Natural history and surgical outcomes for isolated discrete subaortic stenosis in children

C V Rohlicek, S Font del Pino, M Hosking, J Miro, J-M Côté, J Finley

Abstract

Objective—To document the natural history and surgical outcomes for discrete subaortic stenosis in children.

Design—Retrospective review.

Setting—Tertiary care paediatric cardiology centres.

Patients—92 children diagnosed between 1985 and 1998.

Main outcome measures—Echocardiographic left ventricular outflow gradient (echograd), and aortic insufficiency (AI).

Results—The mean (SEM) age at diagnosis was 5.3 (0.4) years; the mean echograd was 30 (2) mm Hg, with AI in 22% (19/87) of patients. The echograd and incidence of AI increased to 35 (3) mm Hg and 53% (36/68) ($p < 0.05$) 3.6 (0.3) years later. The echograd at diagnosis predicted echograd progression and appearance of AI. 42 patients underwent surgery 2.2 (0.4) years after diagnosis. Preoperatively echograd and AI incidence increased to 58 (6) mm Hg and 76% (19/25) ($p < 0.05$). The echograd was 26 (4) mm Hg 3.7 (0.4) years postoperatively, with AI in 82% (31/38) of patients. Surgical morbidities included complete heart block, need for prosthetic valves, and iatrogenic ventricular septal defects. Eight patients underwent reoperation for recurrent subaortic stenosis. The age at diagnosis of 44 patients followed medically and 42 patients operated on did not differ (5.5 (0.6) v 5.0 (0.6) years, $p < 0.05$). However, the echograd at diagnosis in the former was less (21 (2) v 40 (5) mm Hg, $p < 0.05$) and did not increase (23 (2) mm Hg) despite longer follow up (4.1 (0.4) v 2.2 (0.4) years, $p < 0.05$). The incidence of AI at diagnosis and at last medical follow up was also less (14% (6/44) v 34% (13/38); 40% (17/43) v 76% (19/25), $p < 0.05$).

Conclusions—Many children with mild subaortic stenosis exhibit little progression of obstruction or AI and need not undergo immediate surgery. Others with more severe subaortic stenosis may progress precipitously and will benefit from early resection despite risks of surgical morbidity and recurrence.

(Heart 1999;82:708-713)

Keywords: subaortic stenosis; congenital heart disease; cardiac surgery

management remain unclear. Subaortic stenosis can be divided into discrete and tunnel forms.¹ The former type is more common and consists of a fibrous ridge alone or is associated with a muscular base located below the aortic valve in the left ventricular outflow tract.¹⁻⁵ In about half of the cases subaortic stenosis occurs in isolation, although it can be associated with other cardiac malformations.¹⁻⁶ Subaortic stenosis seems to be acquired as it has only rarely been reported in neonates,⁷⁻⁸ and has been diagnosed after previous documentation of a "normal" left ventricular outflow tract.⁹⁻¹⁰ A higher incidence of subaortic stenosis has been noted in males.⁴⁻¹¹⁻¹⁵ A genetic influence is suggested by reports of familial cases¹⁶⁻¹⁷ and by genetic studies in the Newfoundland dog.¹⁸⁻²⁰

The severity of subaortic stenosis has generally been felt to be progressive,¹⁻⁴⁻¹¹⁻²¹ although some cases remain stable for many years.¹² Aortic valve insufficiency (AI) is common with subaortic stenosis and may also be progressive.¹⁻¹³⁻²² A high incidence of infective endocarditis has been previously reported,¹⁻¹¹⁻¹⁹⁻²³ although this was not the case in a recent large series.¹² Surgical resection of subaortic stenosis has generally resulted in satisfactory relief of LVOTO,¹⁻³⁻⁴⁻²¹ and a reduced incidence of infective endocarditis.¹ Unfortunately the progression of AI may not be arrested by surgical resection of subaortic stenosis.¹⁻²¹⁻²⁴ Surgery for subaortic stenosis carries a low risk of mortality although recognised morbidities include complete heart block, damage to the aortic or mitral valves, as well as the creation of a ventriculoseptal defect.⁴⁻¹²⁻²¹⁻²³⁻²⁵⁻²⁶ In addition a recurrence rate of 7-27% has been reported in various series.²¹⁻²⁴⁻²⁶⁻³⁰

The optimal medical management and timing of surgery for isolated subaortic stenosis remains controversial. Surgical resection at diagnosis, regardless of the degree of LVOTO, is advocated by some because such an obstruction is regarded as being progressive with increasing risk of aortic valve damage and infective endocarditis.³⁻⁴⁻¹¹⁻²¹⁻²⁵⁻²⁸⁻³¹ However, data regarding the natural history of subaortic stenosis are generally limited to series involving patients who have ultimately come to surgical attention¹⁻²¹⁻²⁴⁻²⁵⁻²⁷⁻²⁸ or that include patients with additional cardiac malformations.¹⁻³⁻⁵⁻²²⁻²³⁻²⁵⁻²⁷⁻²⁹ Other series include many patients who were diagnosed by angiography before the advent of good quality two dimensional echocardiographic imaging and colour Doppler technology.¹⁻³⁻⁴⁻¹¹⁻¹²⁻²³⁻²⁵⁻²⁷⁻²⁹⁻³² Thus the management of patients with isolated subaortic stenosis

Division of Cardiology,
Montréal Children's
Hospital, 2300 Tupper
Street, Montréal,
Québec H3H 1P3,
Canada

C V Rohlicek
S Font del Pino

Division of Cardiology,
Children's Hospital of
Eastern Ontario,
Ottawa, Ontario,
Canada
M Hosking

Departement de
Cardiologie, Hôpital
Ste Justine, Montréal,
Québec, Canada
J Miro

Departement de
Cardiologie, Centre
Hospitalier de
l'Université Laval,
Québec, Québec,
Canada
J-M Côté

Division of Cardiology,
Izaak Walton Killam
Hospital, Halifax,
Nova Scotia, Canada
J Finley

Correspondence to:
Dr Rohlicek.

Accepted for publication
30 July 1999

diagnosed today is largely based on previous experience with cases that were likely to be exhibiting more severe LVOTO complicated by associated cardiac malformations.

In this retrospective multicentre review of data collected between 1985 and 1998 at five paediatric referral centres in eastern Canada we have sought to document the natural history of isolated discrete subaortic stenosis in children in terms of LVOTO and AI. In those patients operated on for subaortic stenosis we have also examined the results of surgery as well as its associated morbidity. Our data represent the largest series of paediatric patients with isolated discrete subaortic stenosis diagnosed and followed in the era of high quality echocardiography and colour flow Doppler technology.

Methods

PATIENT SELECTION

The hospital records for the years 1985 to 1998 of five tertiary care paediatric cardiology centres in eastern Canada (Montréal Children's Hospital, Montréal; Hôpital Ste Justine, Montréal; Children's Hospital of Eastern Ontario, Ottawa; Centre Hospitalier de l'Université Laval, Québec; Izaak Walton Killam Children's Hospital, Halifax) were reviewed retrospectively. Data were included for children diagnosed with subaortic stenosis consisting of either a thin ridge or a thicker but discrete obstruction with a muscular base,¹ without additional intracardiac malformations apart from a non-stenotic bicuspid aortic valve.

DIAGNOSTIC PROCEDURES AND SURGERY

Echocardiography was performed and/or reported by paediatric cardiologists. All of the institutions were equipped with colour Doppler technology during the study period. Pulsed and continuous wave Doppler techniques were used to measure the peak flow velocity across the left ventricular outflow tract. The peak instantaneous echocardiographic left ventricular outflow pressure gradient (echograd) was calculated using the simplified Bernoulli equation.³³ Doppler colour flow mapping was used to grade AI as absent, mild, moderate, or severe.

Cardiac catheterisation was performed in 28 patients. The peak to peak gradient across the left ventricular outflow tract (cathgrad) was measured by catheter pull back or by simultaneous left ventricular and ascending aorta pressure monitoring. The presence and severity of AI was assessed from biplane angiography.

Surgery was performed at five institutions by 12 surgeons over a 14 year period.

STATISTICS

Age, length of follow up, echograd, and cathgrad are expressed as mean (SEM). Significant differences between two group means of these variables were evaluated by a two tailed *t* test. Fisher exact test analysis was used to compare the presence of AI with the presence of a bicuspid aortic valve. Simple linear correlation analysis was performed on the

preoperative echograd and cathgrad. Two way analysis of variance was performed on the data concerning the echograd at diagnosis and at later follow up of those patients who did not undergo an operation and those who were subsequently operated on. One grouping factor was the treatment (no operation versus subsequent operation) while the other was the time of assessment (diagnosis versus later follow up, with repeated measurements). Post hoc pairwise means comparisons were made using the Tukey multiple comparisons test. Multiple regression analysis was performed with the outcomes of: echograd at late or preoperative follow up; the presence of AI at late or preoperative follow up; the presence of AI at late postoperative follow up; and operation. The independent variables included: age at diagnosis; sex; institution; length of follow up; echograd at diagnosis; echograd immediately postoperatively; presence of AI at diagnosis; presence of AI immediately preoperatively; and the presence of a bicuspid aortic valve. The null hypothesis of no effect was rejected at $p < 0.05$.

Results

SUBJECTS

Ninety two children were diagnosed with subaortic stenosis. The mean age at diagnosis was 5.3 (0.4) years. The male to female ratio was 1.6:1.

NATURAL HISTORY OF THE COHORT

The mean echograd at diagnosis in 88 of 92 children was 30 (2) mm Hg. AI assessed by colour Doppler was absent in 68 patients and was graded as mild in 19 patients. A bicuspid aortic valve was noted in 13 of 92 patients. The presence of AI was independent of the finding of a bicuspid aortic valve.

The cohort of patients was followed medically and 68 of the children were reassessed echocardiographically 3.6 (0.3) years after diagnosis. In these patients the mean echograd had increased from 25 (2) mm Hg at diagnosis to 35 (3) mm Hg (fig 1). In all of these patients subaortic stenosis remained discrete. The incidence of AI (all mild) increased from 12/68 (18%) to 36/68 (53%) (fig 1). There was no association between the presence of AI and a bicuspid aortic valve.

Cardiac catheterisation was performed on 28 of the patients 1.5 (0.4) years after diagnosis. The mean cathgrad was 50 (6) mm Hg. AI assessed angiographically was mild in 17 patients and absent in 11 individuals. Eighteen of these 28 patients were assessed echocardiographically within six months (2.4 (0.5) months) of their cardiac catheterisation. In these patients the mean cathgrad was 45 (8) mm Hg and the mean echograd was 58 (9) mm Hg. There was a significant correlation between these two variables ($r = 0.85$) (fig 2). AI was graded by angiography as mild in 12 patients and absent in the rest, and by echocardiography as mild in 11 patients and absent in seven. There was agreement between angiographic and colour Doppler assessment of AI in 13 of 18 cases.

Figure 1 Echocardiographic assessment of left ventricle (LV) to aorta (Ao) gradient (mm Hg on left vertical axis) and aortic insufficiency (AI) (patient number on right vertical axis) in 68 patients at diagnosis and again at the last medical follow up ($n = 44$) or before surgery ($n = 24$) versus age in years (horizontal axis). Peak instantaneous left ventricular outflow tract gradient is indicated by the solid points and line (bars represent SEM). The number of patients with AI is indicated in the bar graphs.

Figure 2 Comparison of the left ventricle (LV) to aorta (Ao) gradient measured at cardiac catheterisation versus that measured by echocardiography in 18 patients undergoing these assessments within six months of each other. The solid line indicates the best linear fit to these points. The correlation coefficient (r) is indicated.

RESULTS OF SURGERY

Forty two patients underwent excision of their subaortic ridge as well as a wedge resection of underlying left ventricular outflow tract muscle 2.2 (0.4) years after diagnosis. In 25 of the 42 patients operated on, echocardiographic reassessment was performed 0.4 (0.1) years before surgery. In these patients the echograd was 58 (6) mm Hg. AI was mild in 19 patients and absent in six. In only four of the patients with AI was the echograd < 40 mm Hg. In 17 patients echocardiography was not repeated preoperatively. Echocardiography in six of these patients at diagnosis had shown an echograd of 50 (15) mm Hg, with mild AI in three of these patients. In 11 other patients cardiac catheterisation was performed 0.5 (2) years before surgery and showed a cathgrad of 53 (10) mm Hg, with mild AI in six of these patients. In all 42 patients the operative findings were of a discrete subaortic stenosis. Echocardiography before hospital discharge in 39 of 42 patients showed a significant reduction in the echograd to 16 (3) mm Hg. AI was absent in 13 patients, mild in 25, and moderate in one patient. The patients operated on were

followed for 3.7 (0.4) years, with echocardiographic assessment in 38 of 42 patients showing an average echograd of 26 (4) mm Hg. AI was absent in seven patients, mild in 27, moderate in two, and severe in two patients. The presence of AI either preoperatively or postoperatively was independent of the presence of a bicuspid aortic valve.

There was no surgical mortality after primary resection of subaortic stenosis. Two patients required placement of permanent cardiac pacemakers for complete heart block. A prosthetic aortic valve was placed in one patient for severe AI noted postoperatively, and a prosthetic mitral valve was placed in another patient for severe mitral insufficiency also noted postoperatively. Surgery resulted in small restrictive iatrogenic ventricular septal defects in two patients.

Eight patients required reoperation for recurrent subaortic stenosis 4.8 (0.9) years after their first operation. The initial surgery had provided good relief of their subaortic stenosis with postoperative echocardiography showing an echograd of 25 (11) mm Hg, with mild AI in four patients and none in four. However, echocardiography 3.8 (0.7) years postoperatively showed the echograd to have increased significantly to 53 (11) mm Hg, with no AI in three patients, mild AI in four, and severe AI in one. In seven patients the recurrent subaortic stenosis remained of the discrete form. Three of these patients underwent excision of the recurrent subaortic ridge as well as a wedge resection of underlying left ventricular outflow tract muscle, three others underwent simple resection of the recurrent subaortic ridge, and one patient with severe AI underwent a Konno procedure with placement of a prosthetic aortic valve. The latter patient died during the immediate postoperative period. One patient was reoperated on for a diffuse tunnel obstruction (modified Konno and Ross procedures). One patient underwent a third operation for recurrence of subaortic stenosis, this time of the tunnel form, and required a mechanical aortic valve prosthesis.

SUBACUTE BACTERIAL ENDOCARDITIS

Subacute bacterial endocarditis was not diagnosed in any patient during the study period. This included 249 patient years of follow up without any surgical intervention.

COMPARISON OF PATIENTS MANAGED MEDICALLY AND SURGICALLY

Forty four children were followed medically and never operated on while 42 ultimately underwent surgery. There was no difference in the age at diagnosis (5.5 (0.6) *v* 5.0 (0.6) years) or in the male to female ratio (1.6:1). However, the echograd at diagnosis in those followed medically was significantly less than in those ultimately operated on (21 (2) *v* 40 (5) mm Hg). The children followed medically were last reassessed echocardiographically 4.1 (0.4) years after diagnosis, while 25 of 42 patients subsequently operated on were last reassessed echocardiographically before surgery 2.7 (0.5) years after diagnosis. The inter-

Figure 3 Comparison of the left ventricle (LV) to aorta (Ao) gradient measured echocardiographically in patients followed only medically with that in patients subsequently operated on at diagnosis and again at the last medical follow up or before surgery, versus patient age. Bars represent SEM; n, number of patients assessed.

val between diagnosis and the last reassessment in those never operated on was significantly greater than the time from diagnosis to surgery in those ultimately operated on. In those who never underwent surgery the echograd did not change significantly (21 (2) v 23 (2) mm Hg), while in those who were subsequently operated on the echograd increased significantly (41 (5) v 58 (6) mm Hg), and was significantly greater than the echograd at the last follow up in those not subsequently operated on (58 (6) v 23 (2) mm Hg) (fig 3). The proportion of patients with AI at diagnosis as well as at follow up was considerably greater in those subsequently operated on (34% (13/38) at diagnosis v 76% (19/25) at follow up) compared to those followed only medically (14% (6/44) at diagnosis v 40% (17/43) at follow up).

Comparison of the eight patients who required reoperation with the remainder of the patients operated on showed that there was no difference in age at diagnosis (5.6 (1) v 4.9 (0.7) years). However, the echograd at diagnosis was significantly greater (66 (10) v 34 (5) mm Hg), although the period between diagnosis and initial operation was significantly shorter (0.5 (0.2) v 2.5 (0.4) years).

MULTIPLE REGRESSION ANALYSIS

Multiple regression analysis of the data showed that the echograd at diagnosis was predictive of subsequent progression of the echograd. The length of follow up, age at diagnosis, and sex were not predictors of echograd progression. The echograd at diagnosis was predictive of new AI at subsequent follow up (odds ratio 0.95, 95% confidence interval (CI) 0.91 to 0.99). The age at diagnosis, length of follow up, presence of a bicuspid aortic valve, or sex were not factors in the appearance of new AI. The odds of having surgery were influenced by the echograd at follow up (odds ratio 1.25, 95% CI 1.08 to 1.44) which was itself predicted by the echograd at diagnosis. The age at diagnosis, length of follow up, presence of AI, or sex were not predictive of having surgery. The chance of AI at late postoperative follow up was predicted by the presence of AI preoperatively (odds ratio 0.18, 95% CI 0.04 to 0.88). The echograd at early as well as at late postoperative follow up,

the presence of a bicuspid aortic valve, age at diagnosis, sex, and the length of postoperative follow up were not predictive of late postoperative AI.

Discussion

An important management concern in regard to patients with subaortic stenosis has been progression of LVOTO and the development of AI. The medical follow up and the timing of surgery has been strongly influenced by the impression of almost inevitable progression in this regard.^{1 9 11 21} Our findings indicate that a large proportion of patients diagnosed with mild subaortic stenosis at our centres over a recent 14 year period had little progression of LVOTO. Other patients with more significant subaortic stenosis showed notable and rapid increases in LVOTO. Although we found a major incidence of AI at diagnosis that increased with time, this AI remained mild in all of our patients during medical follow up. The echograd at diagnosis was predictive of the progression of LVOTO and of the appearance of new AI. Similar findings have been reported by deVries and colleagues.¹² However, other older reports based on cardiac catheterisation data have shown that LVOTO progresses notably, as was seen in some of our patients, in almost all patients of particular series.^{1 9 11} This may reflect a previous bias towards selection of patients with more severe obstruction introduced by the need to perform cardiac catheterisation to diagnose subaortic stenosis. The possibility that our patients have been followed for too short a time to allow development of significant LVOTO seems unlikely since those whose left ventricular outflow tract gradient increased considerably in our series were followed for a shorter period of time than those whose gradient did not change significantly. Our findings suggest that progression of LVOTO and development of significant AI is not inevitable in a substantial number of children with discrete isolated subaortic stenosis.

The indication for surgery in patients with subaortic stenosis has been the relief of LVOTO and the prevention of AI.³³ The vast majority of our patients had good relief of their LVOTO as has been reported in numerous previous series.^{1 3 4 21} However, surgery did not have a beneficial impact on AI as both the incidence and severity of AI increased after surgery. Similar findings have been reported by leading cardiac centres.^{1 11 24} Whether this is a result of the natural evolution of these patients, surgical intervention, or a combination of the two is difficult to determine. However, our finding that AI at late postoperative follow up was predicted by the presence of AI preoperatively suggests that surgery had little beneficial impact on the function of insufficient aortic valves.

As has been previously reported,^{21 26-28} a small but significant proportion of our patients experienced recurrence of LVOTO. Our observation is that these patients had more severe LVOTO at diagnosis than the other patients operated on, which is in agreement with the

findings of Brauner and colleagues.²¹ These children may represent a subset of patients with more severe and difficult pathology. An important finding in our series was the significant incidence of surgical morbidities such as complete heart block, iatrogenic ventricular septal defect, and the need for valve replacement. These morbidities are known risks of surgical resection of subaortic stenosis, and their incidence is comparable to previous reports.^{4 12 21–23 25 26} Nevertheless such risks must be placed in the context of largely asymptomatic patients, many of whom may be referred for surgery prophylactically.

Of interest is our finding of a significant correlation between the peak instantaneous left ventricular outflow tract gradient obtained by Doppler echocardiography (echograd) and the peak to peak gradient measured at cardiac catheterisation (cathgrad). Similarly good correlations between these measures of LVOTO have been reported previously.^{34 35} There is no doubt that the two techniques measure different aspects of a pressure gradient and are not always interchangeable, with a tendency of Doppler echocardiography to overestimate the peak to peak gradient measured at cardiac catheterisation that is particularly notable at low gradients.^{34 35} This tendency is evident in our own results as a rightward shift of the relation between the cathgrad and echograd. Nevertheless our data show that the echograd directly reflects the severity of LVOTO. The finding that in those patients whose LVOTO will progress this occurs in a significant fashion, as well as the good correlation found between echocardiographic and angiographic assessment of AI, calls into question the necessity of cardiac catheterisation.

Bacterial endocarditis has been considered an important risk in the setting of subaortic stenosis.^{1 11 19 23} No patient in our study experienced bacterial endocarditis, suggesting that the risk in patients with subaortic stenosis is possibly less than previously feared. However, the total patient years of medical follow up in our study is small (249 patient years) and, despite the freedom of our patients from bacterial endocarditis, their risk of bacterial endocarditis may nevertheless be similar to other moderate risk groups—that is, 40–500/100 000 patient years.³⁶

An important strength of this study is that it represents the largest series of paediatric patients with subaortic stenosis that have been followed from diagnosis onwards. Numerous previous studies have involved only patients that have ultimately come to surgical attention and/or that have had additional structural cardiac lesions.^{1 3–5 21–25 27–29} Our patient cohort is also unique because they all have been followed in the era of high quality echocardiography/Doppler technology. This contrasts with most other series that have included many patients diagnosed only by cardiac catheterisation.^{1 3 4 11–13 23 25 27–29 32} Finally, because of the health care system in place in Canada it is very likely that this series of patients represents almost all children diagnosed with subaortic stenosis in eastern

Ontario, Québec, New Brunswick, Prince Edward Island, and Nova Scotia. Census data from 1998 indicate a population of over 10 million in this region, with some 1.75 million children aged 0–14 years.³⁷

Some limitations of this work must be recognised. Although this is the largest series of its type the number of patients is small. In addition they have been followed at several institutions by numerous cardiologists and surgeons. These limitations arise from the relatively rare nature of subaortic stenosis. The inclusion of data from multiple institutions has prompted us to study only a relatively few robust measures. More detailed analysis of the left ventricular outflow might have given insight into the evolution of this lesion in our patients.³⁸ For instance it has been suggested that the distance of the subaortic ridge from the aortic cusps is important in the development of AI,³⁹ while recent work indicates that the alignment of the interventricular septum relative to the aorta may be important in the development of subaortic stenosis.^{40 41} Such analysis would have required a more uniform and prospective approach. A further limitation is the relatively short period of follow up for these patients. This is the result of our decision to study only patients diagnosed since the use of modern echocardiography/Doppler equipment in order to make our study applicable to current practice.

In conclusion, our data indicate that many children with mild discrete subaortic obstruction experience little progression over several years. Similarly mild AI in these children may remain mild for some time. We feel that such patients can be safely followed medically with the aid of echocardiography and need not be referred for immediate surgery. However, there are patients who present with important LVOTO that will progress sometimes rapidly, who will benefit from surgery. Thus the management of children with discrete isolated subaortic stenosis must involve careful and frequent assessment by the paediatric cardiologist and the close collaboration of the paediatric cardiac surgeon.

The clinical collaboration of the various cardiac surgeons at our centres during the period of this study is gratefully acknowledged. We thank Dr A Dobell for his helpful comments during preparation of the manuscript as well as Dr R Platt for assistance with the statistical analysis.

- 1 Wright GB, Keane JF, Nadas AS, et al. Fixed subaortic stenosis in the young: medical and surgical course in 83 patients. *Am J Cardiol* 1983;52:830–5.
- 2 Deutch V, Shem-Tov A, Yahini JH, et al. Subaortic stenosis (discrete form). *Radiology* 1971;101:275–86.
- 3 Reis RL, Peterson LM, Mason DT, et al. Congenital fixed subaortic stenosis. *Circulation* 1971;43 (suppl 1):111–18.
- 4 Newfeld EA, Muster AJ, Paul MH, et al. Discrete subvalvular aortic stenosis in childhood. *Am J Cardiol* 1976;38:53–61.
- 5 Choi JY, Sullivan ID. Fixed subaortic stenosis: anatomical spectrum and nature of progression. *Br Heart J* 1991;65:280–6.
- 6 Baltaxe HA, Moller JH, Amplatz K. Membranous subaortic stenosis and its associated malformations. *Radiology* 1970;95:287–91.
- 7 El Habbal MH. Discrete subaortic stenosis in a newborn. *Pediatr Cardiol* 1991;12:243–4.
- 8 Kleinert S, Ott DA, Geva T. Critical discrete subaortic stenosis in the newborn period. *Am Heart J* 1993;125:1187–9.
- 9 Freedom RM, Fowler RS, Duncan WJ. Rapid evolution from “normal” left ventricular outflow tract to fatal subaortic stenosis in infancy. *Br Heart J* 1981;45:605–9.

- 10 Leichter DM, Sullivan I, Gersony WM. "Acquired" discrete subvalvular aortic stenosis: natural history and hemodynamics. *J Am Coll Cardiol* 1989;14:1539-44.
- 11 Shem-Tov A, Schneewiss A, Motro M, et al. Clinical presentation and natural history of mild discrete subaortic stenosis. *Circulation* 1982;66:509-12.
- 12 de Vries AG, Hess J, Witsenburg M, et al. Management of fixed subaortic stenosis: a retrospective study of 57 cases. *J Am Coll Cardiol* 1992;19:1013-17.
- 13 Freedom RM, Pelech A, Brand A, et al. The progressive nature of subaortic stenosis in congenital heart disease. *Int J Cardiol* 1985;8:137-43.
- 14 Cabrera A, Galdeano JM, Zumalde J, et al. Fixed subaortic stenosis: the value of cross-sectional echocardiography in evaluating different anatomical patterns. *Int J Cardiol* 1989;24:151-7.
- 15 Kitchiner D, Jackson M, Malaiya N, et al. Incidence and prognosis of obstruction of the left ventricular outflow tract in Liverpool (1960-91): a study of 313 patients. *Br Heart J* 1994;71:588-95.
- 16 Gale AW, Cartmil TB, Bernstein L. Familial subaortic membranous stenosis. *Aust N Z J Med* 1974;4:576-81.
- 17 Richardson ME, Menahem S, Wilkinson JL. Familial subaortic stenosis. *Int J Cardiol* 1991;30:351-3.
- 18 Pyle RL, Patterson DF, Chacko S. The genetics and pathology of discrete subaortic stenosis in the Newfoundland dog. *Am Heart J* 1976;92:324-34.
- 19 Muna WFT, Ferrans VJ, Pierce JE, et al. Discrete subaortic stenosis in Newfoundland dogs: association of infective endocarditis. *Am J Cardiol* 1978;41:746-54.
- 20 Jones M, Picon AL, Ferrans VJ, et al. Subaortic stenosis in Newfoundland dogs: an acquired congenital heart disease. *Circulation* 1982;66(suppl II):II-317.
- 21 Brauner R, Laks H, Drinkwater DC, et al. Benefits of early surgical repair in fixed subaortic stenosis. *J Am Coll Cardiol* 1997;30:1835-42.
- 22 Firpo C, Azcárate MJM, Jiménez MQ, et al. Discrete subaortic stenosis (DSS) in childhood: a congenital or acquired disease? Follow-up in 65 patients. *Eur Heart J* 1990;11:1033-40.
- 23 Katz NM, Buckley MJ, Liberthson RR. Discrete membranous subaortic stenosis. *Circulation* 1977;56:1034-8.
- 24 Coleman DM, Smallhorn JF, McCrindle BW, et al. Postoperative follow-up of fibromuscular subaortic stenosis. *J Am Coll Cardiol* 1994;24:1558-64.
- 25 Somerville J, Stone S, Ross D. Fate of patients with fixed subaortic stenosis after surgical removal. *Br Heart J* 1980;43:629-47.
- 26 van Son JAM, Schaff HV, Danielson GK, et al. Surgical treatment of discrete and tunnel subaortic stenosis: late survival and risk of re-operation. *Circulation* 1993;88(suppl II):II-159-69.
- 27 Brown JW, Stevens LS, Holly S, et al. Surgical spectrum of aortic stenosis in children: a thirty year experience with 257 children. *Ann Thorac Surg* 1988;45:393-403.
- 28 Sung M, Price GC, Cooley DA. Discrete subaortic stenosis in adults. *Am J Cardiol* 1978;42:283-90.
- 29 Vogt J, Dische R, Rupprath G, et al. Fixed subaortic stenosis: an acquired secondary obstruction? A twenty-seven year experience with 168 patients. *Thorac Cardiovasc Surg* 1989;37:199-206.
- 30 Stewart JR, Merrill WH, Hammon JW, et al. Reappraisal of localized resection for subvalvular aortic stenosis. *Ann Thorac Surg* 1990;50:197-203.
- 31 Douville EC, Sade RM, Crawford FA, et al. Subvalvular aortic stenosis: timing of operation. *Ann Thorac Surg* 1990;50:29-34.
- 32 Khan MM, Varma MPS, Cleland J, et al. Discrete subaortic stenosis. *Br Heart J* 1981;46:421-31.
- 33 Snider AR, Serwer GA. *Echocardiography in pediatric heart disease*. Chicago: Year Book Medical Publishers, 1990:98-102.
- 34 Currie PJ, Hagler DJ, Seward JB, et al. Instantaneous pressure gradient: a simultaneous Doppler and dual catheter correlative study. *J Am Coll Cardiol* 1986;7:800-6.
- 35 Bengur AR, Snider AR, Serwer GA, et al. Usefulness of the Doppler mean gradient in evaluation of children with aortic valve stenosis and comparison to gradient at catheterization. *Am J Cardiol* 1989;64:756-61.
- 36 Steckelberg JM, Wilson WR. Risk factors for endocarditis. *Infect Dis Clin North Am* 1993;7:9-19.
- 37 Statistics Canada data for 1998. <http://WWW.StatCan.CA/english/Pgdb/People/Population/demo31a.htm> [Accessed 20 December 1998.]
- 38 Freedom RM. The long and short of it: some thoughts about the fixed forms of left ventricular outflow tract obstruction. *J Am Coll Cardiol* 1997;30:1843-6.
- 39 Motro M, Schneewiss A, Shem-Tov A, et al. Correlation of distance from subaortic membrane to base of the right aortic valve cusp and the development of aortic regurgitation in mild discrete subaortic stenosis. *Am J Cardiol* 1989;64:395-6.
- 40 Cape EG, VanAuker MD, Sigfússon G, et al. Potential role of mechanical stress in the etiology of pediatric heart disease: septal shear stress in subaortic stenosis. *J Am Coll Cardiol* 1997;30:247-54.
- 41 Sigfússon G, Tacy T, VanAuker MD, et al. Abnormalities of the left ventricular outflow tract associated with subaortic stenosis in children: an echocardiographic study. *J Am Coll Cardiol* 1997;30:255-9.