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ORIGINAL ARTICLE

Bradyarrhythmias in Repaired Atrioventricular Septal Defects: Single-Center Experience Based on 34 Years of Follow-Up of 522 Patients

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Abstract

Atrioventricular Septal Defect (AVSD) is a rare congenital heart defect (CHD) often associated with genetic syndromes, most commonly Down syndrome (DS). Over the last four decades, surgical repair has increased survival and improved quality of life in these patients. The prevalence of bradyarrhythmias namely, atrioventricular block (AVB) and sinus node dysfunction (SND) in AVSD is partially known. 522 cases with both partial and complete AVSD (38.7% with DS), undergoing intracardiac repair from 1982 to 2016 at our institution, were reviewed from our system database. 38 (7.3%) patients received permanent PM implantation for AVB (early or late) or SND. On one hand, AVB requiring PM was found in 26 (4.98%). This was further subdivided into early-onset 14 (2.6%) and late-onset AVB 12 (2.2%) (median 4 [IQR 1–7] years). On the other hand, 12 (2.3%) experienced late SND requiring PM (median 11 [IQR 3.5–15.2] years). Early and late AVB were independent from the type of AVSD (partial or complete), whereas the late SND was remarkably observed in complete AVSD compared to partial AVSD ($p=0.017$). We classified the cohort into two main categories: DS (202, 38.7%) and non-DS (320, 61.3%). At Kaplan–Meier survival analysis, DS was significantly associated with late-onset bradyarrhythmias ($p=0.024$). At Cox regression analysis, we identified DS as an independent predictor of PM implantation (HR 2.17). In conclusion, about 7% of repaired AVSD patients need PM implantation during follow-up. There are no differences in early and late AVB occurrence according to the type of AVSD. There is a higher incidence of late SND in repaired complete AVSD, with a later timing onset in patients with associated DS. Moreover, DS seems to be an independent predictor of PM implantation.

Keywords Congenital heart disease · Atrioventricular septal defect · Atrioventricular block · Sinus node dysfunction · Down syndrome · Pacemaker implantation

Abbreviations

AVSD	Atrioventricular septal defect
CHD	Congenital heart defect
DS	Down syndrome
AVB	Atrioventricular block
SND	Sinus node dysfunction
PM	Pacemaker

Introduction

Atrioventricular septal defects (AVSD) represent nearly 7% of all congenital heart diseases, with an incidence of approximately 4–5.3 per 10,000 live births [1]. AVSD comprise a broad spectrum of cardiac anomalies characterized by incomplete development of the septal tissue at the atrial and/or ventricular level, abnormalities of the atrioventricular valves, and can be either complete or partial [1]. AVSD can be an isolated finding or it can be associated with other cardiac defects or extracardiac abnormalities constituting a syndromic form (in almost 50% of AVSD). Many syndromes are associated with AVSD such as Down syndrome (DS), Heterotaxy, CHARGE Syndrome, Rasopathies, Holt Oram

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Syndrome, and many other genetic syndromes. Almost 50% of DS patients show AVSD (commonly complete and rarely partial AVSD) [2]. Conduction system injury remains the leading cause of postoperative cardiac morbidity. In the last decade, the incidence of postoperative complete or advanced high-degree atrioventricular block (AVB) has progressively declined compared to its first description by Lillehei at al. [3]. However, it continues to be a serious complication in approximately 1–3% of surgically repaired major CHDs [3–7]. The incidence of late AVB and sinus node dysfunction (SND), and their timing after surgery, are still unknown. AVB may variably occur months or years after surgery [8–11]. Indeed, postoperative arrhythmias, including AVB and SND, are serious complications in different AVSD forms including DS and non-DS populations [12]. So far, there are conflicting data in literature regarding the relationship between DS and bradyarrhythmias as a determinant factor for long-term outcomes [13–15].

The aim of this study was to explore the incidence of early and late AVB and SND requiring pacemaker (PM) implantation in a large single-center cohort of surgically repaired AVSD children and to determine the prognostic impact of DS during a long-term follow-up.

Materials and Methods

Study Design

In this single-center observational cohort study, we reviewed the medical records and operative findings of all patients with partial or complete AVSD who underwent intracardiac repair from 1982 to 2016 at our Institution. For each patient enrolled, data regarding demographics, cardiac diagnosis, age at first surgical repair, age at PM implantation, and genetic abnormalities were collected from the system database.

Length of follow-up was calculated as the time from the first operation to the date of the last follow-up visit at our Institution.

Informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

Study Population

The characteristics of the study population with inclusion and exclusion criteria are depicted in Fig. 1.

According to the International Pediatric and Congenital Cardiac Code [16], complete AVSD included an ostium primum atrial septal defect and a non-restrictive inlet ventricular septal defect with a single atrioventricular valve annulus

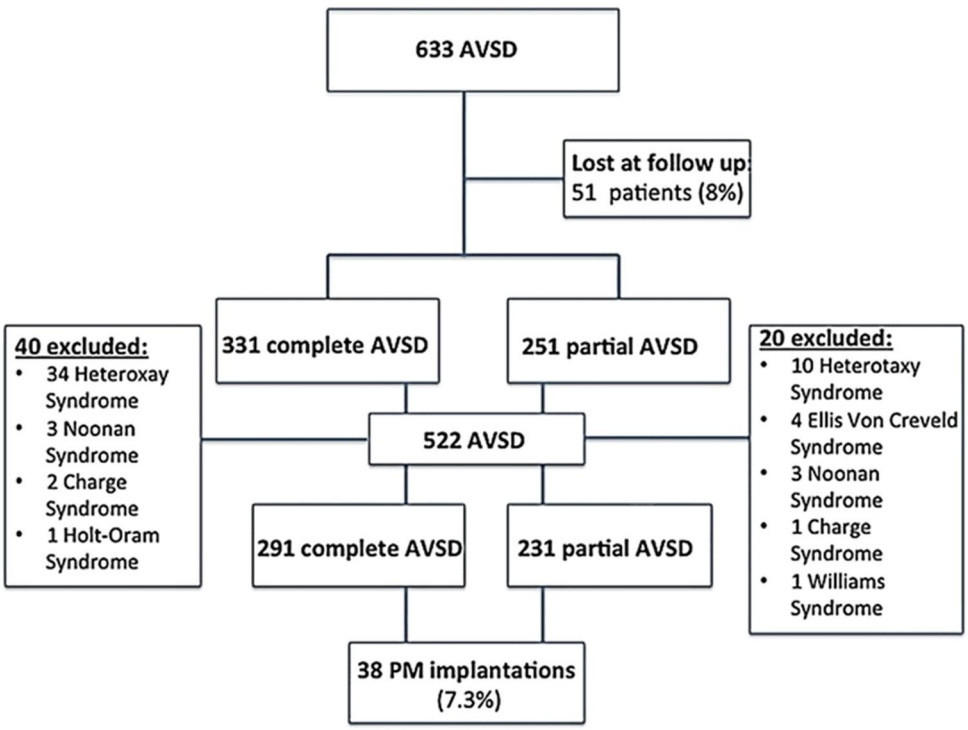

Fig. 1 Flow-chart of the study population. *AVSD* atrioventricular septal defect, *PM* pacemaker

and a common atrioventricular valve. Partial AVSD was defined as an AVSD with an isolated atrial component, also known as primum or ostium primum atrial septal defect, where the attachment of the bridging leaflets to the ventricular septum results in two orifices and shunting occurs at the atrial level. Ventricular septal defect in cAVSD was considered medium defined as aortic annulus, without difference between Down and not-Down subjects, but its prognostic impact on long-term arrhythmic complications was not significant.

DS was genetically confirmed in all patients by cytogenetic analysis.

We have excluded genetic syndromes, such as heterotaxy syndrome, Noonan, CHARGE usually associated to ASVD because it is still widely debated the influence of a genetic condition on surgical outcomes [17]. Indeed, in these patients, coexisting extracardiac malformations may predispose to a different preoperative and postoperative risk stratification. For example, heterotaxy syndrome carries a higher arrhythmic risk associated to anatomic and hemodynamic factors, as the intrinsic propensity to experience bradyarrhythmias [18].

Patients developing AVB or SND after a subsequent cardiac operation, unrelated to initial repair, were excluded because the AVB/SND was assumed as not due to AVSD repair.

The diagnosis of AVB or SND was documented on hospital records, ECG, 24-h Holter monitoring, exercise testing, and PM or Loop Recorder interrogation, whenever available.

AVB was defined as "early" if occurred within 30 days after first surgery, persisting for at least 7–10 days. It was considered "late" AVB if diagnosed at more than 30 days after first surgery, requiring PM implantation with class I indication according to the ACC/AHA/NASPE and ACCF/AHA/HRS guidelines and recent literature data [5, 19–23].

According to current guidelines, postoperative SND requiring PM implantation was considered as a late bradyarrhythmic condition [24].

Surgical Repair

Repair was accomplished by standard cardiopulmonary bypass with bicaval cannulation, mild-to-moderate hypothermia (28–32 °C), and intermittent infusion of anterograde blood cardioplegic solution. All preexisting shunts were divided at initiation of cardiopulmonary bypass.

All children with complete AVSD had closure of septal defects using the 2-patch technique. The ventricular patch was made of glutaraldehyde-treated autologous or heterologous pericardium and was shaped like a comma. The cleft of the left atrioventricular valve was closed with multiple interrupted monofilament sutures, and competence of the valve was assessed by filling the left ventricle with cold saline solution. Closure of the ostium primum atrial septal defect followed repair of the left atrioventricular valve and was also achieved by an autologous or heterologous pericardial patch, always leaving the coronary sinus on the right atrial side [25, 26].

Statistical Analysis

Categorical variables were reported as counts (percentage) and compared with Chi-square test. Continuous variables were first tested for Gaussian distribution with the one-sample Kolmogorov–Smirnov test. They were expressed as mean ± standard deviation (SD), and compared with unpaired Student *t* test, if normally distributed. They were instead reported as median and 1st–3rd quartiles and compared with Mann–Whitney *U* test if not normally distributed. Event-free survival was estimated by Kaplan–Meier method and compared by the log-rank test. Cox proportional hazards regression was used to calculate hazard ratios (HR) for PM implantation. Stochastic level of entry into the model was set at a p value of 0.10, and interaction terms were explored for all the variables in the final model. In the analysis, the time to event was the time from AVSD repair to PM implantation for late onset of bradyarrhythmias in years. A p value < 0.05 was considered as statistically significant.

Statistical analysis was performed using IBM SPSS Statistics, version 22 (SPSS Inc., Chicago, IL).

Results

The characteristics of the whole cohort of 633 pediatric patients screened, with inclusion and exclusion criteria, are shown in Fig. 1.

During follow-up (maximum 34 years, median 18, interquartile range [IQR] 11–23 years) 51 (8%) patients were lost. After excluding patients with isomerism and genetic syndromes other than DS, a total of 522 patients with partial and complete AVSD were recruited. DS was present in 202/522 patients (38.7%). There were four late deaths: three for end-stage heart failure and one for acute respiratory infection.

Thirty-eight patients (7.3%) underwent permanent PM implantation after first surgical correction for early or late AVB or SND. AVB occurred in 26 patients (~ 5%), with early onset in 14 (2.6% of all operated AVSD) and late onset in 12 (2.2%) (Median 4 [IQR 1–7] years; the latest at 17 years). Twelve patients (2.3%) experienced late-onset SND after surgery, with 10 patients developing late SND and 2 postoperative SND (median 11 [IQR 3.5–15.2] years; the latest at 19 years).

Patients requiring postoperative PM implantation were well balanced for gender, age at first surgical correction, DS prevalence, timing of late AVB and SND, age at PM

implantation, and mortality (Table 1). In these patients, there were major associated cardiac lesions such as 3 tetralogy of Fallot associated with complete AVSD, 1 cor triatum associated with complete AVSD, 3 aortic coarctation (2 associated with complete AVSD and 1 with partial AVSD), 1 partial abnormal pulmonary return associated with complete AVSD, 1 persistent left superior vena cava associated with complete AVSD, 1 double outlet right ventricle associated with complete AVSD, 1 subaortic stenosis associated to partial AVSD. Among minor associated cardiac lesions there were 5 posterior clefts (4 associated with partial AVSD and 1 with complete AVSD). None of them was associated to arrhythmic complications.

A progressive but not statistically significant decrease in postoperative bradyarrhythmias was observed from 1994 to 2016, with a more pronounced reduction in the occurrence of SND (Fig. 2a).

Complete AVSD Versus Partial AVSD

No differences in early AVB were found according to type of AVSD and a tendency towards a higher frequency of late AVB was found in partial AVSD patients. Conversely, a significant difference was observed in the incidence of late SND, which was significantly higher in patients with complete AVSD than with partial AVSD ($p=0.017$).

Down Syndrome Versus Non-Down Syndrome

There was no significant difference in mortality between DS and non-DS patients ($p=0.59$).

Table 1 Characteristics of patients with partial and complete AVSD undergoing PM implantation

	Partial AVSD ($n=17$)	Complete AVSD ($n=21$)	p
Male gender	10 (59)	9 (43)	0.32[a]
Age at first surgery (years)	4.1 ± 7.9	2.7 ± 3.9	0.5[b]
Down syndrome	7 (41)	13 (62)	0.2[a]
Age at PM implantation (years)	7.0 ± 8.6	8.9 ± 8.3	0.5[b]
Early AVB	7 (41)	7 (33)	0.62[a]
Late AVB	8 (47)	4 (19)	0.06[a]
Late SND	1 (6)	9 (43)	0.01[a]
Timing of AVB onset (years)	4.3 ± 3.5	6.6 ± 7.2	0.45[b]
Timing of SND onset (years)	2 ± 0	10.6 ± 6	0.22[b]
Mortality	2 (12)	2 (9.5)	0.55[a]

Values are expressed as number (%) or mean ± SD

AVB atrioventricular block, *AVSD* atrioventricular septal defect, *SND* sinus node dysfunction, *PM* pacemaker

[a]Chi-square test

[b]Independent *t* test

Dividing patients who received a PM according to the presence (20, 9.9%) or absence of DS (18, 5.6%), gender, age at first surgery, age at PM implantation, and type of AVSD were not significantly different (Table 2).

Moreover, no significant differences were found in early or late AVB occurrence in non-DS category, requiring PM implantation. Conversely, a significant difference was recorded in late vs early AVB occurrence among DS patients ($p=0.02$).

No significant differences were found in the incidence of late SND, requiring PM implantation, when comparing DS versus non-DS patients, but only during long-term follow-up, in timing of onset after surgical correction.

Whereas a significant difference was observed in timing of SND onset after surgical correction, which occurred later in DS patients (median 15 [IQR 8.5–17.5] years; the latest at 19 years) than in non-DS patients (median 4 [IQR 2–11] years; the latest at 13 years) ($p=0.019$).

At Kaplan–Meier survival analysis, the presence of DS was significantly associated with late onset of both bradyarrhythmic disorders requiring PM implantation (DS vs. non-DS patients: median 5 [IQR 0.6–15] years vs. median 4 [IQR 2.5–8.5] years) (log-rank test: $p=0.024$) (Fig. 2b).

Furthermore, at Cox regression analysis adjusted for other possible confounding variables, such as age and type of AVSD, DS was found to be an independent predictor of PM implantation in the overall population (HR 2.17 [IQR 1.12–4.46], $p=0.029$).

Discussion

So far, this is one of the longest follow-up studies that investigated the occurrence of bradyarrhythmias requiring PM implantation in a large single-center cohort of children who had undergone surgical repair of both complete and partial AVSD between 1982 and 2016. Despite the improvement of surgical techniques over the past decades, AVSD repair is still associated with a high incidence of postoperative arrhythmias [27]. Our PM implantation rate (7.3%) was higher compared with previous data [26, 28, 29], probably because all types of AVSD were considered in our cohort. The children who needed PM for early AVB represented 2.6% of the whole population, a proportion similar to that reported by St. Louis et al. [28] in a multicenter data analysis of only complete AVSD operated in the recent era. However, AVB may also occur late from a few months to as late as more than 30 years after the initial surgical repair, with a highly variable incidence ranging from 0.1 to 4.5% [8, 12, 22, 29]. Importantly, different from other large cohort studies with long-term follow-up after repair surgery, our population was composed exclusively of patients with complete

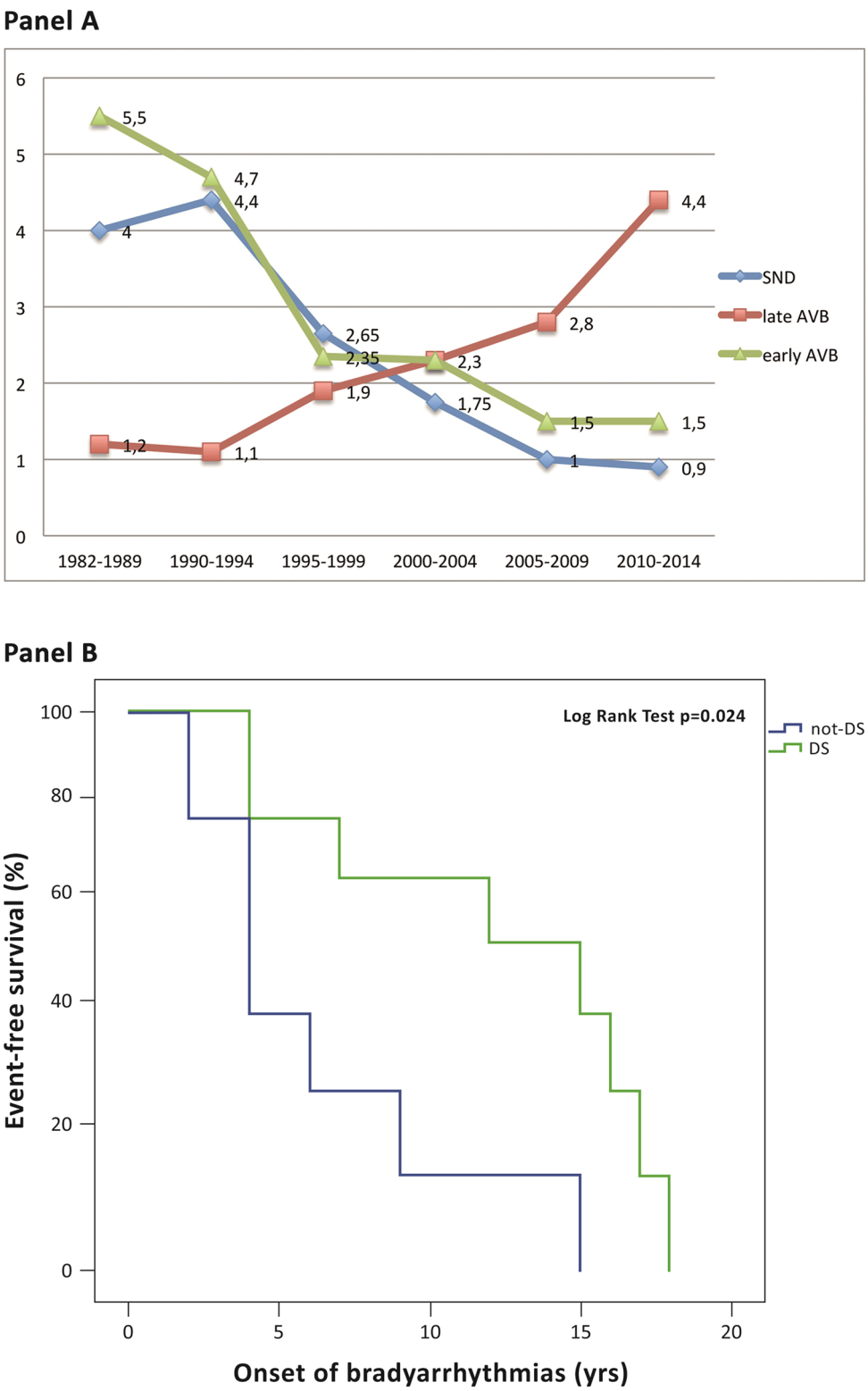

Fig. 2 Temporal trends in the incidence of postoperative bradyarrhythmias according to the year of intervention, mostly grouped in 4-year intervals. **a** *AVB* atrioventricular block, *SND* sinus node dysfunction; **b** Kaplan–Meier event-free survival curves for patients with late-onset bradyarrhythmias requiring pacemaker implantation. *DS* Down syndrome patients, *not-DS* non-syndromic patients

or partial AVSD and we found an overall incidence of 2.2% late AVB.

Early occurrence of postoperative AVB may be a consequence of surgical procedures near the atrioventricular node, whereas late onset of AVB has been postulated as a result of progressive fibrosis in the surgical site near the atrioventricular node with slow sclerosis extending over the fragile conduction pathway [8]. In our population, occurrence of early or late AVB not significantly differed between partial and complete AVSD, not affecting their postoperative follow-up.

Table 2 Characteristics of patients with and without Down syndrome undergoing PM implantation

	DS ($n=20$)	Non-DS ($n=18$)	p
Male gender	10 (50)	9 (50)	1.0[a]
Age at first surgery (years)	3.2 ± 7.4	3.4 ± 4.2	0.94[b]
Complete AVSD	13 (65)	8 (44)	0.2[a]
Partial AVSD	7 (35)	10 (56)	0.2[a]
Age at PM implantation (years)	9.8 ± 9.8	6.1 ± 6.0	0.16[b]
Early AVB	6 (30)	8 (44)	0.36[a]
Late AVB	8 (40)	4 (22)	0.24[a]
Late SND	5 (25)	5 (28)	0.85[a]
Timing of AVB onset (years)	5.6 ± 5.7	4.0 ± 2.4	0.61[b]
Timing of SND onset (years)	13.4 ± 5.6	6.0 ± 4.8	0.05[b]
Mortality	1 (5)	3 (17)	0.5[a]

Values are expressed as number (%) or mean ± SD

AVB atrioventricular block, *AVSD* atrioventricular septal defect, *DS* Down syndrome, *SND* sinus node dysfunction, *PM* pacemaker

[a]Chi-square test

[b]Independent *t* test

This could be probably explained by the fact that the surgery risk of AVB is correlated to the posterior displacement of the conduction system, located close to the coronary sinus, which can be observed both in partial and complete AVB.

In our study, the development of late SND (2.1%) and its significant association with complete AVSD, rather than with partial AVSD (Table 1), could be explained by the more complex surgical techniques used and the longer procedural operative time [24].

Notably, in our experience, the incidence of postoperative bradyarrhythmic complications has decreased since 1994, with a more marked reduction in SND onset. Thus, the presence of a learning curve in performing AVSD operations, the development of advanced surgical instruments and, as recently shown by Murray et al. [30], reduced extracardiac circulation times may account for the decreasing annual rates of PM implantation (Fig. 2a), as also reported in other populations after 1993 [29]. Nonetheless, we observed a slight, progressive increase in the incidence of late AVB, which could be related to earlier surgical repairs and to a concomitant increase in AVSD repairs over time (Fig. 2a).

Interestingly, in our study, no proportional difference between the presence of DS or age at first operation was found in patients who required PM implantation, as shown by St. Louis et al. [28]. In particular, we did not find any difference in neither early nor late development of AVB between DS and non-DS patients, in contrast with literature data, although in the vast population of Tucker et al. the risk of AVB was analyzed only after isolated perimembranous ventricular septal defect surgery and was significantly associated with a lower age at surgical repair [26, 29]. Conversely, a higher incidence of late vs early AVB was observed in patients with DS after surgical repair of AVSD ($p=0.02$), similarly to what reported by Banks et al. [12]. In addition, DS patients underwent PM implantation later than non-DS patients ($p=0.024$, Fig. 2b). Of note, the impact of DS on the need for PM placement could be probably related to less detectable clinical symptoms or surgical better outcomes of these patients compared with non-syndromic subjects [15]. The role of DS in determining long-term outcomes of patients with prior AVSD surgical repair is still a controversial issue. Children with DS have been described at increased risk for perioperative and long-term mortality and have a predisposition to postoperative complications [31]. Nonetheless, previous studies suggested improved outcomes for patients with DS undergoing AVSD surgery [14, 15]. Other studies reported no significant differences in 30-day mortality and 20-year survival between patients with and without DS [13, 14]. At our Cox regression analysis adjusted for age and type of AVSD, DS was a predictive factor for PM implantation probably because, "the AV node remains in dorsal position close to the coronary sinus ostium with a long non branching bundle that runs through of the AV node and ventricular conduction system in AVSD and DS differs from normal development, which can be a causative factor in the development of AV conduction disturbances" [32].

Thus, although the risk of late development of bradyarrhythmias has decreased over time, it remains a significant cause of morbidity and of increased costs due to the need for PM implantation [5], suggesting that a close follow-up is advisable for patients undergoing surgical repair of both partial and complete AVSD.

Limitations of the Study

The observational nature of this study is the main limitation. Another important limitation is that the surgical techniques used in all patients were not examined in detail and, considering the long follow-up, these could have evolved over time.

In addition, our large population consists of both partial and complete AVSD.

Finally, we could not ascertain whether the late onset of AVB and SND was related to the first cardiac surgery or to further cardiac surgeries that were not considered in this study.

Conclusion

In conclusion, our experience suggests that about 7% of repaired AVSD patients need PM implantation during a long-term follow-up. There are no differences in early and

late AVB occurrence according to the type of AVSD. Of note, there is a higher incidence of late SND in repaired complete AVSD, with a later timing onset in patients with associated DS. Moreover, DS seems to be an independent predictor of PM implantation. So, a close and long-term follow-up may be useful for the early identification of potential life-threatening arrhythmias in high-risk patients.

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Compliance with Ethical Standards

Conflict of interest The authors have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Informed Consent Informed consent was obtained from all individual participants included in the study.

References

1. Calkoen EE, Hazekamp MG, Blom NA et al (2016) Atrioventricular septal defect: from embryonic development to long-term follow-up. Int J Cardiol 202:784–795
2. Christensen N, Andersen H, Garne E et al (2013) Atrioventricular septal defects among infants in Europe: a population-based study of prevalence, associated anomalies, and survival. Cardiol Young 23:560–567
3. Lillehei CW, Sellers RD, Bonnabeau RC, Eliot RS (1963) Chronic postsurgical complete heart block. With particular reference to prognosis, management, and a new P-wave pacemaker. J Thorac Cardiovasc Surg 46:436–456
4. Bonatti V, Agnetti A, Squarcia U (1998) Early and late postoperative complete heart block in pediatric patients submitted to open-heart surgery for congenital heart disease. Pediatr Med Chir 20:181–186
5. Gross GJ, Chiu CC, Hamilton RM, Kirsh JA, Stephenson EA (2006) Natural history of postoperative heart block in congenital heart disease: implications for pacing intervention. Heart Rhythm 3:601–604
6. Anderson JB, Czosek RJ, Knilans TK, Meganathan K, Heaton P (2012) Postoperative heart block in children with common forms of congenital heart disease: results from the KID database. J Cardiovasc Electrophysiol 23:1349–1354
7. Weindling SN, Saul JP, Gamble WJ, Mayer JE, Wessel D, Walsh EP (1998) Duration of complete atrioventricular block after congenital heart disease surgery. Am J Cardiol 82:525–527
8. Laurens P, Gavelle P, Piwnica A, Farge C, Dubost C, Maurice P (1983) Severe postoperative heart blocks appearing late. 16 cases. Arch Mal Coeur Vaiss 76:1132–1139
9. Nishimura RA, Callahan MJ, Holmes DR Jr et al (1984) Transient atrioventricular block after open-heart surgery for congenital heart disease. Am J Cardiol 53:198–201
10. Godman MJ, Roberts NK, Izukawa T (1974) Late postoperative conduction disturbances after repair of ventricular septal defect and tetralogy of Fallot. Analysis by his bundle recordings. Circulation 49:214–221
11. Moss AJ, Klyman G, Emmanouilides GC (1972) Late onset complete heart block. Newly recognized sequela of cardiac surgery. Am J Cardiol 30:884–887
12. Banks MA, Jenson J, Kugler JD (2001) Late development of atrioventricular block after congenital heart surgery in Down syndrome. Am J Cardiol 88:A7:86–89
13. Lange R, Guenther T, Busch R, Hess J, Schreiber C (2007) The presence of Down syndrome is not a risk factor in complete atrioventricular septal defect repair. J Thorac Cardiovasc Surg 134:304–310
14. Al-Hay AA, MacNeill SJ, Yacoub M, Shore DF, Shinebourne EA (2003) Complete atrioventricular septal defect, Down syndrome, and surgical outcome: risk factors. Ann Thorac Surg 75:412–421
15. Saffirio C, Marino B, Formigari R (2008) Better surgical prognosis for patients with Down syndrome. J Thorac Cardiovasc Surg 135:230
16. Giroud JM, Jacobs JP, Spicer D et al (2010) Report from the international society for nomenclature of paediatric and congenital heart disease: creation of a visual encyclopedia illustrating the terms and definitions of the international pediatric and congenital cardiac code. World J Pediatr Congenit Heart Surg 1:300–313
17. Formigari R, Michielon G, Digilio MC et al (2009) Genetic syndromes and congenital heart defects: how is surgical management affected? Eur J Cardiothorac Surg 35:606–614
18. Niu MC, Dickerson HA, Moore JA et al (2018) Heterotaxy syndrome and associated arrhythmias in pediatric patients. Heart Rhythm 15:548–554
19. Gregoratos G, Abrams J, Epstein AE American College of Cardiology/American Heart Association Task Force on Practice Guidelines/North American Society for Pacing and Electrophysiology Committee to Update the 1998 Pacemaker Guidelines et al (2002) ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE Committee to Update the 1998 Pacemaker Guidelines). Circulation 106:2145–2161
20. Epstein AE, DiMarco JP, Ellenbogen KA American College of Cardiology Foundation; American Heart Association Task Force on Practice Guidelines; Heart Rhythm Society et al (2013) 2012 ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Circulation 127:e283–e352
21. Batra AS, Wells WJ, Hinoki KW, Stanton RA, Silka MJ (2003) Late recovery of atrioventricular conduction after pacemaker implantation for complete heart block associated with surgery for congenital heart disease. J Thorac Cardiovasc Surg 125:1291–1293
22. Liberman L, Pass RH, Hordof AJ, Spotnitz HM (2008) Late onset of heart block after open heart surgery for congenital heart disease. Pediatr Cardiol 29:56–59
23. Brignole M, Auricchio A, Baron-Esquivias G et al (2013) 2013 ESC guidelines on cardiac pacing and cardiac resynchronization therapy: the task force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). Europace 15:1070–1118
24. Goldman BS, Williams WG, Hill T et al (1985) Permanent cardiac pacing after open heart surgery: congenital heart disease. Pacing Clin Electrophysiol 8:732–739

25. Alexi-Meskishvili V, Ishino K, Dähnert I et al (1996) Correction of complete atrioventricular septal defects with the double-patch technique and cleft closure. Ann Thorac Surg 62:519–524
26. Devlin PJ, Backer CL, Eltayeb O, Mongé MC, Hauck AL, Costello JM (2016) Repair of partial atrioventricular septal defect: age and outcomes. Ann Thorac Surg 102:170–177
27. Delaney JW, Moltedo JM, Dziura JD, Kopf GS, Snyder CS (2006) Early postoperative arrhythmias after pediatric cardiac surgery. J Thorac Cardiovasc Surg 131:1296–1300
28. St Louis JD, Jodhka U, Jacobs JP et al (2014) Contemporary outcomes of complete atrioventricular septal defect repair: analysis of the Society of Thoracic Surgeons Congenital Heart Surgery Database. J Thorac Cardiovasc Surg 148:2526–2531
29. Tucker EM, Pyles LA, Bass JL, Moller JH (2007) Permanent pacemaker for atrioventricular conduction block after operative repair of perimembranous ventricular septal defect. J Am Coll Cardiol 50:1196–1200
30. Murray LE, Smith AH, Flack EC, Crum K, Owen J, Kannankeril PJ (2017) Genotypic and phenotypic predictors of complete heart block and recovery of conduction after surgical repair of congenital heart disease. Heart Rhythm 14:402–409
31. Morris CD, Magilke D, Reller M (1992) Down's syndrome affects results of surgical correction of complete atrioventricular canal. Pediatr Cardiol 13:80–84
32. Blom NA, Ottenkamp J, Deruiter MC, Wenink ACG, Gittenberger-De Groot AC (2005) Development of the cardiac conduction system in atrioventricular septal defect in human trisomy 21. Pediatr Res 58:516–520