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Incidence and risk factors of post-operative arrhythmias and sudden cardiac death after atrioventricular septal defect (AVSD) correction: Up to 47 years of follow-up☆,☆☆

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ABSTRACT

Background: Atrioventricular septal defect (AVSD) has an incidence of 4–5.3 per 10.000 live births and is associated with Down syndrome (DS). Data on arrhythmias and sudden cardiac death (SCD) after AVSD correction is scarce.
Aim: To analyse the incidence of post-operative arrhythmias and SCD after AVSD correction and explore risk factors.
Methods: This is a retrospective multicenter study including patients after biventricular AVSD correction. Univariate and multivariate analyses were performed to explore risk factors.
Results: A total of 415 patients were included with a mean follow-up duration of 9 years (range; <30 days–47 years). Early post-operative SVTs were documented in 33 patients (8%) and late post-operative SVTs in 15 patients (3.6%). Non-syndromic AVSD ($p = 0.022$, HR = 2.64; 95% CI = 1.15–6.04) and cAVSD ($p = 0.005$, HR = 3.7; 95% CI = 1.39–7.51) were independent risk factors for early post-operative SVTs and significant more late post-operative SVTs occurred in non-syndromic patients ($p = 0.016$, HR = 6.38; 95% CI = 1.42–28.71) and in pAVSD ($p = 0.045$, HR = 3.703; 95% CI = 1.03–13.32). Fifteen patients (3.6%) received a pacemaker. Non-syndromic AVSD ($p = 0.008$, HR = 15.82; 95% CI = 2.04–122.47), pAVSD ($p = 0.017$, HR = 6.26; 95% CI = 1.39–28.28) and re-operation ($p = 0.007$, HR = 4.911; 95% CI = 1.54–15.64) were independent risk factors for postoperative pacemaker implantation.
Late life-threatening ventricular arrhythmias and SCD occurred in 0.5% and 1.7% respectively.
Conclusion: There is good long-term survival after AVSD correction and incidence of SCD is low. Non-syndromic AVSD and cAVSD are independent risk factors for early post-operative SVTs. Non-syndromic AVSD patients have significant more early 3rd degree AVB and late post-operative SVTs. Non-syndromic patients with partial AVSD who have undergone reoperation have a significant higher risk of pacemaker implantation.

1. Introduction

Atrioventricular septal defect (AVSD) represents a spectrum of cardiac anomalies characterized by incomplete development of the atrioventricular septum along with abnormalities of the atrioventricular (AV) valves. The incidence of AVSD is 4–5.3 per 10.000 live births and it is associated with several syndromes, in particular Down syndrome (DS) [1]. Surgical repair can be accomplished with good long-term survival, with an estimated overall survival after 15 years of 88.6% [2].

In patients with an AVSD, the AV node and bundle of His are displaced inferiorly [3], predisposing the conduction system for injury during surgical repair [4]. Furthermore, functional properties of the conduction tissues can be suboptimal and may result in complete heart block [5]. In recent ACC/AHA guidelines regular evaluation of the status of AV conduction with ECG and periodic Holter monitoring in patients with repaired or palliated AVSD is recommended [5].

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An incidence of early and late post-operative supraventricular arrhythmias is reported in 9.6% and 11.7% respectively in patients with a partial AVSD [6] and the reported incidence of pacemaker implantation after AVSD correction ranges from 1.3% to 5.0% [6–11]. There is little data on the incidence of ventricular arrhythmia and sudden cardiac death (SCD) in AVSD patients [12]. Although clinical differences between isolated AVSD and AVSD in the setting of syndromal heart disease are overt [1], the difference between DS and non-syndromic patients with regard to conduction and rhythm disorders is not well established. Literature suggests that non-syndromic AVSD patients tend to have more post-operative arrhythmias, although to date there is no clear evidence about differences in post-operative arrhythmias or the need for permanent pacemaker implantation [13].

The aims of the current study were 1. To analyse the incidence of post-operative arrhythmias, especially late ventricular arrhythmias and SCD, after surgical repair of AVSD and 2. To explore potential factors, including DS and type of AVSD, contributing to the risk of rhythm- and conduction disorders after surgical repair of AVSD.

2. Methods

2.1. Study population and design

This is a retrospective multicenter study including all AVSD patients who underwent biventricular correction between June 1958 and January 2014. Patients were recruited from a surgical database of the Center of Congenital Heart Disease Amsterdam-Leiden (CAHAL) that includes all patients who have undergone surgical procedures at the Leiden University Medical Center (LUMC) and the Amsterdam Academic Medical Center (AMC), the Netherlands. Patients with an unbalanced AVSD who underwent univentricular repair and patients with heterotaxy syndrome were excluded from the study.

Data was obtained during follow-up by analyses of medical files, electronic records, 24-h Holter recordings, catheterisation reports, echocardiographic findings and electrocardiograms (ECGs). The majority of patients underwent routine follow-up at the paediatric or adult Cardiology departments of the LUMC or AMC, some patients underwent routine follow-up at their local hospital. Data, as far as obtainable, of these visits were collected.

Informed consent for retrospective observational studies is not mandatory according to Dutch law, provided the results are reported anonymously.

2.2. Pre-operative, peri-operative & post-operative data

Collected data consisted of gender, type of AVSD, associated cardiovascular anomalies, chromosomal abnormalities, ECG features and documented arrhythmias or conduction disorders. Treatment of all arrhythmias consisting of anti-arrhythmic drug treatment, electrical cardioversion, catheter ablations and pacemaker or implantable cardiac defibrillator (ICD) implantation were registered. Atrioventricular septal defect was subdivided in complete AVSD (cAVSD; both atrial and ventricular shunting) and partial AVSD (pAVSD; atrial or ventricular (intermediate AVSD) shunting). Down syndrome was confirmed by chromosomal analysis.

Collection of ECG-derived data included rhythm, heart rate, PR interval and QRS duration. Paediatric ECGs were scored according to normal values matched by age and heart rate [14]. An experienced researcher, supervised by a Paediatric Cardiologist and a Cardiologist specialized in grown-up congenital heart disease, examined the ECGs.

Peri-operative data consisted of type of surgical repair (single/double patch) and rhythm after cardiopulmonary bypass. As early surgical era may negatively influence survival and risk for reoperation, AVSD repairs were divided into two surgical eras: 1958 to 1995 and 1996 to 2014 [2].

Post-operative data consisted of post-operative arrhythmias and conduction disorders, early and late mortality and cause of death.

Early mortality was defined as mortality within 30 days after surgery or longer when death occurred with the patient still in hospital. Cause of death was classified as cardiac or non-cardiac. Sudden cardiac death (SCD) was defined as unexpected death within 1 h of cardiac symptom onset or unwitnessed death.

2.3. Rhythm & conduction disorders

Arrhythmias documented during the early post-operative period (<30 days) were defined as early onset post-operative arrhythmias and arrhythmias documented during the late post-operative period (>30 days) as late post-operative arrhythmias. Arrhythmias were classified as either tachy-arrhythmias or brady-arrhythmias.

2.4. Tachy-arrhythmias

Supraventricular tachycardia was subdivided in atrial flutter (AFL), atrial fibrillation (AF), atrial tachycardia (AT), junctional ectopic tachycardia (JET), atrioventricular re-entrant tachycardia (AVRT) and AV nodal re-entrant tachycardia (AVNRT).

Ventricular arrhythmias included ventricular tachycardia (VT) and ventricular fibrillation (VF).

2.5. Brady-arrhythmias

Sino-atrial node (SAN) dysfunction was reported as sinus bradycardia (SB), sick sinus syndrome (SSS), SA exit block and atrial or junctional escape rhythm. Rhythm was scored from ECGs and 24-h Holter reports.

Atrioventricular block (AVB) was categorized as 1st and 2nd degree AVB and complete AVB. Second degree AVB was further subdivided in type 1 Wenkebach and type 2 Mobitz block.

Bundle branch block was subdivided in right or left bundle branch block (RBBB, LBBB) and left anterior fascicular block (LAFB).

2.6. Pacemaker/ICD implantation

Pacemaker implantation was subdivided in early post-operative period (<30 days) and late post-operative period (>30 days) implantation. The indications for pacemaker and ICD therapy were documented.

2.7. Statistical analysis

All statistical analyses were performed with IBM SPSS Statistical software (version 20, IBM Corp., Armonk, New York, USA). Descriptive statistics were used to describe post-operative arrhythmias and the incidence of ICD and pacemaker implantation.

Univariate Cox regression analyses were performed to evaluate the effect of multiple variables, DS (DS versus non-syndromal), type of AVSD (pAVSD versus cAVSD), gender (male versus female) and surgical era (before 1996 versus after 1996), on the incidence of arrhythmias and pacemaker implantation. The variables DS and type of AVSD were further entered into a stepwise multivariate cox regression model to assess their independent value. Some variables were analysed in a time-dependent Cox model. A P-value of <0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

Overall, 428 patients underwent biventricular correction at our institute. Patients with other syndromes than Down syndrome ($n = 13$) were excluded from further analysis since the numbers of events were too low for risk stratification. However, an overview of arrhythmias that occurred in these patients is provided in **appendix 1.**

Therefore, 415 patients were included for further analysis with a mean follow-up duration of 9 years (range; <30 days – 47 years) (Fig. 1A). Among these, 238 (57%) had a cAVSD and 253 (61%) were diagnosed with DS (Table 1). In patients with a cAVSD, DS was present in 206 patients (87% of all cAVSD patients). The two most common additional cardiac malformations were patent ductus arteriosus (30%) and atrial septal defect type 2 (25%). Other additional cardiac anomalies are listed in Table 1.

Holter monitoring was available in 44 patients (11% of all patients), consisting of 17 patients with DS (7% of all patients with DS) and 27 non-syndromic patients (17% of all non-syndromic patients).

Overall mortality was 10.3%. In-hospital mortality occurred in 5.5% and late mortality in 4.8%. The main causes of late cardiac mortality were sudden cardiac death (1.7%) and heart failure (0.5%). Eighty-nine patients underwent 128 re-operations. Left atrioventricular valve pathology was the most common indication for reoperation, in 53.0%.

3.2. Tachy-arrhythmias

Among the included 415 patients, at least one episode of a SVT was documented in 48 patients (11.6%), further subdivided in AF ($n = 7$), AFL ($n = 8$), AVNRT ($n = 1$), AVRT (n = 1), JET ($n = 12$), unspecified SVT ($n = 29$), and VT or VF in 6 patients (1.9%) (Table 2). Some patients experienced more than one type of arrhythmia.

According to analyses of both early and late SVTs, significantly more SVTs occurred in non-syndromic patients ($P = 0.049$, HR = 1.79; 95% CI = 1.00–3.20). There were no statistically significant associations between the occurrence of SVT and gender ($p = 0.221$, HR = 1.45; 95% CI = 0.80–2.64), type of AVSD (pAVSD vs. cAVSD, $p = 0.719$, HR =