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Echocardiographic predictors of reoperation for subaortic stenosis in children and adults

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Key question

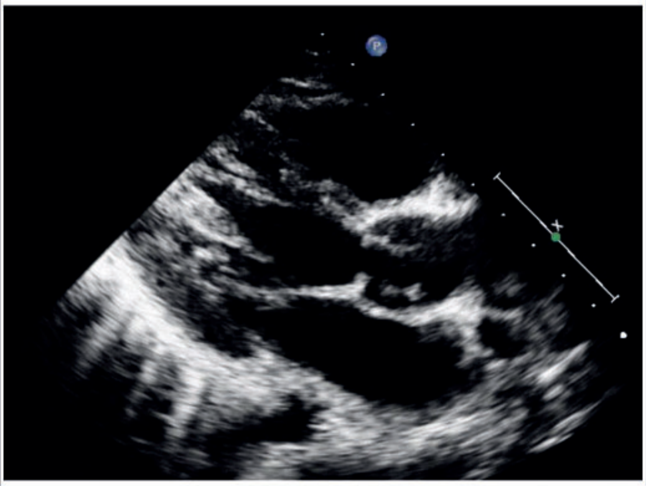
Which are the predictors of reoperation of subaortic stenosis (SAS)?

Key finding

Young age, unfavourable left ventricular (LV) geometry, interrupted aortic arch and higher residual LV outflow tract gradients were associated with recurrence of SAS.

Take-home message

Presence of interrupted aortic arch and unfavourable LV geometry can independently predict reoperation for SAS.



Abstract

OBJECTIVES: Subaortic stenosis (SAS) can present as various types of obstruction of the left ventricular outflow tract (LVOT) below the level of the aortic valve. Even though corrective surgery has been identified as the most effective treatment, SAS more frequently reoccurs requiring reoperation in a significant proportion of the patients. Previous studies have focused on predictors of recurrence in various subgroups of patients with SAS, but rarely in the overall population of patients with SAS. The aim of this study was to determine the predictors of recurrence of SAS after initial corrective surgery.

METHODS: Patients from the database of the Congenital Cardiology Department of the University Hospital of Southampton with significant SAS requiring corrective surgery were included in the study. Data retrieved were obtained and used to determine the predictors of SAS recurrence after the initial corrective surgery.

RESULTS: Eighty-two patients (paediatric, $n = 72$ and adult, $n = 10$) who underwent initial successful resection were included in the analysis. Thirty patients required reoperation for recurrent SAS. These were significantly younger (median age 3.0 vs 6.7 years, $P = 0.002$).

CONGENITAL

The recurrence of SAS was more common in patients with an interrupted aortic arch (23.3% vs 3.8%, $P = 0.010$) and unfavourable left ventricle geometry (43.3% vs 7.6%, $P < 0.001$), with steeper aortoseptal angle (131.0° ± 8.7° vs 136.1° ± 8.6°, $P = 0.030$), shorter distance between the point of obstruction of the LVOT and the aortic valve annulus in systole and diastole (median 4.30 vs 5.90 mm, $P = 0.003$ and 3.65 vs 4.95 mm, $P = 0.006$, respectively) and in those who had higher residual peak and mean LVOT gradients postoperatively (29.3 ± 16.0 vs 19.8 ± 10.7 mmHg, $P = 0.006$ and 15.9 ± 8.3 vs 10.1 ± 5.8 mmHg, $P = 0.002$, respectively). Overall, the presence of an interrupted aortic arch [odds ratio (OR) 10.34, 95% confidence interval (CI) 1.46–73.25; $P < 0.019$] and unfavourable left ventricle geometry (OR 10.42, 95% CI 1.86–58.39; $P < 0.008$) could independently predict reoperation for SAS after initial successful resection.

CONCLUSIONS: Patients who have initial corrective surgery for SAS at a younger age, unfavourable left ventricle geometry, an interrupted aortic arch and higher early postoperative LVOT gradients are more likely to have recurrent SAS requiring reoperation.

Keywords: Subaortic stenosis • Predictors of recurrence of subaortic stenosis • Reintervention for subaortic stenosis • Echocardiography for subaortic stenosis

INTRODUCTION

Subaortic stenosis (SAS) encompasses a range of obstructions of the left ventricular outflow tract (LVOT) below the aortic valve (AV) [1] and is considered an acquired condition [2, 3]. The obstruction progressively increases in approximately 50% of patients and therefore it can become apparent later in infancy or early childhood [4]. SAS is more frequently associated with other congenital lesions such as ventricular septal defect (VSD), coarctation of the aorta, interrupted aortic arch (IAA), double-outlet right ventricle, or atrioventricular septal defect (AVSD) [5]. As an isolated lesion, it accounts for 8–20% of overall LVOT abnormalities [1, 6].

Although surgery for SAS appears to be an effective treatment for the majority of patients, recurrence occurs in up to 55% of cases, and reoperation is required in up to 30% of patients [7–9]. The mechanisms of disease progression and recurrence after initial resection remain unclear. Various anatomical and echocardiographic features have been associated with the development, progression and recurrence of the disease after an initial surgery, but early prediction of which patients will suffer recurrence remains problematic. Abnormal left ventricular geometry causing chronic flow disturbance and turbulent flow may be responsible for increased shear stress, abnormal proliferative response, and increased endothelial cell turnover in the subvalvar region [10]. The characteristics of unfavourable LVOT geometry include a wide mitral-aortic separation, exaggerated aortic dextroposition, a steep aortoseptal angle, the involvement of the anterior mitral valve leaflet and the proximity of the obstructive lesion to the AV. These features and factors such as early surgical resection have been previously associated with the development, more rapid disease progression, recurrence and reoperation of various types of SAS [8, 9, 11, 12]. Previous studies have largely concentrated on subsets of this heterogeneous group, but there is a paucity of studies addressing the group as a whole. It is therefore challenging for the clinician to use published data to treat individual patients.

The aim of this study was to determine the anatomical, clinical and echocardiographic parameters that predict the recurrence of SAS requiring reoperation after initial corrective surgery.

METHODS

Subjects

The database of the Congenital Cardiology Department of the University Hospital of Southampton was used to identify all patients who were diagnosed with subvalvar aortic stenosis between February 1976 and March 2016. Patients were included in the analysis if they fulfilled the following criteria: (i) diagnosis of any type of SAS, (ii) initial successful surgical resection of the SAS, (iii) at least 36 months of follow-up or reoperation during this period and (iv) normal segmental cardiac anatomy postoperatively. Patients with hypertrophic cardiomyopathy were excluded from the analysis. Demographic and clinical data were retrieved from the patients' medical records. Both adult (over 18 years old) and paediatric patients were included in the analysis.

Surgical data

Surgical reports were reviewed for all patients. The following unfavourable left ventricle (LV) geometry characteristics prone to develop SAS were documented at the time of surgery: posterior deviation of outlet septum, extension of structures to LVOT, dextroposition of the aorta, longer and narrower LVOT, steeper aortoseptal angle and wide aortomitral separation by visual inspection, proximity of the stenosis to the AV and concomitant presence of a VSD [11, 13]. All interventions were carried out on cardiac arrest via an aortotomy and care was taken in removing all recognizable lesions. Techniques selectively applied to individual patients included as necessary: membrane complete resection, LVOT myectomy, blunt and/or sharp thinning of aortic and/or mitral valve leaflets, Ross or modifications of Konno procedures and concomitant repair of any other cardiac lesions (e.g. VSD closure of any type, mitral valve repair and aortic coarctation repair). A surgical procedure was considered successful when it obtained:

- Complete removal of a discrete subaortic membrane from the muscular section of the LVOT as well as the anterior leaflet of the mitral valve, and the expected augmentation of the LVOT diameter (demonstrated by probing the LVOT with a Hegar dilator to a size bigger than the adequate *Z*-score diameter, while on cardioplegic arrest, to account for systolic dynamic compression).
- Complete resection of subaortic fibrosis from the ventricular aspect of the AV and trigones. When subaortic fibrosis heavily involved the ventricular aspect of the AV leaflets, resection was limited by the need to preserve integrity of the leaflets and avoid the need for leaflet reconstruction.
- Resection of additional mitral valve tissue including cysts and non-specific fibrous nodules.
- Resection of all accessory subvalvar material including accessory chordae.

- Resection of hypertrophied muscle in the LVOT. For this, the extent of resection into the LVOT was assessed, on preoperative echocardiogram. The depth of the resection was intraoperatively judged, the limiting factor being injury to the left bundle branch and the bundle of His or creation of an interventricular communication. The width of the resected wedge was limited by the standard anatomical criteria: the mitral valve anterior leaflet to the left and the position of the bundle to the right. Hegar dilators were used to size the resection as described above.
- Appropriate complete resection of endocardial fibroelastosis.
- Intraoperative echocardiographic demonstration of rightward movement of interventricular septum when repairing VSD associated with posterior deviation of the septum.

Echocardiographic analysis

The initial preoperative, postoperative and most recent follow-up echocardiograms were reviewed and selected still frames (end-diastole and mid-systole) were used for analysis. Measurements used for the statistical analysis were the means of triplicate measurements performed by 2 experienced echocardiographers (P.T. and N.D.P.) who were blinded to measurements of each other and the patient outcomes. The body surface area was calculated from the recorded height and weight using the Haycock formula which has been validated for infants, children and adults [14]. The SAS type was categorized as discrete subaortic stenosis, which included, as previously defined, subaortic membrane, fibromuscular ridge or fibromuscular ridge associated with membrane [8]; tunnel type; and LVOT obstruction due to accessory tissue associated with AVSD. Two-dimensional echocardiographic images were used to calculate the following, which were measured in all echocardiograms as previously described [10, 11].

- Left ventricular ejection fraction (EF) and fractional shortening according to standard guidelines [15].
- The distance of the lesion from the hinge point of the right coronary cusp of the AV in systole and diastole from the parasternal long-axis view.
- The width of the membrane or fibromuscular ridge (measured from the parasternal long-axis view as the distance from the septal insertion to the free edge of the obstructive lesion).
- The AV annulus diameter *z*-score [16].
- The aortoseptal angle [measured by the method described by Fowles *et al.* [10], by using a protractor superimposed on the angle formed by the long axis of the ascending aorta and the plane of the ventricular septum].
- The distance between the aortic and mitral valves in systole in the parasternal long-axis view measured from the hinge point of the non-coronary aortic cusp to the hinge point of the anterior mitral valve leaflet.
- The degree of aortic dextroposition was graded qualitatively as normal when less than one-third of the annulus was intercepted by an extrapolation of the ventricular septum long axis, as mild when one-third to two-thirds of the annulus was intercepted, and as marked when more than two-thirds was intercepted.

The maximum and mean gradients across the LVOT (using the simplified Bernoulli equation) from the LVOT spectral Doppler tracings were recorded preoperatively and postoperatively. Aortic regurgitation was graded qualitatively as none, mild, moderate or severe as previously described [17]. Associated cardiac lesions, if any, were also recorded. Early postoperative period was considered less than 30 days after the initial operation.

Statistical analysis

Patient demographic, clinical and echocardiographic characteristics were compared between patients with recurrent SAS who required reoperation after initial resection and those who did not. Variables were tested for normality using the Kolmogorov–Smirnov test to eliminate potential sources of errors which could affect the subsequent analysis. Values are expressed as mean ± standard deviation for variables with normal distribution, as median (associated range) for variables without normal distribution and as percentages when appropriate. The differences between group means were compared using independent *t*-tests or Mann–Whitney *U*-tests (for normally and non-normally distributed variables, respectively). The χ^2 test was used to test group differences for categorical variables for data sets of appropriate size (when <20% of the contingency cells of had expected values <5). Otherwise, a Fisher's exact test was used to test group differences for categorical variables. Logistic regression analysis was used to assess multiple-adjusted risk for the recurrence of SAS in relation to demographic, clinical and echocardiographic factors in all subjects. Kaplan–Meier curves were used to schematically demonstrate the effect of each independent predictor on the probability of freedom from reoperation during the follow-up period; patients who did not require reoperation were censored at the time of last follow-up. A *P*-value of <0.05 was considered significant. The SPSS statistical software package (version 15.0 for Windows, SPSS Inc., Chicago, IL, USA) was used.

RESULTS

Subjects

There were 82 patients with SAS who underwent initial successful resection during the study period. The median age of patients at the time of first surgery was 4 years (range 2 months–70 years). There were 10 (12.2%) adults and 72 (87.8%) paediatric patients included in the analysis. Sixty-seven patients (81.7%) were diagnosed with discrete SAS, 10 patients (12.1%) with tunnel type SAS and 5 patients (6.1%) with LVOT obstruction due to accessory tissue following AVSD repair. The indication for initial SAS resection or the need for reoperation remained the same for all patients included in the study. This included clinical and echocardiographic evidence of symptomatic SAS and involved agreement between cardiologists and cardiac surgeons at a multidisciplinary team meeting. The threshold for surgical intervention was a peak LVOT gradient of >50 mmHg or mean gradient of >30 mmHg before surgery; this did not vary significantly during the 40-year study period based on the data retrieved from the patient records. A separate statistical analysis (data available on request) confirmed that there were no significant differences in the demographic, anatomical, surgical and echocardiographic characteristics (that could potentially influence the results of the subsequent analysis), between the patients who had undergone initial successful resection of SAS within the last 10 years and those who had their initial intervention more than 10 years ago.

Table 1: Demographic, anatomical and surgical characteristics of the patients who did and did not require reoperation for SAS

	Reoperation (*n* = 30)	No reoperation (*n* = 52)	*P*-value
Age at first surgery (years), median (IQR)	3.0 (0.0–38.0)	6.7 (0.0–70.0)	**0.002**
Adult patients (%), *n* (%)	1 (3.3)	9 (17.3)	0.084
Body surface area (m^2), median (IQR)	0.56 (0.20–2.12)	0.86 (0.16–2.15)	**0.001**
Male gender (%), *n* (%)	15 (50.0)	36 (69.2)	0.101
Type of SAS (%), *n* (%)			
Discrete SAS	26 (86.8)	41 (78.8)	0.555
Tunnel type	2 (6.7)	8 (15.4)	0.312
Accessory AVSD tissue type	2 (6.7)	3 (5.8)	1.000
Associated lesions (%), *n* (%)			
Shone syndrome	4 (13.3)	2 (3.8)	0.185
Aortic stenosis	3 (10.0)	6 (11.5)	1.000
VSD	1 (3.3)	9 (17.3)	0.084
Coarctation	5 (16.6)	7 (13.4)	0.751
Interrupted aortic arch	7 (23.3)	2 (3.8)	**0.010**
AV morphology (%), *n* (%)			
Unicuspid	0 (0.0)	0 (0.0)	
Bicuspid	9 (30.0)	17 (32.7)	1.000
Tricuspid	21 (70.0)	35 (67.3)	0.808
Thickened leaflets (%), *n* (%)	4 (13.3)	9 (17.3)	0.760
Doming valve (%), *n* (%)	3 (10.0)	4 (7.6)	0.703
Type of surgery (%), *n* (%)			
AV peeling	5 (16.6)	9 (17.3)	1.000
MV peeling	6 (20.0)	13 (25.0)	0.787
Myectomy	16 (53.3)	37 (71.1)	0.150
Ross/Konno	0 (0.0)	5 (10.0)	0.153
Bypass time (min), median (IQR)	69.0 (24.0–256)	61.5 (27.0–201)	0.361
Unfavourable LV geometry (%), *n* (%)	13 (43.3)	4 (7.6)	**<0.001**

Statistically significant values are in bold (<0.05).
AV: aortic valve; AVSD: atrioventricular septal defect; IQR: interquartile range; LV: left ventricle; MV: mitral valve; SAS: subaortic stenosis; VSD: ventricular septal defect.

Surgical procedures and outcomes

All patients underwent resection of a subaortic membrane or fibrous strands at first repair. In 53 patients (64.6%), associated septal myectomy was performed. Aortic and mitral valve leaflets were thinned or underwent resection of fibrous tissue in 14 (17.1%) and 19 patients (23.1%), respectively. One patient underwent a Ross procedure and 4 patients (4.8%) had a Konno procedure. Additional surgical procedures for associated congenital cardiac anomalies (VSD closure, coarctation repair, IAA repair) were performed in 32 patients (39.1%). One patient developed postoperative third-degree atrioventricular block requiring permanent pacemaker insertion. Thirty patients (36.5% of the entire cohort) required reoperation for recurrent SAS. Of those, 1 was an adult (10% of the adult cohort) and the remaining 29 were children (40.1% of the paediatric cohort) ($P = 0.084$). The patients who required reoperation for the recurrence of SAS underwent initial SAS resection at a significantly younger age compared to the patients who did not require reoperation (median age 3.0 vs 6.7 years, $P = 0.002$). A similar outcome was found when only patients under 18 years were analysed: those who required reoperation had initial surgery at a significantly younger age compared to those who did not require reoperation (median age 3.0 vs 5.0 years, $P = 0.005$).

There were no significant differences in the type of SAS, AV morphology, preoperative EF or type of surgery between the patients who did and did not require reoperation. The presence of IAA was significantly more common in the patients who did require reoperation compared to those who did not (23.3% and 3.8%, respectively, $P = 0.010$). Demographic, anatomic and surgical data of the patients requiring reintervention and not requiring reintervention are shown in Table 1.

Predictors of reintervention

There was good correlation between the preoperative echocardiographic findings and the intraoperative surgical findings. Markers of unfavourable LV geometry were much more prevalent in patients who required repeat surgery for SAS (43.3% vs 7.6%, $P < 0.001$). In particular, patients in this group tended to have a steeper aortoseptal angle (131.0°±8.7° vs 136.1°±8.6°, $P = 0.030$) confirmed at surgery. Equally, they had a significantly shorter distance between the point of obstruction of the LVOT and the AV annulus in both systole and diastole (median 4.30 vs 5.90 mm, $P = 0.003$ and median 3.65 vs 4.95, $P = 0.006$, respectively). Other anatomical characteristics associated with reinterventions included IAA. Reintervention was also associated with higher peak and mean residual LVOT gradients at surgery (29.3 ± 16.0 mmHg vs 19.8 ± 10.7 mmHg, $P = 0.006$ and 15.9 ± 8.3 mmHg vs 10.1 ± 5.8 mmHg, $P = 0.002$, respectively). Residual gradients at surgery were deemed to be unrelated to surgically correctable residual lesions, but rather to non-surgically repairable lesions, such as unfavourable geometry, funnel-like LVOT or relatively smaller aortic annulus size. The echocardiographic characteristics of these patients are shown in Table 2.

Multiple-adjusted binary logistic regression analysis for all the significant differences between the 2 groups showed that only unfavourable LV geometry [odds ratio (OR) 10.42, 95%

Table 2: Echocardiographic characteristics of the patients with and without recurrence of SAS that required reoperation

	Reoperation (*n* = 30)	No reoperation (*n* = 52)	*P*-value
Ejection fraction (%), mean ± SD	69.6 ± 10.1	73.3 ± 6.0	0.119
Fractional shortening (%), mean ± SD	35.3 ± 9.5	39.1 ± 8.7	0.157
AV annulus *z*-score, mean ± SD	-1.2 ± 1.3	-0.5 ± 2.0	0.140
AV override (%), *n* (%)	14 (46.6)	17 (32.7)	0.201
Aortoseptal angle (°), mean ± SD	131.0 ± 8.7	136.1 ± 8.6	**0.030**
Lesion-AV distance, systole (mm), median (IQR)	4.30 (2.70–7.00)	5.90 (2.00–28.00)	**0.003**
Lesion-AV distance, diastole (mm), median (IQR)	3.65 (1.70–11.00)	4.95 (2.10–22.50)	**0.006**
Preoperative peak LVOT gradient (mmHg), mean ± SD	70.9 ± 22.7	69.3 ± 28.2	0.788
Preoperative mean LVOT gradient (mmHg), mean ± SD	38.0 ± 12.8	35.8 ± 15.9	0.518
Postoperative peak LVOT gradient (mmHg), mean ± SD	29.3 ± 16.0	19.8 ± 10.7	**0.006**
Postoperative mean LVOT gradient (mmHg), mean ± SD	15.9 ± 8.3	10.1 ± 5.8	**0.002**
>Mild AR (%), *n* (%)	2 (6.6)	5 (9.6)	0.135

Statistically significant values are in bold (<0.05).
AR: aortic regurgitation; AV: aortic valve; IQR: interquartile range; Lesion-AV: distance between the point of the obstructive lesion in the LVOT and the aortic valve annulus; LVOT: left ventricle outflow tract; SAS: subaortic stenosis; SD: standard deviation.

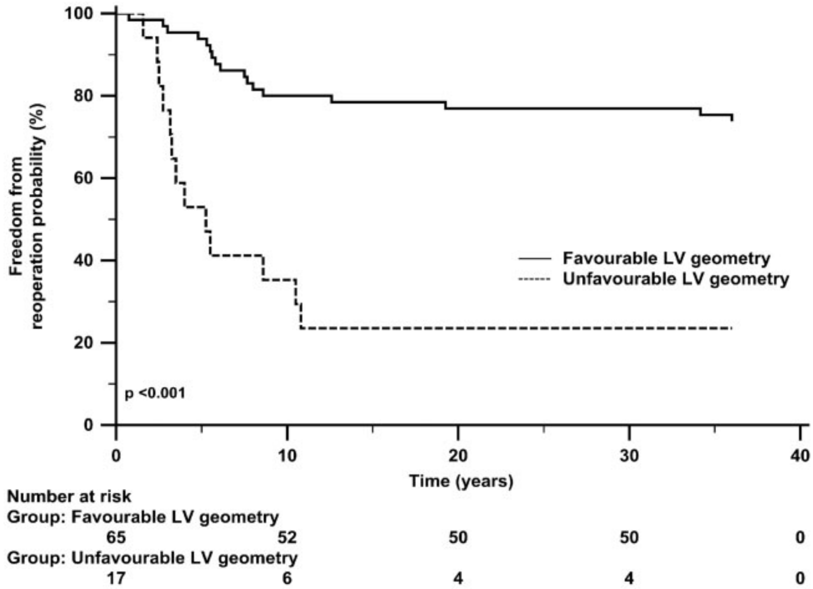


Figure 1: Kaplan–Meier curve showing freedom from reintervention by LV geometry type. Patients with unfavourable left ventricular geometry were significantly more likely to require reoperation ($P < 0.001$). LV: left ventricle.

confidence interval (CI) 1.86–58.39; $P < 0.008$] and IAA (OR 10.34, 95% CI 1.46–73.25; $P < 0.019$), but not postsurgical residual gradients, were independent predictors of reoperation for SAS after initial successful resection. The effects of unfavourable LV geometry and IAA on the probability of freedom from reoperation during the follow-up period are schematically represented in Figs 1 and 2.

DISCUSSION

Our study, that included a large cohort of patients with long postoperative follow-up, demonstrated that IAA and echocardiographic indices of unfavourable LVOT geometry strongly predict the recurrence of SAS requiring reoperation. In contrast to previous studies, the main outcome of this study was the need for reoperation and not the recurrence of SAS. Previous studies that have aimed to determine the recurrence of SAS are difficult to interpret or compare, as they employed inconsistent criteria to define recurrence of SAS or did not report any specific criteria [7, 9, 18–20]. Studies that have used reoperation as their primary outcome have been limited to either adult or paediatric patients with specific types of SAS [8, 19, 21, 22] differing from the current study, which included both adult and paediatric patients, and a wide range of types of SAS.

Previous studies have suggested that the type of surgical resection can influence the outcome of patients with SAS. In early reviews, it has been suggested that myectomy added to resection of a subaortic membrane at the initial surgery could reduce the risk of recurrence of SAS [19, 23], although this finding has not been supported by other research groups [9, 24]. These differences may be due to inconsistent outcome definitions used or the fact that surgeons' perception of need for myectomy corresponds to more aggressive underlying disease. However, previous reports

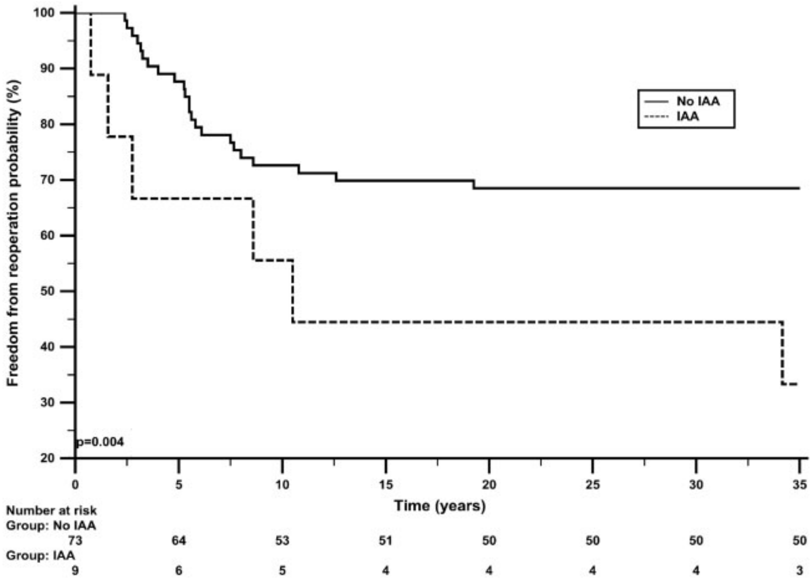


Figure 2: Kaplan–Meier curve showing freedom from reoperation by the presence or absence of an IAA. Patients with IAA were significantly more likely to undergo repeat surgery for subaortic stenosis ($P = 0.004$). IAA: interrupted aortic arch.

have shown that when a more aggressive myectomy is used, higher incidence of postoperative atrioventricular block is observed [18]. The association between recurrent myectomy and incidence of atrioventricular block has been widely recognized and studies with higher rates of recurrent SAS had significantly lower incidence of postoperative atrioventricular block and less extensive myectomy [7, 9, 19, 20]. These findings highlight the trade-off between the 2 strategies. In the present study, the incidence of postoperative atrioventricular block was low, similar to previous studies [7, 9, 19, 20], and interestingly, myectomy did not influence significantly the need for reoperation.

The preoperative mean and peak LVOT gradients did not differ significantly between the patients who required reoperation versus those who did not. The postoperative mean and peak LVOT gradients were significantly higher in the patients who required reoperation for SAS. Data for previous studies have shown that higher preoperative or postoperative LVOT gradients were associated with worse outcomes. There is also evidence indicating that both preoperative and postoperative LVOT gradients can predict recurrence of SAS for patients with various types SAS [8, 9, 18, 24]. In our study, the preoperative LVOT gradients did not predict reoperation for SAS, but patients with higher early postoperative LVOT gradients were more likely to undergo repeat surgery. The residual gradients after an initial successful resection could be attributed to a number of factors. Those may include inherently small LV outflow tracts, for which a Konno procedure or any of its modification were not performed during the first intervention, tight aortoseptal angles for which no specific solutions were adopted, the presence of extensive endocardial fibroelastosis or AV involvement that may have been treated more conservatively at the time of the first intervention, or even other unrecognized multiple causes of obstruction not fully addressed during the initial resection (i.e. membrane and mitral accessory chordae, or AVSD accessory chordae and malposition of the superior bridging leaflet). At the end of each operation, all surgically correctable lesions were judged has having been addressed; in the more recent era, this included echocardiographic assessment, and therefore it is unlikely that important correctable lesions were more frequently left. Furthermore, the postoperative LVOT gradients alone could not independently predict the need for reoperation after adjusting for all the significant differences in the demographic, anatomical, surgical and echocardiographic characteristics between the 2 groups.

It has been previously proposed that young age at first surgery is a surrogate marker for a more aggressive disease process [8]. Similar to previous studies, the current study also showed that patients who required reoperation for SAS had initial surgery at a significantly younger age, but this failed to reach statistical significance at multivariate analysis.

Unfavourable LV geometry markers including steep aortoseptal angle, AV dextroposition, wider mitral-aortic separation and close proximity of the membrane to the AV [25] were found in this study to be strong independent predictors of recurrent SAS requiring repeat surgery. The proximity of the obstructive lesion to the AV was previously reported to be associated with the recurrence of SAS [8]. This finding was confirmed in the current study where the obstructive lesion was significantly closer to the AV in the patients who underwent repeat surgery for SAS. The steeper aortoseptal angle recorded in the patients with recurrent SAS who had repeat surgery is also consistent with previous findings [25]. A steep aortoseptal angle was previously associated with an established or an increased risk of development of SAS [11, 25]. It has also been associated with the presence of an LVOT malformation [11, 25]. It has been suggested that distortion of the LVOT geometry creates chronic LVOT flow disturbance which may trigger an abnormal proliferative endothelial response in the subvalvar region [25]. This supports the findings of the current study that showed that when anatomical or echocardiographic features suggesting unfavourable LV geometry were present, they could independently predict the recurrence of SAS requiring reoperation.

Interestingly, the presence of IAA was an independent predictor of recurrent SAS. IAA has been previously associated with posterior and leftward axial deviation of the outlet septum in its long axis [26], which could further support the hypothesis that unfavourable LV geometry can strongly predict the recurrence of SAS even after an initial complete resection.

On the other hand, there are very limited data available to inform the development of strategies to minimize the need for reoperation in the presence of unfavourable LV geometry during the initial resection of SAS. We would recommend that every effort should be made to fashion a shorter patch in cases of VSD with posterior deviation of the interventricular septum (IVS) in order to 'pull' the septum rightward. In cases of SAS following AVSD repair, resection of all residual secondary chordae and when appropriate a transposition of the superior bridging leaflet with an interposition patch could be an effective surgical intervention. A more accurate localization and quantification of septal hypertrophy could be used to guide intraoperative LVOT remodelling. Furthermore, a wider use of LVOT-enlarging techniques (such as Konno procedure and its modifications) at the time of the first resection in cases of funnel-like LVOT could possibly also be considered. Finally, recent advances in Cardiac computed tomography have now provided the option of performing three-dimensional (3D) modelling in patients with challenging LVOT geometry in order to facilitate planning of a future procedure. 3D printed models have been successfully used in adult patients with a challenging LVOT anatomy [27, 28]. Similar 3D printed models could be used to plan a future resection of SAS in case of unfavourable LV and LVOT geometry.

Limitations

This was a retrospective study and outcomes should be confirmed by prospective studies following the evolution of young patients with SAS over several decades. Although criteria for initial or subsequent operation involved agreement between cardiologists and cardiac surgeons that the severity of the LVOT obstruction or degree of aortic regurgitation warranted intervention, those criteria were not standardized. Operations were carried out over a long period of time by different surgeons and techniques might have changed over time. We used a multivariate regression analysis that controlled for different types of SAS and other identifiable confounding variables, but the low number of adult patients included in the current study did not allow us to determine differences in the predictors for reoperation for SAS between adult and paediatric patients. The heterogeneity of our patient population could also be considered as one of the limitations of the study. However, we sought to reflect true clinical practice. The aim of our study was to identify significant factors and the independent predictors of outcomes in all patients with SAS without focusing on a specific group.

CONCLUSIONS

SAS can be a recurring problem for patients undergoing surgical resection. Echocardiographic markers of unfavourable LV geometry, as well as the diagnosis of IAA, strongly predict postoperative recurrence of SAS requiring reintervention. Surgery performed at a younger age, lesions closer to the AV and higher early postoperative LVOT gradients are also associated with a higher rate of reinterventions.

Conflict of interest: none declared.

REFERENCES

[1] Katz NM, Buckley MJ, Liberthson RR. Discrete membranous subaortic stenosis. Report of 31 patients, review of the literature, and delineation of management. Circulation 1977;56:1034–8.
[2] Wright GB, Keane JF, Nadas AS, Bernhard WF, Castaneda AR. Fixed subaortic stenosis in the young: medical and surgical course in 83 patients. Am J Cardiol 1983;52:830–5.
[3] Leichter DA, Sullivan I, Gersony WM. "Acquired" discrete subvalvular aortic stenosis: natural history and hemodynamics. J Am Coll Cardiol 1989;14:1539–44.
[4] Bezold LI, Smith EO, Kelly K, Colan SD, Gauvreau K, Geva T. Development and validation of an echocardiographic model for predicting progression of discrete subaortic stenosis in children. Am J Cardiol 1998;81:314–20.
[5] Keane JF, Lock JE (eds). NADAS' Pediatric Cardiology. 2nd edn. Philadelphia, PA: Saunders Elsevier, 2006.
[6] Newfeld EA, Muster AJ, Paul MH, Idriss FS, Riker WL. Discrete subvalvular aortic stenosis in childhood. Study of 51 patients. Am J Cardiol 1976; 38:53–61.
[7] Ayari M, Ben Farhat M, Betbout F, Maatouk F, Jarrar M, Gamra H. Surgical treatment of fixed subvalvular aortic stenosis. Immediate and long-term hemodynamic results. Arch Mal Coeur Vaiss 1997;90:1357–62.
[8] Geva A, McMahon CJ, Gauvreau K, Mohammed L, del Nido PJ, Geva T. Risk factors for reoperation after repair of discrete subaortic stenosis in children. J Am Coll Cardiol 2007;50:1498–504.
[9] Brauner R, Laks H, Drinkwater DC Jr, Shvarts O, Eghbali K, Galindo A. Benefits of early surgical repair in fixed subaortic stenosis. J Am Coll Cardiol 1997;30:1835–42.
[10] Fowles RE, Martin RP, Popp RL. Apparent asymmetric septal hypertrophy due to angled interventricular septum. Am J Cardiol 1980;46: 386–92.
[11] Kleinert S, Geva T. Echocardiographic morphometry and geometry of the left ventricular outflow tract in fixed subaortic stenosis. J Am Coll Cardiol 1993;22:1501–8.
[12] Hwang MS, Chu JJ, Su WJ. Natural history and risk stratification of discrete subaortic stenosis in children: an echocardiographic study. J Formos Med Assoc 2004;103:17–22.
[13] Kitchiner D, Jackson M, Malaiya N, Walsh K, Peart I, Arnold R et al. Morphology of left ventricular outflow tract structures in patients with subaortic stenosis and a ventricular septal defect. Br Heart J 1994;72: 251–60.
[14] Haycock GB, Schwartz GJ, Wisotsky DH. Geometric method for measuring body surface area: a height-weight formula validated in infants, children, and adults. J Pediatr 1978;93:62–6.
[15] Lopez L, Colan SD, Frommelt PC, Ensing GJ, Kendall K, Younoszai AK et al. Recommendations for quantification methods during the performance of a pediatric echocardiogram: a report from the Pediatric Measurements Writing Group of the American Society of Echocardiography Pediatric and Congenital Heart Disease Council. J Am Soc Echocardiogr 2010;23:465–95.
[16] Chubb H, Simpson JM. The use of Z-scores in paediatric cardiology. Ann Pediatr Cardiol 2012;5:179–84.
[17] Tani LY, Minich LL, Day RW, Orsmond GS, Shaddy RE. Doppler evaluation of aortic regurgitation in children. Am J Cardiol 1997;80: 927–31.
[18] Parry AJ, Kovalchin JP, Suda K, McElhinney DB, Wudel J, Silverman NH et al. Resection of subaortic stenosis; can a more aggressive approach be justified? Eur J Cardiothorac Surg 1999;15:631–8.
[19] Rohlicek CV, del Pino SF, Hosking M, Miro J, Cote JM, Finley J. Natural history and surgical outcomes for isolated discrete subaortic stenosis in children. Heart 1999;82:708–13.
[20] de Vries AG, Hess J, Witsenburg M, Frohn-Mulder IM, Bogers JJ, Bos E. Management of fixed subaortic stenosis: a retrospective study of 57 cases. J Am Coll Cardiol 1992;19:1013–17.

[21] Oliver JM, Gonzalez A, Gallego P, Sanchez-Recalde A, Benito F, Mesa JM. Discrete subaortic stenosis in adults: increased prevalence and slow rate of progression of the obstruction and aortic regurgitation. J Am Coll Cardiol 2001;38:835–42.
[22] de Lezo JS, Romero M, Segura J, Pan M, Pavlovic D, Mazuelos F *et al*. Long-term outcome of patients with isolated thin discrete subaortic stenosis treated by balloon dilation: a 25-year study. Circulation 2011; 124:1461–8.
[23] Chan KY, Redington AN, Rigby ML, Gibson DG. Cardiac function after surgery for subaortic stenosis: non-invasive assessment of left ventricular performance. Br Heart J 1991;66:161–5.
[24] Coleman DM, Smallhorn JF, McCrindle BW, Williams WG, Freedom RM. Postoperative follow-up of fibromuscular subaortic stenosis. J Am Coll Cardiol 1994;24:1558–64.
[25] Barkhordarian R, Wen-Hong D, Li W, Josen M, Henein M, Ho SY. Geometry of the left ventricular outflow tract in fixed subaortic stenosis and intact ventricular septum: an echocardiographic study in children and adults. J Thorac Cardiovasc Surg 2007;133:196–203.
[26] Al-Marsafawy HM, Ho SY, Redington AN, Anderson RH. The relationship of the outlet septum to the aortic outflow tract in hearts with interruption of the aortic arch. J Thorac Cardiovasc Surg 1995;109:1225–36.
[27] Guo HC, Wang Y, Dai J, Ren CW, Li JH, Lai YQ. Application of 3D printing in the surgical planning of hypertrophic obstructive cardiomyopathy and physician-patient communication: a preliminary study. J Thorac Dis 2018;10:867–73.
[28] Andrushchuk U, Adzintsou V, Nevyglas A, Model H. Virtual and real septal myectomy using 3-dimensional printed models. Interact CardioVasc Thorac Surg 2018;26:881–2.