add to the risk of device implantation. As new devices and new approaches to device implantation are developed, we will be better able to reduce mortality and delay heart transplantation in pediatric DCM patients.

1. Background

Dilated cardiomyopathy (DCM) is the most common cardiomyopathy worldwide, as well as the most frequent cause of heart transplantation in adults and children [1,2]. Pediatric DCM has many causes, including primary cardiomyopathy due to genetic or familial causes, or secondary cardiomyopathy due to myocarditis, neuromuscular disorders, inborn errors of metabolism, or toxins [1–4]. Some forms remain idiopathic, but unlike adults, ischemia is rare etiology in children. The incidence of DCM in children is approximately 0.57 cases per 100,000 per year; higher in boys and infants (< 1 year of age) [2,5].

DCM is characterized primarily by left ventricular (LV) chamber dilation with normal wall thickness, resulting in impaired contractility and systolic dysfunction, leading to progressive congestive heart failure (CHF) and arrhythmias, including sudden cardiac death (SCD). [1,3] There can also be right ventricular dysfunction that adds to the severity of the disease [2]. One multicenter study with a cohort of 1803 children with DCM determined the incidence of SCD in this population to be 3% cumulatively over 5 years [6]. The prognosis for DCM patients varies with the etiology, but overall, one and five-year rates of death or heart transplantation for pediatric patients in the cardiomyopathy registry were 31% and 46% respectively [2,4].

Medical treatment of DCM is mainly centered on managing the symptoms of CHF. Generally accepted therapeutic regimens include angiotensin-converting enzyme inhibitors, beta-blockers, and/or diuretics, along with anti-arrhythmic medications if indicated. Device therapies such as implantable cardioverter defibrillator (ICD) placement for primary or secondary prevention of SCD and cardiac resynchronization therapy (CRT) for management of mechanical dyssynchrony are used in these patients at all ages. ICD and CRT placement have been shown to provide significant benefits in the adult population with DCM, but the results are less clear in children [3,6,7].

1.1. Implantable Cardioverter Defibrillators in Pediatric Dilated Cardiomyopathy

Ventricular arrhythmias are present in 50% of children who die from DCM, and in 63% of pediatric patients who are awaiting heart transplantation [8]. Overall, SCD is a leading cause of mortality in adolescents with congenital heart disease (CHD) and a major concern in

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children with DCM [9]. ICDs can provide multiple functions, including anti-bradycardia pacing, anti-tachycardia pacing, and defibrillation. Large, randomized trials have demonstrated the benefit of ICD therapy in adults for the prevention of SCD [6,10]. As such, there are clear indications regarding ICD placement in adults, but no specific guidelines for pediatric DCM patients. For adults with DCM, ICD therapy is indicated for patients with a left ventricular ejection fraction (LVEF) less than or equal to 35%, and a New York Heart Association (NYHA) functional Class of II or III (Class I guideline) [11]. ICD placement is the preferred treatment for primary or secondary prevention of adults with non-ischemic DCM [11]. For pediatric patients, recommendations are extrapolated to follow adult guidelines for secondary prevention of SCD. However, it is noted that there are no randomized controlled trials of ICD therapy for primary prevention of SCD, and thus there are no specific guidelines for pediatric DCM patients. As noted in the updated guidelines, careful considerations should be made regarding the benefit of prevention of SCD vs. the probability of adverse events including inappropriate shocks and the resultant decrease in quality of life [12]. This is especially true given the relatively low estimated rate of SCD of 3% in this population [6].

Nevertheless, pediatric patients are receiving these devices as treatment, and it is evident that ICD therapy can abort sudden arrhythmic death events. Ventricular tachyarrhythmias are effectively terminated by an ICD, using either programming antitachycardia pacing or prompt delivery of a defibrillation shock (Fig. 1). A multicenter retrospective study of 443 pediatric patients with ICDs demonstrated that 23% of the cohort had a primary diagnosis of cardiomyopathy [13]. However, the study also showed that the rate of inappropriate shocks in this population is as high as 21%, primarily due to lead failure, as well as sinus or atrial tachycardias and T-wave oversensing (Fig. 2). The majority of DCM patients who receive ICDs tend to be older patients and those who have already had aborted SCD, as opposed to younger patients with CHF without arrhythmias [8]. This may be due to the added complications of placing an epicardial system in younger patients as opposed to a transvenous system in older children. Regarding patients who are awaiting transplant (all comers), the risk of SCD does not appear to be different between those who have ICDs placed and those who do not [7]. Although the retrospective cohort contained 426 patients with and 4646 patients without ICDs, the authors hypothesized that the survival benefit seen in adults may not have been appreciated in this study for a variety of reasons. The low incidence of SCD, the heterogeneous nature of underlying diagnoses, the shorter wait times for transplantation, and the higher likelihood of being listed as status 1A may all have contributed to this finding [7]. The small sample size of most pediatric clinical studies also hampers statistical power to determine the impact of having an ICD on morbidity and mortality.

1.2. Cardiac Resynchronization Therapy in Pediatric Dilated Cardiomyopathy

CRT is an effective treatment for adult patients with left ventricular failure who have not responded to maximal medical therapy [8,14,15]. Studies have shown that in adult patients in LV failure with electrical dyssynchrony, CRT can produce a hemodynamic improvement in LV function, as well as an increase in exercise tolerance, quality of life, and survival [8]. Multiple multi-center registry trials show a clear mortality benefit for CRT in adults with ischemic and nonischemic cardiomyopathy [8]. Moreover, the addition of ICD capability to provide CRT (CRT-D) reduces mortality in adult patients even more than compared to CRT alone (CRT-P) [8,16]. However, even in adults, up to 30% of patients can end up being non-responders to CRT [15]. This begets the importance of having specific guidelines for CRT placement as well as implant techniques to maximize likelihood of resynchronization responsiveness. Currently, initiation of CRT is a Class I recommendation in patients who have LVEF less than or equal to 35%, sinus rhythm, a left bundle branch block (LBBB) pattern with a QRS duration greater than or equal to 150 ms, and NYHA Class II, III, or ambulatory IV. If a patient does not have a QRS duration > 150 ms or a LBBB pattern, the recommendation falls to Class IIa [12]. The European Society of Cardiology has similar recommendations for adult patients, but not in pediatric patients. Their meta-analysis revealed that although there is no mortality benefit seen from CRT plus ICD, it has the highest probability of being the best treatment. The study also predicted that the highest responders to CRT are more likely to be female, have non-ischemic cardiomyopathy, have a wider QRS duration, and have a LBBB pattern [17].

In pediatric patients with DCM, the benefit of CRT and indications for use are not as well established. It is difficult to apply adult criteria directly to pediatric patients [15]. One study demonstrated that only 9% of pediatric patients with CHF present with a LBBB pattern and a QRS duration > 120 ms [15]. It is also unclear what the appropriate cutoff for QRS duration should be given the variation in normal QRS duration with age. Schiller et al. determined that in a single-center cohort of 52 pediatric patients with various etiologies of LV DCM, none of these patients met adult criteria for CRT [14]. Even though adult data has shown that there is little benefit in treating patients without LBBB pattern with CRT, it is possible that the indications for CRT in pediatrics may not fully be directly related to electrical dyssynchrony [8,12].

Several single-center and multi-center studies have been done to evaluate the use of CRT in pediatric patients (Table 1). Khairy et al.

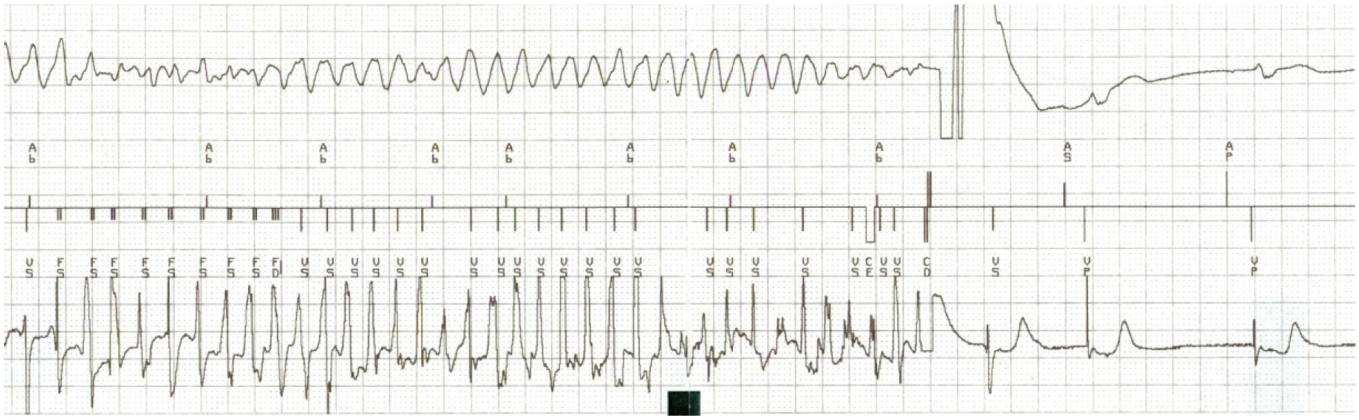

Fig. 1. Intracardiac electrogram from implanted defibrillator showing ventricular fibrillation on the left, with rapid rates. The marker channel notations include atrial sensing (AS), atrial pacing (AP), ventricular sensing (VS), fibrillation sensing (FS), fibrillation detection (FD) which begins charging, charge end (CE), followed by cardioversion (CD). The shock effectively converts the ventricular fibrillation and is followed by a DDD paced rhythm.