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Review Article

Permanent Pacemaker Implantation after Orthotopic Heart Transplantation. A Review of the Pediatric Literature

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Abstract

Allograft rejection and transplant coronary artery disease continue to be significant causes of morbimortality in patients after orthotopic heart transplantation, so non-invasive predictors have been seeking to determine when coronary angiography and endomyocardial biopsies may be required to evaluate for these conditions. In this article, we reviewed the pediatric literature about the subject, highlighting that the paediatric patient presenting with sinus node dysfunction or atrioventricular block requiring PPM implantation over 3 months after transplantation should be aggressively worked up for rejection or coronary disease, as it may be their first symptom.

Keywords: *Orthotopic Heart Transplant; Pacemaker; Sinus Node Dysfunction; Atrioventricular Block; Children*

Abbreviations

OHT: Orthotopic Heart Transplant; AR: Allograft Rejection; TCAD: Transplant Coronary Artery Disease; AVB: Atrioventricular Block; SND: Sinus Node Dysfunction; PPM: Permanent Pacemaker

Introduction

Significant advances in surgical techniques and immunosuppressive strategies have resulted in increased overall survival after orthotopic heart transplant (OHT). However, allograft rejection (AR) and transplant coronary artery disease (TCAD) continue to be significant causes of morbimortality, so non-invasive predictors have been seeking to determine when coronariography and endomyocardial biopsies may be required to evaluate for these conditions [1]. Adult studies suggest a strong relationship between brady arrhythmias in the form of an atrioventricular block (AVB) or sinus node dysfunction (SND) requiring a permanent pacemaker (PPM) after OHT and AR or TCAD [1]. The occurrence of arrhythmias after pediatric OHT is common (41%) [2], so their potential connection with outcome could be crucial in these patients too. However few data, limited by small sample size in single-centre analyses, are available regarding the incidence and indications for PPM implantation after paediatric OHT and the relationship between PPM and AR or TCAD [3-7]. In this article, we review the paediatric literature about the subject.

Review of the Pediatric Literature

Complete AVB or SND after OHT is a major complication potentially requiring PPM, with a reported incidence of 1% - 6.6% in pediatric OHT [2,3,5-7]. PPM implantation after OHT follows a bimodal distribution of early (< 3 months after OHT) and late (> 3 months after OHT) implantation.

Early postoperative PPM implantation is rare (0.41 - 1.9%) [4,6,7] in paediatric OHT and usually occurs in the immediate post-transplant period. It has been associated with biatrial anastomosis, antiarrhythmic use, and older donor age, and disruption of the sinoatrial nodal blood supply during surgery is thought to be an essential factor [6]. Patients with early sinus node dysfunction are asymptomatic and not pacemaker-dependent at three months; however, those with early atrioventricular block will require long-term pacing [4,6,7]. Although PPM recipients had higher incidences of infections and dialysis, PPM implantation did not adversely impact survival of these patients [6], and no association with AR or TCAD has been reported [6].

Late postoperative PPM implantation occurs in approximately 1.5 - 5.2% of paediatric patients [3-5,7]. The underlying mechanism is probably not related to the surgical technique but could be the result of the ischemia involving the sinoatrial or atrioventricular node. The limited existing literature shows that this situation is an ominous sign and portends a poor outcome that should prompt a search for the presence of AR or TCAD.

Chinnock., *et al.* reported seven infants with PPM after OHT. Indications were SND in 5 and complete AVB in 2 patients. 1 patient (AVB) had an acute AR and died. 6 survivors were alive, asymptomatic and without complications during the study period (8 - 50 month). The authors did not find a correlation with graft cold ischemic time, rejection history, donor age or recipient age at transplantation [7].

Kertesz., *et al.* found that only new-onset Wenckebach periodicity was noted in the presence of either AR or TCAD in 6 patients. All patients with Wenckebach periodicity returned to sinus rhythm, except for 1 with TCAD who received a PPM because of an episode of complete AVB [5].

Cannon., *et al.* reported 5 patients requiring late PPM. Indications for pacing were complete AVB in 1 patient and SND in the remaining 4 patients. All patients were symptomatic (syncope or dizziness), and all had a resolution of symptoms and no complications after PPM implantation. Of note all patients requiring late PPM had TCAD diagnosed within 1 year of PPM implantation (22% of all OHT recipients diagnosed with TCAD in the population study). Three patients were diagnosed with TCAD before their symptoms precipitating PPM placement. 2 of the 5 patients had a PPM placed before angiographic evidence of TCAD. In these 2 patients, TCAD was diagnosed 5 and 10 months after PPM implantation, despite a normal evaluation before PPM placement. Four of the patients in this group subsequently underwent OHT, and all of them had evidence of TCAD on their explanted heart specimen. None of the patients had an acute AR episode [4].

Collins., *et al.* reported 12 patients (5.2%) with late PPM implantation. 7 pacemakers were placed for SND and 5 for complete AVB. At the time of pacemaker placement, 1 patient with SND and 3 with sudden complete AVB had cardiac biopsies positive for AR, and 1 patient with SND was documented to have TCAD. None of the patients with AVB had TCAD at the time of pacemaker placement. Patients with permanent pacemakers had poor clinical outcomes, with death or re-transplant rates significantly higher compared to patients without a pacemaker (75 vs. 34%; p 0.01). 4 cases of SND and 3 cases of complete AVB were death or re-transplanted secondary to AR or TCAD. Notably, patients with complete AVB either died or were re-transplanted in a relatively short period (1 month vs. 4.9 years) [3].

Discussion and Conclusions

After reviewing the literature, we highlight that the paediatric patient presenting with SND or AVB (including Wenckebach periodicity) requiring PPM implantation late after OHT should be aggressively worked up for AR and TCAD, as it may be their first symptom. If normal results are obtained a close follow-up is warranted because TCAD is usually diagnosed after pacemaker placement, probably because it is not detected or underestimated by routine coronary angiography because of its diffuse and concentric nature. PPM implantation should always be considered in those patients with symptomatic SND or asymptomatic complete AVB block because pacemakers can be safely performed when necessary with excellent clinical results. However, despite pacemaker implantation, these patients have a worse outcome than patients without pacemakers, and many succumb to the underlying disease process often with a precipitous decline, and re-transplantation should be considered.

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Conflict of Interest

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