Fixed subaortic stenosis: anatomical spectrum and nature of progression

Jung Yun Choi, Ian D Sullivan

Abstract
Retrospective echocardiographic review identified 58 consecutive infants and children with fixed subaortic stenosis. Mean (SD) age at diagnosis was 4.8 (3-6) years (range two days to 14.7 years), and diagnosis occurred in infancy in eight. Associated cardiac abnormalities were present in 41 (71%) whereas fixed subaortic stenosis was an isolated lesion in 17 (29%). Four types of fixed subaortic stenosis were identified: short segment (47%), long segment (12%), posterior displacement of the infundibular septum with additional discrete narrowing of the left ventricular outflow tract (3%), and redundant tissue arising from the membranous septum (1%).

Echocardiographic studies had been performed before the diagnosis of fixed subaortic stenosis in nine patients, all with associated abnormalities. These were performed in infancy in each and showed a "normal" left ventricular outflow tract in six and posterior deviation of the infundibular septum in three. In 16 patients serial echocardiographic studies had been performed after the diagnosis of fixed subaortic stenosis but before surgery of the left ventricular outflow tract. Rapid evolution of short segment to long segment narrowing was seen in one patient, and tethering of the aortic valve or mitral valve developed in a further four patients. Aortic valve or mitral valve involvement was not seen before the age of three years but was common thereafter (10/40 patients, 25%).

Fixed subaortic stenosis may be an "acquired" lesion with the potential for changes in form as well as progression in severity of left ventricular outflow tract obstruction.

Fixed subaortic stenosis progresses in severity and may even present as an "acquired" condition. The mechanism of progression is unknown. Further knowledge of the course would be a useful guide to optimal management, which is controversial. Cross-sectional echocardiography can define the nature of subaortic stenosis and can easily be repeated. Consequently, this study was performed to detail the echocardiographic findings of subaortic stenosis at different ages and to identify the nature of progression on serial studies.

Patients and methods
Echocardiographic and surgical records at the Hospital for Sick Children between April 1981 and December 1986 were reviewed. Fifty-eight cases of subaortic stenosis with normal cardiac connections were diagnosed. The criterion for diagnosis was the demonstration of a localised subvalvar discrete ridge or long segment narrowing in the left ventricular outflow tract at echocardiographic examination. This was confirmed by inspection at operation or necropsy whenever possible. Long segment narrowing was diagnosed when the length of the obstruction in the left ventricular outflow tract was more than three times the diameter of the aortic valve. Patients with posterior deviation of the infundibular septum were excluded unless there was additional discrete narrowing in the left ventricular outflow tract. Similarly, patients with obstruction of the left ventricular outflow tract caused by hypertrophic cardiomyopathy were excluded. Mitral valve involvement was diagnosed when abnormal tissue was attached to the anterior mitral valve leaflet which tethered the anterior mitral leaflet during systole. Aortic valve involvement was diagnosed when abnormal tissue in the left ventricular outflow tract seemed to be tethered to the base of the aortic valve.

All available echocardiograms performed before or after the diagnosis of subvalvar aortic stenosis, but before surgical procedures on the left ventricular outflow tract, were reviewed to determine sequential changes. The echocardiograms had been recorded on U-matic or VHS video tape by an ADR SC-2000, ATL mark 5, or ATL 8000, Ultramark 4, or Ultramark 8 machine. During the course of the study, operation to the left ventricular outflow tract was undertaken in 30/58 (52%) patients, twice in three of them. Five patients died and a necropsy was performed in three of them.
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Anomalies associated with subaortic stenosis

<table>
<thead>
<tr>
<th>Nature of subaortic stenosis</th>
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<td>Short segment</td>
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<tr>
<td>49 0-1-14-7 (4-5)</td>
<td>19 13 6 5 7 6 1 1 2 1 1 1 0</td>
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<tr>
<td>2 days</td>
<td>0 0 0 0 1 0 0 0 0 0 0 0 0</td>
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<tr>
<td>Membranous septum</td>
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APW, aortopulmonary window; ASD, atrial septal defect; AVSD, atrioventricular septal defect; BAV, bicuspid aortic valve; Coa/IAA, coarctation or interruption of aortic arch; distal Ao, diffuse narrowing of distal aorta and iliac vessels; Inf PS, infundibular pulmonary stenosis; LSVC, persistent left superior vena cava; PDA, persistent ductus arteriosus; PVS, pulmonary valve stenosis; SVMS, supravalvar mitral stenosis with or without mitral valve stenosis.

**Results**

**ASSOCIATED ANOMALIES**

The table shows the clinical characteristics and type of subvalvar aortic stenosis. Age at diagnosis ranged from two days to 14.7 years (mean 4.8 (3.6) years). There were 35 boys and 23 girls (sex ratio 1.5:1). Associated anomalies were present in 41 (71%) patients (table), whereas 17 (29%) had “isolated” subaortic stenosis. Common associated anomalies were ventricular septal defect (21 (36%)) and lesions resulting in obstruction to left heart flow such as coarctation or interruption of the aortic arch (16 (28%)), bicuspid aortic valve (nine (16%)), or supravalvar mitral stenosis (six (10%)). There was a persistent left superior vena cava draining to coronary sinus in 9 (16%) patients.

**NATURE OF SUBAORTIC STENOSIS**

Four types of subaortic stenosis were identified on echocardiographic review. There was short segment narrowing in 47 patients, long segment narrowing in seven patients, displacement of the infundibular septum with additional discrete obstruction in three, and abnormal tissue with a unique appearance in one patient. Figure 1 shows the echocardiographic findings at diagnosis of subaortic stenosis.

Short segment narrowing, apparently the result of a fibrous ridge or localised muscular bulging, was usually seen in long axis views. In almost all cases the parasternal long axis allowed better visualisation of the obstructing tissue in the left ventricular outflow tract than apical or subcostal views. Tilting the transducer slightly to either side of the true parasternal long axis plane showed whether the fibrous ridge was attached to the anterior leaflet of the mitral valve. The extent to which the ridge protruded into the left ventricular outflow tract varied according to the exact plane of the ultrasound beam in parasternal long axis views. The reason was apparent on careful parasternal short axis scans of the left ventricular outflow tract which showed the extent of the attachment of the subaortic ridge. This was sometimes confined to the left ventricular aspect of the infundibular septum but more often extended from the infundibular septum around the margins of the left ventricular outflow tract to the anterior leaflet of the mitral valve (fig 2). The ridge came into

**Figure 1**

Echocardiographic findings at diagnosis of subaortic stenosis. Squares are patients with coarctation or interruption of the aortic arch with or without a ventricular septal defect. Circles are patients with a ventricular septal defect but without obstruction of the aortic arch. AV, aortic valve involvement; Coa, coarctation; DEV INF SEP, deviation of the infundibular septum into the left ventricular outflow tract; IAA, interruption of the aortic arch; LS, long segment; MEMB, membranous; MV, mitral valve involvement; SS, short segment; VSD, ventricular septal defect.

**Figure 2**

(A) Cross sectional echocardiogram (parasternal long axis view) showing short segment subaortic stenosis in a 2 year old boy. (B) Parasternal short axis view in the same patient showing that the attachment of the obstructing ridge extended around the margins of the left ventricular outflow tract to the anterior mitral valve leaflet so that the lumen of the outflow tract was reduced to a slit. The curved arrows indicate the base of the anterior mitral valve leaflet. A, anterior; AL, aortic valve leaflets; Ao, ascending aorta; L, left; LA, left atrium; SAS, subaortic stenosis.
In diastole the obstruction in the left ventricular outflow tract was separate from the aortic valve leaflets but attached to the anterior mitral leaflet. (A) In systole the anterior mitral valve leaflet was pulled anteriorly at the site of attachment of the subaortic obstruction (curved arrow). AL, aortic valve leaflets; LV, left ventricle; LA, left atrium.

and out of the plane of the parasternal short axis section very quickly because of heart movement during the cardiac cycle; frame by frame analysis was necessary to assess it adequately. A localised ridge that did not affect the mitral or aortic valves was the most common type of subaortic stenosis; it was present in 37 (65%) patients (fig 1). Mitral valve (fig 3) or aortic valve (fig 4) involvement was confined to patients with short segment narrowing and was not seen in any patient aged less than 3 years (fig 1). After that age the aortic or mitral valve or both, were often affected (10/34 (30%)) in patients with short segment narrowing and in (10/40 (25%)) the entire group (fig 1). All the patients in whom subaortic stenosis was diagnosed after infancy who had associated coarctation or interruption of the aortic arch had undergone previous repair of the arch abnormality (figs 1 and 5).

There was long segment narrowing in seven (12%) patients (fig 1). The youngest two of these had subaortic stenosis diagnosed at 10 and 16 months of age and each had coarctation of the aorta without a ventricular septal defect. The five others were aged 5 to 13 years at diagnosis (fig 1): one had a ventricular septal defect and another persistence of the arterial duct but there were otherwise no additional abnormalities in these patients.

There were three patients in whom a posteriorly displaced infundibular septum was complicated by an additional discrete subaortic lesion (fig 1). All of these had aortic arch anomalies (two coarctation, one interruption). The patient with interruption of the aortic arch developed long segment narrowing in infancy after neonatal repair of the arch and ventricular septal defect closure, whereas the remaining two patients developed localised narrowing that was first apparent beyond infancy (fig 1). During the period of the study there were 12 additional patients who had malalignment ventricular septal defects with posterior deviation of the infundibular septum into the left ventricular outflow tract who did not develop additional discrete subaortic obstruction.

One infant had unusual redundant tissue obstructing the left ventricular outflow tract. Necropsy confirmed that this was fibrous tissue arising from the membranous septum.
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Figure 5  Parasternal long axis view in a 10 year old boy with long segment subaortic stenosis. See legend to fig 2 for abbreviations.

Figure 6  Echocardiographic appearances of subaortic obstruction in patients who had more than one study. LVOT, left ventricular outflow tract. See legends to figs 1–3 for other abbreviations and symbols.

SEQUENTIAL CHANGES
Echocardiograms had been performed before the diagnosis of subaortic stenosis in nine (16%) patients. In six of these the left ventricular outflow tract was considered to be "normal" at the time of the first echocardiogram, performed in infancy in each case (fig 6). Each of these infants had clinically evident associated cardiac anomalies. Careful retrospective review with frame by frame analysis showed subtle irregularity in the location in the left ventricular outflow tract in two of these patients, suggesting that very early ridge formation might have been apparent at the initial study (undertaken at 3 and 4 weeks of age respectively). Careful retrospective review of the echocardiograms recorded in infancy in the remaining four patients considered to have a "normal" left ventricular outflow tract did not show any abnormality (fig 7).

The three patients with posterior displacement of the infundibular septum into the left ventricular outflow tract who subsequently developed additional discrete subaortic stenosis (fig 6) have been described above.

Ten of the 14 patients who had further echocardiograms after the diagnosis of subaortic stenosis had persistence of short segment narrowing (fig 6). In one infant who had undergone coarctation repair there was rapid evolution of short segment to long segment narrowing (figs 6 and 8). The long segment narrowing was confirmed at operation. Acquired valve involvement was seen in four patients. Short segment narrowing evolved to include tethering of the mitral valve (two patients) or aortic valve (two patients, fig 6). Ages at diagnosis of new valve involvement ranged from 5 to 16 years (fig 6).

In three patients with repaired coarctation, short segment narrowing with aortic or mitral valve involvement was diagnosed at 3–5 years of age (fig 1). In another, long segment narrowing was diagnosed at 16 months of age (fig 1). Subaortic stenosis had not been diagnosed at the time of coarctation repair in infancy in any of these patients but, because echocardiograms from that time were not available, serial changes in the shape of the left ventricular outflow tract could not be described.

Discussion
CLASSIFICATION OF SUBAORTIC STENOSIS
At least nine mechanisms for subaortic obstruction have been described.11 Almost all cases, however, are examples of "fibrous diaphragm" or "fibromuscular" narrowing if posterior displacement of the infundibular septum and hypertrophic cardiomyopathy are excluded.11 These categories inevitably overlap because "fibrous diaphragm" refers to narrowing over a short but unspecified length whereas "fibromuscular" narrowing occurs over a longer but variable length. Our classification of subaortic lesions into short segment, long segment, and displaced infundibular septum with additional localised narrowing was based purely on echocardiographic appearances without inferring the composition of the subaortic tissue. In one infant we described an unusual appearance as "aberrant tissue"; this was shown at necropsy to be an extension of fibrous tissue from the membranous septum. The distinction between short segment narrowing and long segment narrowing was based on previous work10 but was nevertheless arbitrary. In practice, there was little difficulty classifying the appearances in individual cases. "Fixed subaortic stenosis" may be the preferred term to encompass these lesions.

PROGRESSION OF SUBAORTIC STENOSIS
Subaortic stenosis may cause progressively more severe obstruction of the left ventricular outflow tract.7 Significant obstruction has developed even in the absence of a systolic pressure difference between left ventricle and aorta at a previous catheterisation,7 showing that lesions can present as an "acquired" disorder that increases in haemodynamic severity, presumably when there is a pre-existing anatomical substrate.7 Most patients in these studies7 were first seen before cross sectional echocardiography became available. We used echocardiography in an attempt to
assess the anatomical range of fixed subaortic stenosis and the nature of its progression in a consecutive unselected series of infants and children.

Our data confirmed that short segment narrowing is by far the most common form of fixed subaortic stenosis and that most cases are associated with congenital heart defects, typically ventricular septal defect and obstructive lesions of the left heart. The association between obstructive lesions of the left heart and fixed subaortic stenosis was recognised as long ago as 1963. Persistence of the left sided superior vena cava was a notable feature, which we found in nine (16%) of our patients. We previously noted a similar association between persistence of the left superior vena cava and supravalvar mitral stenosis (6/16 patients, 38%) but not in patients with cor triatriatum (0/6 patients) or with congenital mitral stenosis without a supravalvar membrane (1/16 patients, 6%). This suggests that persistence of the left superior vena cava with consequent enlargement of the coronary sinus may restrict left ventricular filling during prenatal life and that the diminished flow may contribute to the development of the various "downstream" fixed obstructive lesions.

The classification of the fixed subaortic lesion did not change in most infants and children in this study, but follow up before surgical procedures on the left ventricular outflow tract was short (maximum six years). Short segment narrowing, however, caused progressively more important obstruction of the left ventricular outflow tract.

Tethering of the mitral valve or aortic valve or both, was not seen before the age of 3 years but developed or was present in most children (7/13, 54%) who had at least one serial assessment at age 5 years or more. The development of aortic regurgitation when fixed subaortic stenosis is present is almost certainly the result both of tethering of the aortic valve and the trauma to the valve from the turbulent ejection jet during left ventricular systole.

In rare cases, however, long segment subaortic stenosis can rapidly develop in infancy. An infant in whom severe long segment narrowing developed within four months of repair of aortic coarctation has been reported. The left ventricular outflow tract had been considered...
normal on initial echocardiographic and angiocardio graphic assessment at age 7 weeks. In the two patients in this study who followed a similar course after repair of coarcta tion, the "substrate" in the left ventricular outflow tract was short segment narrowing in one and displacement of the infundibular septum in the other. In two additional children, we saw the development of a localised ridge superimposed on a posteriorly displaced infundibular septum after repair of coarctation in infancy.

Consequently, the potential for changes in form as well as for progression in haemodynam ic severity of left ventricular outflow tract obstruction exists. Reports of long segment subaortic stenosis described patients who were much older than those in our series. Perhaps short segment narrowing would have evolved into long segment narrowing in more of our patients during a longer prospective follow up. The term "transitional" was used to describe a form of subaortic stenosis intermediate between "discrete" and "tunnel" types in a study that included young adults.

In infants with coarctation or interruption of the aortic arch the left ventricular outflow tract is fixed narrowing because of the absence of an aortic valve abnormality or of a malalignment ventricular septal defect with posterior deviation of the infundibular septum. Reduced aortic valve diameter and increased mitral valve separation were identified in a pathological study of patients with isolated subaortic stenosis. It was suggested that the altered flow characteristics in a narrow and elongated left ventricular outflow tract during early heart development could cause embryonic cells near the crest of the ventricular septum to accumulate and later differentiate into a ridge or band of tissue.

When subaortic stenosis occurs in association with a ventricular septal defect but without other abnormality, the obstruction in the left ventricular outflow tract is typically at the lower margin of a perimembranous defect. Maximum turbulence at this site in the presence of a left to right shunt through the ventricular septal defect might explain this and also the tendency for subaortic stenosis to be especially associated with malalignment ventricular septal defects in which there is anterior deviation of the outlet septum where the flow disturbance at the lower margin of a perimembranous defect is likely to be even greater.

CLINICAL IMPLICATIONS

We studied infants with clinically evident congenital heart defects. Subaortic stenosis was seen in six young children who had an apparently normal left ventricular outflow tract in infancy; this accords with the contention that fixed subaortic stenosis is a lesion acquired because of flow disturbance in the left ventricular outflow tract. A review of the echocardiographic studies to examine the left ventricular outflow tract showed that very early "ridge" development in the outflow tract may have been present in two patients. A similar appearance was described in an infant, but it was not stated whether subaortic stenosis developed subsequently.

The sequential changes that we saw emphasise the need for careful serial echocardiographic assessment of the left ventricular outflow tract in infants with other obstructive lesions of the left heart, especially if physical signs of left ventricular outflow tract obstruction might be obscured by coexisting abnormalities. Similarly, patients about to undergo ventricular septal defect closure should have a detailed echocardiographic assessment to detect possible incipient subaortic stenosis because surgical removal of any fibrous tissue with the potential to cause subsequent left ventricular outflow tract obstruction is advisable, even when this is only an "echodense area at the crest of the ventricular septum" seen during preoperative echocardiographic assessment.

When fixed subaortic stenosis is "isolated", the likelihood of increasing left ventricular outflow tract obstruction, tethering of the aortic and mitral valves, and the risk of endocarditis argue in favour of early operation. However, recurrent or residual postoperative left ventricular outflow tract obstruction is an important complication of operation, and some children with fixed subaortic stenosis do not develop increasingly severe left ventricular outflow tract obstruction or other complications during follow up for many years. Surgical results are probably satisfactory for at least a decade provided the obstruction of left ventricular outflow tract is effectively relieved at the initial operation. The postoperative prognosis of patients with short segment subaortic stenosis was better than with long segment narrowing. It might therefore be argued that indications for operation should include evidence of important or increasing left ventricular outflow tract obstruction, the development of mitral or aortic valve tethering, or evidence of possible transition from short segment to long segment narrowing on serial studies. Certainly, serial echocardiographic assessment of the left ventricular outflow tract is mandatory for medical management.

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PLANTS IN CARDIOLOGY

Veratrum alkaloids

The *Veratrum* species (Liliaceae) contain over 20 alkaloids with important cardiovascular, neuromuscular, and respiratory actions. They lower the blood pressure by an unusual mechanism first elucidated in 1867 by A von Bezold. Stimulation of vagal afferent fibres in the left ventricle causes the vasomotor centre to reset homeostatic control at a lower level and to reduce the peripheral vascular resistance through the sympathetic nervous system. When pure alkaloids became available, they were shown by A E Doyle and F H Smirk (*British Heart Journal* 1953;15:439–49) and by others to reduce considerably the blood pressure in hypertensive patients. But toxicity, especially nausea and vomiting also caused by vagal action, made treatment difficult and their use stopped despite their attractive vasodilator mode of action. *Veratrum* was used in eclampsia before its pharmacology was studied. It had been given for mania and epilepsy early in the nineteenth century and prompted Dr P de L. Baker of Eufala, Alabama, to prescribe *Veratrum viride*, the American or green hellebore, with success in 1859 for a lady with eclamptic fits. This was well before the association between eclampsia and hypertension was recognised. The plant and its alkaloids were used with good effect in toxaemia of pregnancy and eclampsia for the next 100 years.

The *Veratrum* species are handsome perennial plants with large-plated leaves and tall spikes of flowers—well worth growing in the garden. The two European species, *V album* and *V nigrum*, are common on alpine meadows. There are 43 other species, the best known being *V viride* and *V sabadilla*. The alkaloids come from the rhizome and root, or occasionally from the seed. Their common name, from antiquity, is hellebore but they are quite different from the genus *Helleborus*—the Christmas and Lenten roses. *Veratrum* has always been known as a highly poisonous plant causing vomiting, subternal constriction, faintness with a weak pulse, convulsions, and death. In 1985 a Frenchman made wine from it, believing it to be gentian, and developed complete atrioventricular block. It is also known as a strong teratogen; ewes that eat it can have lambs with a central eye.

Other medicinal members of the Lily family include those that contain cardiac glycosides, such as squill (*Drimia maritima*) and lily of the valley (*Convallaria majalis*). Colchicine is found in the meadow saffron ("autumn crocus") *Colchicum autumnale* while sisal (*Agave sisalana*) provides the starting material for steroid synthesis.


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