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Long-term outcome after surgical correction of sinus venosus defect in a nationwide register-based cohort study

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ABSTRACT

Objectives: Long-term results after sinus venosus defect (SVD) closure are sparse and many studies lack a proper control cohort. This nationwide cohort evaluated the long-term outcome after SVD surgery.

Methods: The study enrolled every surgical SVD correction from the nationwide hospital discharge registry (FHDR) and surgical registries of two tertiary centers. Patients with more complex congenital heart defects were excluded. Surgeries were performed from 1969 to 2019. Five sex and birth-year-matched controls per SVD patient were gathered from the general population.

Results: In total, 182 surgical SVD corrections were performed during the study period. The median age at the time of surgery was 8.3 years (range 0.06–75.7), and the majority (77.5%, $n = 141$) were under 18 years old. The median follow-up period was 18 years (range 0.1–53).

There was no significant difference in mortality during the follow-up (logrank $p = 0.62$, MRR 0.78, 95% CI: 0.30–2.0). However, SVD patients had elevated risk for new-onset atrial fibrillation (RR 4.9, 95% CI: 2.2–10.9), heart failure (RR 4.0, 95% CI: 1.2–13.2), ischemic heart disease (4.3, 95% CI, 1.5–11.7), migraine (RR 3.6, 95% CI: 1.5–9.1) and sick sinus syndrome, II- or III-degree AV-block or pacemaker implantation (RR 11.3, 95% CI: 2.9–43.8).

Conclusion: Young patients with SVD have an excellent survival prognosis after the surgery. Risk for sick sinus syndrome or conduction disorders, atrial fibrillation, and heart failure remains elevated in the long-term follow-up.

1. Introduction

Sinus venosus defect (SVD), described for the first time in 1858, accounts for an estimated 5% of all atrial septal defects (ASD) [1,2]. Defects are divided into superior and inferior types, with the superior type accounting for most instances. The most prevalent abnormality is an interatrial connection produced by a defect in the common wall between the superior vena cava (SVC) and the right-sided pulmonary veins [3,4], often resulting in anomalous pulmonary venous return (PAPVR). Some experts even suggest that SVD should be considered a venovenous defect [5].

The basic idea behind SVD surgical repair is to divert the pulmonary venous blood back to the left atrium and close the atrial septal defect without jeopardizing adjacent tissues.

Different techniques for SVD surgery include single patch, double patch, Warden procedure, and channelling the SVD with PAPVC using an autologous right atrial appendage. Compared to secundum ASD repair, the surgical technique for SVD is more intricate and carries a risk of SVC or pulmonary vein stenosis, residual shunting, and sinoatrial node dysfunction.

More recently, a transcatheter approach has been developed for SVD closure [6]. As the transcatheter approach is making its way to superior sinus venosus-type defects, it is important to study the prognosis after closure with current methods. However, many studies to date are

Abbreviations: ASD, Atrial septal defect; CI, Confidence interval; FHDR, Finnish hospital discharge registry; IQR, Interquartile range; NYHA, New York Heart Association; OR, Odds ratio; PAPVR, Partially anomalous pulmonary venous return; RR, Risk ratio; SVD, Sinus venosus defect.

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limited by a small study series, short follow-up time or a lack of a control cohort.

This study was set up to examine the outcomes of patients who underwent SVD correction, focusing on patient survival and the development of comorbidities during the long-term follow-up.

2. Methods

2.1. Study population

All patients with a diagnosis code for sinus venosus type atrial septal defect (Q2112) were gathered from the Finnish hospital discharge registry (FHDR) ($n = 299$), and patients with more complex congenital heart defects were excluded ($n = 125$). This exclusion included all diagnoses for congenital heart defects except patent foramen ovale, patent ductus arteriosus, or partial anomalous pulmonary venous return. Of the remaining 174 patients, 108 did not have procedural codes for ASD closure and were excluded from the analysis. After exclusions, 66 patients were included from the FHDR.

In addition, Children's hospitals' and Turku University Hospitals' surgical registers were combined with the FHDR data. All pediatric cardiac surgery patients in Finland are referred for surgery to the Helsinki Children's Hospital. We gathered all patients with sinus venosus diagnosis codes from the Children's Hospital surgical registry. Children's Hospital's data was further validated by reviewing surgical operation notes. Patients with more complex congenital heart defects were not included in the study. After duplicate deletion, in total 116 patients were included from the surgical registries.

Follow-up data were gathered until the end of 2019. However, 59 patients from the.

Children's Hospital surgical registry had long-term mortality data available only until 2012. Follow-up data consisted of mortality data from Statistics Finland's causes of death registry and diagnosis data from the Finnish hospital discharge registry. Control population was gathered from the digital and population data services agency and consisted of five sex and birth-year-matched controls per one SVD patient.

2.2. Statistical analysis

The results are expressed as mean (standard deviation) or median (range). Counts and percentages were used to summarize categorical variables. Cumulative events of deaths and a composite outcome of atrial fibrillation, heart failure, heart surgery, or death events were plotted using Kaplan-Meier estimates. Follow-up was set to start from the date of the operation. Poisson regression with 95% confidence intervals was used to calculate incidence risk ratios (RRs) based on first-event incidence rates. The Chi-square test or Mann-Whitney *U* test was used to compare baseline characteristics. In addition, odds ratios were calculated for major comorbidities prior to surgery. All analyses were performed using R software, version 4.2.1.

2.3. Ethics

The Helsinki University Hospitals Ethics Committee accepted this study on 11.7.2019 (number HUS/1820/2019), which was carried out following the Helsinki Declaration. For registry-based research, no patient permission was required.

3. Results

3.1. Study cohort

In total, 182 (Women 99 (54.4%)) sinus venosus type ASD patients were included in the study (Table 1). Median follow-up was 18.2 years (range 0.1–53.8 years), resulting in a total follow-up time of 3378 patient-years. The median age at the time of surgery was 8.3 years (range 0.06–75.7 years), and the majority (77.5%, $n = 141$) were under 18 years old (Fig. 1). The patients operated on before 2000 were, on average, younger at the time of operation compared to patients operated during 2000–2019, 8.3 years vs. 23.5 years ($p < 0.001$).

Table 1
Baseline characteristics.

	Controls	SVD	*p*-value
	***N* = 888**	***N* = 182**	
Date of the surgery	NA	2000 (1987–2012)	NA
Age at the time of surgery	NA	8.34 (4.37–16.74)	NA
Sex (female)	489 (55.1%)	99 (54.5%)	0.93
HF*	3 (0.51%)	5 (4.07%)	**0.005**
Stroke*	4 (0.67%)	4 (3.25%)	**0.033**
AF*	4 (0.67%)	9 (7.32%)	**<0.001**
SSS*	1 (0.17%)	0 (0.86%)	1.00
CAD*	11 (1.85%)	5 (4.07%)	0.17
Hypertension*	10 (1.69%)	4 (3.25%)	0.43

Data is presented as median (interquartile range) or number of events (percentage).
* Data available for 123 cases and 593 controls. AF = Atrial fibrillation, CAD = Coronary artery disease, HF = Heart failure, SSS = Sick sinus syndrome, SVD = Sinus venosus defect.

All pediatric patients were operated on at a single center. A single patch closure technique was used for pediatric patients whenever the anatomical relation of right pulmonary vein openings and septal defect would allow. Otherwise, a second patch was used to enlarge the upper vena cava continuity to the right atrium. The exact number of each technique used was not available. Cardiopulmonary bypass was used in every surgery.

3.2. Mortality

The whole cohort of 182 patients was used to study long-term mortality. The follow-up was until the end of 2019 in 123 patients and until 2012 in 59 patients. There were five deaths among SVD patients and 31 deaths among controls during the follow-up. There was no surgery-related mortality and no deaths in the 30-day period following the surgery. Mortality risk ratio was 0.78 (95% CI: 0.30–2.01) during the follow-up period. There was no difference in mortality in any of the subgroups shown in Table 2 (sex, year of the surgery, age at the time of surgery) (Table 2).

3.3. Morbidity

123 SVD patients and 593 controls were used to study the long-term morbidity after the sinus venosus surgery. SVD patients had more often heart failure, stroke, or atrial fibrillation before the surgery when compared to controls. The odds ratio prior to surgery for heart failure was 8.1 (95% CI: 1.9–42.4), for atrial fibrillation 12.6 (95% CI: 4.1–48.1), and for stroke 4.9 (95% CI: 1.1–22.0).

During the follow-up, SVD patients had an elevated risk for new-onset atrial fibrillation (AF), heart failure, ischemic heart disease, migraine and sick sinus syndrome, II- or III-degree AV-block, or pacemaker implantation (Fig. 3). Four patients (3.3%) got pacemaker during the follow-up, and no pacemaker implantations were seen in the control population.

Atrial fibrillation was seen in 9 patients before the surgery and 12 patients during the follow-up, totaling an AF risk of 17% at the end of follow-up. Patients with atrial fibrillation during the follow-up were older at the time of operation than those without atrial fibrillation (mean age 40.8 years vs. 18.0 years, $p = 0.009$). The risk ratio for composite outcome of death, atrial fibrillation, stroke, or heart failure was 2.40 (95% CI:1.36–4.22) (Fig. 2).

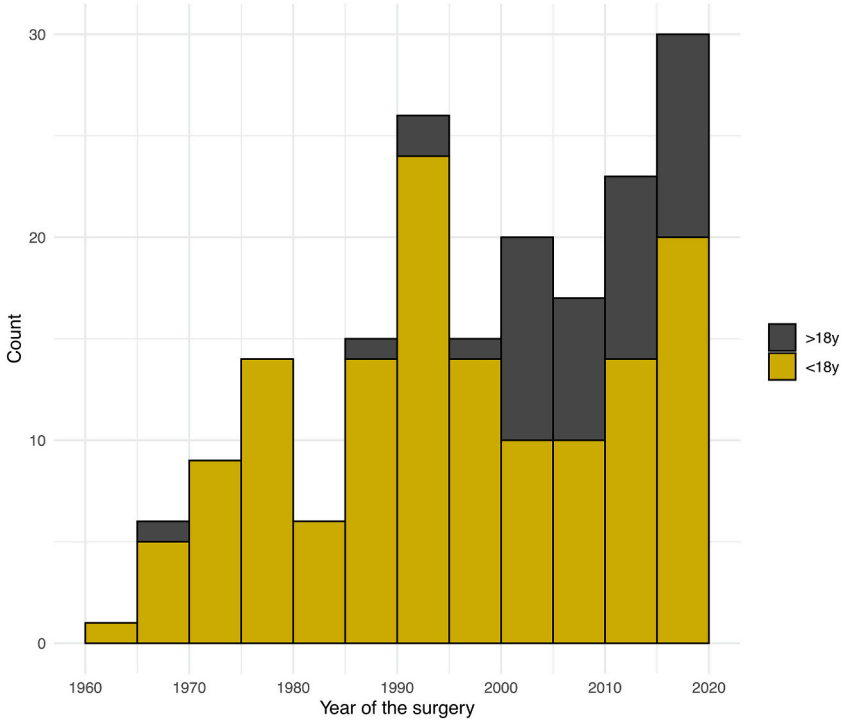

Fig. 1. Sinus venosus defects operated per five-year period.
Caption: Yellow bars indicate pediatric patients, and dark grey bars adult patients. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2
Follow-up time, number of deaths, and all-cause mortality rates (per 1000 person-years) in different groups.

	SVD				Controls			
	Group	P-years	Event	Rate (95% CI)	P-years	Event	Rate (95% CI)	MRR (95% CI)
Sex	Male	1489	3	2.0 (0.42–5.89)	7192	17	2.36 (1.38–3.78)	0.85 (0.25–2.91)
	Female	1988	2	1.0 (0.12–3.63)	9635	14	1.45 (0.79–2.44)	0.69 (0.16–3.05)
Age at the time of surgery	≤ 18	2978	2	0.67 (0.08–2.43)	14,448	11	0.76 (0.38–1.36)	0.88 (0.20–3.98)
	> 18	499	3	6.01 (1.24–17.57)	2380	20	8.40 (5.13–12.98)	0.72 (0.21–2.41)
Year of the surgery	< 1980	1262	1	0.79 (0.02–4.41)	6325	8	1.26 (0.55–2.49)	0.63 (0.08–5.01)
	1980–2000	1506	2	1.33 (0.16–4.80)	7112	8	1.12 (0.49–2.22)	1.18 (0.25–5.56)
	> 2000	708	2	2.82 (0.34–10.20)	3391	15	4.42 (2.48–7.30)	0.64 (0.15–2.79)

The risk ratios reported are crude risk ratios. The exact approach is used to compute confidence intervals. MRR = Mortality risk ratio, P-years = Person-years, SVD = Sinus venosus defect.

4. Discussion

We report the long-term outcomes of the largest cohort of SVD to date. We showed excellent long-term survival after surgical SVD correction, and the mortality was similar to the individualized controls.

Studies on the mortality of all ASD patients suggest that the mortality is similar to the control population if the defect is closed before age 30 [7,8]. This study shows that this also applies to SVD patients, as most patients were under 30 years of age at the time of surgery in this study. Previous studies have also found that there does not seem to be a difference in the long-term outcome between patients with secundum or sinus venosus type ASD if the defect is closed at a young age [9,10]. However, when comparing the short-term prognosis of inferior type sinus venosus defects to secundum defects, there seem to be worse technical outcomes and a higher reintervention rate [11]. In this study, no distinction was made between superior and inferior SVD.

SVD patients had significantly more cardiac morbidity during the follow-up (atrial fibrillation, heart failure, sick sinus syndrome, AV-block, and ischemic heart disease). A major known comorbidity after SVD surgery is sinus node dysfunction. We found sick sinus syndrome, II- or III-degree AV block, or pacemaker implantation in 7 of the 123 (5.6%) patients. This finding aligns with previous study, that found a risk of 6% for sinus node dysfunction or pacemaker implantation during follow-up [12].

Atrial fibrillation is common among SVD patients. This study showed that 7.3% had AF before surgery, and 9.8% developed new-onset AF during the follow-up. The higher incidence of atrial fibrillation was seen mainly in patients with SVD closed at older age. It can be speculated whether these patients would benefit from simultaneous maze procedure. Similarly Canadian series of 44 closed sinus venosus defects (1 to 13 years old) found that during follow-up of 1–14 years, over 80% of patients were in sinus rhythm [13]. A Mayo Clinic study showed that 14% had atrial fibrillation 12 years after the surgery [12]. In postoperative ECGs after the SVD surgery, only 41% of the patients operated on with double patch technique were in sinus rhythm, compared with 81% in one-patch and 89% in Warden procedure [14].

SVD patients had more ischemic heart disease in the long-term follow-up. Similar results were found in our previous study of transcatheter closed secundum type atrial septal defects [15]. In addition to previous speculations, the incidence of ischemic heart disease can be

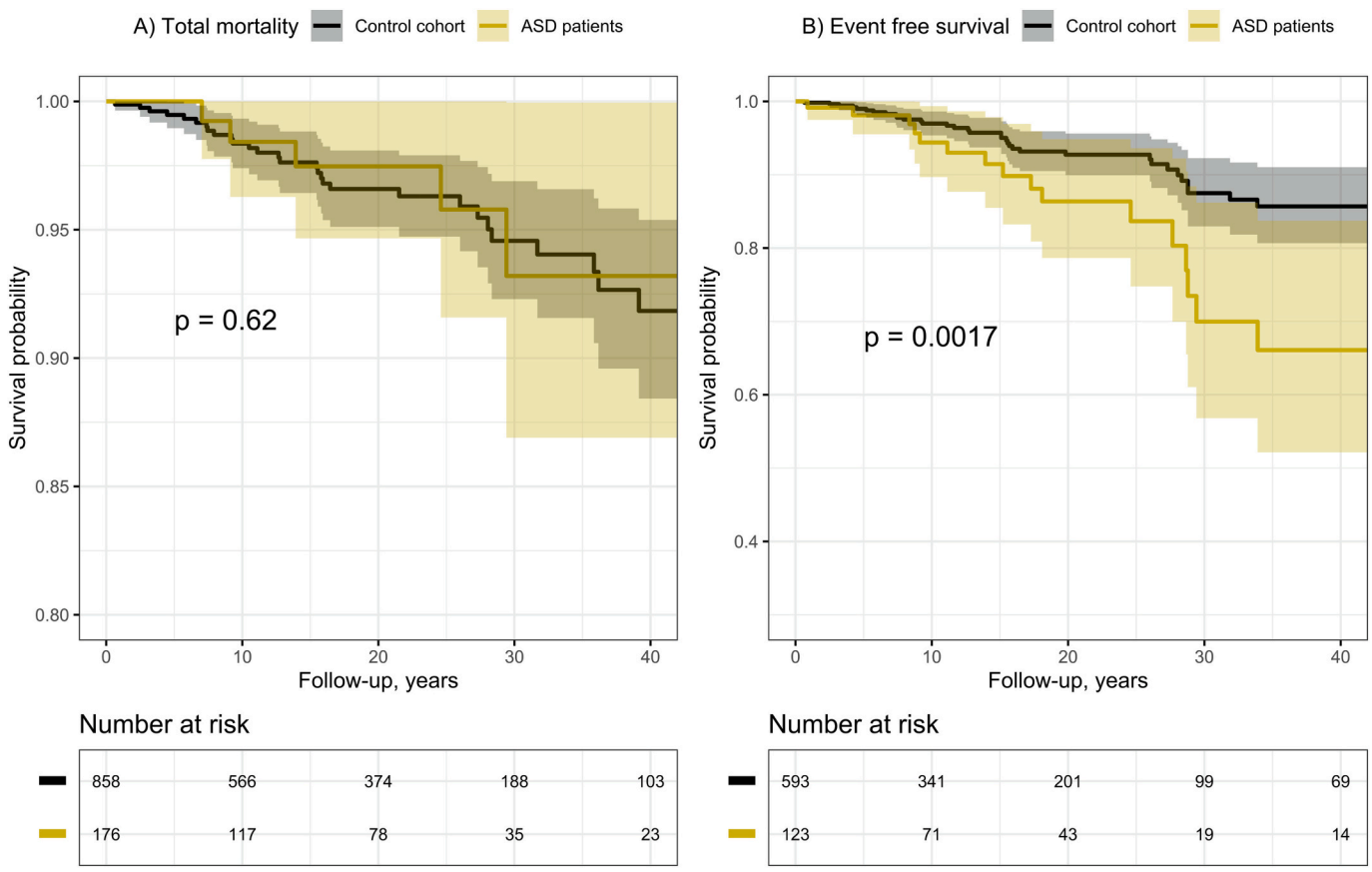

Fig. 2. Long-term mortality and event-free survival.
Caption: Long-term mortality according to study groups(A) and event-free survival (B). Events are defined as new-onset atrial fibrillation, new heart failure, new stroke or death.

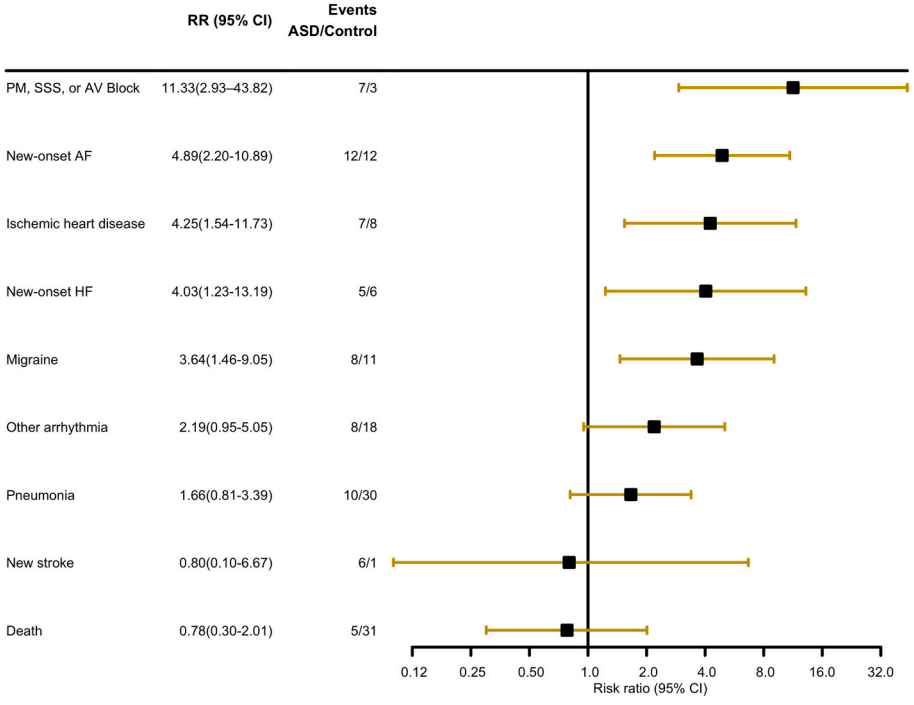

Fig. 3. Long-term outcomes and incidence risk ratios for events during the follow-up after sinus venosus defect correction.
Caption: AF = atrial fibrillation, SVD = Sinus venosus defect, AV = atrioventricular, CV = Cardiovascular, PY = Person year, aRR = Adjusted risk ratio.

higher due to more thorough cardiac follow-up compared to the matched general population.

Several other studies have examined the outcome after sinus venosus-type defect correction. Most of these studies are limited by a small study population or a lack of a control cohort [16–19]. The most extensive case series are published by Mayo Clinic with 115 patients (mean age 34 years) and from Verona, Italy, with 104 SVD patients (mean age 29 years) [12,20].

The Mayo Clinic's study has a series of 115 surgically closed SVD during 1972–1996. Mean age at the time of surgery was 34 years [12]. The inclusion of older patients resulted in more events in their study. However, the study was limited by a lack of a control group. Survival was 79% at 30 years in the Italian study. Yet it must be considered that there were only 13 patients with 30-year follow-up [20]. This study had a much younger population at the time of the repair, and most of the patients were pediatric. Thus, these results are not directly comparable with these previous studies.

4.1. Limitations

Despite being the largest cohort of sinus venosus defects with a control population and long follow-up time, the study is limited by a small number of events of interest. Also, the retrospective nature of the study limited availability of more specific information, and in-depth electronic health record data was unavailable, e.g., size of the defect and the location of PAPVD. The type of procedure was not available in every case. However, we know that most defects are operated using a single patch technique. Data regarding the surgical reinterventions was partly available from the discharge registry. However, we could not confirm these results to be accurate, and the results were not included in the final manuscript. Finally, analyzing register-based data has inevitable limitations, and the quality of diagnoses in the registries is dependent on the clinicians who provide the data.

5. Conclusion

Young patients with SVD have comparable survival prognosis to matched general population after the surgery. Risk for sick sinus syndrome or conduction disorders, atrial fibrillation, and heart failure remains elevated after the surgical SVD correction.

Contributions

VM is the corresponding author and contributed to every phase of the study. JS and MJ contributed to the design, writing, interpretation, and reviewing. JH contributed to the design and statistical analysis. AV and TP contributed to data collection, writing, and editing. All authors approved the final version.

Declaration of Competing Interest

None.

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