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Recall of patients discharged from follow-up after repair of isolated congenital shunt lesions

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ABSTRACT

Background: Discharge from follow-up after closure of isolated congenital shunt lesions in childhood was common practice in the past. The aim of the present study was to recall these patients to evaluate their current status.
Methods: Patients included in the database of pediatric and congenital heart disease of our tertiary center with repaired secundum atrial septal defect (ASD) or ventricular septal defect (VSD) before the age of 18 years, and discharged from follow-up, were invited for clinical and echocardiographic check-up.
Results: Forty-six ASD patients (age 30 ± 7 years, 37% male) responded. Median age at ASD repair was 6 (IQR 4–8) years. All but one functioned in NYHA class I. Eight (17%) patients reported palpitations. No patient developed pulmonary hypertension (PH). Right ventricular (RV) dilatation was present in 7 (15%). RV fractional area change (FAC) was <35% in 7 (15%), TAPSE <17 mm in 12 (26%).
Forty-seven VSD patients (age 34 (IQR 29–40) years, 57% male) participated. Median age at VSD repair was 4 (IQR 1–5) years. Six (13%) patients functioned in NYHA class II. Seventeen (36%) patients reported palpitations. Four (9%) patients presented PH. Left ventricular dilatation was present in 4 (9%), RV dilatation in 6 (13%). RV FAC was <35% in 7 (15%), TAPSE <17 mm in 17 (36%). Seven (15%) patients had dilated ascending aorta.
Conclusions: Patients with closure of isolated secundum-type ASD in childhood do well, but some have persistent RV dilatation and dysfunction. By contrast, more patients after VSD closure were symptomatic and presented with RV dilatation and dysfunction, PH, and a dilated ascending aorta.
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1. Introduction

In the early period of congenital cardiac surgery, many patients with a repaired simple congenital heart defect (CHD) were considered definitively cured after a relatively short postoperative follow-up. This has resulted in a large population of patients with repaired CHD discharged from further medical cardiac care. However, these patients may still have residua or sequelae requiring lifelong specialized care [1].

The birth prevalence of atrial septal defect (ASD) is estimated around 1.6 per 1000 live births [2]. Secundum-type ASD accounts for 75% of all ASD, and there is a female predominance of 2:1 [3]. ASD complications that often occur in the long-term are (supraventricular) arrhythmias and right heart failure [4]. A smaller percentage of patients may develop pulmonary arterial hypertension [3,5].

Isolated ventricular septal defect (VSD) is the most common CHD, apart from bicuspid aortic valve, accounting for 30–40% of all congenital cardiac malformations, with a birth prevalence of 2.6 per 1000 live births [2,4,6]. The clinical presentation and natural history can vary from small VSD with insignificant left-to-right shunt to VSD with significant left-to-right shunt that, if unrepaired, may cause pulmonary vascular disease or even Eisenmenger syndrome [4,7,8]. Patients with a small or repaired VSD are considered to remain event-free during follow-up. However, several problems may develop later in life, with the most important being endocarditis, left ventricular (LV) dilatation and heart failure, aortic valve complications, arrhythmias, and complete heart block [4].

(Surgical) repair of small isolated ASD or VSD in childhood is generally considered curative. Therefore, it is stated in the guidelines that for ASDs, no further follow-up is needed in the absence of a residual shunt,

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residual right heart disease, or pulmonary hypertension (PH) [4]. For repaired VSDs without residua, follow-up every 5 years is advised [4]. Discharge from follow-up after repair in childhood or adolescence of isolated congenital shunt lesions such as secundum-type ASD and VSD was also common practice in our tertiary university center in the seventies and eighties.

The aim of the present study was to recall these patients to evaluate their current health and clinical status and the global heart function by detailed echocardiography. Indeed, at present there is no data if patients discharged from follow-up remain event-free or if they actually need lifelong follow-up. Furthermore, it was intended to include these patients subsequently in the Belgian Registry on Adult Congenital Heart Disease. This will lead to more accurate estimations of true incidence and prevalence of CHD-related morbidities and mortality, since studying only the patients in continuous follow-up and included in registries may introduce a selection bias [3,9].

2. Methods

2.1. Patient selection

All patients, aged 18 years or older, with secundum-type ASD or VSD, included in the local database of pediatric and congenital heart disease of our tertiary university center and with the latest clinical follow-up more than 5 years ago, were selected. The local database was started in 1992 and includes all patients with congenital heart disease, examined or treated in our tertiary university hospital. The database is accurately updated at each patient visit, or with each new cardiac or non-cardiac event. The large majority (86%) of these patients remain in specialized follow-up through adulthood [10]. Patients who did not undergo defect repair or underwent repair after the age of 18 years were excluded. Patients with associated congenital heart lesions, with spontaneous ASD or VSD closure, or who lived outside Belgium were also excluded. A letter was sent to the patients who met the inclusion criteria, to invite them for a clinical check-up. A reminder was sent 5 months later to those who did not respond the first time. Each participant signed informed consent. The Ethics Committee of the hospital approved the study protocol (Belgian protocol number: B322201421767. Approval date: 25th August 2014. http://www.uzleuven.be/commissie-medische-ethiek).

2.2. Review of the patient records

Data on catheterization prior to defect repair and details on defect closure were retrieved from the patients' records. In patients who underwent invasive hemodynamic measurements prior to ASD/VSD repair, pulmonary artery pressures (PAP) were measured, and shunt ratio (Qp/Qs) was calculated through series of oxygen saturation by the Fick method. PH at baseline was defined as mean PAP (PAPm) ≥ 25 mmHg, according to the 2015 ESC/ERS guidelines [11]. Most patients underwent transthoracic and/or transesophageal echocardiography (TTE and/or TEE) at baseline before defect closure, mainly focusing on anatomical and shunt characteristics. Defect size was defined as the maximal defect diameter. The electronic patient files of all patients who met the inclusion criteria were checked for survival status. There are two main resources by which the death of a patient is registered in this electronic patient file. First, death is registered automatically when the patient dies in our university hospital, or in one of the 17 hospitals connected to this electronic patient file network. Second, there is a link between the electronic hospital database and the central national database containing the population data (managed by the Federal Public Service Interior), among other the status alive or deceased.

2.3. Clinical and echocardiographic reassessment

At inclusion, demographic, clinical and electrocardiographic data were acquired. Cardiac symptoms, such as palpitations and syncope, and hours of exercise per week (with lack of physical activity defined as 0 h of exercise per week) were actively asked for. All patients underwent comprehensive TTE at study visit. TTE was performed with a Vivid 9 ultrasound system (General Electric Vingmed Ultrasound, Horten, Norway). TTE included two-dimensional, M-mode, pulsed wave, continuous wave, and color Doppler measurements. A single observer performed the on-line and off-line analyses. All measurements were made in triplicate and the means were used for data analysis. Analyses were done according to the 2015 guidelines for cardiac chamber quantification [12]. LV systolic function was assessed by ejection fraction using the Simpson's method. LV hypertrophy was defined by LV mass indexed to body surface area (BSA), measured by two-dimensional echocardiography. LV diastolic function was assessed by E/e' in case of normal ejection fraction and by E/A in case of reduced ejection fraction. Right ventricular (RV) systolic function was assessed by RV fractional area change (FAC) and tricuspid annular plane systolic excursion (TAPSE). Atrial and ventricular dimensions were graded as normal, mild, moderate, or severe dilatation, based on absolute measurements of diameters, areas, and volumes. Ascending aortic diameter was measured in diastole, in a parasternal long-axis view, and indexed for BSA. Valvular regurgitations were graded semi-quantitatively on color Doppler echocardiography on a scale of 0 to 4. The probability of PH in patients without residual shunt after repair was estimated upon the tricuspid regurgitation velocity (TRV), obtained by TTE, taking into account a series of other parameters as right atrial dimensions, pulmonary artery diameter, inferior cava diameter, and collapsibility. Three different PH categories were defined, following the 2015 ESC/ERS guidelines [11]. Low PH probability was defined as TRV ≤ 2.8 m/s in the absence of other TTE signs of PH; intermediate PH probability was defined as 2.9 ≤ TRV ≤ 3.4 m/s or as TRV ≤ 2.8 m/s in the presence of other TTE signs of PH; high PH probability was defined as TRV > 3.4 or as 2.9 ≤ TRV ≤ 3.4 m/s in the presence of other TTE signs of PH. In patients with residual shunt, PH was estimated by means of the peak pressure gradient across the VSD (difference of LV and RV systolic pressure, estimated by 4 times the VSD peak velocity squared, cutoff of 4 m/s) and the pulmonary artery acceleration time (PAAT, cutoff of 100 milliseconds [13]).

Finally, patients were asked to complete the Short-Form 36 (SF-36) questionnaire (Dutch Version). This is a commonly used tool to measure the patient's subjective physical and mental health status along 8 dimensions [14]. The SF-36 generates a score for each dimension, ranging from 0 to 100. Higher scores indicate a better health status. Using norm-based scoring, the health domain scales all have a mean of 50 and a standard deviation of 10, based on the results from a large sample of the U.S. general population in 1998. A score < 50 indicates a subjective health status below the general population average [14].

2.4. Statistical analysis

Statistical analyses were performed with SPSS software (version 23.0, Chicago, USA). For continuous variables, data are reported as means ± standard deviation, or as medians + interquartile ranges (IQR) if data were not normally distributed. Discrete variables are presented as frequencies and/or proportions. Comparison of two means was done by a Student's t test, comparison of two medians by a Mann–Whitney U test. Levene's test was performed to assess for equal variances. Proportions were compared by the chi-square test (or Fischer's exact test in case of small sample size). All tests were two-sided, and a p-value <0.05 was considered statistically significant.

3. Results

3.1. Patient selection

A total of 519 patients with secundum-type ASD and 1144 patients with VSD, aged 18 years or older and with the latest clinical check-up more than 5 years ago, were selected (Fig. 1). The information provided in the local database of pediatric and congenital heart disease of our tertiary university center was screened to look for exclusion criteria. This led to the omission of 346 ASD and 918 VSD patients. After in depth analysis of the remaining patient records, there were still another 56 ASD and 103 VSD patients found that met at least one of the exclusion criteria. One hundred seventeen patients with ASD and 112 patients with VSD, who underwent repair before the age of 18 years, were selected as eligible study candidates. A total of 79 (34%) patients responded positively to the first letter and an additional 14 (6%) patients to the reminder letter. These 93 patients were analyzed in the present study. Of these, 73 (78%) were actively discharged from follow-up, 17 (18%) were unintentionally lost to follow-up, and 3 (3%) were referred for external follow-up. Three (1%) patients refused to participate. The remaining 133 (58%) did not respond.

A comparison was made between responders and non-responders, considering age and gender distribution. For patients with ASD, mean age was lower in the responders compared to non-responders (30 ± 7 years versus 33 ± 8 years, $p = 0.019$). No gender difference was seen (37% versus 51% male, $p = 0.18$). In the VSD group, there was no gender difference (57% versus 53% male, $p = 0.70$) and no difference in median age between responders and non-responders (34 (IQR 29–40) years versus 34 (IQR 29–39) years, $p = 0.85$).

3.2. Patient baseline characteristics

Forty-six patients with ASD repair (age at study visit 30 ± 7 years, 37% male) were analyzed. Median defect size was 16 (IQR 11–22) mm. ASDs were closed between May 1979 and August 2003. Median age at ASD repair was 6 (IQR 4–8) years. Forty (87%) ASDs were closed surgically (22 primary closure, 15 patch closure, 3 unspecified), 6 percutaneously with an Amplatzer Septal Occluder Device (St. Jude Medical). Heart catheterization was performed in 17 (37%) patients prior to repair. Mean Qp/Qs ratio was 2.4 ± 0.5 and PH was only present in 1

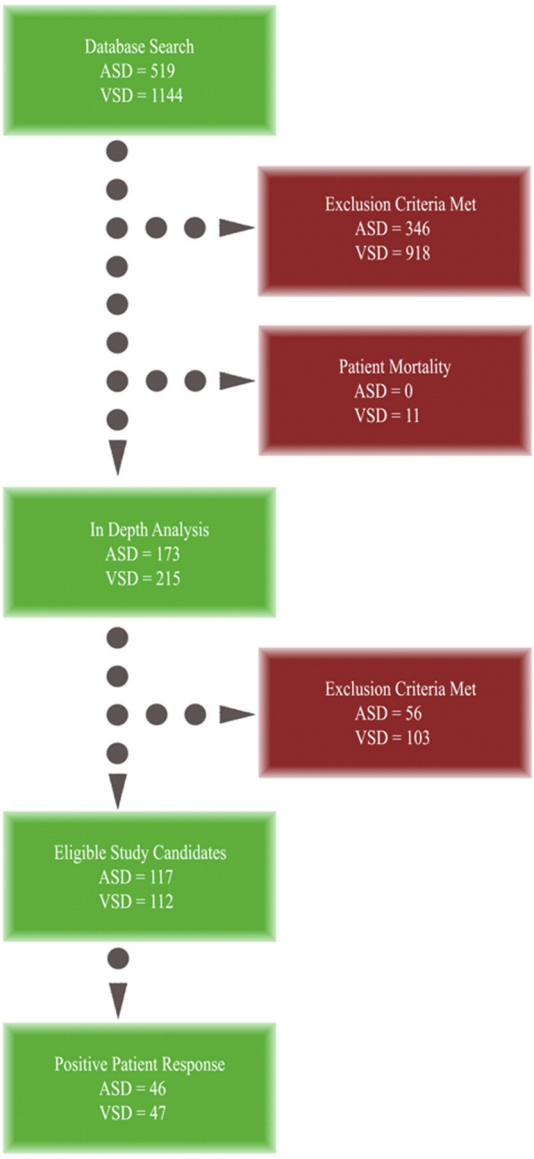

Fig. 1. Flowchart of patient inclusion.

(2%) patient before repair. Median PAPm was 12 (IQR 11–16) mm Hg. Familial ASD occurred in 3 (7%).

Forty-seven patients with VSD repair (age at study visit 34 (IQR 29–40) years, 57% male) were analyzed. The type of VSD was perimembranous in 44 (94%), muscular in 2 (4%), and doubly committed in 1 (2%). Median defect size was 9 (IQR 5–10) mm. Repair took place between October 1966 and March 1997. Median age at VSD repair was 4 (IQR 1–5) years. All patients had surgical repair (15 primary closure, 29 patch closure, 3 unspecified). Heart catheterization was performed in 16 (34%) patients prior to repair. Mean Qp/Qs ratio was 2.6 ± 0.8, and PH was present in 21 (45%) before repair. Mean PAPm was 32 ± 19 mmHg. Familial VSD was present in 1 (2%).

3.3. Patient survival after discharge from follow-up

No patient with ASD, who underwent repair before the age of 18 years and was no longer in follow-up, died. Eleven patients with VSD (45% male), repaired between November 1960 and January 2006, died. Causes of mortality were non-cardiac in 2 (bacterial sepsis in 1, asbestosis in 1) and unknown in 9 (of which 2 were out-of-hospital cardiac arrest at the age of 25 and 30 years, with a high suspicion of cardiac arrhythmia, although not documented).

3.4. Outcome in patients with secundum-type ASD repair

3.4.1. Current health and clinical status

All patients with ASD functioned in NYHA class I, except one in NYHA class II. Median SF-36 norm-based score for physical health was 56 (IQR 53–57), for mental health 55 (IQR 51–57) (Fig. 2). Six (13%) patients had a score for physical health below the general population average, and eight (17%) patients had a score for mental health below the population average. Results for the eight SF-36 health dimensions separately are shown in Fig. 3. Eight (17%) patients reported palpitations. No history of arrhythmia was documented. Eight (17%) patients suffered from vasovagal syncope. The prevalence of cardiovascular risk factors is shown in Table 1. Surprisingly, almost half of patients lack physical activity, with a significantly higher proportion of females (66% versus 18%, $p = 0.002$). Also the prevalence of arterial hypertension and hyperlipidemia was clearly higher compared to the general Belgian population in a similar age group.

3.4.2. Global heart function

All patients were in sinus rhythm at study visit. Only one patient presented with first degree atrioventricular (AV) block. Four (9%) patients had a rightward axis and 19 (41%) had an incomplete right bundle branch block.

No residual atrial shunt could be detected on TTE. LV systolic and diastolic functions were within the normal range in all patients. Mild right atrial (RA) dilatation was present in 2 (4%) patients. Mild RV dilatation was present in 7 (15%). RV dysfunction was not uncommon: RV FAC was below 35% in 7 (15%) patients, and TAPSE was below 17 mm in 12 (26%). Tricuspid regurgitation was mild in 37 (80%) and moderate in 9 (20%). No patient had echocardiographic criteria for PH. Thirteen (28%) patients had an increased peak systolic pressure gradient across the LV outflow tract (LVOT), ranging from 10 to 17 mmHg. One patient developed aortic coarctation with a peak instantaneous gradient of 23 mmHg.

Comparative analyses were done for RV dilatation and RV dysfunction (defined as FAC < 35%) (Tables 2 and 3). Variables studied included age at study visit, gender, clinical parameters, invasive hemodynamic measurements prior to repair, age at repair and procedural details, subjective health status, and TRV at follow-up TTE. No statistically significant results were retained. Mean systolic PAP at catheterization tended to be higher in the group with RV dilatation.

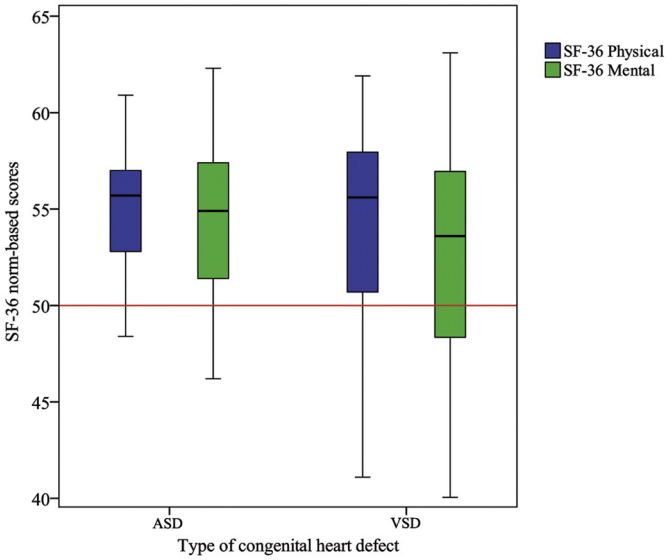

Fig. 2. Box plot of SF-36 norm-based scores by type of congenital heart defect.

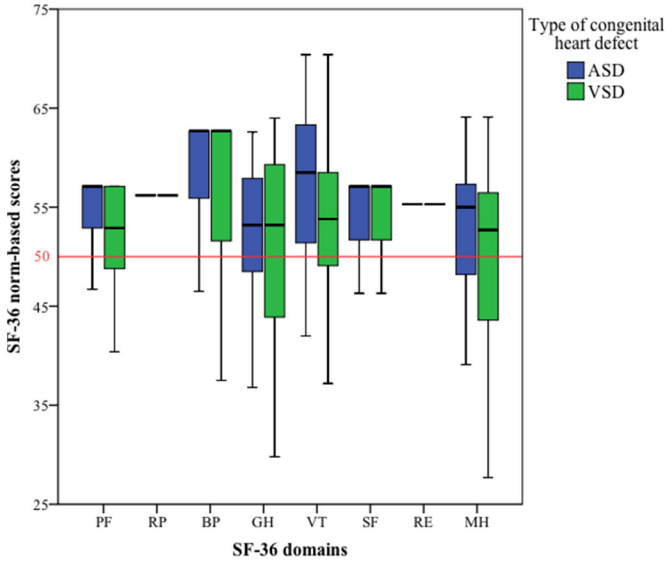

Fig. 3. Box plot of SF-36 norm-based scores by health dimension. PF = physical functioning; RP, role limitations due to physical health; BP, bodily pain; GH, general health perceptions; VT, vitality; SF, social functioning; RE, role limitations due to emotional problems; MH, general mental health.

3.5. Outcome in patients with VSD repair

3.5.1. Current health and clinical status

Six (13%) patients with VSD functioned in NYHA class II, the remaining in class I. The median SF-36 norm-based score for physical health was 56 (IQR 51–58), for mental health 54 (IQR 48–57) (Fig. 2). Ten (21%) patients had a score for physical health below the general population average, and 16 (34%) patients had a score for mental health below the population average. Results for the eight SF-36 health dimensions separately are shown in Fig. 3. Compared to ASD patients, patients with VSD scored lower in the dimensions of physical functioning, vitality, and general mental health. Seventeen (36%) patients reported palpitations. No history of arrhythmia was documented. Six (13%) patients suffered from vasovagal syncope. The prevalence of cardiovascular risk factors is shown in Table 1. More than half (55%) of female patients and 30% of male patients lack physical activity (no gender difference, $p = 0.13$). The prevalence of arterial hypertension and hyperlipidemia was clearly higher compared to the age-matched Belgian population. Current smoking was less frequent in VSD patients.

Table 1
Prevalence of cardiovascular risk factors.

	ASD ($n = 46$)	VSD ($n = 47$)	Belgian population[a]
Diabetes	0 (0%)	1 (2%)	0.6% (0.3–0.9%)
Arterial hypertension	5 (11%)	9 (19%)	2.0% (1.1–2.9%)
Overweight (25 ≤ BMI < 30)	17 (37%)	13 (28%)	37.3% (33.4–41.1%)
Obesity (BMI ≥ 30)	4 (9%)	7 (15%)	10.3% (7.9–12.8%)
Current smokers	10 (22%)	7 (15%)	26.2% (22.1–30.4%)
Former smokers	3 (7%)	4 (9%)	15.8% (−)
Hyperlipidemia[b]	4 (9%)	10 (21%)	3.0% (1.7–4.3%)
Lack of physical activity	22 (48%)	19 (40%)	25.7% (21.3–30.0%)

ASD = atrial septal defect; VSD, ventricular septal defect; BMI, body mass index.
[a] Source: Drieskens S., Charafeddine R., Demarest S., Gisle L., Tafforeau J. & Van der Heyden J. Health Interview Survey, Belgium, 1997–2001 - 2004–2008 - 2013: Health Interview Survey Interactive Analysis. Brussels: WIV-ISP. https://hisia.wiv-isp.be/. Data originate from the 2013 analyses in the Belgian population aged 25–34 years and are presented as mean (95% confidence interval).
[b] Data available for 11 ASD patients and 24 VSD patients.

Table 2
Comparative analysis for RV dilatation in secundum-type ASD.

	RV dilatation ($n = 7$)	No RV dilatation ($n = 39$)	p-value
Gender (male:female)	2:5	15:24	1[a]
Age at study visit (years)	28 ± 6	30 ± 7	0.52[b]
BMI (kg/m^2)	24 ± 4	24 ± 4	0.95[b]
SBP (mm Hg)	127 ± 8	128 ± 11	0.81[b]
Defect size (mm)	12 (10–19)	17 (13–25)	0.06[c]
sPAP (mm Hg)[d]	26 ± 2	22 ± 4	0.07[b]
Shunt ratio (Qp:Qs)[d]	2.4 ± 0.4	2.4 ± 0.5	0.79[b]
Age at repair (years)	5 (4–5)	7 (4–10)	0.13[c]
Type of repair (primary/patch/percutaneous)	3/2/2	19/13/4	0.54[a]
Procedure time (clamp time in minutes)	11 (8–17)	12 (8–17)	0.77[c]
SF-36 Physical Health	56 (53–57)	56 (53–57)	0.77[c]
TRV (m/s) on TTE	2.4 ± 0.2	2.5 ± 0.2	0.13[b]

RV = right ventricular; ASD, atrial septal defect; BMI, body mass index; SBP, systolic blood pressure; sPAP, systolic pulmonary artery pressure; TRV, tricuspid regurgitation velocity.
[a] Fisher's exact test.
[b] Unpaired t test.
[c] Mann–Whitney U test.
[d] Invasive measurements prior to repair.

3.5.2. Global heart function

All patients were in sinus rhythm at study visit. Signs of LV hypertrophy were present in 3 (6%), RV hypertrophy in 1 (2%). Thirty-two (68%) patients had right bundle branch block, incomplete in 15 and complete in 17.

A residual ventricular shunt was found on TTE in 6 (13%) patients. One patient needed surgical reintervention, 2 years after initial VSD repair. LV systolic and diastolic functions were within the normal range in all but 1 patient. LV dilatation was present in 4 (9%). LV hypertrophy was present in 9 (19%). Mild left atrial (LA) dilatation was present in 8 (17%) patients, mild RA dilatation in 1 (2%). Four (9%) patients had PH diagnosed on echocardiography, 3 with intermediate and 1 with high probability. RV dilatation was present in 6 (13%) patients. All of these 6 patients underwent VSD closure by patch. RV dysfunction was frequent: RV FAC <35% in 7 (15%) patients, TAPSE <17 mm in 17 (36%). Tricuspid regurgitation was mild in 39 (83%), moderate in 4 (9%) and severe in 3 (6%). Nine (19%) patients had an increased LVOT gradient, ranging from 10 to 23 mmHg. Nineteen (40%) patients had mild, 5 (11%) moderate and 1 (2%) severe aortic regurgitation (AR). Seven (15%) patients had a dilated ascending aorta, ranging from 19 till 23 mm/m^2. Six of these patients were male.

Comparative analyses were done for RV dilatation and RV dysfunction (Tables 4 and 5). RV dilatation tended to be more prevalent in

Table 3
Comparative analysis for RV dysfunction in secundum-type ASD.

	RV dysfunction ($n = 7$)	No RV dysfunction ($n = 39$)	p-value
Gender (male:female)	3:4	14:25	1[a]
Age at study visit (years)	31 ± 9	29 ± 7	0.59[b]
BMI (kg/m^2)	25 ± 4	24 ± 4	0.71[b]
SBP (mm Hg)	128 ± 13	128 ± 11	0.98[b]
Defect size (mm)	20 (9–38)	16 (12–21)	0.57[c]
sPAP (mm Hg)[§]	24 ± 4	22 ± 4	0.43[b]
Shunt ratio (Qp:Qs)[§]	2.8 ± 0.4	2.4 ± 0.5	0.26[b]
Age at repair (years)	5 (4–7)	6 (4–8)	0.72[c]
Type of repair (primary/patch/percutaneous)	2/3/1	20/12/5	0.49[a]
Procedure time (clamp time in minutes)	8 (8–13)	11 (8–19)	0.37[c]
SF-36 Physical Health	54 (52–57)	56 (53–57)	0.56[c]
TRV (m/s) on TTE	2.5 ± 0.3	2.5 ± 0.2	0.88[b]

Same legend as Table 2.

patients with patch closure of VSD, compared to primary closure. RV dysfunction was more prevalent in patients with RV dilatation.

4. Discussion

Patients with closure of isolated secundum-type ASD in childhood do well and report SF-36 Norm-based Scores for physical and mental health, comparable with or above the general population average. However, some presented persistent RV dilatation and dysfunction. By contrast, more patients after VSD closure were symptomatic. One in 5 patients had a score for physical health below the general population average, and one in 3 patients had a score for mental health below the population average. More patients presented with RV dilatation and dysfunction, PH, and a dilated ascending aorta.

4.1. Patient survival

No patient with isolated secundum ASD, operated in childhood and without follow-up afterwards, died. Eleven patients with isolated VSD, repaired between November 1960 and January 2006, died after discharge from follow-up. Two patients died suddenly out-of-hospital at a young age, presumably as a consequence of cardiac arrhythmia. For the majority of patients, the mortality cause is unknown, because no family member or general practitioner could be contacted or, if contacted, they did not know the cause. Nevertheless, the mortality rate in the present study was low, and most certainly not always related to cardiovascular causes.

Overall survival has greatly improved in the past decades, due to the earlier diagnosis, advancements in surgical techniques and postoperative care [15,16]. Some studies have shown that the survival curves of patients with ASD and VSD are within the normal range of the survival for the general population [17–19]. In others, survival was slightly lower [20].

4.2. Outcome in patients with secundum-type ASD repair

Patients after ASD repair report SF-36 Norm-based Scores for Physical and Mental Health, comparable with or above the general population average (Fig. 2). However, 17% of patients reported palpitations, without a history of arrhythmia detection. These patients probably have a high risk of developing atrial tachyarrhythmias or atrial fibrillation in their fifth or sixth decade [3,19,21].

No patient had a residual shunt on TTE. A residual shunt after ASD repair is rarely reported, especially in the later era of surgery [22]. Next to advancements in surgical techniques, the lower sensitivity of TTE compared to TEE in detecting a small residual shunt needs to be taken into account because of the superior image quality of TEE in adults [4].

Table 4
Comparative analysis for RV dilatation in VSD.

	RV dilatation ($n = 6$)	No RV dilatation ($n = 41$)	p-value
Gender (male:female)	4:2	23:18	1[a]
Age at study visit (years)	33 (31–38)	35 (29–41)	0.70[b]
BMI (kg/m^2)	24 (22–30)	24 (21–26)	0.85[b]
SBP (mm Hg)	132 (131–140)	133 (124–140)	0.58[b]
Age at repair (years)	1 (0–4)	4 (1–5)	0.06[b]
Type of repair (primary:patch)	0:6	15:23	0.08[a]
SF-36 Physical Health	53 (50–58)	56 (51–58)	0.63[b]
RV dysfunction	3 (50%)	4 (10%)	0.035[a]
TRV (m/s) on TTE	2.6 (2.4–2.9)	2.5 (2.3–2.7)	0.38[b]

RV = right ventricular; VSD, ventricular septal defect; BMI, body mass index; SBP, systolic blood pressure; TRV, tricuspid regurgitation velocity.
[a] Fisher's exact test.
[b] Mann–Whitney *U* test.

Table 5
Comparative analysis for RV dysfunction in VSD.

	RV dysfunction ($n = 7$)	No RV dysfunction ($n = 40$)	p-value
Gender (male:female)	4:3	23:17	1[a]
Age at study visit (years)	35 (31–42)	34 (29–40)	0.63[b]
BMI (kg/m^2)	25 (21–30)	24 (21–26)	0.68[b]
SBP (mm Hg)	138 ± 11	131 ± 13	0.21[c]
Age at repair (years)	3 (0–6)	4 (1–5)	0.94[b]
Type of repair (primary:patch)	1:5	14:24	0.65[a]
SF-36 Physical Health	51 (41–59)	56 (51–58)	0.30[b]
RV dilatation	3 (43%)	3 (8%)	0.035[a]
TRV (m/s) on TTE	2.5 (2.5–2.6)	2.5 (2.3–2.7)	1[b]

Same legend as Table 4.
[a] Fisher's exact test.
[b] Mann–Whitney *U* test.
[c] Unpaired *t* test.

RV dilatation and dysfunction were rather commonly found after ASD repair. RV dilatation was seen in 15% of patients, comparable to 11% in a study of 135 Dutch patients with ASD and similar time interval since ASD repair [23]. There are several possible explanations. First, the chronic RV volume overload caused by left-to-right shunt before ASD repair may lead to RV remodeling [24]. Second, although difficult to prove scientifically, one could presume that young age at repair, the surgical technique, and procedure time may also cause RV damage, as suggested by others [25]. Moreover, a small residual left-to-right shunt could have been missed on TTE, and so these patients are preferably further investigated with TEE to exclude a residual shunt with more certainty. Comparative analyses in our study did not retain statistically significant associative factors, presumably because of rather limited patient numbers. Mean systolic PAP at catheterization and median defect size before repair tended to be higher in the patients with RV dilatation.

No patient developed PH. The same observation was made by others [22,23]. Main reasons may include the young age of our study group, and the fact that all but 1 patient had normal PAP before ASD repair. Higher age at repair and elevated PAP and pulmonary vascular resistance before repair are known important predictors of PH after ASD repair [3,26].

4.3. Outcome in patients with VSD repair

Thirteen percent of patients functioned in NYHA class II. One in 5 patients had a score for Physical Health below the general population average, and 1 in 3 patients had a Mental Health score below population average (Fig. 2). By contrast, patients after VSD repair in a Dutch cohort obtained significantly better scores than the reference population [20]. However, their maximal workload at exercise testing was clearly lower than the reference population. In our population, the lack of physical activity in a substantial part of patients could partly explain the lower perceived health status, next to country-specific sociocultural differences.

One in 3 patients reported palpitations. Only a minority had Holter-ECG monitoring, but no arrhythmias were detected. Prevalence of atrial arrhythmias after VSD closure reported in literature varies from 0% to 23% [18,27,28]. The age of onset of atrial arrhythmias or atrial fibrillation is usually between the fifth and sixth decade [21]. Since the present VSD population is younger, this might explain why no atrial arrhythmias were seen.

A residual shunt on TTE was present in 6 (13%), similar to other studies [16,18,28]. One patient needed reintervention.

Four (9%) patients had PH diagnosed on echocardiography, confirming that early VSD repair successfully prevents progressive pulmonary vascular disease in the majority of patients [27,28].

RV dilatation and RV dysfunction were frequent, present in around 15% of patients. Similar prevalence of RV dysfunction was recently

described in a Dutch cohort of 91 VSD patients [20]. There is no rheological explanation. Again, surgical damage of the RV can be hypothesized. No associations with age at repair, surgical details or RV systolic pressure could be found in the present study, most likely because of low patient numbers.

Seven (15%) patients had a dilated ascending aorta, of which six were male. This seems a quite high prevalence compared to other observations [29]. To our knowledge, there are only case reports published about the association of VSD and dilated ascending aorta [30]. There could be a hemodynamic explanation for dilatation of the ascending aorta, due to arterial stiffness, turbulent blood flow and shear stress [31,32]. Furthermore, anatomical, surgical, and genetic causes could also explain the ascending aortic dilatation. VSD anatomy but also repair may give rise to a changed angulation of the ascending aorta and perhaps elevated aortic stiffness. Patients with familial VSD might also be genetically predisposed to maldevelopment of the adjacent ascending aorta. However, to our knowledge, no literature on these hypotheses is published. Severe AR as the cause of ascending aortic dilatation in patients with VSD is postulated by others [30]. In the present study, only 1 patient with aortic dilatation had severe AR.

Nine (19%) patients had an elevated LVOT gradient. Associated AR was mostly absent or mild. The phenomenon of LVOT obstruction was also noted in 14% of patients with surgical repair of isolated VSD that remained in continuous follow-up in our center. Also, the occurrence of AR after VSD repair is an important issue [20]. In the present study, 19 (40%) patients had mild and 6 (13%) moderate or severe AR.

4.4. Indication for systematic follow-up

For isolated ASD repair without residual lesions, no regular follow-up is required according to the guidelines [4]. For isolated VSD repair without residua or sequelae, the guidelines advise periodic follow-up every 5 years, in a specialized adult congenital heart disease center.

In the present study, 8 (17%) of 46 ASD patients and 23 (49%) of 47 VSD patients required further follow-up. The majority of these (68%) was actively discharged from follow-up. Only a minority of these (26%) was in follow-up with a general cardiologist. The remaining 74% were included in the ambulatory system of regular follow-up at our center. Main reasons for follow-up encompassed ascending aortic dilatation, residual shunt, PH, valvular lesions, and device closure. In the CONCOR study, additional cardiac follow-up was necessary within 1 year in 22% of the patients examined [29].

4.5. Future perspectives for patients discharged from follow-up

Although the majority of patients included in the present study were actively discharged from follow-up because they were considered to be cured, some still presented important residua and sequelae requiring follow-up. This is a rather unique study because it mainly includes patients actively discharged from follow-up and because of the focus on two specific congenital heart lesions, whereas most published studies report patients lost to follow-up and include all CHD.

The present results will hopefully stimulate more research on patients with congenital heart lesions that were discharged from follow-up after repair. There clearly exists a subgroup that would benefit from continuous follow-up. Formalized transition programs and outreach programs to identify patients lost to follow-up may also be used to identify those patients discharged from follow-up, to help to ensure the continuity of care into adulthood and may prevent significant morbidity and the need for urgent interventions [10,33,34].

5. Limitations

This study presents a single center experience, making it difficult to generalize the present findings to other populations. Furthermore, because most studies in literature are published on patients still in specialist follow-up, it is difficult to compare event rates with those of a population of patients discharged from follow-up. Moreover, the patient numbers were rather limited, with low event rates and consequently insufficient statistical power to perform comparative and other statistical analyses. Lastly, a certain selection bias is not excluded in this study since only 41% of eligible study candidates responded positively. There were no significant age and gender differences between responders and non-responders in the VSD group. In patients with ASD, mean age was lower in the responder group. However, the clinical significance of this difference is negligible.

6. Conclusions

Patients with closure of isolated secundum-type ASD in childhood do well, but some have persistent RV dilatation and dysfunction. By contrast, more patients after VSD closure were symptomatic and presented with RV dilatation and dysfunction, PH and a dilated ascending aorta, which would require systematic follow-up.

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Conflicts of interest

No funding resource was involved in the study design, data collection and interpretation, writing, and submission of the present study.

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