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Review

Postoperative complete heart block among congenital heart disease patients: Contributing risk factors, therapies and long-term sequelae in the current era☆

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ABSTRACT

Although postoperative complete heart block is a relatively rare complication after cardiac surgery for congenital heart disease in the current era, it has significant repercussions if there is no recovery of atrioventricular conduction in the early postoperative period. Insertion of a permanent pacemaker in an infant, child or adolescent remains an important medical decision considering all potential adverse physical and physiological side effects commonly associated with device implant among these younger patients. In this review, the current incidence, morbidity and mortality of postoperative complete heart block is presented as well as contributing anatomical and perioperative risk factors along with potential therapies and long-term sequelae of this unwanted complication.

1. Introduction

Complete heart block (CHB), after cardiothoracic surgery in pediatric patients, is a complication that has been reported since the onset of surgical interventions for congenital heart disease (CHD) [1,2]. The etiologies of this complication are multifactorial, although the presence of unique variations in the anatomical configurations of the atrioventricular node, that intrinsically can occur among several congenital heart defects, is one of the main reasons for this occurrence. Even though many patients recover atrioventricular (AV) conduction within a few days following surgical intervention, there remains a small percentage of them that will require permanent pacemaker placement due to persistent AV conduction problems. In recent years, with the multiple advances in all the aspects of pediatric cardiothoracic surgery and increasing knowledge of AV nodal anatomies, this number has decreased, yet, depending on surgical database studies, is still reported from 0.9–3% of patients undergoing surgical intervention for various congenital heart defects, although, as indicated below, higher percentages have been noted [3–6].

2. Genetic Risk Factors

Despite the development of innovative and modern techniques designed to avoid close manipulation of the AV conduction system, postoperative CHB still occurs [5]. The “two-hit theory”, where the first “hit” is the genetic predisposition and the second “hit” an environmental factor, may contribute to this persistent incidence. It has been reported that a mutation in the connexin-40 gene (Cx40-Q58L) impairs gap junction formation at cell-cell interfaces which is highly detrimental for action potential propagation in the specialized heart conduction system [7]. In a retrospective study of 1199 patients, Murray et al. recently reported their 8 year CHD surgical experience and found the incidence of complete heart block after surgical repair to be 4.7%. They also reported that a common polymorphism in the gene encoding connexin-40 (GJA5 rs10465885 TT genotype; OR 2.1, 95% CI 1.2–3.8) was independently associated with postoperative CHB in their patient cohort [8]. Interestingly, several genetic polymorphisms in the connexin-40 gene have also been associated with atrial fibrillation but not heart block among non-congenital heart adult patients [9,10]. This raises the issue that more research is required to better understand the contribution of a genetic predisposition to AV node dysfunction,

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postoperative CHB and arrhythmias.

3. Perioperative Risk Factors Including Anatomy

In the above mentioned study that evaluated the connexin-40 gene association with CHB, additional perioperative factors independently associated with postoperative CHB included preoperative digoxin therapy (OR 2.4, CI 1.3–4.4; $p < 0.005$), length of aortic cross-clamp time (OR 1.08, CI 1.04–1.11; $p < 0.005$) and ventricular septal defect (VSD) closure (OR 2.2, CI 1.2–4.1; $p < 0.005$) [8]. Furthermore, in a previous study from 1998, Weindling et al. reported their experience with postoperative CHB at Boston Children's Hospital ($n = 1964$) during a 3 year period. Congenital heart disease surgical interventions most commonly associated with a risk for postoperative CHB were those associated with left ventricular outflow tract obstruction, congenitally corrected transposition of the great arteries (L-TGA), VSD and Tetralogy of Fallot (TOF) [6].

In a major pediatric hospital in Turkey, data on 1550 patients who underwent cardiothoracic surgery for various congenital cardiac defects, revealed that 96 (6.2%) had postoperative AV block. Of these, the most frequent CHD diagnoses were TOF ($n = 22/96$; 23%), complete atrioventricular septal defect ($n = 15/96$; 16%), and VSD ($n = 13/96$; 14%) [11]. Moreover, Mah et al. recently analyzed the data from the Pediatric Heart Network's Single Ventricle Reconstruction Trial involving 549 patients and outlined that tricuspid valve repair during stage 1 surgical palliation and obstruction of pulmonary venous drainage requiring intervention before stage 1 surgical palliation were independently associated with a 6% incidence of postoperative CHB [12].

Furthermore, a recent analysis of the Pediatric Health Information System database (45 hospitals in the United States) found that the surgical interventions associated with the highest incidence of postoperative CHB and need for placement of a permanent pacemaker were the double switch operation (15.6%), tricuspid valve (7.8%) and mitral valve (7.4%) replacements, arterial switch (Jatene procedure) with ventricular septal defect repair (6.4%) and the Rastelli procedure involving the right ventricular outflow tract (4.8%) [3]. In addition, Anderson et al. performed a retrospective review of the Kids Inpatient Database (KIDS) over a 10-year period (2000–2009), which only included patients who underwent surgical repair for VSDs, atrioventricular canal defects (AVC), and TOF. They reported that among these defects, AVC repair was associated with the highest incidence of postoperative CHB reported at 7.7% when compared with other CHDs (OR 1.77; CI: 1.32–2.38; $p < 0.005$) [5].

Several studies have attributed additional risk factors to the population of children specifically undergoing VSD repair; given that the anatomic characteristics of the conduction tissue can be very variable, for example, in membranous VSDs the conduction tissue runs along the posteroinferior border of defect while in inlet VSDs the conduction tissue is anterosuperior to the defect. Within this population, a report from Stanford University (California) noted that patient weight < 4 kg vs > 4 kg (4.2% vs. 1%; $p \leq 0.01$) and the inlet vs perimembranous VSD location (11.6% vs. 1.4%; $p \leq 0.01$) were risk factors for postoperative CHB. Of note, this report indicated that the risk of postoperative CHB was not influenced by the presence of chromosomal abnormalities or other congenital heart disease [13]. This somewhat contradicted an earlier study by Tucker et al. who performed an elegant analysis of the Pediatric Cardiac Care Consortium database of all patients who had CHB after surgical repair of a perimembranous VSD. The most significant risk factor for development of CHB was the association of Down's syndrome (OR 3.62, CI 2.02–6.39; $p < 0.005$) [14]. In a major university hospital in Egypt, infants with isolated VSD repair and who also had tricuspid valve detachment (TVD) as part of the surgical procedure, had a higher incidence of postoperative CHB although not statistically significant (7% for VSD/TVD vs. 3.75% for VSD alone, $p = 0.6$) [15]. In summary, the unique anatomical configurations of the atrioventricular conduction system in congenital heart defects such as ventricular septal defects, endocardial cushion defects, and congenitally corrected transposition of the great arteries (L-TGA) are major non-modifiable risk factors for the onset of postoperative CHB.

4. Early Recovery of Atrioventricular Conduction and Recommendations for a Permanent Pacemaker

In the above-mentioned studies by Weindling and Murray, over half of patients with postoperative CHB had spontaneous normalization of AV conduction. In the former report, this occurred among 32 of the 51 study patients (63%). Additionally, among patients who regained AV conduction within the first postoperative month, 81% did so by postoperative day 7 and 97% by postoperative day 9 [6]. In the latter study, also 63% of patients demonstrated recovery of AV conduction, with median recovery time of 3 days (IQR 2–8 days) [8]. Moreover, the study performed by Lin et al. reported that 62% of patients recovered AV conduction within 3 postoperative days (inter quartile range [IQR] 1–14 days) [4].

As reported in the KIDS database study, 72.6% of patients with CHB had spontaneous resolution of surgical AV block on an average of 9.7 postoperative days [5]. A comparable study by Ayyildiz et al. noted that 68.7% of patients recovered AV conduction spontaneously and among those, 97% of the patients regained AV conduction within the first 10 postoperative days [11].

In an attempt to better delineate those prognostic factors that might favor recovery of AV conduction, Driscoll et al. performed early invasive electrophysiological studies among 14 patients with postoperative CHB to identify site of block in regard to the bundle of His. They reported the site to be above in 5, within in 2, and below the His bundle in 4 patients. Site of block could not be determined in 3 patients. Spontaneous recovery of AV conduction occurred in 3/5 patients with block above the His bundle while recovery occurred in 0/2 patients with bock within and 1/4 patients with block below the His bundle, indicating that injury/damage to the more proximal AV conduction system might have a more favorable prognosis for recovery than more distal damage [16].

The recommendation Guidelines from the American College of Cardiology/American Heart Association/Heart Rhythm Society (ACC/AHA/HRS) for permanent pacemaker therapy for persistent CHB following cardiothoracic surgery in children and adolescent have remained relatively unchanged in this topic over the last two editions: 2008 and 2012. The Guidelines state as a Class I recommendation that permanent pacemaker placement is indicated if postoperative advanced second or third degree AV block persists for at least 7 days after surgical intervention or is not expected to resolve [17,18].

Whether a single ventricular or dual AV sequential pacemaker should be implanted will depend on cardiac anatomy, intrinsic ventricular contractility and patient size. In the current era of small diameter transvenous pacing leads, the debate of endocardial vs epicardial pacing has been less of an issue than in previous years. Although newer 4.1Fr diameter leads can be applied for use even in small children with minimal damage to valves and vessel diameters when compared to older larger diameter leads, epicardial steroid-eluting leads, implanted at the time of CHD surgical repair, remain a ready alternative since the leads can be inserted during the initial or subsequent surgeries [19,20]. Among patients with otherwise normal ventricular contractility, single chamber ventricular pacing may be sufficient to maintain effective cardiac output [21]. However, dual chamber pacing to maintain AV synchrony is typically required for patients with single ventricle physiology [22]. In the longest follow-up study to date, those CHD patients with postoperative CHB who develop heart failure due to ventricular dysfunction, have been shown to benefit clinically from biventricular or cardiac resynchronization pacing [23].

In summary, more than half of pediatric patients affected by postoperative CHB will recover 1:1 AV conduction and the recovery of AV synchrony occurs more frequently when the block is above the His