Implication of anterior septal malalignment in isolated ventricular septal defect

Mei-Hwan Wu, Jou-Kou Wang, Chung-I Chang, Ing-Sh Chiu, Hung-Chi Lue

**Objective**—The aim was to define the long term prognosis of isolated ventricular septal defect (VSD) with anteriorly malaligned outlet septum.

**Design**—Cohort study.

**Setting**—University hospital, tertiary medical care centre.

**Patients**—Between July 1986 and June 1993, 63 patients were studied with an isolated VSD and anteriorly malaligned outlet septum (59 perimembranous; 4 muscular outlet).

**Main outcome measures**—The diagnosis of septal malalignment, aneurysmal transformation, right ventricular obstruction, subaortic ridge, and aortic valve prolapse was based on echocardiographic criteria, then confirmed by angiography in 33 patients and by surgery in 28. An actuarial curve for each event was obtained by Kaplan-Meier non-parametric analysis and the significance was examined by log-rank test.

**Results**—Aneurysmal transformation decreased the size of the VSD in 52% of the patients, but was also associated with the appearance of subaortic ridge (p < 0.05). Progressive obstruction in the right ventricle was observed in 51%, more often in those without aneurysmal transformation (p < 0.05). Aortic valve prolapse was quite common whether or not aneurysmal transformation occurred (33% and 23%, respectively). This was attributed to the location of the VSD and the anterior malalignment of the outlet septum. Surgery was performed in 28 patients at a median age of 50 months because of significant left to right shunt (n = 5), or the development of obstruction in right ventricle (n = 9), aortic valve prolapse (n = 3), or combinations (n = 11). The presence of subaortic ridge per se was not considered to be a surgical indication.

**Conclusions**—Anteriorly malaligned VSDs have variable presentation. Careful echocardiographic evaluation is needed to identify various combinations of progressive right ventricular obstruction, aneurysmal transformation, subaortic ridge, or aortic valve prolapse. In extreme cases a patient may have a pathology complex comprising right ventricular outflow obstruction, subaortic ridge, aortic valve prolapse, and anteriorly malaligned VSD.

**Methods**

**STUDY POPULATION**

From July 1986 to June 1993, 1119 patients with isolated VSD were identified from our paediatric echocardiographic laboratory. Anterior malalignment of the outlet septum towards the right ventricular side had been documented in 63 patients (41 boys and 22 girls). Patients with Fallot’s tetralogy, or who eventually showed Fallot’s tetralogy, were excluded from the study. Tetralogy of Fallot was defined in those with associated infundibular hypoplasia and obstruction, mainly at the distal ostium of the right ventricular infundibulum, though the obstruction in a double chambered right ventricle was at the proximal ostium of the infundibulum, and was usually caused by excessive or high take off moderator bands, or a combination of both. The presence of pulmonary valvular...
steno
tic or peripheral pulmonary arterial
stenosis also suggested the diagnosis of
Fallot’s tetralogy.

Echocardiographic studies were performed
with an Acuson 128 XP module (from June
1991 to June 1993) or an Aloka 880 module
(from Jan 1986 to May 1991) with colour,
pulsed, and continuous wave Doppler capaci-
ties. The studies were recorded on videotape
and were independently reviewed by at least
two of the authors. Cardiac pathology was
confirmed by cardiac catheterisation (in 33
patients) and surgery (in 28 patients).

DEFINITION AND DIAGNOSTIC CRITERIA

Localisation of the VSD was made according
to previous reports.9 10 The VSD was morpho-
logically characterised as perimembranous,
muscular, or subarterial. Anterior malalign-
ment of the outlet septum was diagnosed from
the echocardiographic findings of anterior
deervation of the outlet septum toward the
right ventricular side on the parasternal long
axis view (fig 1A).11 Care was taken not to
produce a false positive picture as a result of a
too cephalad position of the transducer.
Aneurysmal transformation was defined as a
sac-like structure over the VSD, which pro-
truded into the right ventricle during systole
and less so during diastole (fig 1B), A subas-
totic ridge indicated a protrusion from the crest
of interventricular septum into the left ven-
tricular outflow tract seen in the parasternal
long axis or apical five chamber views, and
was not necessarily associated with a pressure
gradient through this ridge (fig 1B and C).4 5 12
Aortic valve prolapse was diagnosed when a
defomed aortic cusp pivoted from the crest of
the interventricular septum, noticeable in a
parasternal long axis view (fig 1D & E).13 14
Obstruction in the right ventricle was defined as
the presence of systolic turbulence through the
right ventricular outflow tract caused by
echodense structures protruding at right
angles to the interventricular septum and
right ventricular free wall (fig 1F).15 Since the es-
imation of right ventricular outflow obstruc-
tion gradient might be limited because of
mixing with the jet of the VSD, only those cathe-
erisation derived pressure gradients
through the right ventricular outflow tract
were analysed.

STATISTICS

Data are expressed as mean (SD). Actuarial
event-free curves were obtained by using
Kaplan–Meier analysis to calculate the
expected probability of events.16 The differ-
ences between curves were evaluated by the
log-rank test.17 Probability was defined as the
percentage of events expected during a set
period of time, given that the condition was
diagnosed at a specific age. For calculation of
each actuarial event-free curve, the follow up
The aneurysmal transformation process occurred exclusively in patients with perimembranous VSD. Left ventricular angiograms confirmed the location of the VSD in 32 patients.

FREQUENCY OF LESIONS IN SUBSEQUENT FOLLOW UP

The frequency of development of aneurysmal transformation, subaortic ridge and aortic valve prolapse in the subsequent follow up is summarised in fig 2. An analysis of the association between these lesions showed that only the subaortic ridge development was closely related to the appearance of aneurysmal transformation (P < 0.01), and there were no significant associations between the rest of the lesions. Nonetheless progressive obstruction in the right ventricle tended to be present in those without aneurysmal transformation.

DEVELOPMENT OF OBSTRUCTION IN THE RIGHT VENTRICLE

By actuarial analysis, event-free curves showing the proportion of patients with progressive obstruction in the right ventricle were obtained both from patients with and without aneurysmal transformation (fig 3). Patients without aneurysmal transformation are prone to have progressive obstruction in the right ventricle at subsequent follow up (P < 0.05). By the age of 60 months, the chance of having obstruction in the right ventricle was 46% and 64%, respectively, for those with and without aneurysmal transformation. The median highest pressure gradient between the right ventricular outflow tract was 36 mm Hg [37 (20) mm Hg]. The severity of right ventricular obstruction was not related to the location of ventricular septal defect, the presence of aneurysmal transformation, or the development of subaortic ridge and aortic valve prolapse.

---

**Figure 2** The frequency of the appearance of aneurysmal transformation, obstruction in right ventricle (RV), subaortic ridge, and aortic valve prolapse in patients with ventricular septal defect and anteriorly malaligned outlet septum.

Period of a case ended at the time the event occurred. The follow up period for those receiving surgical correction ended at the time of surgery. The association between the frequency of events was tested by Fisher's exact probability test.

**Results**

Median follow up period of these 63 patients was 45 months (mean 46, SD 40, months). Median age for surgery was 50 months (mean 49, SD 41, months).

**LOCATION OF VENTRICULAR SEPTAL DEFECT**

The echocardiograms showed a perimembranous VSD in 59 patients and a muscular outlet VSD in the other four. These four patients all developed progressive obstruction in the right ventricle during the subsequent follow up, and two had combined aortic valve prolapse.

---

**Figure 3** Actuarial event-free curves show the probability of having right ventricular obstruction in patients with and without aneurysmal transformation at each follow up time period. The numbers in parentheses indicate the numbers of patients still receiving follow up at that time period. The definition of follow up period is described in Methods.
DEVELOPMENT OF SUBAORTIC RIDGE AND AORTIC VALVE PROLAPSE

By actuarial analysis, patients with aneurysmal transformation tended to have a higher chance of developing a subaortic ridge (fig 4) (P < 0.05). By the age of 60 months, the chance of having a subaortic ridge was 64% and 42%, respectively, for patients with and without aneurysmal transformation. Doppler echocardiography showed progressively accelerated flow in the left ventricular outflow tract in 12 patients [pressure gradient 23(9) mm Hg].

Aortic valve prolapse occurred in a substantial number of patients (fig 5). However, no significant differences were noted between those with and without aneurysmal transformation (P = 0·10). Mild aortic regurgitation was found in six patients.

HAEMODYNAMIC DATA AT CATHETERISATION

Cardiac catheterisation was performed in 33 patients at a median age of 45 months [50(38) months] because of the presence of right ventricular outflow tract obstruction, aortic valve prolapse, or subaortic ridge detected on echocardiography (29 cases), or significant left to right shunt suspected by the clinical picture (four cases). The median ratio of pulmonary to systemic flow was 1·5 [1·68(0·6)]. A significant left to right shunt (pulmonary to systemic flow ratio greater than 2) was only noted in patients without obstruction in the right ventricle or aneurysmal transformation. The median ratio of pulmonary arterial to systemic pressure was 0·26 [0·29(0·14)]. Higher pulmonary arterial pressure was associated with a significant left and right shunt.

Figure 4 Actuarial event-free curves show the proportion of patients having subaortic ridge in those with and without aneurysmal transformation at each follow-up time period. Numbers in parentheses as in fig 3.
MORPHOLOGICAL DESCRIPTION DURING SURGERY

The cardiac pathology described by echocardiography was then confirmed by surgery in 28 patients (three of them were not catheterised). Surgical indications included a large left to right shunt \( n = 2 \); median age 6.5, mean 6.5(0-7) months, a pulmonary to systemic flow ratio greater than 2 after 2 years of age \( n = 3 \); median age 31, mean 29(8) months), a gradient through right ventricular outflow tract greater than 30 mm Hg \( n = 9 \); median age 45, mean 56(32) months), aortic valve prolapse \( n = 3 \); median age 10, mean 31(26) months), a combination of aortic valve prolapse and obstruction in right ventricle \( n = 6 \); median age 71, mean 74(52) months), a combination of obstruction in the right ventricle and the left ventricle or aortic regurgitation \( n = 3 \); median age 56, mean 102(40) months), and others \( n = 2 \); median age 46, mean 46(59) months). The median age of surgical induction of those patients was 24(10) months.

Subaortic ridge on its own was not considered to be a surgical indication. The subaortic ridge was attributed to tissue proliferation from the crest of the interventricular septum. Fibrotic jet lesions with hypertrophic septoparietal and moderator bands in the right ventricle contributed to the progressive right ventricular obstruction. A superiorly inserted moderator band was not clearly documented in our patients. The fibrotic lesion was described as a continuation from a fibrotic complex formed by adherence of tricuspid tissue to the margin of the ventricular septal defect and the subaortic ridge in 10 cases. Prolapsing aortic valve was found herniated into the right ventricle through the septal defect and was partly aggravated by the dextroposed aorta. None of our patients had documented anomalies of the aortic valve commissure. A deformed sinus of Valsalva wall, with severe angulation towards the right ventricular outflow tract, was frequently found in patients with aortic valve prolapse.

Discussion

Infants who have congestive heart failure due to a VSD with anteriorly malaligned outlet septum are usually thought to have a variant of the tetralogy of Fallot.18 Progressive right ventricular outflow tract obstruction is expected at subsequent follow up and a diagnosis of Fallot's tetralogy will then be established. However, the progressive obstruction in the right ventricle in patients with ventricular septal defect has often been described as a double chambered right ventricle, which is characterised by muscular narrowing which partitions the ventricle into an inflow and outflow chamber and is distinct from the tetralogy of Fallot.19 Furthermore, a close association between the development of a subaortic ridge and the presence of anterior septal malalignment has been described in patients with a VSD.14 Additionally, a malaligned VSD may also be associated with a wide right ventricular outflow tract and increased pulmonary flow, with early pul-monary arterial hypertension.1 Therefore the natural history of those patients who initially have an isolated VSD with an anteriorly malaligned outlet septum needs to be clarified. Our longitudinal study of 63 patients with isolated anteriorly malaligned VSD, excluding those with Fallot's tetralogy, confirms a wide clinical spectrum in this disease entity.

Progressive obstruction in the right ventricle occurred in about half the patients with isolated VSD and anteriorly malaligned outlet septum. Although the clinical features at the time an obstruction was evident might simulate those seen in Fallot's tetralogy, the right ventricular outflow lesion as disclosed during surgery was not caused by an antero-cephalad deviation of the outlet septum, as suggested for Fallot's tetralogy; instead it was attributed to the combination of a fibrotic band and a hypertrophic septoparietal and moderator band and subaortic ventricle. Such an anomalous right ventricular muscle bundle has been suggested as an acquired lesion in patients with VSDs and divides the right ventricle into two chambers, the so-called “double chambered right ventricle”10,19. In a substantial number of patients, a subaortic ridge developed in the subsequent course, especially in those in whom tricuspid tissue adhered to the defect margins. Furthermore, aortic valve prolapse was noted in about one third of the patients. These late complications could clearly further distinguish these patients from those with Fallot's tetralogy.

A close association between the presence of anterior septal malalignment and a subaortic ridge had been described by Zielinsky et al.5 In their series, apposition of tricuspid valve tissue over the margins of the VSD was observed in about two thirds of the patients. Our own data also indicate that diminution of the size of the defect by the aneurysmal transformation process may occur in patients with a VSD and an anteriorly malaligned outlet septum. However, this closing mechanism was found to be closely associated with the development of a subaortic ridge. Therefore, it is suggested that in patients with a VSD, the presence of anterior malalignment of the outlet septum predisposes to the development of a subaortic ridge, which can be further stimulated by the appearance of the aneurysmal transformation process.

Ando and Takao reported a high incidence of aortic valve prolapse in patients with ventricular septal defect and anteriorly malaligned outlet septum.8 In 64% of their patients, a deformed sinus of Valsalva wall, with severe angulation towards the right ventricular outflow tract, was found. In about one third, they found a coexisting bicuspid aortic valve. Our study echoed their results by showing a high likelihood of developing aortic valve prolapse in patients with anteriorly malaligned ventricular septal defects. However, no significant intrinsic aortic valve anomalies were identified. It was the location of the outlet septum of the VSD which predisposed to the development of aortic valve prolapse, which
was further facilitated, in the presence of septal malalignment, by an angulation of the sinus of Valsalva.

In conclusion, we have proved the heterogeneous nature of isolated VSD with anteriorly malaligned outlet septum. Close echocardiographic evaluation is needed to delineate the wide spectrum of clinical presentation, including various combinations of progressive obstruction in the right ventricle, aeurysmal transformation, subaortic ridge, or aortic valve prolapse. In extreme cases, a patient may have a pathology complex involving right ventricular outflow obstruction, a subaortic ridge, aortic valve prolapse, and the VSD.

The authors thank Ms Su-Chin Chien for her technical assistance and Ms Chiu-Yu Chen for her preparation of the manuscript.

Implication of anterior septal malalignment in isolated ventricular septal defect.

M. H. Wu, J. K. Wang, C. I. Chang, I. S. Chiu and H. C. Lue

Br Heart J 1995 74: 180-185
doi: 10.1136/hrt.74.2.180

Updated information and services can be found at:
http://heart.bmj.com/content/74/2/180

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/