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When Is It Better to Wait? Surgical Timing and Recurrence Risk for Children Undergoing Repair of Subaortic Stenosis

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Abstract

Background—Recurrence of subaortic stenosis (SAS) after surgery is common in children. The effects of patient characteristics and surgical timing on disease recurrence are largely unknown.

Material and Methods—We performed a retrospective study, assessing the relative effects of patient age and left ventricular outflow tract (LVOT) gradient on the need for reoperation for recurrent SAS. We included all children 20 years of age who underwent initial surgical resection of SAS at our center, January 2003–December 2013. Stratified logistic regression was performed, considering the effects of patient demographics, clinical characteristics, echocardiographic parameters, and operative technique, and clustering standard errors by surgeon. The multivariable model was used to simulate predicted probabilities of recurrent SAS for children at varying ages and baseline LVOT gradients.

Results—Sixty-three patients (38 males) underwent initial operation for SAS. Patients were followed for a median of 3.7 years (IQR 1.2–7.1). Twenty-one percent of patients (n=13) underwent reoperation for SAS. Twelve were male. For every 10mmHg increase in preoperative peak gradient in boys the odds of reoperation for SAS doubled (OR 2.01, CI 1.5–2.72, $p<0.001$), and for every additional 6-months of age the odds of reoperation decreased by 14% (OR 0.86, CI 0.84–0.88, $p<0.001$).

Conclusions—Both younger age and higher preoperative outflow tract gradient are independently associated with risk of reoperation. Clinicians should consider the age and rate of LVOT gradient change—and not just the absolute gradient—in determining initial surgical timing.

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Keywords

Subaortic stenosis; surgical timing; congenital heart disease; left ventricular outflow tract obstruction

Introduction

Subaortic stenosis (SAS) accounts for approximately 8-20% of left ventricular outflow tract (LVOT) obstruction in pediatrics [1,2]. Despite advances in operative technique, the lesion has challenged surgeons and cardiologists with a high predilection for recurrence, even in the face of relatively uncomplicated and seemingly successful operative repairs, with reported recurrence rates ranging from 4-53% [3–10]. While previous studies have identified some potential risk factors [11,9,10,12,13], the effects of patient characteristics and surgical timing on recurrence rates remain largely unknown. We performed a retrospective cohort study, to assess the relative effects of patient age and LVOT gradient on the recurrence of SAS.

Material and Methods

Study population

We included all children ≥ 20 years of age who underwent surgical resection of SAS at NewYork-Presbyterian/Morgan Stanley Children's Hospital, Columbia University Medical Center, January 2003-December 2013. Data was collected via manual review of hospital charts. The presence of SAS and indications for initial surgery were determined from operative referral letters and preoperative echocardiograms and confirmed by operative notes. Patients with severe valvular aortic stenosis, single ventricle anatomy, hypertrophic cardiomyopathy or a history of Ross/Konno procedure were excluded. Patients whose initial surgery was performed at another institution were also excluded.

Outcome variables

The primary outcome of interest was reoperation for SAS. Secondary outcome was echocardiographic evidence of SAS recurrence, defined as postoperative peak LVOT gradient >50 mmHg. The presence of new or worsening aortic valve insufficiency on transthoracic echocardiogram and other operative complications were also assessed.

Predictors of recurrence

The primary predictors of interest were 1) age at initial surgery and 2) peak and mean LVOT gradient (in mmHg) on preoperative transthoracic echocardiogram.

Other predictors of interest

Demographic variables included sex and weight at surgery. Clinical variables included the presence of prematurity (gestational age <37 wks), extracardiac malformations, genetic disorders, other cardiac diagnoses, a history of previous cardiac surgeries, and operative technique (SAS resection alone or SAS plus myomectomy). Concomitant surgical procedures were also recorded.

Echocardiographic variables

Preoperative, postoperative and most recent echocardiograms were evaluated for every patient by two independent reviewers on manual review of echocardiographic images (JT, JG). Each measurement was obtained in triplicate and the average of the reviewers' measurements was used for data analysis for all continuous variables. Preoperative echocardiographic variables collected included the SAS subtype (membranous, fibromuscular ridge, tunnel-like, or other—including posterior deviation of the conal septum or accessory mitral valve attachments), aortic valve morphology (tricuspid, bicuspid, or functionally bicuspid), sizes at the aortic valve annulus, aortic root, and sinotubular junction, distance from the SAS to the right coronary cusp, left ventricular mass indexed to body surface area (BSA), and the presence and degree of aortic insufficiency. The distance of the SAS to the hinge point of the right coronary cusp was also measured using a technique described previously by Kleinert and Geva [14]. The degree of LVOT obstruction was assessed from an apical and suprasternal notch window by calculating the maximal instantaneous gradient from the peak spectral Doppler velocity using the simplified Bernoulli equation. The highest peak and mean gradients obtained from either acoustic window were recorded. Preoperative quantitative assessment of left ventricular mass was performed via 5*6 area length method for all patients for whom appropriate imaging was available. All distances were assessed as absolute values and indexed to BSA; only indexed values were considered in multivariable analyses. All anatomic descriptions (such as valve morphology) were confirmed on intraoperative reports from the surgeon of record.

Perioperative and Operative Management

At our institution, decision to operate for SAS is made jointly at the discretion of the primary cardiologist and operating surgeon. Timing and procedure subtype are typically based on a combination of LVOT gradient and diameter (indexed) on transthoracic echocardiogram and the presence of other cardiac lesions / the need for other cardiac interventions. In the operating room, the membrane is sharply resected, including any attachments to the undersurface of the aortic valve leaflets or anterior leaflet of the mitral valve. Decision to perform a myomectomy is based on the presence of septal hypertrophy in the LVOT seen on preoperative echocardiogram, and is at the discretion of the operating surgeon. Prior to 2010, surgeons at our center used myomectomies conservatively on primary repairs [9]. After 2010, surgeons at our center tended to use myomectomies more aggressively. In addition, for patients with evidence of significant membrane extension on the anterior leaflet of the mitral valve, the fibrous trigones were typically mobilized and lateral attachments of the anteriorlateral papillary muscle to the free wall of the left ventricle were freed, as previously described by Yacoub and colleagues [15]. All patients are recovered postoperatively in our pediatric cardiac care unit and receive transthoracic echocardiograms prior to discharge and are followed longitudinally thereafter. Timing of follow-up visits and echocardiograms post discharge are based on the discretion of the primary cardiologist.

Statistical Analysis

All statistical analyses were conducted in Stata software, version 13 (StataCorp, College Station, Texas). Demographic and clinical variables were described using standard summary statistics. To assess the marginal associations between predictor variables and the outcomes of interest, chi squared or Fishers exact tests were used for categorical variables, and t-tests or Kruskal-Wallis were used for continuous variables. Collinearity of continuous predictor variables was tested using Pearson and Spearman correlation as appropriate. Logistic regression was used to determine the associations between preoperative peak LVOT gradients and patients' ages and each of the measured outcomes, considering the effects patient baseline demographic and clinical characteristics, as well as echocardiographic and surgical parameters. Multivariable models were built via a forward stepwise procedure. Variables with p values ≤ 0.10 in univariable analyses were evaluated together in multivariable models. Other variables were retained in the final models if their p values met the significance criterion or if their inclusion changed the magnitude of the coefficient for age or peak preoperative gradient by $\geq 10\%$. Model-based confidence intervals were constructed and hypothesis testing was performed using robust standard errors, with clusters corresponding to surgeons. Models considered the effects of confounding and effect modification. P values of <0.05 were considered statistically significant. Because age was highly collinear with weight and intra-cardiac dimensions, weight for age and sex z-scores were used. Given that patients with various concomitant cardiac lesions might have different reasons for restenosis, sensitivity analyses were performed to test the robustness of our results, rerunning all models while excluding patients with other congenital heart diseases.

The results of the final multivariable model were then used to simulate predicted probabilities of recurrent SAS for children at different ages and with varying baseline LVOT gradients, including 5th and 95th percent prediction intervals. These results were displayed graphically.

This study was approved by the Columbia University Medical Center Institutional Review Board, with a waiver of informed consent.

Results

Preoperative and operative characteristics

Sixty-three patients (38 males) underwent initial operation for SAS. Baseline characteristics are described in Table 1. The median age at initial operation was 3.6 years (IQR 1.6-7.7). The average peak and mean preoperative LVOT instantaneous gradients were 63.6mmHg (SD 30.5mmHg) and 36.2mmHg (SD 18.0mmHg) respectively. Most patients had discrete membranous SAS (83%, n=52). A fibromuscular ridge SAS was reported in 11% (n=7) and a tunnel-like LVOT in 3% (n=2). Three percent of patients (n=2) were classified as "other" (one with obstruction primarily caused by accessory mitral valve tissue and one with obstruction caused by posterior deviation of the conal septum). The majority of aortic valves were trileaflet (83%, n=52). The remaining valves were true bicuspid valves. The mean aortic valve annulus diameter was 12.9 mm (SD 3.9) and the median aortic valve annulus Z-score was -0.8 ($-2.0 - +1.2$). All but one patient had no or mild aortic insufficiency

preoperatively. Additional cardiac anomalies were present in 57% of patients (n=36). The most commonly associated cardiac lesions were ventricular septal defects (32%, n=20) and coarctation or arch hypoplasia (18%, n=11). Forty-one percent of patients (n=26) had a history of previous cardiac surgery, the most common of which were aortic arch repair (16%, n=10) and ventricular septal defect closure (14%, n=9). See Table 2. One child had a urologic disorder, one had developmental delay and respiratory insufficiency requiring tracheostomy, two children had seizure disorders, and three children had primary pulmonary hypertension.

Just over 40% (43%; n=27) of patients undergoing SAS resection also underwent myomectomy. The frequency of myomectomy differed by surgeon (0/4, 2/15, 5/12, 20/32; p=0.003). One third of patients (n=21) underwent additional concurrent cardiac surgery, the most common being VSD repair (19%, n=12). Four surgeons operated during the study period; half of the patients were operated on by a single surgeon (51%, n=32). Two surgeons each performed approximately 20% of cases (24% and 19%; n=15 & 12). The remaining six percent (n=4) were operated on by a fourth surgeon.

On predischARGE echocardiogram, the average peak and mean LVOT instantaneous gradients were 18.2mmHg (SD 13.1mmHg) and 9.1mmHg (SD 6.9mmHg), respectively—significantly improved from preoperation (p<0.001 for both).

Reoperation

Patients were followed for a median of 3.7 years (IQR 1.2-7.1). Median age at last follow-up was 7.6 years (IQR 4.7-13.2 years). Twenty-one percent of patients (n=13) underwent reoperation for SAS. Median age at reoperation was 7.5 years (IQR 2.5-9.0); median time to reoperation was 2.7 years (IQR 1.9-5.4 years). Of those who underwent reoperation, mean peak and mean LVOT gradient at reoperation were 65mmHg (SD 13) and 36mmHg (SD 8)—similar to the mean peak and mean LVOT gradients at initial operation. Approximately half of these patients also underwent myomectomy at reoperation (46%, n=6); 30% underwent Ross/Konno (n=4); 15% underwent SAS resection alone (n=2); and 7% (n=1) underwent aortic valve repair and modified Konno procedure. No patients underwent a third procedure.

The median age at initial operation for children requiring reoperation appeared lower than for those who did not (2.9 versus 4.3 years [IQR 1.1-4.8 versus 1.6-10.3], though this difference did not meet statistical significance (p=0.064). Children requiring reoperation had a higher mean preoperative peak LVOT gradient (81mmHg vs. 59mmHg, p=0.023) and a smaller mean aortic valve annulus Z-score (-2.0 vs. 0.04, p= 0.002) at the time of first SAS repair than those that did not. Differences in preoperative mean LVOT gradients did not meet statistical significance (44mmHg vs. 34mmHg, p=0.108). No children older than 7 years of age, with initial peak gradients <45mmHg, or with an aortic valve annulus Z-score > 1.2 at initial surgery required reoperation. Preoperative peak LVOT gradient and aortic valve annulus Z-score were highly negatively correlated ($\rho=-0.37$, p=0.004), but were not associated with any other preoperative or operative characteristic, including operative technique, age, or weight. Preoperative peak and mean LVOT gradients were significantly associated with postoperative (predischARGE) peak and mean gradients (p<0.001 and

$p < 0.001$), though were not correlated with age at initial operation. Both postoperative (predischARGE) peak and mean gradients were predictive of reoperation ($p = 0.019$ and $p = 0.021$, respectively); the average peak and mean LVOT instantaneous gradients postoperatively were 30mmHg [SD 19mmHg] and 15mmHg [SD 11mmHg] respectively for patients who required reoperation and 15mmHg [SD 9mmHg] and 7mmHg [SD 4mmHg] for those who did not.

Female sex appeared to be protective; boys had a significant higher reoperation rate than girls (31.5% vs. 4.0%, $p = 0.008$). Sex was not significantly associated with any other measured preoperative or operative characteristic. There were no statistical differences in any other clinical characteristic, preoperative echocardiographic parameters, or surgical technique between those requiring and not requiring reoperation. Notably, there were no significant differences in SAS subtype, aortic valve morphology, or presence of other congenital heart lesions (see Table 1 & 2).

In stratified, multivariable analyses, for every 10mmHg increase in preoperative peak gradient in boys the odds of reoperation for SAS doubled (OR 2.01, CI 1.5-2.72, $p < 0.001$), and for every additional 6-months of age the odds of reoperation decreased by 14% (OR 0.86, CI 0.84-0.88, $p < 0.001$), after considering the effects of other patient demographics, clinical characteristics, echocardiographic parameters, and operative technique, and clustering standard errors by surgeon (Table 3). Given the strong collinearity between LVOT gradient and aortic valve annulus Z-score, and given the presumed causal association, aortic valve annulus size was excluded from multivariable modeling. Figure 1 graphically displays the simulated expected probabilities of reoperation for three-month old and five-year old boys as a function of the peak preoperative LVOT gradient. These results were similar when excluding patients with other congenital heart lesions.

Long-term follow-up

Among all patients, median peak and mean LVOT gradient at last follow-up were 17mmHg (IQR 10-32) and 9mmHg (IQR 4-16), respectively. There were no difference in final gradients between those who underwent reoperation and those who did not ($p = 0.575$ and $p = 0.110$). Initial LVOT gradients and aortic valve annulus Z-score were both predictive of LVOT gradients at last follow-up, but age at initial operation was not. Prematurity and the presence of a concomitant surgery at initial operation were significantly associated with lower peak and mean LVOT gradients at last follow-up. No other preoperative or operative variables predicted final LVOT gradients.

Surgical complications

On postoperative echocardiogram, there were no significant difference in the degree of aortic valve insufficiency compared to baseline. Only one patient had greater than or equal to moderate insufficiency postoperatively and this patient had moderate insufficiency preoperatively. Five patients with no insufficiency preoperatively had mild insufficiency postoperatively, and nine patients with mild insufficiency preoperatively had no insufficiency postoperatively. Three patients (4.7%) experienced other complications associated with the initial SAS resection. One patient developed an aneurysm of the LVOT

postoperatively that required surgical resection. Two patients had refractory postoperative pericardiotomy syndrome. No patients developed heart block after initial SAS resection. However, two of the 13 patients who underwent reoperation (15%) developed complete heart block after their second surgeries, requiring permanent pacemaker placement. No other patients experienced complications at reoperation.

Discussion

SAS is a progressive disorder with high recurrence. Debate still exists regarding the effects of patient characteristics and surgical timing on disease recurrence. We examined rates of reoperation among children operated on for SAS. Reoperation occurred in 20% of our patients with a median follow-up period of 3.7 years—similar to previously published data [1,2,4,6]. Lifetime reoperation rates are likely even higher. Higher preoperative LVOT gradients and younger age were both independently associated with a higher risk of reoperation. In fact, no patient over the age of seven at the time of their first surgery required a reoperation for recurrence, regardless of the preoperative gradient.

The development of SAS is clearly multifactorial. Leichter and Gersony, in their natural history study, were the first to describe this disease process as “acquired”. They described 35 patients undergoing catheterizations for other cardiac lesions, who had no evidence of LVOT obstruction on initial catheterization, who subsequently developed SAS with significant obstruction [16]. While not truly an acquired lesion, SAS likely has both genetic and environmental features that stimulate development [17]. Several anatomic features have been identified that may predispose the development of SAS in susceptible individuals. Cape proposed a four-stage etiology in which altered morphology of the LVOT causes septal shear stress triggering a genetic predisposition leading to a cellular proliferation response [18].

Several studies have tried to determine risk factors for recurrence in this group of patients. Geva and colleagues, identified distance from the subaortic membrane to the aortic valve (<6mm) as an independent risk factor for recurrence [11]. Distance of discrete subaortic membrane to the aortic valve, involvement of the anterior leaflet of the mitral valve and initial Doppler gradient across the LVOT [12], and the presence of other congenital heart lesions [13] have also previously been described as risk factors for progressive disease. In our population, none of these was significantly associated with the risk of reoperation, though our subpopulations were small.

Surgical technique has been considered as a risk factor for restenosis. In particular, some at our center have questioned the utility of adding myomectomy to standard enucleation [10]. While risk of recurrence in our present study was not different for patients who did and did not undergo myomectomy as part of SAS repair, we would point out that, beginning in 2010, due to philosophical changes at our center, our surgeons promote a more aggressive use of myomectomies. Patients in our study were not randomized to the various surgical approaches, and so the similarity in outcomes across procedure subtypes might reflect appropriate technique selection for individual patient anatomy.

Our study suggests that age might influence the rates of disease progression and recurrence and that the impact of a rising gradient on SAS recurrence might be more profound in infants than it is in toddlers and school-aged children. In our model, a five year old with a 50mmHg gradient would be expected to have less than a 10% chance of recurrence. Were the gradient to rise to 60mmHg, the risk of recurrence would still remain less than 15%. In contrast, a three month old with a 50mmHg gradient would be expected to have a greater than 35% chance of recurrence, rising to nearly 50% by the time the gradient reached 60mmHg (See Fig. 1).

The implications of these data on clinical decision-making are complex, and surgical timing for these patients needs to be individualized. On the one hand, our data suggests that the younger a child is at initial operation, the higher the risk of recurrence. This might argue for a more conservative approach to initial surgery in infants. That having been said, if one has evidence that the gradient in a particular infant is rising rapidly, as gradients often do in babies with SAS, the more prudent approach might be to operate immediately, at a lower gradient, as the effects of the incremental gradient increase might outweigh the benefits of an extra month or two of age. Conversely, in a child in whom the gradient appears to be rising more slowly (as is often seen in older children), the benefits of age might outweigh the negative effects of a slightly higher gradient.

Unfortunately, given the retrospective nature of this investigation, the causal directions of these associations are not known. We did detect an association between initial aortic valve z-score and initial preoperative LVOT gradient, as well as associations between LVOT gradient *after* initial surgery and both preoperative gradient and reoperation. Median absolute aortic valve diameters were also, obviously, smaller in younger children. It is, therefore, possible that current techniques do not sufficiently relieve LVOT obstruction in infants with smaller aortic valves and that incomplete initial repair this leaves a stratum susceptible for restenosis. It is also possible that younger children or children with higher initial gradients are followed more closely postoperatively and are, therefore, more likely to be referred for reoperation. In contrast, it is also possible that children who develop hemodynamically significant LVOT gradients in infancy have a fundamentally different disease than do children who do not develop significant gradients until their school-aged years. It is notable that we found no difference in gradient at last follow-up between those who underwent reoperation and those who did not, indicating that optimal outcomes are possible for all children.

Our reoperation rate was also significantly affected by sex. Twelve of the thirteen patients who underwent reoperation for recurrence were male. Baseline and operative characteristics for males and females were similar and an explanation for the male predominance in the reoperation group could not be identified. Similar to most left heart obstructive lesions, SAS is known to have a male predominance. Male sex, however, has not been shown previously to be risk factor for recurrence. It is possible that this association was observed by chance. The p-value, however, was 0.008, indicating less than a 1% probability of a Type I error. Of note, a recent study has described female sex as a potential risk factor for recurrence in adults [19].

Limitations

Our study has several limitations. Our analyses were performed on a limited number of patients, derived from a single center, and reviewed retrospectively, and includes patients with concomitant lesions. The decisions for surgical intervention, and reintervention, were determined by individual practitioners and with no standardized criteria. Our follow-up is also limited to the pediatric population, and does not describe the entire natural history of disease progression. Predicted probabilities from our models should be considered in the context of these potential biases and with attention to confidence limits. Larger studies are needed to validate these results and to narrow the predictive interval.

Conclusions

Recurrence for SAS is common, with approximately 20% requiring reintervention. Both younger age and higher preoperative outflow tract gradient are independently associated with reoperation. Clinicians should consider the age and rate of LVOT gradient change—and not just the absolute gradient—in determining initial surgical timing.

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References

1. Newfeld EA, Muster AJ, Paul MH, Idriss FS, Riker WL. Discrete subvalvular aortic stenosis in childhood. Study of 51 patients. The American journal of cardiology. 1976; 38(1):53–61. [PubMed: 937199]
2. Wright GB, Keane JF, Nadas AS, Bernhard WF, Castaneda AR. Fixed subaortic stenosis in the young: Medical and surgical course in 83 patients. The American journal of cardiology. 1983; 52(7):830–835. [http://dx.doi.org/10.1016/0002-9149\(83\)90423-X](http://dx.doi.org/10.1016/0002-9149(83)90423-X). [PubMed: 6684879]
3. Brauner R, Laks H, Drinkwater DC Jr, Shvarts O, Eghbali K, Galindo A. Benefits of early surgical repair in fixed subaortic stenosis. Journal of the American College of Cardiology. 1997; 30(7): 1835–1842. [PubMed: 9385915]
4. Dodge-Khatami A, Schmid M, Rousson V, Fasnacht M, Doell C, Bauersfeld U, Pretre R. Risk factors for reoperation after relief of congenital subaortic stenosis. Eur J Cardiothorac Surg. 2008; 33(5):885–889. DOI: 10.1016/j.ejcts.2008.01.049 [PubMed: 18314346]
5. Erentug V, Bozbuga N, Kirali K, Goksedef D, Akinci E, Isik Ö, Yakut C. Surgical Treatment of Subaortic Obstruction in Adolescent and Adults: Long-Term Follow-up. Journal of cardiac surgery. 2005; 20(1):16–21. [PubMed: 15673405]
6. Lopes R, Lourenço P, Gonçalves A, Cruz C, Maciel MJ. The Natural History of Congenital Subaortic Stenosis. Congenital Heart Disease. 2011; 6(5):417–423. DOI: 10.1111/j. 1747-0803.2011.00550.x [PubMed: 21801312]
7. Parry AJ, Kovalchin JP, Suda K, McElhinney DB, Wudel J, Silverman NH, Reddy VM, Hanley FL. Resection of subaortic stenosis; can a more aggressive approach be justified? European Journal of Cardio-Thoracic Surgery. 1999; 15(5):631–638. DOI: 10.1016/s1010-7940(99)00060-3 [PubMed: 10386409]
8. Uysal F, Bostan OM, Signak IS, Semizel E, Cil E. Evaluation of subvalvular aortic stenosis in children: a 16-year single-center experience. Pediatr Cardiol. 2013; 34(6):1409–1414. DOI: 10.1007/s00246-013-0664-x [PubMed: 23456292]

9. Hirata Y, Chen JM, Quaegebeur JM, Mosca RS. The role of enucleation with or without septal myectomy for discrete subaortic stenosis. *The Journal of thoracic and cardiovascular surgery*. 2009; 137(5):1168–1172. DOI: 10.1016/j.jtcvs.2008.11.039 [PubMed: 19379985]
10. Rayburn ST, Netherland DE, Heath BJ. Discrete Membranous Subaortic Stenosis: Improved Results After Resection and Myectomy. *The Annals of Thoracic Surgery*. 1997; 64(1):105–109. [http://dx.doi.org/10.1016/S0003-4975\(97\)82825-1](http://dx.doi.org/10.1016/S0003-4975(97)82825-1). [PubMed: 9236343]
11. 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. *Journal of the American College of Cardiology*. 2007; 50(15):1498–1504. DOI: 10.1016/j.jacc.2007.07.013 [PubMed: 17919571]
12. Bezold LI, Smith EOB, Kelly K, Colan SD, Gauvreau K, Geva T. Development and Validation of an Echocardiographic Model for Predicting Progression of Discrete Subaortic Stenosis in Children. *American Journal of Cardiology*. 1998; 81:314–320. [PubMed: 9468074]
13. Frommelt MA, Snider AR, Bove EL, Lupinetti FM. Echocardiographic assessment of subvalvular aortic stenosis before and after operation. *Journal of the American College of Cardiology*. 1992; 19(5):1018–1023. [http://dx.doi.org/10.1016/0735-1097\(92\)90287-W](http://dx.doi.org/10.1016/0735-1097(92)90287-W). [PubMed: 1552088]
14. Kleinert S, Geva T. Echocardiographic Morphometry and Geometry of the Left Ventricular Outflow Tract in Fixed Subaortic Stenosis. *Journal of the American College of Cardiology*. 1993; 22(5):1501–1508. [PubMed: 8227811]
15. Yacoub M, Onuzo O, Riedel B, Radley-Smith R. Mobilization of the left and right fibrous trigones for relief of severe left ventricular outflow obstruction. *The Journal of thoracic and cardiovascular surgery*. 1999; 117(1):126–132. discussion 132–123. [PubMed: 9869766]
16. Leichter DA, Sullivan I, Gersony WM. “Acquired” Discrete Subvalvular Aortic Stenosis: Natural History and Hemodynamics. *Pediatr Cardiol*. 1989; 14(6):1539–1544.
17. Cilliers AM, Gewellig M. Rheology of discrete subaortic stenosis. *Heart*. 2002; 88:335–336. [PubMed: 12231585]
18. Cape EG, VanAuker MD, Sigfússon G, Tacy TA, del Nido PJ. Potential Role of Mechanical Stress in the Etiology of Pediatric Heart Disease: Septal Shear Stress in Subaortic Stenosis. *Journal of the American College of Cardiology*. 1997; 30(1):247–254. [http://dx.doi.org/10.1016/S0735-1097\(97\)00048-X](http://dx.doi.org/10.1016/S0735-1097(97)00048-X). [PubMed: 9207650]
19. van der Linde D, Roos-Hesselink JW, Rizopoulos D, Heuvelman HJ, Budts W, van Dijk AP, Witsenburg M, Yap SC, Oxenius A, Silversides CK, Oechslin EN, Bogers AJ, Takkenberg JJ. Surgical outcome of discrete subaortic stenosis in adults: a multicenter study. *Circulation*. 2013; 127(11):1184–1191. e1181–1184. DOI: 10.1161/CIRCULATIONAHA.112.000883 [PubMed: 23426105]

Figure 1.
Probability of recurrence as a function of preoperative outflow tract gradient in 3-month old (left) and 5-year old (right) boys with 95% confidence limits (CI).

Table 1

Baseline Patient Characteristics

	Total N=63	Patients without Restenosis N=50 (79.4%)	Patients with Restenosis N=13 (20.6%)	p-value
Demographics				
Sex (male)	38 (60.3)	26 (52.0)	12 (92.3)	0.008 *
Age (years)	3.6 (1.6-7.7)	4.3 (1.6-10.3)	2.9 (1.1-4.8)	0.064
Weight (kg)	15.7 (10.3-33.0)	16.5 (12.2-39.5)	9.0 (7.9-19.0)	0.055
Clinical Characteristics				
Prematurity	4 (6.3)	3 (6.0)	1 (7.7)	1.000
Genetic disorder	8 (12.7)	5 (10.0)	3 (23.1)	0.345
Other cardiac diagnosis	36 (57.1)	29 (58.0)	7 (53.9)	0.787
Prior cardiac surgery	26 (41.3)	22 (44.0)	4 (30.8)	0.388
Preoperative Echocardiographic Parameters				
Preoperative peak LVOT gradient (mmHg)	64 (31)	59 (30)	81 (28)	0.023 *
Preoperative mean LVOT gradient (mmHg)	36 (18)	34 (18)	44 (15)	0.108
SAS subtype				0.579
Discrete	52 (82.5)	42 (84.0)	10 (76.9)	
Fibromuscular	7 (11.1)	5 (10.0)	2 (15.4)	
Tunnel-like	2 (3.2)	2 (4.0)	0 (0.0)	
Other	2 (3.2)	1 (2.0)	1 (7.7)	
Aortic Valve Morphology				0.216
Trileaflet	52 (82.5)	43 (86.0)	9 (69.2)	
Bicuspid	11 (17.5)	7 (14.0)	4 (30.8)	
Aortic valve annulus (mm)	12.9 (3.9)	13.8 (3.7)	9.4 (2.8)	<0.001 *
Aortic valve annulus Z-score	-0.8 (-2.0 - +1.2)	-0.4 (-1.5 - +1.44)	-2.0 (-2.9 - -1.4)	0.002 *
Distance from SAS to aortic valve (mm)	5.0 (3.3-7.9)	5.5 (4.1-8.7)	2.9 (2.2-3.5)	0.003 *
Distance from SAS to aortic valve, indexed	0.7 (0.5-1.0)	0.8 (0.5-1.1)	0.5 (0.5-0.8)	0.175
Left ventricular hypertrophy (Z-score >2) **	16 (29.1)	14 (31.1)	2 (20.0)	0.706
Aortic Regurgitation				0.628
None	27 (42.9)	20 (40.0)	7 (53.9)	
Mild	35 (55.6)	29 (58.0)	6 (46.2)	
Moderate	1 (1.6)	1 (2.0)	0 (0%)	
Severe	0 (0%)	0 (0%)	0 (0%)	
Surgical Technique				
Myomectomy	27 (42.9)	24 (48.0)	3 (23.9)	0.106
Additional cardiac procedure	21 (33.3)	16 (32.0)	5 (38.5)	0.660

Data presented as numbers (%), means (standard deviations), or medians (IQR). *p*-values describe the association between patient characteristics and restenosis.

* denotes $p < 0.05$.

** Adequate echocardiographic images for 5/6 Area * Length measurements available on 55 subjects (45 without restenosis).

Table 2**Other Cardiac Defects and Interventions**

	Total N=63	Patients without Restenosis N=50	Patients with Restenosis N=13
Other cardiac diagnoses	36 (57.1)	29 (58.0)	7 (53.9)
Atrial septal defect	4 (6.3)	4 (8.0)	0 (0.0)
Ventricular septal defect	20 (31.7)	18 (36.0)	2 (15.4)
Atrioventricular septal defect	7 (11.1)	7 (14.0)	0 (0.0)
Shones complex	2 (3.2)	0 (0.0)	2 (15.4)
Coarctation or arch hypoplasia	11 (17.5)	8 (16.0)	3 (23.1)
Interrupted aortic arch	5 (7.9)	4 (8.0)	1 (7.7)
Mitral stenosis	2 (3.2)	0 (0.0)	2 (15.4)
Supravalvar mitral ring	3 (4.8)	2 (4.0)	1 (7.7)
Double outlet right ventricle	1 (1.6)	0 (0.0)	1 (7.7)
Double chamber right ventricle	1 (1.6)	1 (2.0)	0 (0.0)
Heterotaxy	1 (1.6)	1 (2.0)	0 (0.0)
Aberrant subclavian artery	0 (0.0)	0 (0.0)	0 (0.0)
Prior cardiac surgeries	26 (41.3)	22 (44.0)	4 (30.8)
Coarctation / arch repair	10 (15.9)	7	3 (23.1)
Ventricular septal defect closure	9 (14.3)	8	1 (7.7)
Atrioventricular septal defect repair	7 (11.1)	7 (14.0)	0 (0.0)
Patent ductus arteriosus ligation	7 (11.1)	4 (8.0)	3 (23.1)
Interrupted aortic arch repair	5 (7.9)	5 (10.0)	0 (0.0)
Atrial septal defect closure	4 (6.3)	3	1 (7.7)
Mitral valve replacement	1 (1.6)	1 (2.0)	0 (0.0)
Tricuspid valve repair	1 (1.6)	1 (2.0)	0 (0.0)
Repair of submitral stenosis	1 (1.6)	1 (2.0)	0 (0.0)
Pulmonary artery band	1 (1.6)	1 (2.0)	0 (0.0)
Repair of double outlet right ventricle	1 (1.6)	0 (0.0)	1 (7.7)
Concurrent cardiac surgeries			
Ventricular septal defect repair	12 (19.0)	11 (68.8)	1 (7.7)
Mitral valve replacement	3 (4.8)	1 (2.0)	2 (15.4)
Aortic valve repair	3 (4.8)	2 (4.0)	1 (7.7)
Supravalvar mitral ring repair	2 (3.2)	1 (2.0)	1 (7.7)
Pulmonary artery band takedown	1 (1.6)	1 (2.0)	0 (0.0)
Double chamber right ventricle repair	1 (1.6)	1 (2.0)	0 (0.0)
Tricuspid valve repair	1 (1.6)	0 (0.0)	1 (7.7)
Pulmonary artery plasty	1 (1.6)	1 (2.0)	0 (0.0)
Pacemaker implantation	1 (1.6)	1 (2.0)	0 (0.0)
Pericardectomy	1 (1.6)	1 (2.0)	0 (0.0)
Ligation of a patent ductus arteriosus	1 (1.6)	0 (0.0)	1 (7.7)

There were no significant differences in rates of restenosis among patients with and without various other cardiac diagnoses or prior cardiac surgeries, or those undergoing various concurrent cardiac surgeries.

Table 3

Multivariable predictors of reoperation for subaortic stenosis in boys

Parameter	OR (95% CI)	p value
Preoperative peak LVOT gradient **	2.01 (1.50-2.72)	<0.001 *
Age in years	0.86 (0.84-0.88)	<0.001 *

* Indicates p<0.05.

** Gradient measured in units of 10mmHg.