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Paediatric subaortic stenosis: long-term outcome and risk factors for reoperation

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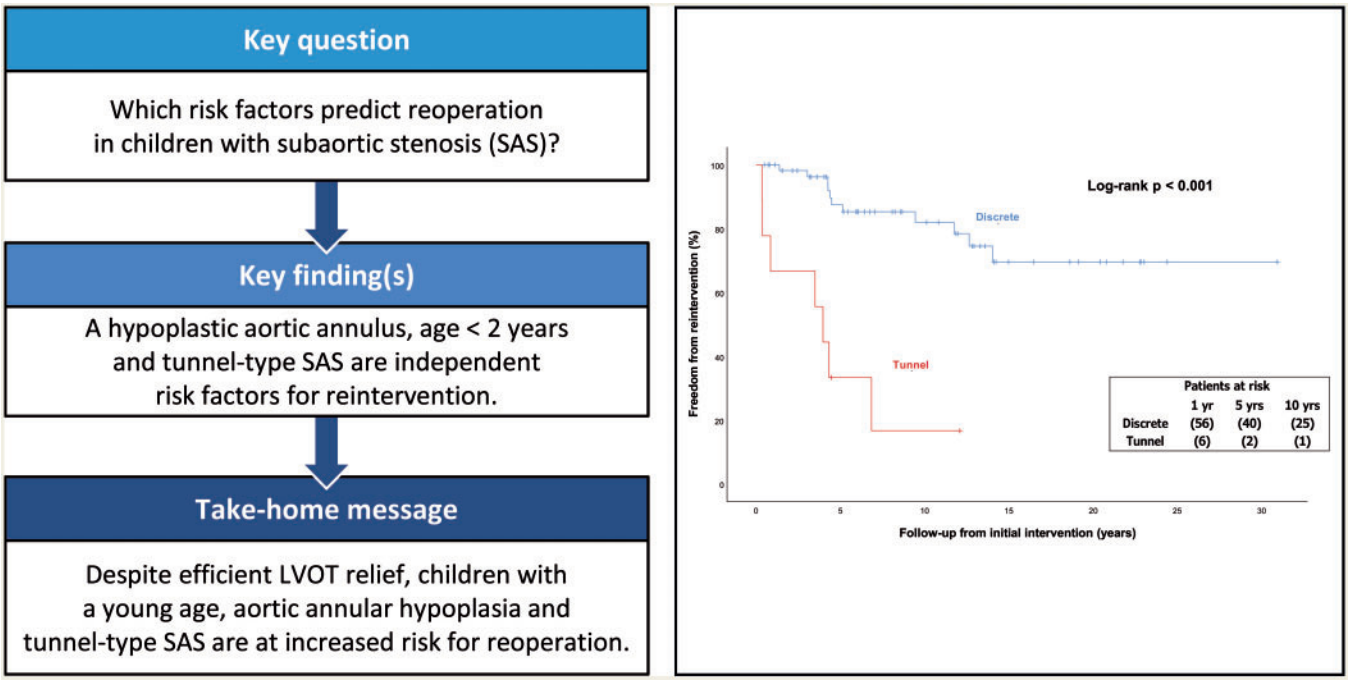

Abstract

OBJECTIVES: Surgical repair of subaortic stenosis (SAS) is associated with a substantial reoperation risk. We aimed to identify risk factors for reintervention in relation to discrete and tunnel-type SAS morphology.

METHODS: Single-centre retrospective study of paediatric SAS diagnosed between 1992 and 2017. Multivariable Cox regression analysis was performed to identify reintervention risk factors.

RESULTS: Eighty-five children [median age 2.5 (0.7–6.5) years at diagnosis] with a median follow-up of 10.1 (5.5–16.4) years were included. Surgery was executed in 83% ($n = 71$). Freedom from reoperation was 88 ± 5% at 5 years and 82 ± 6% at 10 years for discrete SAS, compared to, respectively, 33 ± 16% and 17 ± 14% for tunnel-type SAS (log-rank $P < 0.001$). Independent risk factors for

reintervention were a postoperative gradient >20 mmHg [hazard ratio (HR) 6.56, 95% confidence interval (CI) 1.41–24.1; $P = 0.005$], tunnel-type SAS (HR 7.46, 95% CI 2.48–22.49; $P < 0.001$), aortic annulus *z*-score <-2 (HR 11.07, 95% CI 3.03–40.47; $P < 0.001$) and age at intervention <2 years (HR 3.24, 95% CI 1.09–9.86; $P = 0.035$). Addition of septal myectomy at initial intervention was not associated with lesser reintervention. Fourteen children with a lower left ventricular outflow tract (LVOT) gradient ($P < 0.001$) and older age at diagnosis ($P = 0.024$) were followed expectatively.

CONCLUSIONS: Children with SAS remain at risk for reintervention, despite initially effective LVOT relief. Regardless of SAS morphology, age <2 years at first intervention, a postoperative gradient >20 mmHg and presence of a hypoplastic aortic annulus are independent risk factors for reintervention. More extensive LVOT surgery might be considered at an earlier stage in these children. SAS presenting in older children with a low LVOT gradient at diagnosis shows little progression, justifying an expectative approach.

Keywords: Subaortic stenosis • Congenital heart disease • Left ventricular outflow tract

ABBREVIATIONS

AR	Aortic regurgitation
CI	Confidence interval
DSS	Discrete subaortic stenosis
HR	Hazard ratio
LVOT	Left ventricular outflow tract
LVOTO	Left ventricular outflow tract obstruction
SAS	Subaortic stenosis
VSD	Ventricular septum defect

INTRODUCTION

Subaortic stenosis (SAS) accounts for up to 20% of left ventricular outflow tract obstruction (LVOTO) in children [1]. Two subtypes are distinguished: (i) discrete-type SAS (DSS) consisting of a fibrous membrane and (ii) tunnel-type SAS, wherein LVOTO is longer and more complex, often associated with obstructions at different levels [2]. SAS is considered a progressive disease and early intervention has been suggested [3, 4], although not all patients require surgery during childhood [5]. Aortic regurgitation (AR) is the most common complication but is usually mild [5–7]. Although immediate surgical results are satisfying, reoperation rates remain high in both adults and children, varying between 16% and 31% [8–12]. Several risk factors for reoperation have been identified, such as the magnitude of left ventricular outflow tract (LVOT) gradient at, respectively, diagnosis, preoperatively or postoperatively, younger age at intervention, small size of the aortic annulus and concomitant complex cardiac disease [3, 6, 8, 11, 13, 14].

Currently, there is little consensus on the best surgical technique for DSS. Adding a septal myectomy routinely to membrane enucleation to prevent reoperation is highly debated [10]. In contrast, tunnel-type SAS shows higher reoperation rates, rising up to 70% [15] and frequently warrants more complex surgery [12].

We aimed to review the natural history and risk factors for reintervention in paediatric SAS, thereby assessing differences between DSS and tunnel-type SAS. In addition, we tried to identify which patients could benefit from a septal myectomy at the initial surgery or at reoperation, and those for whom even a more radical first surgery might be considered by analysing risk factors for reoperation. Finally, we assessed the differences between patients undergoing surgery during childhood and those in whom a expectative approach was possible.

METHODS

For this retrospective study, both surgical and cardiology databases of patients diagnosed with SAS at the Ghent University hospital were reviewed. Patient- and disease-related data were retrieved from outpatient and hospitalization files, surgical reports, transthoracic echocardiography and catheterization protocols. Patients with SAS due to hypertrophic cardiomyopathy, intracardiac conduits and/or age >18 years at the time of surgery or diagnosis were excluded, as well as foreign patients without follow-up data. Authorization was granted by the Medical Ethical Committee of Ghent University Hospital (B670201941047). The need for informed consent was waived due to the retrospective nature.

DSS was defined on echocardiography as a localized subaortic fibrous membrane, while tunnel-type SAS was identified as a long segment LVOT narrowing.

Eighty-five patients diagnosed with SAS <18 years between August 1992 and October 2017 were included. Patients with SAS were divided according to the treatment strategy into an intervention group for patients requiring surgical LVOTO relief and a conservative group for patients with expectative follow-up as shown in the flowchart (Fig. 1).

Indications for surgical intervention were symptoms and/or a peak LVOT gradient ≥40 mmHg, AR ≥grade III or any other associated intracardiac defect warranting intervention.

Study end points of interest were need for reintervention and definitive pacemaker implantation, early postoperative (in-hospital) and late mortality. The median follow-up was 10.1 years (5.5–16.4). Follow-up data were not available in 2 (2.4%) patients.

Qualitative and quantitative measurements

Peak LVOT gradient and AR grade were retrieved from catheterization and transthoracic echocardiography protocols. Peak gradient across the LVOT (expressed in mmHg) was recorded at diagnosis, immediately preoperatively and postoperatively if surgical intervention was performed, and finally at the latest follow-up. The preoperative echocardiography was done the day before intervention and the postoperative echocardiography was done

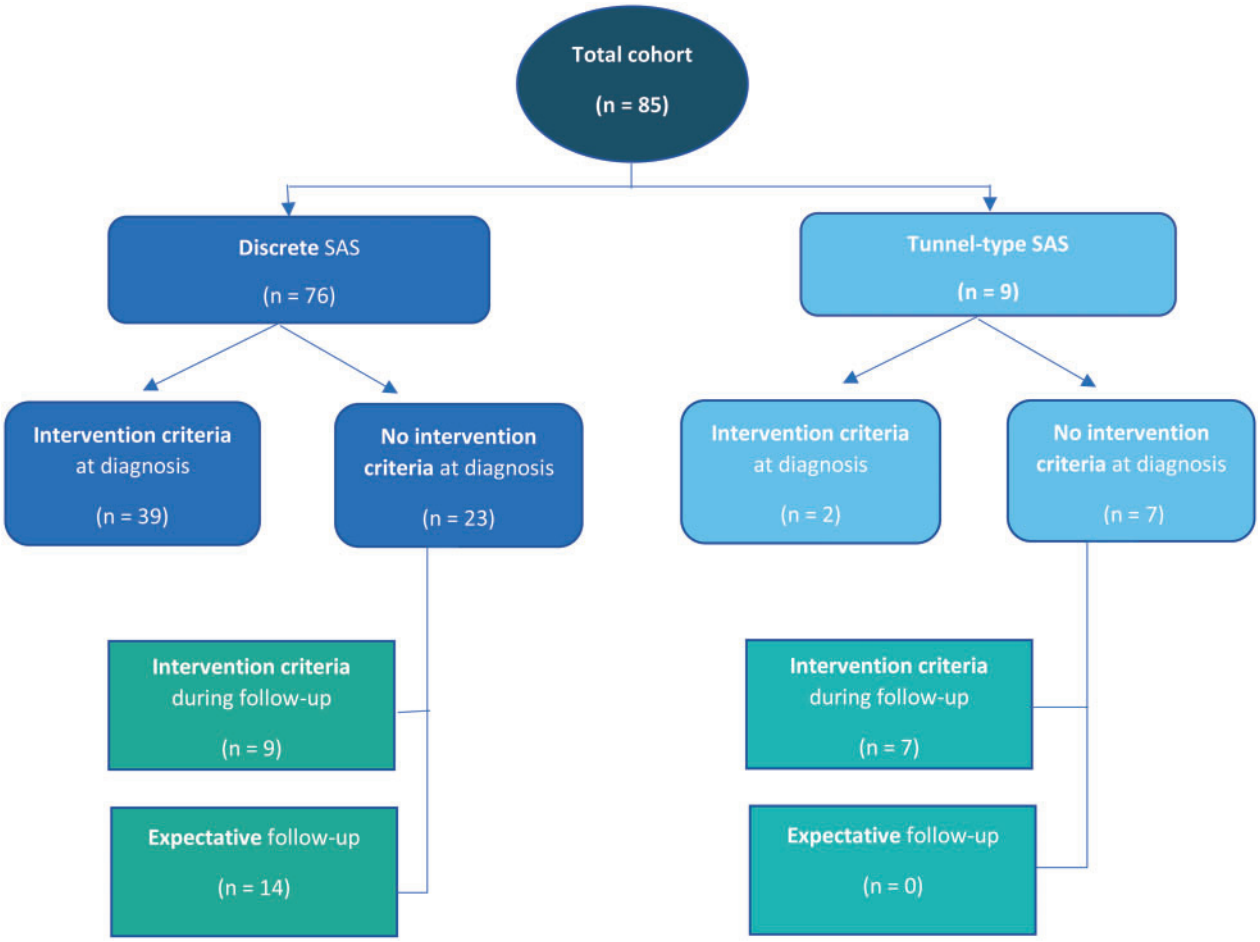

Figure 1: Flowchart representing need for intervention during follow-up. SAS: subaortic stenosis.

at discharge. The presence of AR was evaluated simultaneously and categorized as grade I–IV. The morphology of the aortic valve was assessed for the number of cusps (bicuspid or tricuspid) and for size. The aortic annulus was defined as hypoplastic for a *z*-score of <-2.

Operative procedures

The decision for surgery was made in a multidisciplinary team of paediatric cardiologists and cardiothoracic surgeons. The type of operation was a balanced consideration of the surgical team based on morphology and degree of stenosis, presence of AR and associated intracardiac lesions. All surgical interventions were performed under cardiopulmonary bypass with moderate hypothermia and cardioplegic arrest. Classically the aortic valve and LVOT were visualized through a transverse aortotomy. The fibrous membrane, if present, was completely enucleated by blunt dissection in a circular fashion as first described by Ross [16]. The decision to add a concomitant septal myectomy was based on the intraoperative assessment of the extent of septal bulging and asymmetrical hypertrophy of the outflow septum, after the complete removal of subvalvular fibrous tissue.

A modified Konno septoplasty with patch enlargement of the subaortic interventricular septum was performed for morphological malalignment of the interventricular septum. Aortic valve replacement was done by a Ross or Ross–Konno procedure, using the pulmonary autograft as a root replacement.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation if normally distributed and as median and interquartile range (25th–75th percentile) if skewed. Categorical variables are expressed as number and percentages. Comparison of characteristics between the different patient groups was done with the Student's *T*-test or Mann–Whitney *U*-test for continuous variables, and by Fisher's exact test for dichotomous variables. The Kaplan–Meier method was used to analyse the estimated freedom from reoperation for type of SAS, and the difference was shown by log-rank test. The association between clinical characteristics and the need for reoperation was evaluated through Cox regression analysis. Factors reaching a *P*-value of <0.10 were included into a multivariable stepwise backward regression model. The risk effect was expressed by the hazard ratio and 95% confidence interval. The proportional hazard assumption was verified by the log-log Kaplan–Meier plot and by the Schoenfeld residuals. A *P*-value of <0.05 was considered statistically significant. Statistical analysis was done with IBM SPSS Statistics 25.0 (Armonk, NY, USA; IBM Corp.).

Table 1: Baseline cohort characteristics

	Total ($n = 85$)	Intervention ($n = 71$)	Conservative ($n = 14$)	P-value
Sex (male)	51 (60)	43 (61)	8 (57)	1.00
Age at diagnosis (years)	2.5 (0.7–6.5)	2.3 (0.6–5.9)	4.1 (2.4–9.3)	**0.024**
Concomitant CHD	67 (79)	57 (80)	10 (71)	0.48
Hypoplastic aortic annulus	7 (8)	7 (10)	0 (0)	0.60
Bicuspid aortic valve	18 (21)	16 (23)	2 (14)	0.72
Discrete	76 (89)	62 (87)	14 (100)	
Tunnel	9 (11)	9 (13)	0 (0)	
Peak gradient at diagnosis (mmHg)	31.9 ± 24.4	36.2 ± 24.5	13.6 ± 13.9	**<0.001**
Peak gradient at latest follow-up (mmHg)	11.5 ± 15.1	9.8 ± 15.2	19.3 ± 12.4	**0.030**

Values are presented as n (%), means ± SD or median (Q1–Q3).
CHD: congenital heart disease; SD: standard deviation.
Bold face values are statistically significant.

Table 2: Associated congenital heart defects

	Total ($n = 85$)	Intervention ($n = 71$)		Conservative ($n = 14$)
		Discrete ($n = 62$)	Tunnel type ($n = 9$)	
VSD	37 (44)	31 (50)	4 (44)	2 (14)
AVSD	8 (9)	7 (11)	0 (0)	1 (7)
CoA	17 (20)	13 (21)	1 (11)	3 (21)
ASD	7 (8)	5 (8)	1 (11)	1 (7)
Valvular aortic stenosis	5 (6)	2 (3)	0 (0)	3 (21)
Mitral valve stenosis	4 (5)	3 (5)	1 (11)	0 (0)
DORV	4 (5)	2 (3)	2 (22)	0 (0)
DCRV	3 (4)	3 (5)	0 (0)	0 (0)
Interrupted aortic arch	3 (4)	1 (2)	2 (22)	0 (0)
TGA	2 (2)	2 (3)	0 (0)	0 (0)
TOF	1 (1)	1 (2)	0 (0)	0 (0)
Monoatrium	1 (1)	0 (0)	0 (0)	1 (7)
Cleft mitral valve	1 (1)	1 (2)	0 (0)	0 (0)
PAPVR	1 (1)	1 (2)	0 (0)	0 (0)

Values are given as n (%).
ASD: atrial septal defect; AVSD: atrioventricular septal defect; CoA: coarctation of the aorta; DCRV: double chambered right ventricle; DORV: double outlet right ventricle; PAPVR: partial anomalous pulmonary venous return; TGA: transposition of the great arteries; TOF: tetralogy of Fallot; VSD: ventricular septal defect.

RESULTS

Demographic and clinical characteristics of the total cohort are summarized in Table 1. A total of 85 SAS patients with a median age of 2.5 (0.7–6.5) years at diagnosis were included. The majority (89%; $n = 76$) had DSS. Other congenital heart anomalies were associated in 79% ($n = 67$) (Table 2).

Intervention group

As displayed in Table 3, 84% ($n = 71$) underwent surgery for, respectively, DSS in 87% ($n = 62$) and tunnel-type SAS in 13% ($n = 9$) of patients. Associated heart defects were present in most patients (80%; $n = 57$) (Table 2). Twenty-nine percent ($n = 19$) had mild AR at first diagnosis of SAS, but none had more than grade II. The median follow-up time of this group was 10.8 years (5.4–17.8). Overall mortality in this cohort was 3% (2/71).

Primary intervention

The median time interval between diagnosis and surgery was 0.3 (0.1–1.1) years. Mild preoperative AR was present in 41% ($n = 28$). One patient developed grade III AR, and 2 patients grade IV AR before surgery. Table 4 summarizes the type of initial intervention for the SAS subtypes. Four patients with DSS required complex surgery at the first intervention. A Ross procedure was performed in 2 patients. One patient developed DSS with grade IV AR after neonatal balloon dilatation of a stenotic bicuspid valve. The second patient had previous ventricular septum defect (VSD) closure with residual shunt, resulting in DSS with grade IV AR. The modified Konno procedure was performed in 2 DSS patients with previous interventions for an atrioventricular septum defect and a transposition of the great arteries with VSD and pulmonary atresia. Eleven patients had concomitant VSD closure, and 24 patients had surgical or spontaneous closure of a VSD in the past. The operative result was effective, illustrated by a mean postoperative LVOT gradient of 6.9 ± 11.1 mmHg. One patient

Table 3: Intervention group: comparison between discrete and tunnel-type SAS

	Discrete ($n = 62$)	Tunnel type ($n = 9$)	*P*-value
Sex (male)	39 (63)	4 (44)	0.30
Age at diagnosis (years)	2.6 (0.7–6.0)	0.2 (0.1–4.2)	0.06
Age at first intervention (years)	3.7 (2.0–8.5)	1.3 (0.2–6.7)	0.11
Age <1 year at first intervention	9 (15)	4 (44)	0.052
Age <2 year at first intervention	18 (29)	5 (56)	0.14
Small aortic annulus	5 (8)	2 (22)	0.22
Bicuspid aortic valve	13 (21)	3 (33)	0.42
Reintervention	11 (18)	7 (78)	**0.001**
Peak gradient at diagnosis (mmHg)	38.1 ± 25.3	24.0 ± 13.5	**0.031**
Initial preoperative peak gradient (mmHg)	53.5 ± 31.5	49.4 ± 31.6	0.73
Peak postoperative gradient after first intervention (mmHg)	6.0 ± 10.1	13.0 ± 15.8	0.083
Postoperative gradient >20 mmHg	7 (12)	3 (33)	0.12
Peak gradient at latest follow-up (mmHg)	10.2 ± 14.6	7.0 ± 19.8	0.58

Values are presented as *n* (%), means ± standard deviation or median (Q1–Q3) as appropriate.
SAS: subaortic stenosis.
Bold face values are statistically significant.

Table 4: Surgical procedures at primary intervention

	Discrete ($n = 62$)	Tunnel ($n = 9$)
Membrane resection	29	4
Membrane resection + septal myectomy	29	3
Modified Konno procedure	2	2
Ross procedure	2	0

Table 5: Surgical procedures at reintervention

	Discrete ($n = 11$)	Tunnel ($n = 7$)
Membrane resection	4	1
Membrane resection + septal myectomy	2	1
Modified Konno procedure	3	0
Ross procedure	1	2
Ross–Konno procedure	1	3

required a pacemaker for complete heart block after DSS resection. Early postoperative mortality after the first intervention occurred in 1 patient (1%) with DSS and mitral valve stenosis died. The exact cause of death could not be identified in the patient's record.

Reintervention

Reoperation was necessary in 25% ($n = 18$) at a median interval of 4.3 (2.6–7.5) years after the primary procedure. LVOT gradient before reoperation was 57.8 ± 20.5 mmHg.

Eleven (18%) patients with DSS needed reoperation. Seven children had simple membrane recurrence with progressively increasing LVOT gradient, 3 patients showed worsening of AR and 1 a combination of both. Surgical procedures at reintervention are displayed in Table 5. One patient required a third intervention for LVOTO recurrence and AR grade III, consisting of a repeated enucleation procedure and associated aortic valve repair.

Seven out of 9 tunnel-type SAS patients (78%) underwent at least 1 reintervention (Table 5). A third intervention was necessary in 2 patients for recurrent LVOT gradient, consisting of a Ross, and a modified Konno procedure.

In both DSS and tunnel-type SAS, only half ($n = 4$) of the patients treated with a Ross or Ross–Konno operation at reintervention showed abnormal aortic valve morphology. Two patients had a hypoplastic aortic annulus, 1 patient had a bicuspid aortic valve and 1 patient had both. There was no association between a bicuspid aortic valve and a hypoplastic aortic annulus ($P = 0.17$), nor with tunnel-type SAS ($P = 0.40$).

Definitive pacemaker implantation was necessary in 3 patients, respectively, after the first or second reintervention. One patient with tunnel-type SAS died shortly after reintervention due to an unexplained hyperkalaemia. No late mortality was observed during further follow-up, resulting in a total mortality of 3% ($n = 2$).

Risk factor analysis of reintervention

Patients with a tunnel-type lesion had an increased risk for reintervention in comparison to those with DSS. Kaplan–Meier estimates of freedom from reoperation in patients with DSS were, respectively, 88 ± 5% and 82 ± 6% at 5 and 10 years. In contrast, the tunnel-type group showed a significantly lower freedom from reintervention of 33 ± 16% and 17 ± 14% at 5–10 years (log-rank $P < 0.001$) (Fig. 2).

Univariable analysis identified postoperative peak gradient >20 mmHg, hypoplastic aortic annulus, age <2 years at initial intervention and tunnel-type SAS as significant predictors of reintervention; all factors were confirmed at multivariable analysis (Table 6). Reoperation rate in DSS ($n = 11$) did not differ significantly if a simple enucleation was performed ($n = 3$; 10%), compared to those undergoing additional septal myectomy ($n = 8$, 28%) ($P = 0.11$). DSS children treated with additional septal

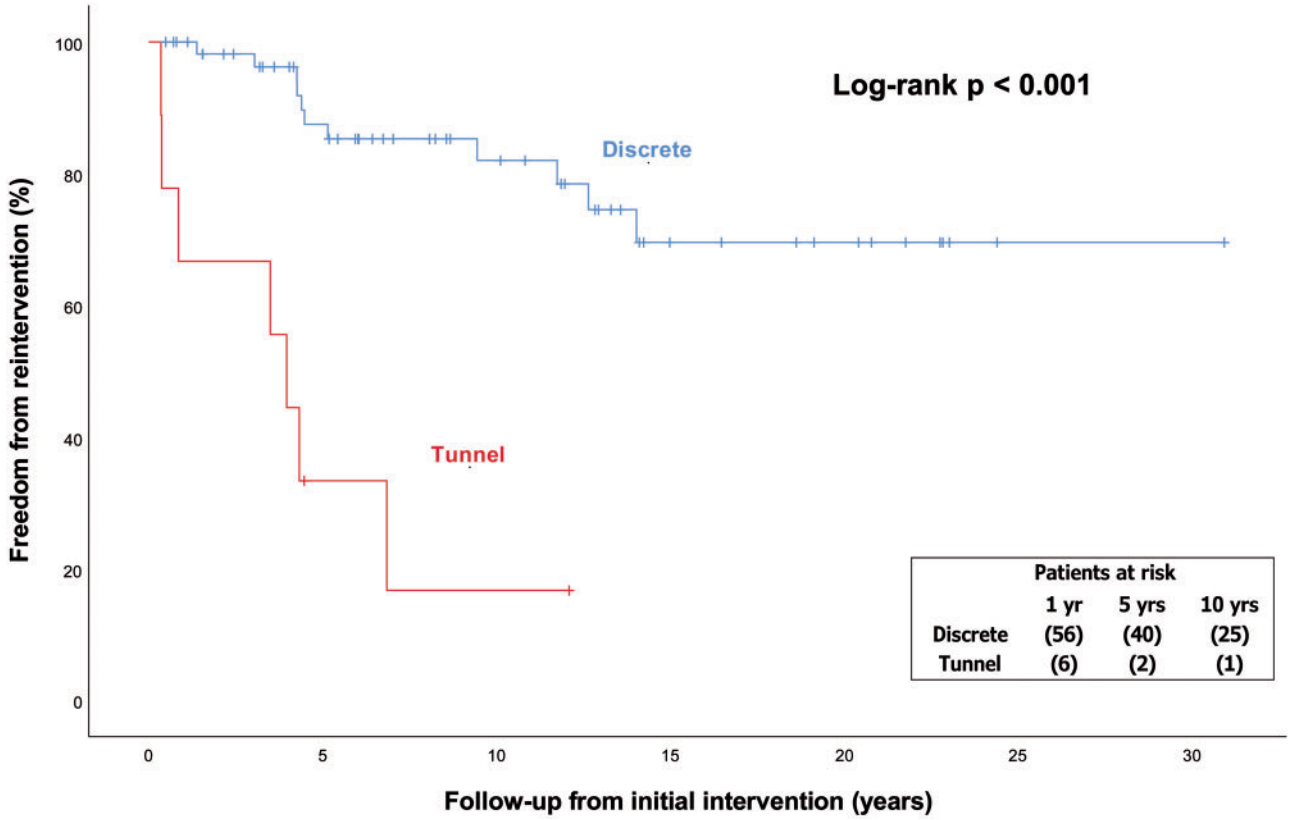

Figure 2: Kaplan–Meier survival curve for freedom from reoperation in patients with discrete and tunnel-type subaortic stenosis.

Table 6: Predictors of reintervention

	Univariable analysis			Multivariable analysis		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Age at diagnosis	0.89	0.76–1.05	0.16			
Age at first intervention	0.90	0.79–1.03	0.12			
Age <2 years at first intervention	2.81	1.11–7.11	**0.029**	3.24	1.09–9.86	**0.035**
Concomitant CHD	1.75	0.65–4.68	0.27			
VSD	0.43	0.16–1.15	0.092			
AVSD	0.63	0.14–2.74	0.54			
CoA	2.61	0.97–6.99	0.057			
Type (tunnel vs DSS)	9.05	3.30–24.80	**<0.001**	7.46	2.48–22.49	**<0.001**
Hypoplastic aortic annulus	4.89	1.59–15.00	**<0.001**	11.07	3.03–40.47	**<0.001**
Bicuspid aortic valve	0.83	0.27–2.52	0.74			
Peak gradient at diagnosis	1.00	0.98–1.03	0.86			
Preoperative peak gradient	1.01	1.00–1.03	0.19			
Postoperative peak gradient >20 mmHg after first intervention	3.96	1.78–11.17	**0.009**	6.56	1.41–24.1	**0.005**

AVSD: atrioventricular septum defect; CHD: congenital heart disease; CI: confidence interval; DSS: discrete subaortic stenosis; HR: hazard ratio; VSD: ventricular septum defect.

Bold face values are statistically significant.

myectomy were significantly younger than those having simple membrane resection [2.3 (0.8–5.2) vs 4.6 (2.3–9.4) years, $P = 0.014$].

Conservative group

Sixteen percent ($n = 14$) of the SAS patients were followed-up conservatively (Table 1). The median age at diagnosis was 4.1 (2.4–9.3) years, and the LVOT gradient at diagnosis was 13.6 ± 13.9 mmHg. Within a median follow-up interval of 9.3 (5.5–13.1) years, the LVOT gradient progressed to 19.3 ± 12.4 mmHg at the latest follow-up. All had DSS, while 71% ($n = 10$) had associated congenital cardiac disease (Table 2). The size and morphology of the aortic valve was normal except for 2 patients with a bicuspid valve. Mild AR was present at diagnosis in 29% ($n = 4$) patients. Despite an increasing number of patients developing AR (57%; $n = 8$) at last follow-up, none had AR >grade

2. In comparison with SAS patients requiring intervention, patients in this group were commonly older ($P = 0.024$) and had a lower LVOT gradient at diagnosis ($P < 0.001$).

DISCUSSION

This study was performed on a heterogeneous paediatric cohort of SAS. Almost 80% showed associated heart defects, which is slightly higher than the 71% reported previously in a comparable group [17]. We demonstrated that a substantial number of children are at risk of LVOTO recurrence despite initially effective LVOT relief. In this cohort, 25% of the children needed at least 1 reintervention, comparable to 20% in other series [8]. The results of the multivariable analysis showed that besides the tunnel-type SAS, a postoperative gradient >20 mmHg, age at initial surgery <2 years and a hypoplastic aortic annulus, defined by a *z*-score of <-2, were significant predictors of reoperation, independent of SAS subtype. Several risk factors for reintervention have been identified, such as a higher LVOT gradient at diagnosis and higher preoperative gradient [3, 9, 18]. We only found that a remnant postoperative LVOT gradient >20 mmHg was predictive for reintervention, confirming earlier findings [13–15]. This might suggest a suboptimal surgical result possibly pointing to an unaddressed anatomical substrate for SAS recurrence and underlines the need for intensified follow-up in this particular group. Younger age at initial intervention has been associated with a higher reintervention rate in previous paediatric studies. Presentation of SAS early in life is seen as surrogate of a more complex disease yielding intrinsically a higher risk for reoperation [8, 10, 11, 13, 18]. First surgery before the age of 2 years was a risk factor for reintervention in our patients as well, strengthening the hypothesis of a more severe cardiac disease phenotype early in life.

Results differ regarding the best surgical method to prevent reintervention in DSS. Some propose a more aggressive initial approach with a beneficial effect of septal myectomy over simple enucleation [4], while others have reported contradictory results [10, 19, 20]. Adding a septal myectomy to simple membrane resection in DSS patients did not enable to decrease the later reoperation rate in our hands. However, the decision to perform a septal myectomy was subjective, leading to results in line with Mazurek *et al.* [10] who did not show either a benefit of the addition of a septal myectomy during SAS membrane resection. The real contribution of this particular technical adjustment is, however, difficult to evaluate as it was more frequently done in older children, probably presenting in a more advanced physiological stage of their disease, entailing increased left ventricular hypertrophy.

Differentiating patients according to the anatomical subtype is important to adopt the correct clinical and surgical strategy in SAS treatment. Reports on complex SAS are scarce in comparison with DSS studies. Reoperation rates vary depending on the complexity of the SAS lesion [12]. Unfortunately, the definition of complex SAS lacks uniformity. We focused on the qualitative aspect of the SAS morphology, independent of associated congenital cardiac disease, and without relying on quantitative measurements to define the tunnel-type SAS subtype more precisely. Reoperation rate in the DSS group (18%) was significantly lower in comparison to the tunnel-type group (78%) during a follow-up period of almost 11 years. Our findings are similar to another study, which reported a reoperation rate of 70% in a mixed population of 50 patients with tunnel-type SAS after a follow-up of 12 years [15]. The higher reintervention rate in tunnel-type SAS was also reported by others, motivating a switch to a more aggressive surgery over the years in this peculiar type of SAS [14].

Surgical treatment of tunnel-type SAS remains challenging. A more elaborate approach at initial surgery as a modified Konno when a normal sized aortic annulus and valve are present or, as a Ross–Konno procedure in case of a diminutive aortic valve size, have been suggested [14, 15, 21]. In our group of 9 patients with tunnel-type SAS, a modified Konno septoplasty, Ross–Konno or Ross procedure was necessary in all except two during follow-up. The high number of reinterventions in tunnel-type SAS patients resulting ultimately in the need for extensive surgery might indirectly justify a more aggressive LVOTO relief during the first surgery in these particular patients. However, it is conceivable that one hesitates to perform such extensive procedure already in early infancy because of the potentially increased complication rate in these small children.

The aortic valve size is another important feature in SAS. A small aortic annulus was previously identified as a risk factor for LVOTO recurrence and reoperation in univariable analysis, though not confirmed by multivariable analysis [8, 14, 18]. In our study, a hypoplastic aortic annulus was an independent risk factor for reintervention, regardless of SAS subtype. This should be taken into consideration when determining the surgical approach for patients with an apparent simple form of SAS in combination with a hypoplastic aortic annulus. As solely adding a septal myectomy to enucleation of the membrane in DSS does not seem to protect against reintervention, performing a Ross procedure might be considered earlier to achieve definitive LVOT relief. Hence, the option for replacing the small sized aortic valve earlier at the first surgery must be outweighed against the long-term drawback of the pulmonary autograft, susceptible to progressive root dilation and valve dysfunction [22].

Further analysis of the reinterventions in our series demonstrated that half of patients who finally were treated with a Ross or Ross–Konno procedure had anatomically and functionally a normal aortic valve at presentation. As the flow turbulences related to a residual subaortic LVOT narrowing are promoting the progressive cicatricial fibrous infiltration of the aortic valve, close follow-up of these patients is mandatory to send them for repeat surgery before unrepairable aortic valve damage has developed [23].

All findings underscore the need for an individualized approach, including a careful preoperative assessment of the LVOT anatomy as well as intraoperatively, to choose the optimal surgical strategy. Additional imaging with 3D reconstruction of the LVOT morphology might be useful to justify more aggressive surgery, if one wants to improve the reoperation rate. On the other hand, for some infants and neonates with complex SAS, a reoperation should not be seen as a surgical failure, if the first procedure is enhancing the survival perspective as well as the quality of life, for example by avoiding the occurrence of a complete heart block and subsequent need for definitive pacemaker therapy, which is commonly low after simple membrane resection [4, 10, 16, 18].

A substantial portion of children did not require surgical treatment and warranted only expectative follow-up with echocardiography. SAS has previously been described as a disease with 2 distinct clinical pathways: an aggressive disease with rapid LVOTO progression and a milder form with no or slow

progression during childhood [5, 24]. Similar to previous findings, this cohort had a lower gradient [25] and was commonly older at the time of diagnosis [5]. Although an important subset of patients has a stable or slowly evolving disease during childhood, the progression continues into adulthood at a slow rate. In case of the presence of a VSD, the progression rate is faster [26]. However, in patients with an intact interventricular septum, a higher gradient of SAS obstruction has been observed beyond the age of 50 years [27]. Since the rate of progression is consistently slow or non-existent in this non-surgical group and does probably not reach significance until the later stages of life, a watchful waiting approach is a safe option. The presence of AR in this cohort doubled during the follow-up period, but none developed more than mild AR. These results are consistent with adult series [26, 27]. Therefore, early surgery for gradients <40 mmHg to prevent damage of the aortic valve is not indicated. But once the LVOT gradient exceeds 40 mmHg in childhood, postponing surgery to reduce the risk for reintervention might be hazardous since the development of moderate to severe AR is associated with LVOT gradients of ≥50 mmHg [28]. Therefore, surgery should not be delayed in children once the aortic gradient exceeds 40 mmHg.

Limitations

This study had several limitations intrinsic to its retrospective nature. Being a single-centre experience, statistical analysis may be biased by the relatively small sample size. The tunnel-type SAS subgroups included only 9 patients. Moreover, data on tunnel-type SAS are limited and no uniform definition exists on complex SAS. Another limitation of this single-centre review is that this study reflects a surgical policy which might differ from other centres, thereby limiting the generalizability of the results. Moreover, the choice for some procedures like the addition of a septal myectomy was merely subjective and not supported by evident quantitative data.

The number of patients with a conservative approach was relatively low compared to the number of patients needing surgery. As 40% of our operated patients are referred from outside the Paediatric Cardiology department, we estimate that at least a comparable percentage of non-operated SAS patients were not included in our database.

CONCLUSION

This study analysed the clinical outcome of a mixed paediatric cohort with SAS. In the surgically treated group, LVOTO recurrence requiring reoperation was significantly determined by an increased residual LVOT gradient after repair, age <2 years and an aortic annular *z*-score of <-2 at initial surgery, independent of SAS subtype. Children with DSS undergoing LVOT surgery do well in the majority of cases. Tunnel-type SAS is significantly associated with an increased risk of reoperation. As a substantial number of patients in both groups are finally ending with extensive LVOT reconstruction including a Ross, Ross–Konno or modified Konno procedure, it opens the discussion whether a more extensive LVOT relief should be performed at an earlier stage in children presenting one of these risk factors, while outweighing the advantage of a decreased reoperation risk against its technical complexity and effect on morbidity and eventual mortality, particularly in the younger aged ones.

In contrast, an expectative approach seems justified in children with DSS presenting with a low gradient during childhood and adolescence, as disease progression is slow and commonly at a low risk for complications later in life.

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Author contributions

Rik De Wolf: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Resources; Supervision; Visualization; Writing—original draft; Writing—review & editing. **Katrien François:** Conceptualization; Resources; Supervision; Writing—review & editing. **Thierry Bové:** Conceptualization; Formal analysis; Resources; Supervision; Writing—review & editing. **Ilse Coomans:** Formal analysis; Resources; Writing—review & editing. **Katya De Groote:** Resources; Writing—review & editing. **Hans De Wilde:** Resources; Writing—review & editing. **Joseph Panzer:** Resources; Writing—review & editing. **Kristof Vandekerckhove:** Resources; Writing—review & editing. **Daniël De Wolf:** Conceptualization; Data curation; Formal analysis; Methodology; Resources; Supervision; Visualization; Writing—original draft; Writing—review & editing.

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