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Clinical predictors of permanent injury to the atrioventricular conduction system after congenital heart disease surgery. A new perspective on an old problem

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ABSTRACT

Objective: Complete heart block develops as a result of damage to the cardiac conduction system after 1–3% of open-heart surgeries for congenital heart disease. This study was performed to identify clinical predictors of permanent complete heart block in the immediate post-operative period.
Design: Retrospective cohort study.
Setting: Cardiac intensive care unit in two quaternary children's hospitals.
Patients: From 2004 to 2015, 5480 open-heart surgeries were performed. Seventy-four patients with complete heart block lasting >6 h were identified.
Measurements: The status of atrioventricular conduction was evaluated using pacemaker checks and 12-lead electrocardiograms. The patient data collected included gender, type of heart defect and surgery, age and weight at surgery, clinical parameters in the immediate post-operative period, presence of complications, and hospital mortality.
Main Results: Complete heart block complicated 1.35% of the open-heart surgeries with 58% representing transient block and 42% permanent block. Comparison between these two groups revealed that a longer surgery is a risk factor for permanent complete heart block. The other main risk factor was morbidity in the immediate post-surgical period, including severe hemodynamic compromise, mechanical ventilation longer than 5 days and a cardiac re-intervention within 14 days after surgery. Mortality was also higher in the group with permanent complete heart block. A multivariable logistic regression analysis showed that the significant risk factors for permanent atrioventricular conduction block included a cardiac re-intervention in the first 2 weeks after the initial surgery and the presence of moderate to severe post-operative complications.
Conclusions: Our study demonstrates that even if the cardiac conduction system suffers acute injury at the time of surgery in children with congenital heart disease and develops post-operative conduction defects, its restitution seems to be intrinsically related to the well-being of the system as a whole during the first 7 to 10 days after surgery.

1. Introduction

Injury to the atrioventricular (AV) conduction system is a well-known complication of surgical repair of congenital heart disease, resulting in 1 to 3% of post-operative patients developing complete heart block (CHB) in the current era [1]. These postoperative cardiac conduction blocks reportedly resolve spontaneously in most cases [2–4], usually within 10 days of the surgery in >90% of patients [5]. Several investigators have attempted to identify prognostic factors for post-operative CHB, including location of conduction disruption [6] and degree of conduction system injury assessed by morphology of the QRS escape mechanism [7]. The question "When to proceed to permanent pacemaker implantation for post-operative CHB in congenital heart disease?" has been addressed by several studies [8]. Current guidelines determined as a Class I indication for permanent pacing are "advanced second- or third-degree AV block that persists for at least 7 days and that is not expected to resolve" [9]. Current practice in most centers includes placement of a permanent pacemaker between post-operative days 7 and 14. Our experience is that patients with post-operative third-degree AV block represent a heterogeneous population and in many cases the current guidelines do not help in practical application, especially when faced to the decision of optimal timing for pacemaker implantation.

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The purpose of this study was to determine acute clinical predictors of permanent vs. temporary injury to the cardiac conduction system, in light of new statistical methods and the tremendous advances in the surgical and post-surgical management of congenital heart disease during the last 10 years.

2. Methods

The pediatric cardiac intensive care unit (CICU) and pacemaker databases of the Pediatric Hospital "Dr. Juan P. Garrahan" in Buenos Aires, Argentina, and of Cliniques Universitaires "St Luc", in Brussels, Belgium were reviewed. Pediatric patients that had CHB lasting >6 h following congenital heart disease surgery from year 2004 to 2015 were identified. The status of AV conduction was evaluated as per temporary pacemaker checks at least twice a day and daily 12- lead electrocardiograms were performed as per the CICU standardized protocols. Patient data collected included gender, presence of trisomy 21 (Down's syndrome), type of heart defect and surgery, and age and weight at surgery. Assessment of clinical parameters in the immediate post-operative period included presence of open chest; mechanical ventilation longer than 5 days; presence of cardiac rhythm abnormalities other than the AV block; need for a cardiac re-intervention within first 14 days after surgery; presence and type of complications; and hospital mortality. Severe hemodynamic compromise within the first 48 h after surgery was defined as the use of ≥2 inotropic drugs to maintain normal invasive mean pressure for age and body size. The US National Institutes of Health (NIH) tables for blood pressure levels according to height percentile in children were used to determine appropriate blood pressure measurements in each case [10]. The risk adjustment in congenital heart surgery 1 (RACHS-1) method for risk adjustment for congenital heart surgery was used to evaluate performance after surgery [11]. The total dataset was analyzed to determine patient characteristics and risk factors for post-operative development of permanent third-degree AV block.

3. Statistical Analysis

Patients were initially divided in 2 groups, depending of the status of AV conduction: permanent and transient AV block groups were compared. The mean comparisons were performed with unpaired Student's *t*-tests, or Mann-Whitney and Kruskal-Wallis tests. Frequencies were cross-tabulated and analyzed with chi-squared tests; and Fisher's exact tests were used when appropriate. Time data was presented as mean and range. Hazard ratio (HR), confidence intervals (CI) and *p*-values were calculated in univariate analysis. A multivariate analysis was adjusted on variables with a p-value < 0.15 in the univariate analysis, using a Cox model. Significance was defined as p-values < 0.05. SPSS version 22 software (IBM, Armonk, NY, USA) was used for all analyses.

4. Results

During the 10 year period from January 2004 to December 2015, 5480 open-heart surgeries were performed on cardiopulmonary bypass. Table 1 depicts the distribution of the type of congenital heart defect and the AV conduction status. Fig. 1 shows the flow diagram of those patients who developed post-surgical heart block. Seventy-four patients developed third-degree AV block lasting at least 6 h (1.35%); of these, 43 had transient AV block (58%) and 31 patients had permanent third-degree AV block (42%).

Comparison of the permanent AV block group with the temporary block group reveals no significant difference in age, weight, or gender at surgery, expressed as median and range (Table 2). There were 6 patients with Down syndrome (2 ventricular septal defects, 2 AV septal defects, and 2 Tetralogy of Fallot) and all of them suffered transient AV block. History of a previous cardiac intervention had no impact on the recovery of AV conduction. Longer surgeries were associated with development of permanent heart block. The presence of an open chest immediately after surgery also significantly reduced recovery of cardiac impulse conduction and resolution of heart blocks. Severe hemodynamic compromise and longer mechanical ventilation were related to permanent third-degree AV block. Interestingly, when evaluated with the RACHS-1 method, no significance could be identified between groups.

Table 1
Distribution of congenital heart defects.

CHD	Transient CAVB	Permanent CAVB	Total
VSD	15 (65)	8 (35%)	23
TOF	7 (64%)	4 (36%)	11
PA-VSD	3 (100%)	0 (0%)	3
SV	3 (60%)	2 (40%)	5
AVSD	3 (38%)	5 (62%)	8
DORV	2 (67%)	1 (33%)	3
MVD	2 (100%)	0 (0%)	2
L-TGA	2 (40%)	3 (60%)	5
D-TGA/VSD	1 (33%)	2 (67%)	3
LVOTO	1 (25%)	3 (75%)	4
APVC	2 (50%)	2 (50%)	4
TVD	1 (100%)	0 (0%)	1
AVD	1 (50%)	1 (50%)	2

APVC indicates anomalous pulmonary venous connection; CAVB, complete atrioventricular block; AVD, aortic valve disease; AVSD, atrioventricular septal defect; ccTGA-VSD, congenitally corrected transposition of great arteries with ventricular septal defect; CHD, congenital heart disease; DORV, double-outlet right ventricle; MVD, mitral valve disease; D-TGA-VSD, transposition of the great arteries with ventricular septal defect; LVOTO, left ventricular outflow tract obstruction; PA-VSD, pulmonary atresia-ventricular septal defect; SV, single ventricle; TVD, tricuspid valve disease; TOF, Tetralogy of Fallot and VSD, ventricular septal defect.

There was no difference in terms of presence of post-operative arrhythmias in patients who recovered AV conduction and those with permanent third-degree AV block. In addition, there was no difference in the number of patients who presented with junctional ectopic tachycardia (JET) between both groups (n = 4; 9% for the transient block group and n = 1; 3% for the permanent block group; $p = 0.39$). This discordance with previously reported literature [12] could be related with the small number of patients in our series.

Severe post-operative complications in the transient block group affected 4 patients (one each of surgical wound infection, endocarditis, pneumonia, and transient myocardial ischemia related to coronary compression after a right ventricle to pulmonary artery tube insertion). Complications in the permanent third-degree AV block group affected 17 patients and were predominantly cases of infection (n = 12, 70% of patients) including 4 sepsis, 3 wound infections, 3 pneumonias, 1 endocarditis, and 1 urinary tract infection, all unrelated to the permanent pacemaker implantation. Other complications for this group included cardiogenic shock, lung injury requiring chronic ventilation, cerebral sinus venous thrombosis, loss of capture of the transitory pacemaker wires, and arterial thrombosis with limb necrosis.

There was no significant difference in the presence of an escape rhythm (the limit of >40 bpm was set arbitrary as lower rates were not usually tested) or its characteristics measured in rate or width of QRS between both groups.

For those patients with transient blocks, the mean time to recovery of AV conduction was 5 ± 3.5 days (range 1 to 14 days). For patients with permanent third-degree AV block, 100% had a pacemaker implanted before discharge from hospitalization, with the device placement done at 9.0 ± 6.8 days after the initial surgery.

Hospitalization was longer in the group with permanent third-degree AV block (30.3 days versus 12.3 days; $p < 0.05$). In-hospital mortality occurred in 2 patients (4.6%) of the transient block group vs. 5 patients (16%) of the permanent block group ($p < 0.05$).

With the same set of clinical parameters, the logistic regression analysis was performed as discussed previously. In the multivariable logistic regression analysis, the significant risk factors for permanent third-degree AV block were length of the surgery (measured in aortic clamp

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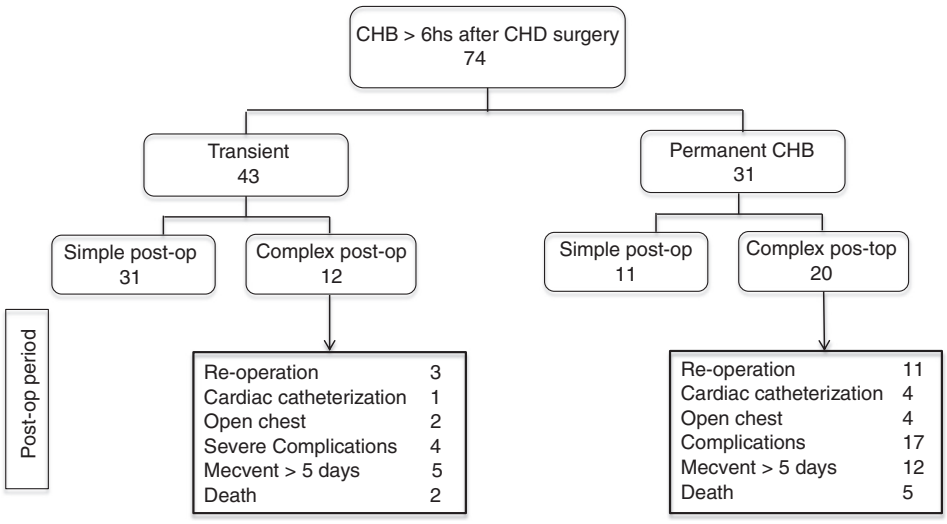

Fig. 1. Flow diagram of the study patients. CHB indicates complete heart block. CHD indicates congenital heart disease; mec vent: mechanical ventilation.

time), severe hemodynamic compromise during the first 2 days after surgery, indication of open-heart re-intervention during the same hospitalization and presence of severe systemic complications (Table 3). Of these, only the need for re-intervention and the presence of complications were statistically significant.

5. Discussion

CHB (or third-degree AV block) continues to be a significant complication following 1 to 3% of open-heart surgeries for congenital heart disease. The majority of these CHB patients (55 to 65%) recover AV conduction within the first 10 days after surgery. Permanent pacemaker implantation is not generally recommended before the end of this 10-day recovery period. However, the clinical features that may predispose an individual to the development of CHB have not previously been reported at length.

This study shows that individual patient characteristics such as sex, age, and weight do not influence the risk of permanent conduction defects. On the other hand, the length of the surgery and post-operative clinical complications are relevant for the recovery of normal AV conduction. One of the main predictors for permanent CHB was overall postsurgical morbidity, measured by number and severity of post-operative complications, with infection unrelated to the pacemaker implantation being at the top of the list. It is difficult to determine whether the longer hospitalization in the permanent block group was related to the requirement for device implantation or to non-conduction related complexities.

Multivariate analysis, which is the best statistical method for this type of study, determined that the 2 variables that increased the risk of permanent CHB with 85% certainty were the presence of post-operative complications and the need for surgical re-intervention in the early post-operative period. This finding supports implantation of a permanent pacemaker in those patients that need a surgical "re-do", even within the minimal 7-day waiting period.

Table 2
Comparison of patient characteristics for transient and permanent AVB.

Patient characteristics	Transient AVB	Permanent AVB	*p*
Age in months (median and range)	21.07 (2.77–211.10)	32.20 (0.27–183.97)	0.85
Weight (kg; median and range)	11.00 (4.00–63.20)	13.00 (3.20–55.00)	0.78
% male/female	25/18	13/18	0.33
Trisomy 21	6 (14%)	0	<0.05*
Previous surgery	15 (35%)	17 (55%)	<0.05*
Aortic clamp time (min)	71.86 ± 44.35	97.16 ± 51.75	<0.05*
Open chest	2 (4%)	4 (13%)	<0.05*
Severe HDC	12 (28%)	17 (55%)	<0.05*
RACHS-1 score	2 ± 0.58	3 ± 0.66	0.53
Ventilation days	1.83	7.74	<0.05*
Re-operation	3 (7%)	16 (52%)	<0.05*
Post-operative cath	1 (2%)	4 (13%)	<0.05*
Post-operative arrhythmia	7 (16%)	3 (12%)	0.75
Complications	12 (28%)	19 (61%)	<0.05*
Presence of escape rhythm	18 (42%)	17 (55%)	0.1
Escape rhythm rate (bpm)	78 ± 26	71 ± 15	0.32
Width of QRS (ms)	110 ± 18	111 ± 23	0.9
Days of hospitalization	12.35 (3–52)	30.35 (7–98)	<0.05*
Mortality (rate)	2 (4%)	5 (16%)	<0.05*

AVB indicates atrioventricular block; cath, catheterization; HDC, hemodynamic compromise; kg, kilogrammes; min, minutes; RASCH, Risk Adjustment in Congenital Heart Surgery.
* Statistically significant *p* value.

6. Conclusions

Our study demonstrates that the clinical status of pediatric congenital heart disease patients in the immediate post-operative period plays a fundamental role in the recovery of AV conduction after open-heart surgery. Is the clinical status preventing CHB from resolving, or are the children with permanent CHB sicker with more complications and hemodynamic instability? It is not yet possible to answer this question, as the controlling factors are interconnected and difficult to isolate.

7. Study Limitations

The present retrospective study reviews nodal conduction only on the short-term post-operative course during hospitalization. Evolution

Table 3
Multivariate logistic regression analysis. Predictors for AV conduction recovery in pediatric patients with post-surgical AVB.

Characteristics	Odds ratio	95% CI	*p* value
Aortic clamp time (min)	0.98	0.97–1.00	0.097
Severe HDC	0.14	0.01–1.94	0.145
Re-operation	0.07	0.014–0.37	<0.05*
Complications	0.13	0.24–0.72	<0.05*

AV indicates atrio-ventricular; AVB, atrioventricular block; HDC: hemodynamic compromise.
* Statistically significant *p* value.

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of cardiac conduction after this period has not been addressed and mortality data was limited to in-hospital deaths.

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Conflict of Interests

None.

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