Morphometric Analysis of Atrioventricular Septal Defect With Common Valve Orifice

KIYOSHI SUZUKI, MD, PhD, SIEW Y. HO, PhD, FRCPATH,*
ROBERT H. ANDERSON, BSc, MD, FRCPATH,* ANTON E. BECKER, MD, PhD, FACC,†
WILLIAM H. NECHES, MD, FACC,‡ WILLIAM A. DEVINE, BSc,‡ KATSUHIKO TATSUNO, MD, PhD,
SHIGEKAZU MIMORI, MD, PhD
Tokyo, Japan; London, England, United Kingdom; Amsterdam, The Netherlands; and Pittsburgh, Pennsylvania

Objectives. We sought to analyze morphometric features of atrioventricular septal defect (AVSD) in autopsy specimens and to consider the developmental implications of obstruction in either ventricular outflow tract.

Background. Left ventricular outflow obstruction (LVO) is more prevalent in patients with Rastelli type A morphology. When tetralogy of Fallot (ToF) complicates this malformation, there is usually a free-floating superior bridging leaflet. The reasons for these associations are uncertain.

Methods. In 133 hearts with AVSD and common atrioventricular (AV) valve orifice, we measured the degrees of horizontal and anterior deviation of the great arteries from the AV valve, the diameters of the ventricular outlets and the great arteries and the degree of deficiency of the ventricular septum.

Results. In Rastelli type A morphology, the great arteries were deviated more leftward than in type C morphology (p < 0.01).

Conclusions. The geometric arrangement of the great arteries correlated significantly with obstruction in either ventricular outflow tract and with the Rastelli subtypes. Malrotation of the developing outflow septum may be an embryologic factor producing obstruction, with horizontal deviation of the outlets also influencing the morphology of the superior bridging leaflet.
Museum of the Children's Hospital of Pittsburgh and the Sakakibara Heart Institute in Tokyo. In 67 cases in which clinical data were available, the patients' ages at death ranged from newborn to 10 years. There were 36 males and 31 female patients, and at least 27 had Down syndrome. Of the overall group of 133 hearts, 74 (56%) had the superior bridging leaflet defined as Rastelli type A, whereas 53 (40%) had a free-floating superior bridging leaflet (type C). The remaining six hearts (4%) showed the arrangement initially depicted as Rastelli type B morphology (Table 1). Specimens with isomerism of the atrial appendages, marked dominance of either ventricle, malalignment between the atrial and the ventricular septums, or those with double-outlet RV or discordant ventriculoarterial connection (transposition), were excluded from this study.

**Measurements.** In each ventricle, we measured the lengths from the ventricular apex to the midpoint of the arterial valve (outlet dimension), to the crux of the heart (inlet dimension), and the shortest length to the crest of the ventricular septum (scoop dimension, Fig. 1, A and B). The minimal diameter of each ventricular outflow tract and the diameters of the great arteries and the aortic isthmus were also taken. After measuring the maximal transverse dimension across the AV valve, we measured the distances from the right and left sides of the AV junction to the midpoints of the arterial valves. From the mathematic formulas illustrated in Figure 2, we determined whether the great arteries were shifted to the right or left from the centerline drawn perpendicular to the line across the AV valve. We described this as horizontal deviation, which usually also reflected the location of the atrial septum in cases with balanced ventricles. We also calculated the distance between the line of the maximal transverse diameter of the AV valve and the midpoints of the arterial valves, and defined this measurement as the extent of anterior deviation. The angle between the line through the midpoints of the arterial valves, related to the line across the AV valve, was also taken to provide the angle of the great arteries (16) (Fig. 3).

Subaortic stenosis (SAS) was diagnosed when the ratio of the diameters of the LV outflow tract and the ascending aorta was <50% or there was overt obstruction caused by a discrete fibrous or fibromuscular ridge, AV valve tissue tags, accessory

| Table 1. Relation Between the Associated Anomalies and Rastelli Classification* |
|-----------------|-----------------|----------------|-----------------|-----------------|-----------------|
| AVSD            | Rastelli Type A | Rastelli Type B | Rastelli Type C | p Value          |
| Without obstruction | 92              | 56 (61%)        | 2 (2%)          | 34 (37%)        |
| With SAS or CoA, or both | 23              | 18 (78%)        | 1 (4%)          | 4 (18%)         |
| With ToF | 18              | 0 (0%)          | 3 (17%)         | 15 (83%)        | <0.01           |
| Total          | 133             | 74 (56%)        | 6 (4%)          | 53 (40%)        |

*The incidence of each Rastelli subtype in each group was compared by the chi-square test. Data are presented as number (%) of hearts. AVSD = atrioventricular septal defect; CoA = coarctation of the aorta; SAS = subaortic stenosis; ToF = tetralogy of Fallot.

![Figure 1. Measurement of the ventricular septum in one heart as seen from the LV (A) and RV (B) aspects. The outlet dimension (LO, RO) was determined as the length from the apex to the midpoint of the arterial valve. The scoop dimension (LS, RS) was considered the shortest length from the apex to the crest of the ventricular septum. The inlet dimension (LI, RI) was determined as the length from the apex to the crux. The minimal diameter of the LV and RV outflow tracts (LD and RD, respectively) was also taken. This specimen shows the Rastelli type A configuration of the superior bridging leaflet. Ao = aorta; LA = left atrium; PT = pulmonary trunk; RA = right atrium.](image-url)
tendinous cords or abnormal papillary muscles (5,7,17). Coarctation of the aorta (CoA) was defined as a clearly demonstrated shelf on the posterior aortic wall. Hypoplasia of the aortic isthmus was determined when the diametric ratio between the isthmus and the ascending aorta was ≤50% (17). The diagnosis of ToF was based on the morphologic features of overriding of the aorta, biventricular connections of the aortic valve leaflets, and anterosuperior displacement of the outlet (conal) septum to obstruct the RV outflow tract (8–14,16).

Analysis of data. To clarify the morphologic differences between hearts with and without obstruction in either ventricular outlet, we compared the following data: degrees of horizontal and anterior deviation of the great arteries, angle of the great arteries, diametric ratios of the left and right ventricular outlets (LD/RD) and of the aorta and pulmonary trunk (Ao/PT), and the ratios between the scoop and outlet, and scoop and inlet dimensions for the ventricular septum as assessed in each ventricle. Data are expressed as mean value ± 1 SD. Comparisons between groups were performed by one-way analysis of variance for continuous variables, followed by the Fisher protected least significant difference test if the probability value was significant. Chi-square analysis was used to compare the incidence of Rastelli subtypes in each group. A p value < 0.05 was considered statistically significant.

Results

Relation between the associated anomalies and Rastelli classification (Table 1). Of the 133 hearts with AVSD and common AV valve orifice, 92 (69%) had no other significant anomalies. In 23 hearts (17%), there was SAS or CoA, or both (the group with LVO), whereas the remaining 18 (14%) showed ToF.

Of the 23 hearts with LVO, 18 (78%) showed the arrangement of the superior bridging leaflet defined as Rastelli type A; 4 (18%) were found to have type C morphology, and at least three of these were associated with Down syndrome. The remaining heart (4%) had type B morphology. SAS and CoA were present in 9 (39%) of these 23 hearts, isolated CoA in 8
Type C with ToF 10

0.07 ± 0.06†a
0.57 ± 0.12

0.13 ± 0.07
0.77 ± 0.09
47 ± 9

*cp < 0.01 between the groups indicated. †p < 0.01 between type C with ToF and the other groups. ‡p < 0.01 between hearts with LVO and the other groups.

†p < 0.01 between type C with obstruction in either ventricular outlet and the other groups. ‡p < 0.01 between those with obstruction in either ventricular outlet and those without obstruction. Values are presented as number of hearts or mean value ± 1 SD, and comparisons were made by the Fisher protected least significant difference test. LVO = left ventricular outflow tract obstruction.

**Discussion**

It is well known that an unwedged (or anteriorly deviated) position of the aorta is a feature of AVSD and that biventricular connection of the aorta is an integral component of the morphology of ToF. Becker et al. (16) described a detailed morphometric difference between that of normal hearts and hearts with ToF. Such analysis, to the best of our knowledge, has not yet been reported for AVSD. Because the leaflets of the AV valve are considered to develop in part from the inner (35%) and isolated SAS in the remaining 6 (26%). The morphology of LVO had no correlation with the configuration of the superior bridging leaflet. Among the 15 hearts with LVO identified as showing SAS, diffuse tubular narrowing of the tract was shown in 9 (61%) of the 15, whereas 2 (13%) had accessory tissue tags derived from the AV valve and 2 (13%) had an abnormally positioned papillary muscle obstructing the outlet. The remaining two hearts (13%), both with type C morphology, were found to have an abnormal muscle bundle within the RV, unrelated to the outlet septum, which extended to obstruct the subaortic tract. All hearts except two with CoA also showed isthmic hypoplasia. Three hearts with SAS and CoA were associated with mild LV hypoplasia.

Of 18 hearts with ToF, 15 (83%) had type C morphology; the remaining 3 hearts (7%) had type B, with the papillary muscle supporting the right side of the superior bridging leaflet obstructing the RV outlet. No heart with type A morphology in our series had associated ToF (p < 0.01).

**Geometric relation between the AV valve and the great arteries** (Table 2). The aorta in hearts with Rastelli type A morphology was deviated significantly to the left of that in hearts with type C morphology (p < 0.01). In the setting of LVO, the aorta in type A morphology was also deviated to the left. It assumed a midline position in hearts with type C morphology. Hearts with type C morphology associated with ToF showed the most dextroposed aorta (p < 0.01). However, the degree of anterior deviation of the aorta was the same in each group. Just as the aorta was displaced leftward, the pulmonary trunk was also deviated farther to the left in hearts with type A than in hearts with type C morphology (p < 0.01).

In the presence of LVO, the pulmonary trunk was deviated farther to the left regardless of Rastelli subtype (p < 0.01). In hearts with type C morphology and obstruction in either ventricular outlet, the pulmonary trunk was disposed more posteriorly than in any other group (p < 0.01). The angle of the great arteries was sharper in hearts with obstruction in either ventricular outlet than in hearts without obstruction; that is, the arrangement of the great arteries, was more oblique (p < 0.01, Fig. 3).

**Diametric ratios of the great arteries and ventricular outlets** (Table 3). The hearts with Rastelli type C morphology showed greater Ao/PT and LD/RD ratios than did those with type A (p < 0.01). Moreover, the Ao/PA ratio for type A morphology was exactly the same as that of the similar hearts with associated LVO. As might be expected, the group with LVO had the smallest LD/RD ratio (p < 0.01) and the group with ToF had the greatest Ao/PT (1.5 to 2.8) and LD/RD (1.7 to 7.0) ratios.

**Degree of deficiency of the ventricular septum** (Table 4). When ascertained from the LV, hearts with Rastelli type A morphology had a smaller scoop/outlet ratio than did those with type C (p < 0.05). The group with type C morphology with ToF showed the greatest scoop/outlet and scoop/inlet ratios (p < 0.01). In contrast, as assessed from the RV, the scoop/outlet and scoop/inlet ratios were the same among the different groups.

<table>
<thead>
<tr>
<th>Rastelli Type</th>
<th>No.</th>
<th>Ao/PT</th>
<th>LD/RD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type A</td>
<td>56</td>
<td>0.68 ± 0.13</td>
<td>0.64 ± 0.14</td>
</tr>
<tr>
<td>Type C</td>
<td>32</td>
<td>0.78 ± 0.16*</td>
<td>0.85 ± 0.18*</td>
</tr>
<tr>
<td>Type A with LVO</td>
<td>17</td>
<td>0.66 ± 0.11</td>
<td>0.49 ± 0.12</td>
</tr>
<tr>
<td>Type C with LVO</td>
<td>4</td>
<td>0.64 ± 0.06</td>
<td>0.53 ± 0.31</td>
</tr>
</tbody>
</table>

*p < 0.01 between Rastelli type C without obstruction and the other groups. †p < 0.01 between the groups indicated. Values are presented as mean value ± 1 SD, and comparisons were made by the Fisher protected least significant difference test. Ao/PT = diametric ratio between the aorta and the pulmonary trunk; LD/RD = diametric ratio between the left and the right ventricular outflow tracts; LVO = left ventricular outflow obstruction associated with subaortic stenosis or aortic coarctation, or both.
layer of the myocardium of the ventricular septum (18,19), we assume that the morphology of the outlet septum correlates with the configuration of the superior bridging leaflets which, in turn, determines the Rastelli subtype (1,2). However, direct measurement of the degree of curvature of the ventricular septum is almost impossible without cutting specimens (which become increasingly valuable) into pieces. In this study, therefore, we measured the geometric relation between the AV valve and the great arteries, which reflects the arrangement of the outlet septum relative to the rest of the ventricular septum in hearts with concordant ventriculoarterial connections.

**Morphometric differences between Rastelli type A and type C morphology.** Both the aorta and the pulmonary trunk were deviated more to the left in Rastelli type A morphology than in type C (Fig. 4). In other words, hearts with type C morphology had a greater degree of aortic overriding than those with type A, even in the absence of ToF. The angle of the great arteries was the same between the groups. Thiene et al. (8) suspected that, in AVSD with so-called conotruncal malformations, displacement of the developing outlet septum does not allow the outflow ridges to participate in the normal growth of the anterosuperior leaflet, thus producing a free-floating superior bridging leaflet. However, it remains uncertain, why this type of morphology can develop in the absence of conotruncal malformations. We therefore suggest that rightward location of the developing outlet septum is an indispensable factor in producing a free-floating superior bridging leaflet, irrespective of the presence or absence of conotruncal malformation.

**Morphometric differences between hearts with and without obstruction of either ventricular outlet.** The diagnosis of ToF is usually based on the morphologic features of anterocephalad deviation of the outlet septum coupled with muscular subpulmonary stenosis, even in association with AVSD (8,11–14). Vargas et al. (12) reported that the outlet (conal) septum in AVSD with ToF was deviated anteriorly to the right. To the best of our knowledge, however, no previous investigators have ever specifically measured the degree of malalignment of the outlet septum in this combination or considered obstruction of the LV outlet combined with AVSD to be caused by malalignment of the outlet septum. The present study revealed that, in the setting of Rastelli type A morphology, the pulmonary trunk was deviated more to the left in hearts with LVO than in hearts without obstruction.

The great arteries in such cases showed a more oblique position, which can be seen in Figure 4. The deviation of the great arteries was more pronounced in hearts with LVO compared to those without obstruction. Additionally, there were significant morphometric differences between the groups in terms of the degree of obliquity of the great arteries. These findings suggest that the morphologic features of AVSD are influenced by the presence or absence of obstruction in the ventricular outlets.

**Table 4. Degree of Deficiency of the Ventricular Septum**

<table>
<thead>
<tr>
<th>Rastelli Type</th>
<th>No.</th>
<th>Left Ventricle</th>
<th>Right Ventricle</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Scoop/Outlet</td>
<td>Scoop/Inlet</td>
</tr>
<tr>
<td>Type A</td>
<td>56</td>
<td>0.56 ± 0.07</td>
<td>0.76 ± 0.06</td>
</tr>
<tr>
<td>Type C</td>
<td>32</td>
<td>0.60 ± 0.07</td>
<td>0.78 ± 0.07</td>
</tr>
<tr>
<td>Type A with LVO</td>
<td>18</td>
<td>0.57 ± 0.06</td>
<td>0.78 ± 0.07</td>
</tr>
<tr>
<td>Type C with LVO</td>
<td>4</td>
<td>0.59 ± 0.03</td>
<td>0.72 ± 0.08</td>
</tr>
<tr>
<td>Type C with ToF</td>
<td>14</td>
<td>0.65 ± 0.07†</td>
<td>0.83 ± 0.05†</td>
</tr>
</tbody>
</table>

*p < 0.05 between the groups indicated. †p < 0.01 between type C with ToF and the other groups. Values are presented as mean value ± 1 SD, and comparisons were made by the Fisher protected least significant difference test. Abbreviations as in Table 2.
arrangement, with the subaortic tract being sandwiched between the pulmonary trunk and the superior bridging leaflet. In contrast, in hearts with Rastelli type C morphology with LVO, the aorta assumed a neutral position and the pulmonary trunk was displaced posteriorly to the left, producing the same sandwiched arrangement of the LV outflow tract. In type C morphology with ToF, the aorta was deviated more to the right (overriding and biventricular connection of the aorta), again with the pulmonary trunk displaced posteriorly. This geometry permits an oblique arrangement of the great arteries, but the rightwardly deviated and more horizontally situated outlet septum in this instance obstructs the RV outflow tract (Fig. 4). Becker et al. (16) proved that the great arteries in isolated ToF take a more oblique position than in normal hearts, suggesting that malrotation of the developing outlet septum is an integral embryologic factor for ToF. In AVSD, therefore, malrotation of the developing outlets may also be a factor producing obstruction in the LV, as well as the RV, outflow tracts. When the developing outlet septum rotates in a leftward direction, there is LVO associated with type A morphology. In contrast, rightward deviation and rotation result in obstruction of the RV outflow in hearts with type C morphology, namely AVSD with ToF. With the developing outlet septum in a neutral position, but again with abnormal rotation, it contributes to LVO with type C morphology, which can be considered intermediate between the two extremes. This observation correlates well with the fact that there has been no case report of type A morphology in the setting of ToF combined with AVSD. Leftward deviation of the developing outlet septum, we assume, is necessary to produce type A morphology. In contrast, ToF is accompanied by rightward deviation of the developing outlet septum, which is also an embryologic factor leading to a free-floating superior leaflet.

Different diaphragmatic ratios of the great arteries and ventricular outlets among Rastelli subtypes. Type A morphology has already been reported to be associated with a longer (15) and narrower (4,5,7) LV outflow tract than that of the type C variant. This study revealed that the hearts with type A morphology also had a smaller Ao/PT ratio than did those with type C. Moreover, those with type A had the same Ao/PT ratio, irrespective of the presence or absence of LVO. A fibrous shelf or thick cords anchoring the superior bridging leaflet onto the crest of the ventricular septum, or both, in the type A configuration of the superior leaflet surely prevent widening of the LV outflow tract during ventricular systole (4,7). A longer and narrower LV outlet in type A morphology may produce a small aorta with an enlarged pulmonary trunk. Because of lack of clinical data in our series, it remains to be clarified whether these morphometric differences also affect hemodynamic status and surgical outcome.

Cause of subaortic stenosis. Our study is at variance with previous reports on the morphology of LVO, perhaps because our measurements were performed in autopsy specimens. Discrete fibrous or fibromuscular stenosis has previously been considered one of the major causes of SAS (3,6,7,20), but it was not a predominant factor in any heart in our series. It has been thought (6,17) that the abnormal fibrous ridge reflects abnormal turbulence of blood flow and that it progresses both before and after surgical removal. Our hearts, in contrast, presented with much more complex anomalies, and almost all of the patients had died before or after operation in early infancy. Therefore, the discrete variant of SAS may develop in patients with type A morphology even in the absence of malrotation of the outlet septum. As for hearts with LVO and type C morphology, in at least three of our four cases, the patient had Down syndrome. Therefore, obstruction of the LV outlet accompanied by AVSD should be suspected even in patients with Down syndrome, although the combination of AVSD and LVO was less common than AVSD with ToF (21,22).

Deficiency of the inlet ventricular septum. The degree of deficiency of the inlet ventricular septum (‘scooping’) has been reported to be greater in hearts with common AV valve orifice than in those with separate orifices (23–25). We (26–28) have shown previously that the degree of scooping varies even within each subtype, and that this correlates significantly with the electrocardiographic (ECG) findings. The LV scoop/inlet ratio, which probably influences the ECG findings, was higher in hearts with ToF than in any other group in our series. Patients with ToF and deficient AV septation may have a milder degree of left axis deviation, an intermediate axis or even right axis deviation (12,29). The RV scoop/outlet and scoop/inlet ratios did not differ among groups, although the degree of scooping has previously been considered to affect RV morphology.

Study limitations. Our data from fixed hearts may differ from measurements in live patients, as the hearts we studied could potentially be altered by perioperative and postmortem artifacts. To minimize each artifact, we obtained data from as many hearts as possible, and we chose those with the best preservation. The geometric relation calculated between the AV valve and the great arteries may not always reflect malalignment of the outlet septum. We believe, nonetheless, that such measurements provide a more reliable approach when assessing morphometric features of congenital heart disease than does mere inspection. Lack of clinical data in our series made it difficult to clarify some important issues, such as the morphometric-hemodynamic relation in this disorder and differences between hearts from patients with and without Down syndrome. Another point to be clarified is whether a cause and effect relation exists for the geometric arrangement of the great arteries, obstruction in either ventricular outlet and the morphology of the superior bridging leaflet, or whether they are all consequences of the same cause.

Conclusions. The geometric arrangement of the great arteries correlated significantly not only with the morphology of the superior bridging leaflet, but also with stenosis of either ventricular outflow tract in AVSD with common AV valve orifice. Both the aorta and the pulmonary trunk were positioned more to the left in Rastelli type A than in type C morphology. Hearts with obstruction in either ventricular outlet showed a more oblique position of the great arteries than did those without obstruction. Abnormal rotation of the
developing outlet septum may be an embryologic factor producing obstruction of the LV, as well as the RV outlets, with its horizontal deviation potentially influencing the configuration of the superior bridging leaflet.

We thank Mr. Terauki Kawai, Dr. Kazuo Nitta and Mr. Tadahiko Moriyama from the MOA Health Science Foundation, Tokyo and Drs. Katsuhiko Mori, Yasuo Murakami and Yoshiho Hatai from the Sakakibara Heart Institute, Tokyo for their help in preparing the manuscript.

References