Management of Total Anomalous Pulmonary Venous Return

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SUMMARY
The effects of age, type of return, presence of pulmonary venous obstruction, obstruction to left heart filling, systemic arterial oxygen saturation (Ao O₂%), pulmonary-to-systemic flow ratio (Qp/Qs), pulmonary-to-systemic resistance ratio (Rp/Rs%), and mean pulmonary artery-to-mean systemic arterial pressure ratio (MPAP/MSAP%) in 35 cases of total anomalous pulmonary venous return seen in the last 5 years, were studied in relation to prognosis and management. The surgical mortality was increased in patients with anomalous venous return to the right common cardinal system (right superior vena cava andazygos vein) regardless of age and was significantly lower in patients over 6 months of age and in those who had preoperative intensive medical management. No relation was found between surgical mortality and Ao O₂%, Rp/Rs, MPAP/MSAP%, or the presence of pulmonary venous obstruction. The small size of the left atrium rather than the small size of the left ventricle is felt to be one of the reasons for operative failure. The importance of obstruction to left heart filling at the atrial level was stressed. Until technics for surgical treatment of this group of anomalies in early infancy become more successful, we recommend balloon atrial septostomy in combination with intensive medical management as effective palliative treatment for most of these patients in the first 6 months of life.

Additional Indexing Words:
Pulmonary veins Balloon atrial septostomy Atrial pressure gradient
Medical management

TOTAL anomalous pulmonary venous return (TAPVR) comprises a group of anomalies of different anatomic and hemodynamic types, most of which can be corrected surgically with structural and functional cure. Successful operation for these defects, unlike some of the other operable malformations of the heart, avoids many postoperative problems. The timing of the operation has been

and remains the important question because of the high natural mortality in the untreated infant and the high surgical risk in this age group.

Gersony and associates1 and Barratt-Boyes and co-workers2 recently reported the successful surgical correction of TAPVR in 11 of 16 babies under the age of 5 months. These reports are encouraging and probably represent the coming trend in surgery of TAPVR. However, until the time that such results of early surgical treatment are obtainable in all centers, vigorous medical management can offer a safe and effective form of palliative treatment with a greater overall survival.

This paper presents the total management of 35 cases of TAPVR seen at Texas Children's Hospital in the last 5 years. Two previous articles3,4 from this center discuss the cases prior to 1966.
Methods

Of the 35 patients with TAPVR (cases 1–35) followed for varying lengths of time during the 5 year period from 1966 to mid 1970, 28 presented in heart failure.

For each patient the diagnosis was confirmed by hemodynamic and angiographic studies. A special effort was made during catheterization to enter the left atrium (LA), the common anomalous pulmonary venous channel, and the pulmonary artery wedge position in order to measure the pressure gradients between the left and right atrium, between the anomalous pulmonary vein and right atrium (RA), and between the pulmonary artery wedge (PAW) and RA. Both phasic and mean pressures were recorded at high gain to measure accurately any pressure gradients. To visualize any areas of pulmonary venous obstruction, biplane, large-film selective angiocardiography was used, often with separate injections into the right and left pulmonary arteries. In some cases, injections were made directly into the common anomalous pulmonary venous channel or into the individual pulmonary veins. The quantity of pulmonary blood flow in relation to the quantity of systemic flow \( Q_p/Q_s \) and the pulmonary-to-systemic resistance ratio \( R_p/R_s \) were calculated as follows:

\[
\frac{Q_p}{Q_s} = \frac{\text{Ao O}_2 \text{ saturation} - \text{mixed venous O}_2 \text{ saturation}}{\text{Pulmonary vein or 95% O}_2 \text{ saturation} - \text{PA O}_2 \text{ saturation}}
\]

\[
\frac{R_p}{R_s} = \frac{\text{MPAP} - \text{mean RA pressure/quantity of pulmonary flow}}{\text{MSAP} - \text{mean RA pressure}} \times 100
\]

where \( \text{Ao O}_2 \text{ saturation} \) denotes systemic arterial oxygen saturation; mixed venous \( \text{O}_2 \text{ saturation} \) equals superior vena caval oxygen saturation plus two times the inferior vena cava oxygen saturation divided by 3; \( \text{PA} \), the pulmonary artery; \( \text{MPAP} \), the mean pulmonary artery pressure; and \( \text{MSAP} \), the mean systemic artery pressure (table 1).

In calculating the pulmonary resistance, the difference between MPAP and mean RA pressure (rather than PA wedge pressure) was used, thus deriving total pulmonary vascular resistance (PVR) in preference to pulmonary arteriolar resistance. The frequent variance between PA wedge and RA pressure in these patients precludes the interchangeable use of these two values as was done in a previous study.\(^4\) The difficulty in obtaining a reliable wedge pressure in babies with elevated PA pressure also makes the RA pressure a more reproducible reference point for comparison.

Associated cardiac defects in the subjects of this study include: persistent left superior vena cava, 12; mild right pulmonary artery branch stenosis, one; small arteriovenous fistula in right lower lobe, one; cleft anterior leaflet of the mitral valve, one; and nodular sclerosis of the tricuspid valve, one.

The classification of the anatomic type of anomalous pulmonary venous return chosen for this investigation was proposed by Neill\(^5\) employing both an embryologic and an anatomic basis. In Neill's scheme, anatomic type I returns pulmonary venous blood directly to the body of the RA (excluding return to the coronary sinus), type II returns it to the right common cardinal system (right superior vena cava [SVC] orazygos vein), type III to the left common cardinal system (left innominate vein or coronary sinus), and type IV to the umbillicovitelline system (portal vein or ductus venosus). This classification defines the specific anatomy of the site of return, rather than simply identifying the site as cardiac, supracardiac, or infracardiac.

The criteria selected for diagnosis of pulmonary venous obstruction were as follows:

a. Infra diaphragmatic return either to ductus venosus or to portal vein. (While infra diaphragmatic return to the inferior vena cava may not result in obstruction to venous return, this type of return was not encountered in the study.)

b. Higher mean pulmonary artery wedge pressure than mean RA pressure by 8 mm Hg or more. (High value was selected arbitrarily to avoid gradients due to increased flow.)

c. Higher mean pressure in common pulmonary venous trunk than in the right atrium by 5 mm Hg or more.

d. Angiocardiographic evidence of discrete localized obstruction in the pulmonary venous channels.

Direct observation of the size of the atrial communication was made at operation or by examination of nonsurgical specimens at necropsy. The size of the communication was graded as (1) "small" foramen ovale (presumably obstructing left atrial filling), (2) "adequate" foramen ovale (not obstructing left atrial filling), and (3) atrial septal defect (ASD). The size of the atrial communication was compared to the atrial pressure gradients to determine the significance of the gradient in assessing the size of the atrial communication. In addition, the RA–LA pressure gradients were compared to (1) age of onset of symptoms, (2) \( Q_p \), (3) \( \text{Ao O}_2 \%), (4) \frac{R_p}{R_s} \%, and (5) \frac{\text{MPAP}}{\text{MSAP}} \%.

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In view of the high surgical mortality in infancy, operations on 19 patients were postponed until they reached at least 1 year of age. The following regimen of medical management was instituted: (1) the usual calculated dosage of digoxin; (2) administration of both furosemide and spironolactone daily to each infant; (3) prolonged hospitalization, if necessary, for infants with persistent tachypnea, distress with feeding, and failure to thrive; and (4) balloon septostomy whether or not a RA-LA pressure gradient can be identified. This last procedure did not become a routine part of the regimen until the latter phase of this study.

Results

Age

Twenty patients were referred for diagnosis and treatment before they were 6 weeks of age; five were between 6 weeks and 6 months, seven between 6 months and 2 years, and three were first examined when 2 years of age or more (fig. 1). The difference in Ao O2% and Rq/Rc% between the patients who presented before and after age 6 months were not statistically significant; however, the average pulmonary blood flow and the MPAP/MSAP% were higher in those younger than six months (table 1).

Anatomic Type of Pulmonary Venous Return

Five subjects had type I return; seven had type II (six to the right superior vena cava and one to the azygos vein); 20 had type III (12 to the vertical vein, eight to the coronary

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### Table 1

Hemodynamic Changes Related to Age of Presentation, Pulmonary Venous Obstruction, Atrial Gradient and Surgical Survival

<table>
<thead>
<tr>
<th>Factor</th>
<th>No. of cases</th>
<th>Ao O2 (%)</th>
<th>Qp/Qo</th>
<th>Rq/Rc (%)</th>
<th>MPAP/MSAP (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Below 6 mo</td>
<td>25</td>
<td>80.0 ± 8.0</td>
<td>1.9 ± 1.1</td>
<td>&lt;0.1</td>
<td>59 = 57</td>
</tr>
<tr>
<td>Above 6 mo</td>
<td>10</td>
<td>80.0 ± 8.0</td>
<td>1.3 ± 0.8</td>
<td></td>
<td>49 = 73</td>
</tr>
<tr>
<td>Pulmonary venous</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>obstruction</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>16</td>
<td>80.0 ± 8.7</td>
<td>2.0 ± 1.1</td>
<td>NS</td>
<td>42 = 30</td>
</tr>
<tr>
<td>Absent</td>
<td>6</td>
<td>84.0 ± 7.0</td>
<td>1.5 ± 1.0</td>
<td>NS</td>
<td>28 = 26</td>
</tr>
<tr>
<td>Mean RA-LA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>gradient:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>14</td>
<td>81.0 ± 8.7</td>
<td>2.1 ± 1.2</td>
<td>&lt;0.05</td>
<td>39 = 32</td>
</tr>
<tr>
<td>Absent</td>
<td>18</td>
<td>79.0 ± 8.2</td>
<td>1.3 ± 0.8</td>
<td></td>
<td>53 = 62</td>
</tr>
<tr>
<td>Surgery:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival</td>
<td>14</td>
<td>81.0 ± 7.0</td>
<td>1.3 ± 0.8</td>
<td>NS</td>
<td>70 = 84</td>
</tr>
<tr>
<td>Death</td>
<td>11</td>
<td>79.0 ± 10.0</td>
<td>1.9 ± 0.9</td>
<td>NS</td>
<td>49 = 38</td>
</tr>
<tr>
<td>Total patients:</td>
<td>35</td>
<td>80.0 ± 7.8</td>
<td>1.7 ± 1.0</td>
<td></td>
<td>57 = 61</td>
</tr>
<tr>
<td>Mean of total cases</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: NS = not significant; see text for other abbreviations.
Pulmonary Venous Obstruction

Sixteen patients had one or more criteria for pulmonary venous obstruction (table 1). Of these, 11 presented before they were 6 months of age. Statistically, the MPAP/MSAP% was significantly higher in patients with obstruction, but the other factors studied were not statistically significant.

Size of Atrial Communication

The left atrium was entered during catheterization in 32 of the 35 investigations permitting a comparison of LA and RA pressure as a means of assessing the size of the atrial communication. In 26 of these 32 patients, the atrial opening was observed directly either at operation or at autopsy. Five of these 26 patients had a mean RA to LA pressure gradient of 2 to 3 mm Hg and each had a small, presumably obstructing, foramen ovale. Another five patients had pressure that was only 1 mm Hg higher in the right atrium than in the left atrium, and three of these five were proved by direct observation to have only a small foramen ovale through which the total systemic flow passed. Among the 16 patients in whom the two atrial pressures were identical and direct observation of the atrial communication was possible later, two of them proved to have a small obviously obstructing foramen ovale. As to the possible influence of the size of the atrial communication on the hemodynamics and the clinical course, 80% of the patients with an atrial pressure gradient presented in heart failure before 6 months of age and the pulmonary blood flow was higher in patients with an atrial pressure gradient. However, there was no significant difference between the two groups in the Ao O₂ saturation, the Rp/Rs, or the MPAP/MSAP% (table 1).

Medical Treatment

In the 19 patients treated medically, weight gain was slow but progressive. Two of these 19 died during the medical treatment phase—one death (at age 3 months) from intractable heart failure occurred within 30 days of instituting therapy, and another death (at age 45 days) associated with pneumonia occurred after 40 days of treatment. The death from congestive heart failure occurred in an infant who proved to have a small foramen ovale (fig. 2, from case 33). In this patient, the demonstration of only a 1-mm Hg pressure gradient unfortunately led us away from performing balloon septostomy. After it was realized that a patient died primarily from an atrial communication that was too small, a balloon catheter was used routinely to check the size of the atrial communication and to do septostomy. Balloon atrial septostomy was carried out in the last two patients of the series (in case 34, at age 1 month, and in case 35, at age 3 months) with immediate, marked improvement in the condition of both patients. Both had a right-to-left atrial gradient of 3 mm Hg before septostomy. Figure 3 demonstrates the disappearance of the gradient after septostomy in case 34. In the same patient, immediately after septostomy, the left ventricular pressure rose from 60/0.7 to 70/0.8 and the systemic arterial oxygen saturation rose from 83% to 88%. Pulmonary artery pressure dropped from 80/30 with a mean of 45 mm Hg to 55/15 with a mean of 23 mm Hg, and right ventricular pressure dropped from 80/0.10 to 55/0.8. The clinical condition continued to improve.

Patients with sufficient data to calculate Ao O₂%, Qp/Qs, Rp/Rs, and MPAP/MSAP% who died during medical treatment were too few to allow significant statistical comparison with the group who lived. Medical complications other than congestive heart failure included pneumonia in seven cases and subacute bacterial endocarditis in one.
The right atrium in case 33, showing a small patent foramen ovale (PFO) through which blood had to pass to the left side. Its small size can be compared to the large size of the coronary sinus (CS) through which the pulmonary venous blood returned to the right atrium. The small opening above and to the right of the PFO is a blind recess (BR).

Surgical Treatment
A total of 25 patients had surgical treatment during this 5-year period (table 1 and fig. 4), of whom 11 died (44% total mortality). All deaths were in the early postoperative period. Operation was performed shortly after the diagnosis was confirmed by cardiac catheterization in 16 of these patients and 10 of the deaths occurred in this group (62.5% mortality). Nine patients, all of whom were more than 6 months of age, had surgical treatment after a period of intensive medical treatment, and one died (11% mortality). Among the patients who had immediate operation, 10 were under 6 months of age, and eight of the 10 infants died (80% mortality). Among the six
patients who had immediate operation and who were over 6 months of age, two died (33% mortality).

Considering age alone (fig. 5), eight of the 11 deaths occurred in infants under 6 months of age (72.7% of surgical deaths). Considering the influence of previous intensive medical treatment on surgical survival, two of the three deaths after operation performed in the favorable age group (over 6 months) occurred in patients who had not had a previous period of intensive medical treatment. Of the nine patients operated on after a period of medical treatment, only one died (11% mortality). The mortality during intensive medical treatment alone in 19 critically ill infants was 10.5%. The two deaths occurred in infants who unfortunately did not have balloon septostomy included in the medical treatment regimen.

The operative mortality was tabulated for each of the four anatomic types of anomaly according to the Neill classification (fig. 6). None of the five patients with type II defects survived (three of them were over 10 months of age), whereas three of the four with type I defects survived (all three were under 10 months of age), 10 of the 13 with type III defects survived (the three who died were under 8 months of age) and one of the three with the notoriously lethal type IV defect lived and thrived after operation at 1 year 11 months of age.
In regard to Ao O₂%, Rv/Rp%, and MPAP/MSAP%, no significant statistical differences were found between those who survived surgery and those who died (table 1). The Qp/Qs was higher in those who died (1.9) than in those who survived (1.3) but this was found to be significant only at the 10% level.

Postoperative complications included pulmonary congestion and hemorrhage in every case and arrhythmias in three cases.

**Discussion**

**Age**

Age of the patient unquestionably influences operative survival. Mustard and associates,6 as late as 1962, described 100% mortality for correction of TAPVR in infants. Cooley and associates3 in 1966 and Leachman and co-workers4 in 1969 found a sharp decrease in surgical mortality among patients over 1 year of age. Despite improvements in technic in the past 5 years, operative mortality among the infants reported in this series has not decreased.

The high operative mortality before 6 months of age is related to several factors. Formerly, once the diagnosis was established in a critically ill infant, immediate operation...
was recommended. The moribund condition of the infant at the time of operation increases the risk of thoracotomy alone. Additional considerations include the necessity for cardiopulmonary bypass in corrective surgery of TAPVR. This in infancy adds to the technical difficulty and duration of surgery and contributes to the postoperative problems of electrolyte balance, blood volume regulation, and ventilation.

The critical problems of the small venous anastomoses, venous rechanneling, and repositioning of the atrial septum make the mechanics of such surgery in tiny infants difficult. The suture lines in a small vessel must react and swell postoperatively to a degree equal to that in a larger vessel, rather than to a relatively smaller degree. Very likely a combination of such areas of postoperative pulmonary venous obstruction produced by the anastomosis and the small newly functioning left atrium rather than inadequacy of the left ventricle cause the pulmonary edema often encountered in the infant in the postoperative period.

**Anatomy of the Anomalous Returning Vessels**

The anatomy of the returning vessels also appears to have a bearing on postoperative survival (fig. 6). Vetto and associates,7 in a survey of the literature between 1950 and 1960, found that the best postoperative survival rate (83%) among the 65 patients studied was in those with venous return to the RA, while the lowest (35%) was in those with return to the left innominate vein. However, in 49 of these cases, extracorporeal circulation was not used. Cooley and associates3 and Leachman's group4 reported 68 cases for which correction of TAPVR was done while using extracorporeal circulation. They found that the overall survival rate was not significantly influenced by the site of anomalous return; however, they did not separate supracardiac return into the right or left common cardinal systems. The anatomic and embryonic classification5 used in our study more precisely defines the site of return. In our series, the highest mortality rate occurred among patients with type II defects; all five who had surgery died. In type II defects, the left pulmonary veins form a trunk posteriorly and to the right of the heart, then as a confluence pass anterior to the hilus of the right lung, where the return from both lungs combine. The trunk then enters the posterior aspect of the right SVC. Anastomosis of these veins to the LA requires surgical creation of a new, long, venous channel or tunnel from near the hilus of the right lung to the LA. On the other hand, survival rate was good in 10 of 13 patients with type III return, in which the pulmonary veins from both lungs form a confluence immediately posterior to the LA, making direct anastomosis possible. The venous trunk arising from the hilus of the left lung and passing cephalad toward the left innominate vein is then ligated and is no longer required to transport pulmonary venous return.

**Pulmonary Venous Obstruction**

While obstruction is an important factor in the onset of symptoms, it alone may not be an important factor in postoperative survival. Among the 14 surviving patients, six have signs of obstruction, and among the 11 who died, six also had signs of obstruction. The one patient with infradiaphragmatic return who had surgery after age 6 months lived.

**Hemodynamic Studies**

Comparing hemodynamics in relation to postoperative survival, we found no statistically significant differences in Ao O₂%, Rp/Bsp, Qp/Qs, or MPAP/MSAP%. Previous studies3,4 reported that the surgical mortality increases with an increase in PVR above normal and a decrease in Ao O₂% below 85%. In the cases of Gathman and Nadas,8 the older patients had lower PVR. We did find the Qp/Qs and the MPAP/MSAP% to be higher in patients who presented before age 6 months but we did not find any difference in PVR. The absence of increase of pulmonary arteriolar resistance after age 6 months may again be analogous to the atrial septal defect in which the incidence of hypertension associated with the obligatory and nonpressure related shunts is low in comparison to that associated with ventricular
or aortopulmonary communications, for in the latter incidence of small muscular pulmonary artery obstructive disease is increased.

**Right-Left Atrial Gradient**

That the foramen ovale (PFO) can be the site of obstruction has often been described.9-12 Bonham-Carter and associates12 reported that all their patients who survived beyond the first year of life had a secundum ASD. Serrato and associates11 performed atrial balloon septostomy in five infants in congestive heart failure who had no extracardiac pulmonary venous obstruction. Four showed marked clinical and hemodynamic improvement but the fifth died. The death in this group was attributed to rupture of the balloon.

In 14 cases in our study, the mean pressure was 1 to 3 mm Hg higher in the RA than in the LA. In another 18 cases, the LA was entered at catheterization, and there was no pressure gradient between the atri. Two of these patients had only a small patent foramen ovale. The absence of gradient in the presence of an obviously small atrial communication is explained by the anatomic characteristics of the RA13 which allows a large volume to develop without concomitant high pressure. The patients with a gradient generally showed earlier symptoms and had more pulmonary blood flow. In TAPVR, pulmonary venous blood as well as systemic venous blood returns to the right atrium. The preferential flow will be to the right ventricle. In TAPVR, even minute obstruction between RA and LA will potentiate this type of preferential flow. In patients with TAPVR and inadequate atrial communication, the blood will be sequestered in the lungs, right heart, and large systemic veins. As the body attempts to maintain or increase systemic flow, the pulmonary flow increases to the point of presenting signs of severe “left heart failure” with rales, grunting respirations, and over-expanded lungs. In our two most recent cases with an atrial gradient, balloon septostomy resulted in dramatic clinical and hemodynamic improvement and decreased cardiac size concomitant with the disappearance of the atrial gradient (fig. 3). Balloon septostomy was employed in five other cases during the writing of this manuscript with equally dramatic response in the clinical, radiologic, electrocardiographic and hemodynamic parameters.

The presence of only a patent foramen ovale was confirmed at surgery or autopsy or both in eight of our 10 patients with even a small right-to-left atrial gradient. The response of the seven patients undergoing septostomy mentioned above is additional evidence for significant obstruction. The presence of a localized area of pulmonary venous obstruction does not preclude additional obstruction at the atrial septum. Figure 7, also from case 34 in whom the atrial gradient is illustrated in figure 3, shows a gradient on pullback from the anomalous pulmonary vein to the RA.

Performing balloon septostomy in infants with TAPVR is especially difficult because of the small LA and this problem is compounded by the difficulty in determining the actual location of the catheter without the usual landmarks of pulmonary veins or difference in atrial oxygen saturations. Also, the pressure recording in an anomalous vein may simulate the pressure in the LA. We have found that using a double-lumen catheter and injecting a small amount of contrast medium helps identify the catheter position. Pullback across the septum must be rapid, since the inflated balloon obstructs the entire LV return, and thus the systemic output. These difficulties are far outweighed by the benefits derived from relieving obstruction. Surgical atrial septostomy by the Blalock-Hanlon technic is virtually impossible with the absence of the usual pulmonary venous landmarks, and would require inflow occlusion. Following balloon septostomy, medical treatment will be more effective.

**Planning and Suggestions**

The variety of factors involved in this syndrome make setting universal rules difficult; however, based on our cases and a review of the literature, our proposal for management of TAPVR is as follows:

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1. Immediate, thorough catheterization, not just to confirm the diagnosis, but to delineate precisely the anatomy of the anomalous vessels, to measure pulmonary blood flow and resistance, and atrial gradients, and to determine the sites of pulmonary venous obstruction.

2. Balloon septostomy for all patients and especially for patients under 3 months of age.


4. Delay of definitive surgery until the age of at least 6 months unless pulmonary edema persists in the presence of an adequate atrial septal defect and maximum medical management.

Repeat catheterization if there is clinical deterioration primarily to confirm the adequacy of the atrial communication.

References


8. GATHMAN GE, NADAS AS: Total anomalous pulmonary venous connection: Clinical and physiologic observations on 75 pediatric patients. Circulation 41: 143, 1970


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