Pulmonary Atresia and Intact Ventricular Septum: A Revised Classification


SUMMARY The dismal outlook for patients with pulmonary atresia with intact ventricular septum may be related to associated right ventricular hypoplasia. Study of 32 autopsy specimens and 46 angiograms of neonates with this lesion suggested that the cavitary hypoplasia was related to massive hypertrophy of the right ventricular wall. This hypertrophy was sufficient to obliterate the trabecular and/or infundibular portion of the ventricular cavity entirely in one-third of the cases; this observation forms the basis for a revised classification of these hearts. Three autopsies and 14 angiograms of neonates with critical pulmonary stenosis were examined. Hearts with obliterated infundibular and trabecular cavities had thicker walls and smaller tricuspid valves, as estimated angiographically or at autopsy, than those in which the normal three portions of the ventricular cavity were represented.

PULMONARY ATRESIA with intact ventricular septum (PA:IVS) has a high early and late mortality. The pathologic classification of Greenwold et al. into commoner type 1 (cases with a small right ventricular cavity) and type 2 (with a normal or dilated cavity) has been the key to the description and management of the disease. The implication at that time was that patients with smaller cavities were less likely to survive and that the abnormality was not ultimately correctable. However, morphologic studies of PA:IVS have revealed a continuum of right ventricular cavity size; and, as clinical series were increasingly reported, it emerged that some cavities can grow.

We propose a revised classification of the right ventricular appearances in this condition, based on the tripartite approach to right ventricular morphology. This new classification has relevance for the surgical management of PA:IVS. Ventricular size is important, but there are limitations to the angiographic determination of the volume of these bizarrely shaped cavities.

We therefore prefer to measure the tricuspid annulus diameter and relate tricuspid valve size to our morphologic classification.

In the neonatal period, patients may present with a hemodynamic disturbance indistinguishable from PA:IVS (suprasystemic right ventricular pressure, obligatory right-to-left atrial shunt and a persistent ductus arteriosus) but with a pinhole patency of the pulmonary valve visible on angiography. The ventricular morphology of these patients was examined for comparison.

Materials and Methods

Thirty-two specimens from patients who died with PA:IVS during the neonatal period were available from the pathologic collection at the Hospital for Sick Children. Three specimens from patients with critical pulmonary stenosis from the same age group were also studied. Each specimen was examined to determine the presence or absence of the inlet, trabecular and infundibular portions of the right ventricular cavity. The inlet portion is defined as the part of the ventricle that incorporates the tricuspid valve apparatus. The trabecular portion lies beyond the insertion of the papillary muscles of the tricuspid valve toward the apex, while the infundibulum or outlet portion leads to the atretic pulmonary valve. The tricuspid diameter was measured using Hegar dilators, as this appeared more clinically meaningful than the conventional pathologic measurement of tricuspid annulus circumference. Maximal wall thickness, usually toward the apex of the cavity, was also measured.

Forty-five angiograms of newborns with
PA:IVS were reviewed to determine the presence or absence of the trabecular and infundibular portions of the ventricular cavity. The corresponding pathologic specimens were available in 23 cases. Angiographically, the trabecular cavity is recognized by its irregular outline, compared with the characteristically smooth inlet and outlet portions of the ventricle. During systole, trabecular spaces tend to be obliterated, while sinusoids opacify further, but the distinction can be difficult. Any recognizable infundibular area was considered present, however restrictive it appeared. The diameter of the tricuspid valve was estimated by measuring the annulus as seen in diastolic frames in both anteroposterior and lateral right ventricular angiograms, using the diameter of the catheter as the magnification factor and taking a mean of the anteroposterior and lateral estimates. The validity of this method was tested by comparing angiographic estimates of tricuspid valve diameter with direct measurements of 17 corresponding autopsy specimens.

For comparison, 14 angiograms of patients with critical pulmonary stenosis and suprasystemic right ventricular pressures who required surgery during the first month of life were reviewed in the same way.

Contingency tables were analyzed using the chi-square test and grouped data illustrated with 95% confidence limits around the mean value. The least-squares regression equation was calculated for two related variables. Where groups of data are presented in systematically ordered categories (according to ventricular morphology), a nonparametric test for monotonic trend was applied.10

Results

All hearts with PA:IVS had concordant atrioventricular and ventriculoarterial connections, a patent foramen ovale and a patent ductus arteriosus. They were classified anatomic and angiographically into three groups. In the first group, all three portions of the right ventricular cavity were present and the anomaly consisted in a more-or-less severe degree of generalized hypoplasia. All cases of pulmonary stenosis with IVS but one were in this group (figs. 1A and 2A). In the other hearts, besides the smallness of the cavity, at least one portion was missing. All cases by definition have a patent tricuspid valve and thus an inlet portion to the ventricle, but the trabecular portion (figs. 1B and 2B) or both trabecular and infundibular portions of the cavity (figs. 1C and 2C) can be so overgrown by hypertrophied myocardium as to be effectively absent. No specimen with a trabecular portion but no infundibular cavity was found. The distribution into the three groups of the hearts examined at autopsy and angiographically is shown in tables 1 and 2.

The tricuspid valve diameters measured at autopsy are shown in figure 3, according to morphologic group. For comparison, a normal range of tricuspid valve diameters in the neonatal period, derived from the data of Rowlatt et al.9 (who measured tricuspid valve circumference in centimeters) is included. Among patients with PA:IVS, the largest tricuspid valve annuli were in the group in which all components of the ventricular cavity were present and the smallest in those with only an inlet portion to the ventricular cavity; the trend between groups was significant (p < 0.01). All were, however, smaller than normal (p < 0.01).

Angiographic estimates of tricuspid valve diameter are presented by category in figure 4, which includes patients with critical pulmonary stenosis. The group with the smallest tricuspid valves had PA:IVS with only an inlet cavity. Those with the largest tricuspid valves had critical pulmonary stenosis in which all portions of the ventricular cavity were represented (test for trend, p < 0.001). Many of the latter tricuspid valve diameters lie within the 95% confidence limits for normal, allowing a correction factor for angiographic rather than autopsy measurement. Figure 5 relates autopsy and angiographic estimates of tricuspid valve diameter. While the two measurements correlate closely, the angiographic figures exceed the autopsy estimates by a factor of approximately 1.43:1.
TABLE 1. Autopsy Specimens: Ventricular Morphology

<table>
<thead>
<tr>
<th></th>
<th>All portions present</th>
<th>No trabecular cavity</th>
<th>No infundibular cavity and no trabecular cavity</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA:IVS</td>
<td>17</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>PS</td>
<td>3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: PA:IVS = pulmonary atresia with intact ventricular septum; PS = pulmonary stenosis.

The maximal thickness of the right ventricular wall was measured in autopsy specimens and the data along with the "normal range" are shown in figure 6. All groups with PA:IVS had a right ventricular wall thickness substantially greater than the normal newborn proportions demonstrated by Rowlatt et al.⁹ (p < 0.01), though no trend between groups was demonstrated (p > 0.2).

Discussion

The pathologic features of PA:IVS are well known; little can be added to the early descriptions of the condition.¹¹ Less well understood are the reasons for the disappointing surgical results for PA:IVS compared with apparently more complex anomalies.¹²⁻¹⁴

The tripartite approach to right ventricular morphology was developed by Goor and Lillehei,⁷ who defined a sinus (inlet) portion, a trabecular part and a conus (infundibulum). These areas can be distinguished embryologically, angiographically, functionally and certainly morphologically.

Trabeculations appear very early in the primary heart tube.¹ In nontrabecular portions, cell multiplication is maximal at the endocardial surface, tending to invade the flow pathway.¹⁵ In the trabeculated portion, cell multiplication and maturation occur, mainly at the epicardial surface with regression at the endocardial surface, tending to increase chamber size. Thus, in fetal life, the trabecular portion is the main determinant of cavity size and growth.

At birth, the trabecular portion can be distinguished angiographically; Goor and Lillehei⁷ illustrated the original description of the tripartite concept using the right ventricular appearance in PA:IVS and showed a miniature right ventricle in which all three portions were present.

Functionally, the three areas are distinguishable. Studies of blood flow velocity patterns within the right ventricle suggest that the inlet portion constitutes part of the ventricular filling mechanism, while the trabecular and infundibular portions contribute mainly to systolic pump function.¹⁶

FIGURE 2. Right ventricular angiograms of neonates with pulmonary atresia and intact ventricular septum showing ventricles with inlet trabecular and infundibular portions (top), no trabecular cavity (middle), and no infundibular or trabecular cavity (bottom). Catheter sizes (A) 5F, (B) 5F, and (C) 6F.
We hope to show that the tripartite approach is also helpful in understanding pathology. Emphasis on right ventricular cavity hypoplasia in PA:IVS may have obscured its cause—massive thickness of the right ventricular wall (fig. 6). Myocardial hypertrophy can even obliterate the intertrabecular spaces and infundibular cavity, and this observation forms the basis of our classification of the condition. While an autopsy study inevitably includes the worst end of the spectrum of a disease, in almost half the specimens of PA:IVS we reviewed, myocardial hypertrophy was sufficient to obliterate the trabecular cavity, with no infundibular portion present in about half this subgroup (tables 1 and 2). If the trabecular cavity is entirely overgrown, the mass of muscle toward the apex of the ventricle, however hypertrophied, cannot contribute to the ventricular stroke volume should the obstruction to right ventricular outflow be relieved. However, with reduction of the afterload, the hypertrophy may regress, as occurs in the left ventricle after relief of aortic stenosis.17 The trabecular cavity can then dilate or even become excavated for the first time. Such progression has been illustrated in some reports of right ventricular growth after pulmonary valvotomy for this condition.18,19

### Table 2. Angiographic Evaluation: Ventricular Morphology

<table>
<thead>
<tr>
<th></th>
<th>No infundibular cavity</th>
<th>No trabecular cavity</th>
<th>No infundibular cavity and no trabecular cavity</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA:IVS</td>
<td>20</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>PS</td>
<td>16</td>
<td>1</td>
<td>12</td>
</tr>
</tbody>
</table>

$\chi^2 = 10.034$,

$p < 0.01$.

Abbreviations: PA:IVS = pulmonary atresia with intact ventricular septum; PS = pulmonary stenosis.

**Figure 4.** Tricuspid valve diameter (TV Dia) angiographically estimated, according to ventricular morphology of neonates with critical pulmonary stenosis and pulmonary atresia with intact ventricular septum (95% confidence limits). The 'normal' column is derived from the data of Rowlatt et al.,9 corrected as in figure 5.

**Figure 3.** Tricuspid valve diameter (TV dia.) as measured at autopsy, according to category of ventricle (95% confidence limits around the mean for each group are shown). The 'normal' column is derived from the data of Rowlatt et al.9

**Figure 5.** Tricuspid valve diameter as assessed angiographically and at autopsy.
Right Ventricular Size

While perhaps appropriate for the documentation of ventricular growth, there are two main objections to the use of angiographically derived ventricular volumes for the classification and management of PA:IVS. First, the accuracy of these determinations has not been validated at autopsy or intraoperatively; the assumptions required by Simpson’s rule have been applied to the bizarrely shaped right ventricular cavities often found in this condition. Second, even if the measurements are reasonably accurate, the implications of having a right ventricular volume of 2 ml, 10 ml/m² or even 30% of normal have not been delineated in surgical terms.

We explored the use of estimates of tricuspid valve diameter, both because a restrictive tricuspid valve has implications for the surgical management of PA:IVS and because the tricuspid valve serves as an indirect indicator of right ventricular cavity size. We have usually found a proportionality between tricuspid valve and right ventricular cavity size in the presence of an IVS; this has been confirmed for PA:IVS in an autopsy study by Zuberbuhler and Anderson and angiographically by Patel et al., although they did not discuss this aspect of their data. Tricuspid annulus size is also related to our morphologic classification (figs. 3 and 4). In the current study, a close correlation between angiographic estimates and direct measurements of the tricuspid valve annulus at autopsy (fig. 6) was shown. Angiographic estimates of tricuspid valve diameter were consistently greater than the autopsy measurements. This may be due to shrinkage of the specimen during preservation or to a systematic overestimation inherent in the angiographic method of measurement.

The tricuspid valve has an important role in PA:IVS. Although a degree of tricuspid valve dysplasia is common in this condition, we do not attach great significance to the appearance of tricuspid incompetence on right ventricular angiograms. With power injections into an already hypertensive right ventricle, such appearances could easily be spurious; indeed, the dominant wave in the right atrial pressure trace usually corresponds to atrial systole (fig. 7).

Right Ventricular Cavity and Wall Thickness

Tricuspid valve diameter and right ventricular wall thickness were inversely related, though this relationship did not quite achieve significance. The specimens with the smallest tricuspid valves have the thickest walls and obliterated trabecular and infundibular cavities (fig. 4). In contrast to PA associated with ventricular septal defect, when the ventricular septum is intact the pulmonary annulus is almost always adequate. The tricuspid annulus and hypoplastic right ventricular cavity thus provide the main restriction to forward flow after valvotomy.

Origins of Right Ventricular Dysplasia

Extremes of tricuspid valve and cavity hypoplasia are associated with extremes of derangement of right ventricular myocardial development. The semilunar valve primordia do not appear until after the partitioning of the truncus and the completion of ventricular septation. The stage at which the cusps fuse is unknown and may be variable. Although it must occur late relative to the development of the flow pathways of the heart, which are complete within the first month or so of fetal life, fusion may occur early enough to impair the development and differentiation of the substance of the heart — the myocardium, connective tissue and blood supply.

At the stage of pulmonary valve development, the blood supply of the heart is still derived from its own lumen. Only later do coronary arteries appear and come to communicate with the intertrabecular spaces deep in the myocardium. By this time the heart has
already been beating for 3 weeks, supporting a small embryonic and relatively larger extraembryonic (placent) circulation. If the pulmonary valve primordia fuse, preventing the right ventricle from emptying into the pulmonary artery and ductus, systolic filling of the interventricular spaces and sinusoidal-coronary communications may allow the abnormal pathways to persist. Such sinusoids have been described after birth in the left ventricles of patients with aortic atresia,23 and even atrioventricular discordance with pulmonary atresia,24 suggesting that their persistence is secondary to a hemodynamic disturbance rather than a primary abnormality of right ventricular development.

If successful pulmonary valvotomy is not achieved in the neonatal period, a small cavity with high intracavity pressures remains. Parts of the right and left ventricular myocardium remain perfused through sinusoids from the right ventricle during systole rather than from the aortic root in diastole. The coronary arteries involved in the fistulous communications can become nodular and thickened.25 26 This, together with the severe desaturation of the right ventricular blood, may contribute to myocardial ischemia. The high intracavity pressures generated by the right heart may also be associated with the development of ventricular endocardial fibroelastosis. Fibroelastosis has not been described in the right or left ventricle with pulmonary or aortic atresia when there was also atresia of the corresponding atrioventricular valve.27 In these cases, the ventricle is isolated from the circulation and presumably is not hypertensive. Fibroelastosis is detrimental to the diastolic compliance of the ventricle. Theoretically, small cavity size and high intracavitary pressures are inevitably associated.28 The Laplace relationship between the wall tension, intracavitary pressure and chamber dimension (or any of the modifications applied to describe the properties of the ventricular wall) predict the highest pressures in the smallest cavities at a given wall tension.

Thus, in a neonate with no trabecular or infundibular portion to the right ventricular cavity, severe myocardial hypertrophy, cavitary hypoplasia and abnormalities of the diastolic properties and blood supply of the right ventricular wall may combine to make the prospects for eventual attainment of normal right ventricular size and function very poor. However, the extent to which the potential for enlargement is already impaired by the time of birth is unclear, so early decompression by pulmonary valvotomy seems indicated in all hearts with an infundibular portion to the right ventricular cavity.

A tripartite view of the right ventricle also demonstrates the differences in the spectrum of ventricular morphology in pulmonary stenosis compared with PA-IVS in the neonatal period. Ventricles with pulmonary stenosis were at the best end of the spectrum; all but one had a trabecular portion to the ventricular cavity and, as angiographically estimated, they had the least restrictive tricuspid valves.

Recognition of the varieties of right ventricular mor-

phology in PA-IVS may have practical implications. The surgical options for patients with tripartite right ventricles, absent trabecular but patent infundibular and absent trabecular and infundibular cavities are different. This revised classification constitutes the background from which we have reviewed our surgical management of PA-IVS.

References
6. Graham TP Jr, Bender HW, Atwood GF, Page DL, Sell CGR: Increase in right ventricular volume following valvulotomy for pulmonary atresia or stenosis with intact ventricular septum. Circulation 50 (suppl II): II-69, 1974

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Pulmonary Atresia and Intact Ventricular Septum: Surgical Management Based on a Revised Classification


SUMMARY Sixty patients with pulmonary atresia and intact ventricular septum (PA:IVS) presenting from 1970 to 1980 are reviewed. Three groups of patient are discussed: those with tripartite right ventricles, those with no trabecular portion to the cavity, and those with neither trabecular nor infundibular portions. The decrease in early mortality for neonates with PA:IVS since 1977 (one death in 15 patients) supports our current management policy of preoperative prostaglandin E1 infusion with transpulmonary valvotomy (for patients with an infundibular cavity) combined with a left modified Blalock-Taussig shunt using a Gore-Tex prosthesis. Tricuspid valve growth, estimated by serial angiograms in 12 patients, was greater if right ventricle-to-pulmonary artery continuity was established. Later definitive repair was attempted in nine patients, with two early deaths. Five underwent right ventricular outflow tract reconstruction and four had modified Fontan procedures. Neonates with critical pulmonary stenosis are also discussed. Their neonatal mortality (nine deaths in 20 patients) was similar to that of comparable patients with PA:IVS, but their actuarial survival at 5 years (55%) was superior (36% at 5 years).

ACCOUNTS of the management of pulmonary atresia with intact ventricular septum (PA:IVS) often constitute a catalog of early and late failures of surgical treatment.1-3 The dismal outlook in this condition has been attributed to the associated right ventricular hypoplasia.4 In a recent anatomic and angiographic study,5 we reported that cavitary hypoplasia in PA:IVS is related to massive hypertrophy of the right ventricular wall and proposed a classification of the condition based on the tripartite approach to right ventricular morphology. We distinguished three types of ventricles: those with generalized cavitary hypoplasia, those without a trabecular portion to the cavity and those in which both trabecular and infundibular portions are entirely overgrown by hypertrophied myocardium.

With this appreciation of the variety of ventricular morphology encountered, we have reviewed the results of our surgical management of PA:IVS over the past 10 years. This retrospective study forms the basis of a prospective management protocol both for the neonatal period, when mortality is high, and for definitive repair later. The question of right ventricular growth and the comparability of critical pulmonary stenosis to PA:IVS are also discussed.

Methods

The records of 81 patients admitted to the Hospital for Sick Children from 1970 to 1980 inclusive were examined. Sixty patients had PA:IVS and 21 had critical pulmonary stenosis. Patients with critical pulmonary stenosis were included only if they required operation in the first month of life, with suprasystemic pressures in the right ventricle, right-to-left shunting at atrial level and a pinhole patency of the pulmonary valve at angiography. Patients with PA:IVS were included regardless of age at initial operation. Even in the presence of extreme right ventricular hypoplasia, both lesions were considered amenable to surgical treatment throughout the period reviewed.

Details of the use of prostaglandin infusion, the na-
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C Bull, M R de Leval, C Mercanti, F J Macartney and R H Anderson

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