Benefits of Early Surgical Repair in Fixed Subaortic Stenosis

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Objectives. **We sought to determine whether early resection can improve outcome in fixed subaortic stenosis.**

Background. **The diagnosis of subaortic stenosis (SAS) is often made before significant gradients occur. Whereas resection is the accepted treatment, it remains uncertain whether surgical intervention at this early stage can reduce the incidence of recurrence or influence the progression of aortic valve damage.**

Methods. **Follow-up was available for 75 of 83 consecutive patients operated on for fixed SAS; the average duration of follow-up was 6.7 years. The lesion was discrete in 68 patients (91%) and of a tunnel type in 7, with associated ventricular septal defect in 28 (37%). All underwent transaortic resection.**

Results. **There were no deaths. There were 18 recurrences of SAS in 15 patients (20%). Thirteen patients (17%) underwent 17 reoperations for recurrence or aortic valve disease. The cumulative hazard of recurrence was 8.9%, 16.1% and 29.4% ± 2.3% (mean ± SEM), and the hazard of events, including recurrence and reoperation, was 9.2%, 18.4% and 35.1% ± 3.5% at 2, 5 and 10 years, respectively. Residual end-operative left ventricular outflow tract (LVOT) gradients (>10 mm Hg, n = 8) and tunnel lesions were univariate predictors of recurrence (p = 0.0006 and p = 0.003, respectively). Multivariate predictors included higher preoperative LVOT gradient ($p < 10^{-4}$) and younger patient age (p = 0.002). Only two recurrences (0.87 per 100 patient-years of follow-up) were noted in patients with a preoperative peak LVOT gradient ≤40 mm Hg (n = 40), whereas higher gradients (n = 35) were associated with a greater than sevenfold recurrence rate (6.45 events per 100 patient-years, p = 0.002). The aortic valve required concomitant repair in 17 cases in the high gradient group (48.6%) but in only 8 in the low gradient group (20%, p = 0.018). Despite relief of the obstruction, progressive aortic regurgitation was noted at follow-up after 14 procedures in the high gradient group (40%) but after only 5 procedures in the low gradient group (12.5%, p = 0.014).**

Conclusions. **The data suggest that surgical resection of fixed subaortic stenosis before the development of a significant (>40 mm Hg) outflow tract gradient may prevent recurrence, reoperation and secondary progressive aortic valve disease.**

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Cure of fixed subaortic stenosis (SAS) remains a surgical challenge. Whether a congenital (1) or acquired (2–4) anomaly, the disease is uniformly progressive, although at a variable rate, both in isolated form and when associated with a ventricular septal defect (VSD) (5,6). Secondary damage to the aortic valve may emerge as the predominant feature in untreated cases (2,6–8). An increasing number of young, often asymptomatic patients are diagnosed noninvasively as having subaortic lesions causing minimal or no obstruction. However, early surgery is controversial because of diverging and often conflicting reports on mid- and long-term outcome in patients so treated. A persistent problem is the high postoperative incidence of recurrence of stenosis and late reoperation, as well as the development of aortic regurgitation (AR), even after successful relief of the obstruction (8,9).

In view of reports advocating early surgical intervention (5,9), it has been the institutional policy at the University of California, Los Angeles (UCLA) since the early 1980s to proceed with resection of SAS at the time of patient referral, regardless of the degree of left ventricular outflow tract (LVOT) obstruction or involvement of the aortic valve. To determine whether this strategy improved outcome by reducing recurrence, reoperation and late aortic valve deterioration, we performed this retrospective review of an institutional experience with surgically treated patients with SAS. Although most reports to date include cases with moderate and severe obstructions, the significant number of patients undergoing early intervention in the present series may aid decision-making in the now common clinical setting of young patients with a low gradient but a well defined subaortic lesion.

Methods

Between 1982 and 1995, 83 consecutive patients underwent surgery for fixed SAS at the UCLA medical center. Seventy-five (90.4%) of these had complete follow-up and were included in the analysis. This group does not include patients with hypertrophic obstructive cardiomyopathy or major associated congenital anomalies such as atrioventricular septal defect, univentricular heart, transposition of the great arteries,

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Abbreviations and Acronyms

AR = aortic regurgitation
LVOT = left ventricular outflow tract
ROC = receiver operating characteristic
RVOT = right ventricular outflow tract
SAS = subaortic stenosis
UCLA = University of California, Los Angeles
VSD = ventricular septal defect

double-outlet right ventricle or tetralogy of Fallot. Also excluded were patients with three or more left heart obstructions (Shone's anomaly). Patients with one other obstructive lesion such as coarctation of the aorta were included, as were patients with ventricular septal defects and patients with right ventricular outflow tract (RVOT) obstructions.

The lesions were defined as discrete (short segment) or tunnel type (long segment) (2). In the more common discrete type, a localized shelf of fibrous or fibromuscular tissue protrudes a short segment beneath the aortic valve. Attachments to the anterior mitral leaflet or right coronary aortic cusp, or both, are common (Fig. 1A). The tunnel type implies diffuse narrowing of the LVOT by a long-segment fibromuscular collar (Fig. 1B).

Hemodynamic evaluation. Preoperative cardiac catheterization data were available in 41 patients (54.7%). Instantaneous double-catheter LVOT gradient measurement was not available; therefore, nonsimultaneous peak to peak gradients were used for the purpose of this study. Preoperative echocardiography with Doppler ultrasound was available in 72 patients (86.7%) and was the only technique for estimation of the LVOT gradient in 34 (45.3%). However, because Doppler-derived gradients are based on maximal flow, the resulting maximal Doppler estimates are generally higher than peak to peak gradients by as much as 37% (10). In contrast, a high correlation has been shown (10,11) to exist between directly measured and Doppler calculated mean gradients, and these have been used interchangeably in several studies (12,13). We therefore used the formula derived by Beekman et al. (14) to predict catheter-derived peak to peak LVOT gradients in the patients with no available catheter-derived data (see Appendix), using the mean instantaneous Doppler gradient and the patient's rest blood pressure at the time of echocardiographic examination or inpatient admission. This formula was prospectively validated by Beekman et al. (14) and we found it valid in our patient population. The resulting gradients were used interchangeably with directly measured peak to peak gradients. AR was qualitatively classified as mild, moderate or severe on the basis of aortic root angiographic data when available and, alternatively, on the size of the color Doppler flow jet at aortic valve level, as previously described (15). Invasive estimates of AR grades were used in patients with severe (grades III and IV) AR.

Study groups. The patients were classified for evaluation of outcome into "early" and "late" repair groups. As others before (12,16), we used the degree of obstruction, rather than the highly variable patient age or aortic root size, as the determinant of early versus late surgical intervention. A cutoff based on clinical practice was therefore set at 40-mm Hg catheter-derived peak to peak LVOT gradient to represent mild disease and the threshold for late repair. To validate this cutoff, a post-factum receiver operating characteristic (ROC) sensitivity analysis was performed based on the end points of recurrence, reoperation and progression of aortic valve disease.

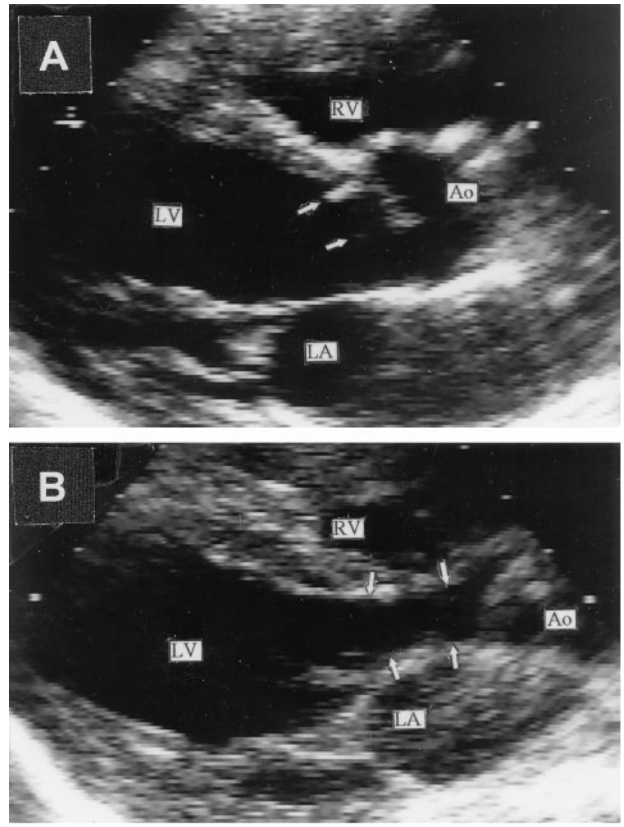

Figure 1. Cross-sectional parasternal long-axis echocardiographic views. **A,** Discrete subaortic ledge in an 8-year old boy with no significant gradient across the lesion. The ledge is seen beneath the right coronary aortic cusp **(arrows)**. After early operation, preoperative symptoms of "asthma" disappeared. **B,** Long-segment fibromuscular tunnel-type lesion **(arrows)** in a 7-year old girl with effort-induced chest pain and a calculated peak LVOT gradient of 90 mm Hg. Resection and extensive septal myomectomy resulted in elimination of the obstruction. Ao = aorta; LA = left atrium. LV = left ventricle; RV = right ventricle.

Surgical technique. A transaortic approach was used for the initial operation in all patients. After cardioplegic arrest with moderate hypothermia, the aortic valve was visualized through a transverse "hockey stick" incision in the ascending aorta; the subaortic lesion was then removed by sharp excision, including any attachment to the mitral and aortic valves and intraventricular septum. A ventricular septal myomectomy with resection of as much ventricular muscle as possible was performed in 73 (84.9%) of 86 resection procedures, starting beneath the left-right aortic commissure and down to the left ventricular apex. Care was taken not to damage the conduction system beneath the noncoronary cusp. If deemed necessary, the aortic valve was then repaired by either commissurotomy or by resuspension of prolapsed or redundant cusps using a standard Trusler (17) pledget-reinforced technique. Transesophageal echocardiography was used routinely since the late 1980s to evaluate end-operative LVOT flow and aortic valve competence.

Statistical analysis. Data are expressed as mean value ± 95% confidence interval. Cumulative hazards curves were derived by the Kaplan-Meier product limit method to analyze recurrence and reoperation hazards, and were compared using the log-rank test. Bivariate correlation coefficients for interval and ordinal data were obtained by the Pearson and Spearman rank correlations. Logistic regression analysis was used to assess univariate predictors for recurrence and reoperation. The influence of multiple covariates as predictive factors for recurrence and reoperation was analyzed with a Cox proportional hazards regression model. Changes in AR and LVOT gradient during follow-up were analyzed using the Wilcoxon signed-rank test for matched pairs. Comparison of means and proportions for continuous variables were based on analysis of variance (ANOVA), two-tailed *t* test, chi-square and Fisher exact tests. The level of statistical significance was set at $p \leq 0.05$. Data analysis was performed with the aid of the UCLA Department of Biomathematics.

Results

Preoperative patient data. Age at operation ranged from 1 month to 44 years (mean 8.6 years, median 6 years). There were 44 male patients (58.7%). Forty-nine patients (65.3%) were asymptomatic at the time of referral. Twenty-six (34.6%) presented with symptoms of mild to moderate congestive heart failure, including exercise intolerance (n = 14), intermittent shortness of breath (n = 8) and failure to thrive (n = 4). The severity of presenting symptoms did not correlate with the preoperative LVOT gradient or with patient age at the time of referral. However, symptoms could be attributed to the presence of a VSD rather than to subaortic obstruction in 14 children (53.8% of symptomatic patients) and to severe AR in 2 others. Bacterial endocarditis was not documented preoperatively.

At the initial operation, 28 patients (37.3%) had a VSD. The aortic valve was bicuspid in 17 patients (22.7%). In addition, right heart obstructions were present in four patients (5.3%) and consisted of double-chamber right ventricle in three and pulmonary valve stenosis in one. Additional cardiovascular anomalies had been repaired at previous operations in 21 patients (Table 1).

The subaortic lesion was initially discrete in 68 patients (90.7%) and of tunnel type in 7 (9.3%). The greater severity of tunnel type lesions was reflected by significantly higher peak LVOT gradients (80.1 ± 28.5 vs. 44 ± 6.2 mm Hg, $p = 6 \times 10^{-4}$). Patient age at initial operation did not correlate with preoperative LVOT gradient, even when patients with tunnel type lesions were excluded. Clinically significant (moderate to severe) AR was present preoperatively in 10 patients (12%). The degree of AR correlated both separately and independently with both higher patient age (p = 0.004) and LVOT gradient (p = 0.003). Bicuspid aortic valves were not more prone to incompetence than were tricuspid valves.

Forty patients (53.3%) had preoperative peak LVOT gradients of ≤40 mm Hg (mean 22.7 ± 3 mm Hg, Group I), and 35 had higher gradients (mean 70.4 ± 7.5 mm Hg, Group II). Preoperative characteristics of the patients in the two study groups were similar with respect to age, gender and presenting symptoms. There were more tunnel type lesions in Group II than in Group I (6 patients vs. 1, p = 0.04) and a higher prevalence of AR (18 vs. 10, p = 0.033). Associated VSD was present in 19 patients in Group I (47.5%) and in 9 in Group II (25.7%, p = NS). The groups were compared with respect to early postoperative and late outcome.

Operative results. There were no operative deaths or major complications (Table 2). Average hospital stay was 5.5 ± 2.6 days; however, a significant decrease was noted from the 1980s (6.5 ± 3.4 days) to the 1990s (4.8 ± 1.3 days, p = 0.02). The peak LVOT gradient was reduced from 45 ± 7 mm Hg before operation to 4.1 ± 2.1 mm Hg after repair ($p < 10^{-4}$). Gradient reduction was greater with tunnel SAS than with discrete lesions (70 ± 35 vs. 38.6 ± 6 mm Hg, p = 0.004), and it was not affected by performance of a left ventricular myomectomy.

Residual gradients (12 to 35 mm Hg) were detected early postoperatively in four patients with discrete SAS (5.9%), and

Table 1. Previous Surgical Procedures in the 75 Study Patients

Procedure	Patients (no.)
Repair of coarctation of the aorta	10
Aortic valve commissurotomy	5
Closure of ventricular septal defect	4
Ligation of patent ductus arteriosus	3
Pulmonary artery banding	2

Table 2. Early Postoperative Outcome After Initial Resection of Subaortic Stenosis in the 75 Study Patients

Complication	Patients	
	No.	%
Deaths	0	0
Persistent AV block requiring permanent pacemaker	1	1.3
Residual subaortic lesion with peak gradient >10 mm Hg	8	10.7
Residual visible subaortic ridge with no LVOT gradient	3	4
Residual VSD	0	0

AV = atrioventricular; LVOT = left ventricular outflow tract; VSD = ventricular septal defect.

Table 3. Late Surgical Outcome in Patients With a Low (Group I) or a High (Group II) Preoperative Left Ventricular Outflow Tract Gradient

	Group I (gradient ≤40 mm Hg, n = 40)	Group II (gradient >40 mm Hg, n = 35)	p Value
Length of follow-up (yr)	6 ± 1.1	7.4 ± 1.4	NS
Late mortality	0	1 (2.9)	NS
Recurrence of SAS			
Patients	2 (5)	13 (37.1)	6×10^{-4}
Per 100 patient-years of follow-up	0.87	6.45	0.002
Recurrence in discrete-type lesions only (n = 68)	1 (2.6)	9 (31)	0.002
Progressive AoV disease			
Regurgitation	5 (12.5)	14 (40)	0.014
Stenosis	0	3 (8.6)	NS
Reoperations			
For subaortic obstruction	1 (2.5)	10 (28.6)	0.002
For progressive AoV disease	1 (2.5)	1 (2.9)	NS
Re-reoperation	1 (2.5)	3 (8.6)	NS
Total	3 (7.5)	14 (40)	0.001

Data are presented as mean value ± SD or number (%) of patients. AoV = aortic valve; SAS = subaortic stenosis.

in four of the seven with tunnel lesions (66%, p = 0.002). The preoperative LVOT gradient in these patients (80 ± 22 mm Hg) was significantly higher than in patients with no residual postoperative gradient (40.8 ± 6 mm Hg, p = 0.0002).

Mild to severe preoperative AR was present in 28 patients (37.3%). Fifteen of these underwent resuspension of aortic valve cusps, including 8 of 10 patients with moderate to severe AR. Concomitant repair of the aortic valve was required in 17 patients in Group II (48.6%) but in only 8 in Group I (20%, p = 0.018). The postoperative improvement in AR grade was significant ($p = 6 \times 10^{-4}$). The degree of AR lessened in all three patients with severe AR (to mild in two and trivial in one) and in six of seven patients with moderate AR, including two who had no valve repair at operation.

Late outcome. Recent evaluation included physical examination by the attending physician and echocardiographic study (including Doppler ultrasound) as well as follow-up with the patients or families. Postoperative follow-up averaged 6.7 ± 0.9 years (range 9 months to 14.6 years) and was similar in the two study groups. There were no cardiac-related late deaths. One patient (in Group II) died of unrelated trauma 5 years after the initial operation. Late surgical outcome in the two study groups is shown in Table 3.

Recurrence of subaortic lesions. Recurrence of SAS during follow-up was defined as the new echocardiographic appearance of previously undetected lesions or Doppler gradients, or as significant progression of a residual lesion, causing a significant LVOT gradient (>20 mm Hg). Nonprogressive echogenic residual lesions were not included.

SAS recurred in 15 patients (20%), at a rate of 3.8 cases per 100 patient-years of follow-up (including re-recurrence). Multivariate hazard analysis demonstrated a strong independent influence of the preoperative gradient on recurrence per patient-year of follow up ($p < 10^{-4}$). Inclusion of an age-gradient interaction variable did not influence outcome in this model, but lower patient age was also an independent predictor of recurrence (p = 0.002). A tunnel-type lesion was five times more likely than a discrete lesion to recur after transaortic resection: Five of seven patients with this type of obstruction (71.4%) had at least one recurrence versus only 10 (14.7%, p = 0.003) of 68 patients with a discrete lesion. In addition, lesions causing residual end-operative LVOT gradients >10 mm Hg progressed in six (75%) of eight patients to cause significant recurrent obstructions ($p = 6 \times 10^{-4}$). Failure to perform a left ventricular myomectomy at the time of initial operation did not increase the likelihood of recurrence in this series.

Time to recurrence was the time between the initial operation and the first detection of a new subaortic lesion or significant progression of a residual obstruction. Average time to recurrence was 4.7 ± 2.3 years (range 8 months to 14.6 years); it was not related to the preoperative LVOT gradient or patient age but was uniformly short in five patients with tunnel type lesions (18.8 ± 8.4 months). Cumulative hazard of recurrence (mean ± SEM) was 8.9%, 16.1% and 29.4% ± 2.3% at 2, 5 and 10 years, respectively (Fig. 2). The cumulative hazard of recurrence at 5 and 10 years was 6.5% in Group I and 28.1% and 57.5%, respectively, in Group II (p = 0.001, Figure 3a). After excluding all seven tunnel lesions, there were nine recurrences (4.08 per 100 patient-years) in the high gradient group (Group II) compared with one recurrence (0.43 per 100 patient-years) in Group I (p = 0.002). In these patients with discrete SAS, the preoperative LVOT gradient was strongly associated with recurrence (p = 0.016) in a multivariate logistic regression model that included patient age and the presence of residual end-operative gradients (in four cases) or coexistent VSD.

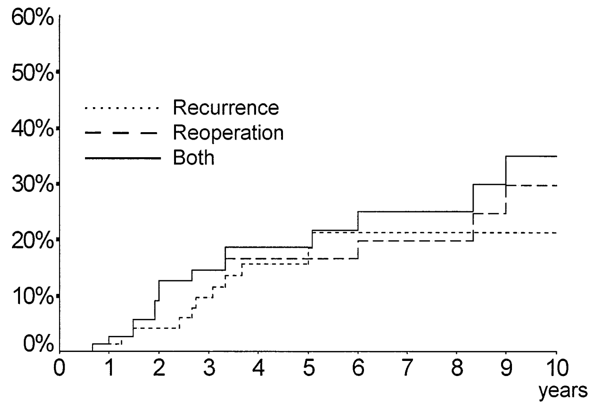

Figure 2. Hazard function curves for the recurrence of subaortic obstruction, for reoperation or for both events during follow-up in the total study group of 75 patients.

Postoperative progression of aortic valve disease. AR progressed despite relief of subaortic obstruction in 19 patients (25.3%), including 8 (17%) of 47 patients who had no preoperative AR and 10 (58.8%) of 17 patients who had undergone resuspension of prolapsed cusps with excellent early postoperative results. A higher preoperative LVOT gradient predicted late progression of AR both univariately ($p = 0.002$) and when adjusting for patient age at operation and the length of follow-up ($p = 0.002$). Exclusion of all patients with VSD or tunnel lesions did not alter this result ($p = 0.022$). A significant difference in late progression of AR between the study groups was therefore observed (Table 3) and, because bicuspid aortic valves were not more prone to late AR than were normal valves (38.5% vs. 50%, p = NS), the higher incidence of bicuspid valves in Group II cannot account for this difference.

Figure 3. Hazard function curves for patients with a low (Group I) and high (Group II) preoperative gradient for recurrence of a subaortic lesion (**a**) and reoperation (**b**).

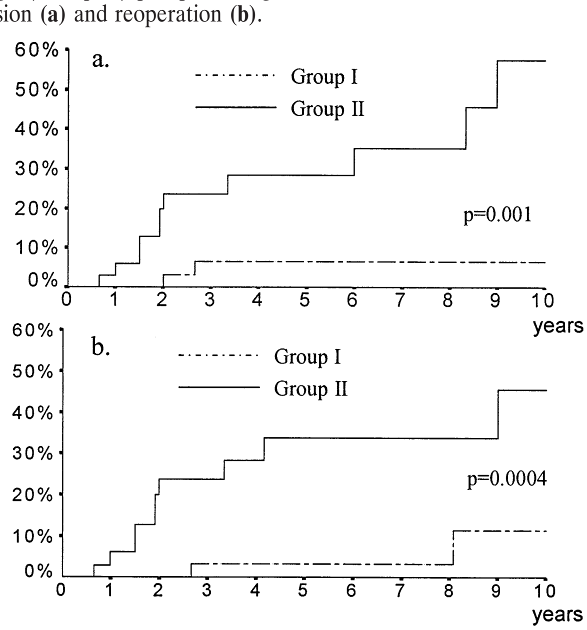

Table 4. Surgical Procedures Performed at the Second Operation in 13 Patients

Procedure	Patients (no.)
Re-resection of subaortic lesion with septal myomectomy	
Alone	4
With AoV commissurotomy	3
With AoV resuspension	2
With pulmonary autograft AoV replacement (Ross operation)	1
Apical to descending aorta valved homograft conduit	1
AoV replacement with pulmonary autograft (Ross operation)	2

AoV = aortic valve.

A higher preoperative degree of AR was the strongest single predictor of persistent AR at late follow-up ($p < 0.001$). Tunnel type lesions were associated with progressive AR in 4 (57.1%) of 7 cases versus 15 (22.1%) of 68 discrete lesions ($p = 0.06$). Initial patient age was not associated with a higher incidence of late AR. Progressive fusion and narrowing of a bicuspid stenosed aortic valve was noted in three additional patients, two of whom had commissurotomy at the initial operation.

Late reoperation. Thirteen patients (17.3%) underwent at least one reoperation (Table 4), including four of the seven patients with tunnel type lesions. Eleven (14.7%) had their second operation to relieve recurrent subaortic obstructions with ($n = 7$) or without ($n = 4$) aortic valve dysfunction, and two had progressive aortic valve disease only, necessitating valve replacement. A higher preoperative LVOT gradient strongly predicted reoperation ($p = 0.0002$), independently of patient age at the initial operation. Performance of a septal myomectomy at initial operation did not lower the hazard of reoperation. Time to initial reoperation was 8 months to 14.6 years (mean 4.4 ± 2.2 years). Cumulative hazard of reoperation at 2, 5 and 10 years was 4.2%, 15.4% and 21.3% ± 1.4%, respectively (Fig. 2). The hazard of reoperation (including re-reoperation) in the high gradient Group II (0.45 events per 100 patient-years) was significantly higher than that in Group I (0.1 events per 100 patient-years, $p = 0.0004$, Fig. 3b).

Four patients had a second reoperation 1.3 to 3.5 years after the first. The reason for the third intervention was severe AR in two patients and progressive aortic valve stenosis in two others, with re-recurrence of long segment subaortic obstruction in one. There was no operative mortality at either the first or the second reoperation.

Clinical outcome. Table 5 compares the clinical outcome in the two study groups. There were no cases of bacterial endocarditis. Overall, 68 patients (91.9%) were asymptomatic, including all but 1 patient in Group I. Significant AR was noted in 14 patients (18.7%). Residual Doppler-derived peak gradients of 15 to 48 mm Hg were present across the subaortic area in eight patients, representing a first unoperated recurrence of SAS in four patients, re-recurrence after reoperation in two and residual mild obstruction in two. Both significant AR and residual LVOT gradients were significantly more prevalent in Group II than in Group I.

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Table 5. Clinical Outcome in Patients With a Low (Group I) or a High (Group II) Preoperative Left Ventricular Outflow Tract Gradient

	Group I (gradient ≤40 mm Hg, n = 40)	Group II (gradient >40 mm Hg, n = 35)	p Value
Gradient ≥15 mm Hg			
Subaortic	2 (5)	6 (17.6)	
On biscupid AoV	1 (2.5)	5 (14.7)	
Total	3 (7.5)	11 (32.3)	0.05
Functional class (NYHA)			
1	39 (97.5)	29 (85.3)	0.06
2	1 (2.5)	2 (5.9)	NS
3	0	3 (8.8)	
Late AoV regurgitation			
None	30 (75)	17 (48.6)	
Mild	7 (17.5)	7 (20)	
Moderate to severe	3 (7.5)	11 (31.4)	0.01

Data are presented as number (%) of patients. AoV = aortic valve; NYHA = New York Heart Association.

Prediction of outcome based on the preoperative peak LVOT gradient. To determine LVOT gradients that best predicted outcome in retrospect based on the results in this series, ROC sensitivity analysis was performed for each of the outcomes of recurrence, reoperation and late progression of aortic valve disease per patient-months during follow-up. For prediction of recurrence of subaortic lesions, the best cutoff was at 45 mm Hg (sensitivity 93%, specificity 64%). Reoperation was best predicted at 46 mm Hg (sensitivity 86%, specificity 63%). Late progression of aortic valve disease during follow-up was best predicted at 46 mm Hg (sensitivity 77%, specificity 69%). These data provide support for our chosen cutoff point (40-mm Hg gradient) as a good predictor of worse clinical outcome in fixed SAS.

Discussion

Since the advent of high resolution echocardiography, the diagnosis of subaortic ridges is frequently made noninvasively in patients with murmurs that hitherto would have been considered functional. Presented with the increasingly common occurrence of young, often asymptomatic patients with minimally occlusive subaortic lesions (such as that seen in Fig. 1A), clinicians have to decide on treatment strategies on the basis of inconclusive existing experience. Although most reports to date encompass patients with moderate to severe obstructive lesions who were more likely to be referred for operative repair, the natural history of low grade lesions is poorly documented. Reports that trivial gradients may remain stable for years (6,8) increase the reluctance to submit these patients to the hazards of early surgery. However, accumulating evidence documenting the progression of untreated low gradient SAS over follow-up periods >6 years indicates that a significant increase in the level of obstruction and progression of AR occur in >80% of such patients (2,5,8). The same is true in the presence of a VSD, as Freedom et al. (6) concluded that progressive LVOT gradients are due to an increase in the severity of LVOT obstruction, rather than to a decrease in VSD size or development of RVOT obstruction.

Because surgical resection can now be accomplished with very low mortality and minimal complications (13), it is attractive to consider surgery at the time of diagnosis provided that late outcome can be improved by this strategy. Potential benefits of early intervention include prevention of ventricular hypertrophy, bacterial endocarditis and, more important, progressive damage to the aortic valve, which can present a more difficult surgical problem (9). In the context of late AR, several investigators (12,16,18) reported better outcome in patients operated on when they were younger or had a lower LVOT gradient. However, the incidence of recurrence of obstructive lesions similar to or more severe than those previously resected remains high, and several well documented studies fail to show any benefit from early surgery (8,19,20). Although resection is the only treatment option for this disease, the optimal timing for surgical intervention remains uncertain.

Outcome. In the present study we documented a highly significant correlation between mid to late outcome in fixed SAS and the preoperative LVOT gradient. This factor predicted both recurrence of the stenotic lesion and progression of aortic valve disease with a high degree of confidence, independent of patient age at operation. Exclusion of patients with the more severe tunnel type obstructions did not alter these findings. Additional exclusion of patients with associated VSD annuls the significance of the gradient-recurrence correlation, but the independent predictive value for late progression of AR remains significant ($p = 0.022$) even in this "pure" population of patients with discrete SAS. This result reproduces findings by Coleman et al. (12) in a similarly pure cohort. In view of the progressive nature of these lesions, the data support the policy of early surgical intervention at the time of diagnosis, with low level of obstruction being the better criterion for definition of early disease stage.

Recurrence rates as high as 55% have been reported (19) after resection of discrete subaortic lesions, with the majority of recurrences recorded during the 1st 5 postoperative years. An interesting etiologic explanation for both the initial lesion and the considerable rate of recurrence is suggested by the finding of Rosenquist et al. (1) that the mitral-aortic separation in SAS is consistently increased. The resulting alterations in the direction of blood flow near the crest of the interventricular septum may lead to differentiation of embryonic cells in this area into a fibrotic tissue variant. The reported lower rates of recurrence after complete blunt enucleation than after sharp excision (21,22) seem to support this hypothesis. In the present series the overall recurrence rate was 20%, an incidence comparable to that of previous surgical experience (23–25). However, the vast majority (87%) of recurrences were observed in patients with initially significant obstructive lesions, whereas recurrence was remarkably rare (two events, 2.5%) in the low gradient group.

Residual gradients. It has been suggested that small residual end-operative gradients do not increase the likelihood of recurrence (24) and may be due to increased immediate postoperative sympathetic tone (26). In our experience, SAS recurred in six of eight patients with mild residual LVOT gradients, a more than fivefold incidence rate, and in one of three patients with residual nonobstructive ledges. In the setting of tunnel type lesions, residual end-operative gradients uniformly progressed to early recurrence in all four such cases. End-operative measurements of LVOT gradients either directly or by transesophageal echocardiography should therefore not be omitted, and residual gradients should be aggressively treated.

Tunnel lesions. Tunnel type lesions are known to be associated with less favorable outcome than are discrete ledges (3). The transformation of discrete SAS to tunnel type is rare in untreated patients, but it has been reported in >90% after an initial resection (13). The long fibrous lesions around the LVOT may represent an abnormal tissue healing response or the response to a residual hemodynamic stimulus caused by abnormal flow patterns. We observed only one such case in 11 reoperations after initial resection of discrete lesions, but all five recurrences in patients with tunnel lesions were of tunnel type. Among seven patients with this type of lesion, we observed significantly higher initial LVOT gradients and worse outcome, including a high incidence of early recurrence (five of seven), re-recurrence and reoperation and consistent postoperative progression of AR. In view of the high incidence of residual postoperative gradients, it seems unlikely that complete removal of these lesions can be accomplished by transaortic resection and myomectomy, and recurrence most likely represents progression of residual disease. Therefore, initial application of more radical surgical techniques such as a Konno-Rastan aortoventriculoplasty (27,28) may be beneficial in these patients. This procedure allows for enlargement of the LVOT and the aortic root, and use of the pulmonary autograft in the aortic position (the "Ross-Konno" procedure [29]) has growth potential and obviates the need for prosthetic aortic valve replacement in young patients.

Aortic valve disease. The aortic valve is secondarily affected by the jet caused by the adjacent subvalvular lesion. This most often results in leaflet redundancy, prolapse and progressive AR, which has been documented even in the presence of mildly obstructive SAS (7). Even after complete surgical relief of the obstruction is achieved, AR can be progressive and often becomes the predominant clinical issue (8). This was observed in eight of our patients (10.7%) who had some degree of late AR even though no AR was detected preoperatively. Persistent abnormal flow patterns in the subaortic region may be involved in late valve damage. The conclusion derived by some investigators (5,18) that postoperative progression of AR can be prevented or stabilized by removal of the obstruction was applicable only to some of our patients in the low LVOT gradient group. Postoperative progression of AR occurred in 5 (7.5%) of these patients and was severe in 1, whereas it occurred in 14 patients (40%) in the high gradient group and became severe in 5. Review of the clinical course of AR in our patients shows that preoperative AR strongly predicts persistent AR at late follow-up, even when the early surgical outcome favorably indicates valve competence. Because we and others (12,13,18) have found that preoperative AR correlates strongly with both initial LVOT gradient and patient age, early intervention is indicated for preservation of the aortic valve.

VSD. The presence of a VSD may partially mask the presence and severity of subaortic obstructive lesions. The incidence of VSD in our study was 47.5% in Group I and 25.7% in Group II (p = NS). A vast majority of VSDs were restrictive and pulmonary/systemic flow ratios when available did not exceed 1.5:1. In the presence of such a VSD it may be difficult both clinically and echocardiographically to accurately appreciate a subaortic obstructive lesion; therefore, any gradient across the LVOT should arouse suspicion and warrants detailed evaluation. We believe that a bias, if any, would only slightly underestimate gradients at the lower end, not significantly altering outcome evaluation.

Clinical implications. In the present study, surgical intervention before the occurrence of a significant (>40 mm Hg) LVOT gradient significantly reduced the incidence of recurrence of SAS, reoperation and progression of secondary aortic valve disease. Furthermore, surgery was remarkably safe, with no operative mortality or major complications. The data suggest that patients with newly diagnosed subaortic lesions may benefit from early referral for surgery regardless of gradient, aortic valve involvement or clinical symptoms. Postoperatively, close follow-up is required to detect and promptly treat early signs of recurrence or progression of aortic valve disease.

Appendix

The following formula was used to calculate the peak systolic LVOT gradient, as proposed and prospectively confirmed by Beekman et al. (14):

$$PSG = 6.02 + 1.49 \cdot (MSG) - 0.44(PP),$$

where PSG = peak systolic gradient; MSG = mean systolic gradient; and PP = pulse pressure.

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