Outcomes in Critically Ill Neonates With Pulmonary Stenosis and Intact Ventricular Septum: A Multiinstitutional Study

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Objective. This study attempted to determine the optimal therapeutic interventions by risk-adjusted comparisons of early and intermediate-term outcomes.

Background. The variety of interventions and the small case load at individual institutions have delayed the generation of reliable information concerning therapy for this condition.

Methods. In this prospective 27-institution study, 101 neonates were consecutively enrolled (between January 1, 1987 and January 1, 1991). Treatment was determined by the physicians. Demographic and morphologic details were tabulated. Dimensions of the pulmonary “anulus” and tricuspid anulus were measured on echocardiograms, and right ventricular cavity size was estimated. Right ventricular-pulmonary trunk pressure gradients were tabulated. Numerous analyses were made.

Results. Severe pulmonary valve stenosis and an intact ventricular septum were present in all patients. The right ventricular-pulmonary trunk junction (“anulus”) was severely narrowed in 15%. Right ventricular cavity size was severely reduced in 4%. The tricuspid valve was small in 15% of patients; its diameter was poorly correlated with right ventricular cavity size. Eighty-nine percent and 81% of patients survived ≥1 month and 4 years, respectively, after the initial procedure. Multivariable analysis identified no patient-specific risk factors for death. Only open pulmonary valvotomy without a support technique was uniformly a procedural risk factor; under some circumstances, transannular patching without a shunt was a risk factor. The right ventricular-pulmonary trunk gradient immediately after valvotomy was <30 mm Hg in 81% of patients and was similar after surgical and balloon valvotomy. In 74% of patients, no intervention was required after the first accomplished intervention.

Conclusions. Marked variation in morphology is uncommon in critical pulmonary stenosis in neonates. Percutaneous balloon valvotomy and certain types of surgical valvotomy are optimal initial procedures. The unusual situation of a small pulmonary “anulus” may initially require a transannular patch and a systemic-pulmonary artery shunt.

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Methods

Patients. One hundred one consecutive patients were entered into the study at 27 institutions between January 1, 1987 and January 1, 1991. Of the 101 patients, 1 (who died) underwent no procedure. 1 (who died) had only an attempted but not an accomplished balloon valvotomy and 1 (who is alive) had only ligation of a patent ductus arteriosus. Five patients were excluded from some analyses because they had an abnormally large right ventricular cavity or Ebstein’s malformation. These patients were excluded because they were believed to have major congenital cardiac anomalies coexisting with critical pulmonary stenosis.

Forty-four percent of the patients entered the study during the 1st day of life and 89% during the 1st week of life. The lowest birth weight was 1.1 kg and birth weight at the 10th, 50th and 90th percentile was 2.4, 3.3 and 3.8 kg, respectively.

Just before the first intervention, 70% of the patients were receiving prostaglandin E1, 26% were intubated and 6% were receiving a continuous infusion of dopamine.

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Morphology. The pulmonary valve was stenotic in all patients. Various degrees of leaflet thickening and immobility were described, but separation of the patients into various categories, including those with pulmonary valve dysplasia (1,2) according to leaflet structure, was not indicated by the data.

The diameter of the right ventricular–pulmonary trunk junction (pulmonary “anulus”) measured by the institutions and usually by echocardiography was available in 49 of the study patients. These dimensions and the body surface area were used to generate the Z value (so-called standard deviation [SD] units) according to the equation:

\[
Z \text{ value} = \frac{\text{Measured diameter} - \text{Mean normal diameter}}{\text{SD of the mean normal diameter}}.
\]

A nomogram for simple estimation of the Z value appears in Appendix A (Fig. A-1); using this nomogram, the Z value and body surface area can also be used to obtain the actual measured diameter. The data for the mean normal diameter (the diameter in a normal individual of the same body surface area as the patient) and the SD values were derived from the studies of Hanseus et al. (3). A Z value \(<-2\) was considered to be outside the 95th percentile of normal values.

Estimation of the dimensions of the tricuspid valve from measurement of a single diameter seemed reasonable because the tricuspid valve in neonates with pulmonary stenosis and intact ventricular septum tends to be round. The diameter and body surface area were used to generate the Z value of the diameter and that of the pulmonary “anulus” (Appendix A, Fig. A-1). Previous anatomic studies (4,5) were used as the source of the mean normal diameters and the standard deviations.

The right ventricular cavity size was estimated for each patient in whom it was possible. The estimate was based on information obtained by echocardiography or angiography, or both, and at operation. Cavity size was graded as follows: 0 = normal (for age), \(-5\) = extreme hypoplasia and \(-1\) to \(-4\) = intermediate degrees of hypoplasia. A similar grading system was used for cavity enlargement.

Management. Physicians at each participating institution followed their own preferred treatment protocols without limitations imposed by the study. Among the 101 patients, 34 had percutaneous balloon pulmonary valvotomy as their initial completed procedure (60 patients underwent cardiac catheterization with the intent of undergoing percutaneous balloon valvotomy; however, in 26, a guide wire could not be advanced across the pulmonary valve and balloon valvotomy could not be attempted). Surgical valvotomy without cardiopulmonary bypass was performed in 25 patients as the initial procedure: a closed operation in 15, an open valvotomy with inflow stasis in 4 and an open valvotomy without support (no inflow stasis or cardiopulmonary bypass) in 6. In 17 patients, valvotomy with cardiopulmonary bypass, in 18 a transannular patch and in 2 an isolated systemic-pulmonary artery shunt was the initial procedure. Some patients had other procedures performed concurrently. Three patients had no completed procedure directed toward relief of pulmonary stenosis.

Among 98 patients undergoing an initial intervention relevant to critical pulmonary stenosis, one or more subsequent interventions were performed in 25, two or more in 9, three or more in 2 and four in 1 patient.

Definition of definitive repair. Patients were considered to have a definitive, completed two-ventricle repair when each ventricle ejected into its respective great artery and no intracardiac shunting remained. A patient was considered to have a definitive, completed one-ventricle repair when a complete Fontan operation had been performed without residual shunting.

Follow-up. On or about March 1 of each year since the beginning of the study, the family or guardian of each patient not known to be dead was contacted and detailed information was obtained. The most recent follow-up evaluation was accomplished during the 1st 3 months of 1991. During the 1991 follow-up evaluation, only one patient not known to be dead could not be traced; that patient was last contacted in the 1988 follow-up effort. The median time of follow-up in surviving patients is 16.8 months (range 1.5 to 47.9); the mean follow-up time is 19.7 ± 12.74 months.

Data collection and analyses. Copies of all hospital documents were sent to the Data and Analysis Center at the University of Alabama at Birmingham. The data were abstracted into computer files and these data and the copies of the hospital documents were retained in confidential storage.

Numerous tabular and life-table analyses (6) were made. Time-related freedom from each outcome event and the hazard function were computed parametrically (7). The hazard function for death was the time-related instantaneous risk (or rate) of death; although related to percent survival, it more directly represented the changing risk of death occurring at specific times after an intervention. Numerous multivariate risk factor analyses were made in the hazard function regression domain (7), but other regression models were used when indicated.

Variables entered into the analyses are given in Appendix B (Table B-1). Variables with a p value ≤ 0.1 were retained in the final equations to avoid overlooking possible explanatory variables (incremental risk factors) in a study whose statistical power was limited by the small size of the sample. The time-related strength of the variables in the final equations was determined by examining nomograms of specific solutions of the multivariate equations. Internal validations of the parametric estimates were made and are available on request; an example is presented in Appendix B (Fig. B-1).
Results

Morphology. An important degree of hypoplasia of the right and left pulmonary arteries was present in only 4% of patients (Table 1). The median Z value of the right ventricular–pulmonary trunk junction (pulmonary "anulus") was -1.6 and the Z value was < -2 (below the 95th percentile in normal neonates) in about 40% of the patients in whom this dimension was available (Fig. 1). The right ventricular cavity size was normal in 44% of patients, mildly or moderately reduced in 49% and severely reduced in about 4% (Table 1). The median Z value for the tricuspid valve was -1.0 and the Z value was < -2 in only about 15% of patients (Fig. 2). The dimensions of the tricuspid valve were poorly correlated with the right ventricular cavity size (r = 0.14, p = 0.04), as well as with the diameter (Z value) of the pulmonary "anulus" (29 paired values [r = -0.28, p = 0.14]). Tricuspid valve incompetence was common and usually of moderate or severe degree and not well correlated with right ventricular pressure (r = -0.1, p = 0.4).

Two patients had a right ventricle to coronary artery fistula, but neither had right ventricular dependency of the coronary circulation. One patient had Wolff-Parkinson-White syndrome and one had a partial anomalous pulmonary venous connection. No patient had an important noncardiac anomaly.

Survival. Three patients had no completed procedure directed toward relief of pulmonary stenosis. Two of the three died during the initial hospital period and the third is alive but the condition is considered uncorrectable.

The survival rate after the initial procedure was 89%, 84%, 83% and 81% at 1, 12, 24 and 48 months, respectively. The time-related hazard function for death had a single rapidly declining phase (Fig. 3). The prevalence of deaths after the various interventions was highly variable (Appendix B, Table B-2).

Multivariate analysis revealed no generally applicable patient-specific risk factors for death at any time after the initial procedure (Table 7). Open pulmonary valvotomy without inflow stasis or cardiopulmonary bypass was the only procedure found to be a risk factor for death; the predicted risk-adjusted survival rate in patients treated initially by this procedure was 20% (Fig. 4). Predicted risk-adjusted survival was 94% in patients undergoing pulmonary valvotomy by percutaneous balloon techniques, open surgical valvotomy using either inflow stasis or cardiopulmonary bypass or closed surgical valvotomy (Fig. 4). In patients whose initial procedure was placement of a transannular patch without a shunt, increased tricuspid incompetence and smaller size of the right ventricular–pulmonary trunk junction (and date of operation) were identified as interaction

Table 1. Size of the Right Ventricular Cavity and Hypoplasia of the Left and Right Pulmonary Arteries in Neonates With Critical Pulmonary Stenosis

<table>
<thead>
<tr>
<th>RV Cavity Size*</th>
<th>No.</th>
<th>% of Total</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
</table>
| Enlarged (grades 1 through 5) | 3 | 4% | 0 | 0%
| Normal (grade 0 reduction) | 37 | 44 | 1 | 3%
| Mildly reduced (grade 1, 2) | 30 | 49 | 0 | 0%
| Moderately reduced (grade 3) | 11 | 1 | 9
| Severely reduced (grade 4, 5) | 5 | 4 | 1 | 33%
| Subtotal | 84 | 3 | 4
| Unknown | 17 | -- | -- |
| Total | 101 | -- | -- |

*Estimated by informal integration of information obtained by echocardiography, angiography and surgery. Excluding the total group of 101 neonates, the 17 with unknown cavity size. No patient had discrete stenosis or unilateral hypoplasia of the pulmonary arteries. The size of the pulmonary arteries was expressed as 0 (no hypoplasia) or hypoplastic grades 1 through 5 by informal integration of the information available. LPA = left pulmonary artery; RPA = right pulmonary artery; RV = right ventricular.
Figure 3. Survival (top panel) and hazard function (bottom panel) for death after the first accomplished procedure. Each circle represents an individual death, positioned along the horizontal axis at the time of death and actuarially (Kaplan-Meier) along the vertical axis. The vertical bars are the 70% confidence intervals of the actuarial estimates. The numbers in parentheses are the number of patients available for follow-up after that actuarial estimate. (By 24, 36 and 48 months after the initial procedure, 29 patients, 14 patients and 1 patient, respectively, were still being followed up.) The solid line is the continuous point estimate of survival (or hazard function in [b]) obtained by a separate hazard function regression analysis. The dashed line encloses the 70% confidence intervals.

Table 2. Incremental Risk Factors for Death at Any Time After the Initial Accomplished Procedure

<table>
<thead>
<tr>
<th>Procedural</th>
<th>Single Hazard</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Open pulmonary valvotomy without inflow stasis or CPB</td>
<td>&lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>Transannular patching without a shunt†</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>(smaller) dimension of the RV-PT junction</td>
<td>0.0002</td>
<td></td>
</tr>
<tr>
<td>(greater) degree of tricuspid incompetence</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>(earlier) date of procedure</td>
<td>0.04</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Incremental Risk Factors for Death at Any Time After the Initial Accomplished Procedure

The strength of the risk factors is shown in Figure 4. The shaping parameters and coefficients are in Appendix C, Table C-1. The variables under this subheading are interaction terms. CPB = cardiopulmonary bypass; RV-PT = right ventricular-pulmonary trunk.

in residual gradients between patients undergoing percutaneous balloon or surgical valvotomy. The immediate reduction in right ventricular peak pressure after valvotomy was ≥35 mm Hg in 71% of the 35 patients in whom these data were available (30 of whom had a balloon procedure). There was no significant difference in this regard (p = 0.8) between balloon and surgical valvotomy.

Reintervention after the initial procedure. Twenty-five patients (26% of those undergoing an initially accomplished procedure) had one or more subsequent procedures for 1) relief of right ventricular outflow obstruction (Fig. 6), or 2) establishment of a systemic-pulmonary artery shunt (Fig. 7). The instantaneous risk (hazard function) of undergoing a shunt operation as the follow-up intervention (the rate of performing the follow-up intervention at any time after the initial procedure) was highest 1 week after the initial inter-
Table 3. Prevalence of Initial Attempted but Failed Percutaneous Balloon Pulmonary Valvotomy, According to the Year in Which the Patient Entered the Study and the Experience ("high volume" vs. "low volume") of the Institution

<table>
<thead>
<tr>
<th>Year</th>
<th>&quot;High Volume&quot; Institution</th>
<th>&quot;Low Volume&quot; Institution</th>
<th>Total</th>
<th>Failed</th>
<th>p Value (chi-square)</th>
<th>Failed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>CL</td>
<td>p value</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>1987</td>
<td>4</td>
<td>25</td>
<td>3%–63%</td>
<td>0.2</td>
<td>9</td>
<td>67</td>
</tr>
<tr>
<td>1988</td>
<td>5</td>
<td>30</td>
<td>29%–86%</td>
<td>0.0004</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>1989</td>
<td>7</td>
<td>22</td>
<td>0%–74%</td>
<td>0.4</td>
<td>3</td>
<td>44</td>
</tr>
<tr>
<td>1990</td>
<td>7</td>
<td>11</td>
<td>2%–41%</td>
<td>27</td>
<td>26</td>
<td>11%–22%</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>92</td>
<td>12%–34%</td>
<td>0.02</td>
<td>29</td>
<td>43</td>
</tr>
</tbody>
</table>

* A "high volume" institution (n = 3) was defined as one in which four or more initial percutaneous balloon pulmonary valvotomy procedures were attempted between January 1, 1987 and January 1, 1991; a "low volume" institution (n = 21) was one in which one to three such procedures were attempted in that time period. No percutaneous balloon pulmonary valvotomy procedures were performed in three institutions whose patients are included in the study. ❧Total No. indicates the total number of attempted procedures in the group of institutions. ❧Failed refers to the number of attempted procedures in which a catheter, with or without a guide wire, could not be passed across the pulmonary valve. CL = 70% confidence limits.

vention, whereas in the case of a procedure for relief of right ventricular outflow obstruction, it was highest 6 months after the initial intervention (Fig. 6 and 7). The only incremental risk factor for reintervention for residual right ventricular outflow tract obstruction found by multivariate analysis was the initial severity of the obstruction as reflected by the ratio between the right ventricular and left ventricular peak pressures before repair (p = 0.002). The risk factors for reintervention by a systemic-pulmonary shunt included small size of the right ventricular cavity (p < 0.0001) and the use of closed surgical valvotomy (p = 0.06).

Definitive repairs. By 48 months after entry, 85% of living patients had a completed two-ventricle repair. The prediction from the multivariate equation (Appendix C, Table C-2) was that by 6 years after entry, nearly all patients would have received a definitive two-ventricle repair.

Only two patients have undergone a definitive one.

Figure 4. Percent freedom from reintervention for relief of right ventricular outflow tract obstruction (RVOTO) after an initial valvotomy by any method (73 patients). The reintervention was by percutaneous balloon dilation in seven, transannular patching in five and surgical valvotomy and pulmonary arterial and right ventricular patching in one. Patients with Eisenmenger’s malformation or enlarged right ventricular cavity size, or both, are excluded. Top, Time-related freedom from the reintervention. Bottom, Time-related hazard function for reintervention. The instantaneous risk of this type of reoperation is highest about 6 months after the initial procedure.

Figure 5. Peak pressure gradient between the right ventricle (RV) and pulmonary artery trunk (PA) immediately after pulmonary valvotomy by any method in the 31 patients in whom this information was available.

Figure 6. Percent free of reintervention for relief of right ventricular outflow tract obstruction (RVOTO) for patients with pulmonary valve stenosis. The reintervention is by percutaneous balloon dilation in seven, transannular patching in five and surgical valvotomy and pulmonary arterial and right ventricular patching in one. Patients with Eisenmenger’s malformation or enlarged right ventricular cavity size, or both, are excluded. Top, Time-related freedom from the reintervention. Bottom, Time-related hazard function for reintervention. The instantaneous risk of this type of reoperation is highest about 6 months after the initial procedure.
ventricle (Fontan) repair: one (who died) at 18 months after
eentry and one 29 months after entry. One of these had had a
systemic-pulmonary artery shunt as initial therapy and the
other had complete right ventricular outflow tract obstruc-
tion at cardiac catheterization at 11 months of age despite
initial open pulmonary valvotomy without inflow stasis or
use of cardiopulmonary bypass.

Discussion

Critique of the study. The 101 neonates in this study
represent a considerably larger group than has been studied
previously. Age at entry into the study and specificity of the
lesion were also more homogeneous than in previous stud-
ies.

The multivariate hazard function regression analysis
technique is particularly useful when the hazard function is
changing across the period of observation as in this study (7).
In >3,000 previous validation exercises, internal validation
of the method has been achieved and prospective validation
has been obtained in several studies (8–10). Internal valida-
tion (Appendix B, Fig. B-1 [additional validations are avail-
able on request]) in the present study also supports the
validity of the method. The classical test of the therapeutic
dilemmas investigated by this study is a multicenter prospective
randomized trial of balloon valvotomy and the most
effective surgical valvotomy techniques. This trial is unlikely
to be performed, however, for many, probably appropriate,
reasons. A valid useful method of risk adjustment by multi-
variate analyses is particularly important in situations
such as this. The remaining problems can probably be
resolved when, in the continuation of this study, the sample
size reaches >400 and the minimal follow-up period is 5
years.

Characteristics of pulmonary stenosis with intact ventricu-
lar septum in neonates (critical pulmonary stenosis). The
absence of any patient-specific risk factors as explanatory
variables for death at any time after intervention—an unus-
usual finding in congenital heart disease—supports the con-
cept that critical pulmonary stenosis is a relatively simple
and homogenous congenital cardiac anomaly. This concept
is supported by the infrequent coexistence of other import-
ant cardiac or noncardiac anomalies in these patients.

Comparison of the results of the current study with those
of a similar study (11) of pulmonary atresia with intact
ventricular septum provides little support for the hypothesis
that critical pulmonary stenosis and pulmonary atresia with
intact ventricular septum are part of the same spectrum.
Instead, they appear to be different entities or at least at
opposite extremes if in the same spectrum. Coexisting
cardiac or noncardiac anomalies rarely occur in patients with
critical pulmonary stenosis but are frequent in those with
pulmonary atresia. Thus, extreme hypoplasia of the tricus-
pid valve is rare (<10%) in patients with critical pulmonary
stenosis but is common in those with pulmonary atresia.
Similarly coronary artery–right ventricular fistulas and se-
vere reduction of right ventricular cavity size are rare in
critical pulmonary stenosis but are common in pulmonary
atresia. In all probability, the most important patient-specific
risk factor for death in patients with pulmonary atresia and
intact ventricular septum—the dimension of the tricuspid
valve—is not a risk factor in those with critical pulmonary
stenosis.

Furthermore, the dimensions of the tricuspid valve and
right ventricular cavity size are poorly correlated in critical
pulmonary stenosis and positively correlated in pulmonary
atresia, suggesting that the reduction in right ventricular
cavity size has different origins in the two conditions.
Speculatively, in patients with critical pulmonary stenosis,
the smallness of the right ventricular cavity results from
hypertrophy of the right ventricular free wall and septum
and, thus, from the severity of the pulmonary stenosis.
Further insight into these associations may be gained as the natural history of these lesions before birth is characterized with fetal echocardiography.

**Optimal therapy.** There is no consensus regarding the most appropriate management protocols for the neonate with critical pulmonary stenosis and intact ventricular septum. As a result, individual institutions have generally approached this lesion according to their own biases, utilizing management protocols based on methods with which they have expertise.

The risk-adjusted information in this study indicates that reduction in valvular gradient and survival are at least as good after percutaneous balloon valvotomy (12–15) as after the best surgical techniques. The theoretic long-term advantages of precision in opening the commissures during pulmonary valvotomy are not supported by this study (the longest follow-up period is 48 months). These data point to percutaneous balloon valvotomy as the current method of choice for critical pulmonary stenosis in neonates (and probably in older patients as well). When expertise with this method is not available at an institution that is experienced in neonatal and infant cardiac surgery, surgical valvotomy, preferably using an open procedure with cardiopulmonary bypass, is indicated.

Initial transannular patching is an unnecessarily aggressive procedure in most patients, as evidenced by the experience with both surgical and percutaneous balloon valvotomy. However, transannular patching may be necessary as an initial or subsequent procedure if the right ventricular–pulmonary trunk junction (="anulus") is very small (a Z value <3). In this uncommon situation, the use of a transannular patch alone is associated with considerable risk (Fig. 4) and a systemic–pulmonary artery shunt should be added. A transannular patch alone seems to present a risk of severe hypoxia postoperatively, speculatively as a result of acute right ventricular failure and resultant shunting from right to left across a patent foramen ovale (which generally should be left open).

Whatever the initial procedure, patients require continual close observation because subsequent interventions are commonly indicated (=25% of patients). Persisting important hypoxia indicates a need for a systemic–pulmonary artery shunt, after which the prognosis is excellent; the shunt should be closed at =1 year, after testing for the adequacy of arterial oxygen levels during temporary closure in the catheterization laboratory. When a persistently high gradient (>50 to 75 mm Hg) between the right ventricle and pulmonary trunk is found during follow-up and valvotomy does not appear to be as complete as possible, repeat valvotomy is indicated, preferably by the percutaneous approach. When a large gradient is present despite an apparently adequate valvotomy, transannular patching is indicated.

Virtually all patients should have a completed two-ventricle repair by the age of 4 to 5 years; a one-ventricle Fontan type of repair is rarely indicated. Again, this obser-
Appendix B

Interventions and Outcomes

Figure B-1. Internal validation of the multivariable risk factor equation for death. The Kaplan-Meier life-table estimate for percent survival after the initial intervention (time zero) in patients who had not had a previous unsuccessful balloon valvotomy is shown by the open circles and for patients who had this before the initial accomplished intervention by the open squares; the vertical bars represent the standard error. (Note that this was not a variable retained in the multivariable equation, Table 2). The solid lines are the predicted percent survival for each group, determined by averaging the time-related patient-specific survival of each patient in the group, predicted from the multivariate equation (Table 2). The 70% confidence intervals around the prediction are indicated by the dashed lines. In both groups, the correspondence is close between the Kaplan-Meier estimates and the predictions from the multivariate equation. Also, the actual and predicted (from the multivariate equation) deaths (n = 16) are shown in the table on the figure, and the p values indicate that the differences are likely to be due to chance alone.

Table B-1. Potential Explanatory Variables (risk factors) Entered Into the Multivariate Analyses

<table>
<thead>
<tr>
<th>1. Patient variables</th>
<th>Total Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic variables</td>
<td></td>
</tr>
<tr>
<td>Age at entry: age at initial procedure; gender; race; birth weight; admission weight; admission body surface area</td>
<td></td>
</tr>
<tr>
<td>Morphologic variables</td>
<td></td>
</tr>
<tr>
<td>Atrial septal defect versus patent foramen ovale: right ventricular cavity size (grade -5 to 0); presence of right ventricular sinusoids; presence of coronary artery-right ventricular fistulas; diometer (Z value) of right ventricle-pulmonary trunk junction (pulmonary &quot;anulus&quot;); diameter (Z value) of tricuspid valve anulus; tricuspid valve incompetence (grades 0 to 5)</td>
<td></td>
</tr>
<tr>
<td>Clinical variables</td>
<td></td>
</tr>
<tr>
<td>Balloon septostomy performed; peak systolic and diastolic pressures in right and left ventricles; ratio of right to left ventricular systolic pressure</td>
<td></td>
</tr>
<tr>
<td>2. Support variables</td>
<td></td>
</tr>
<tr>
<td>Including initial procedure performed using cardiopulmonary bypass</td>
<td></td>
</tr>
<tr>
<td>3. Procedural variables</td>
<td></td>
</tr>
<tr>
<td>Including no procedure; attempted percutaneous balloon valvotomy; achieved percutaneous balloon valvotomy; surgical valvotomy with or without a concomitant systemic-pulmonary artery shunt described as closed transventricular valvotomy, open valvotomy without inflow stasis and without cardiopulmonary bypass, open valvotomy with inflow stasis, open valvotomy with cardiopulmonary bypass; &quot;blunt&quot; valvotomy (balloon or surgical by any technique other than cardiopulmonary bypass) vs. &quot;sharp&quot; valvotomy on cardiopulmonary bypass; transannular patch (entered as [1] with or [2] without a concomitant systemic-pulmonary artery shunt); systemic-pulmonary artery shunt</td>
<td></td>
</tr>
<tr>
<td>4. Institutional variables</td>
<td></td>
</tr>
<tr>
<td>Including date of initial procedure, balloon valvotomy performed at a low volume or high volume institution for this procedure</td>
<td></td>
</tr>
</tbody>
</table>

Table B-2. Initial Interventions and Total Deaths in Neonates With Critical Pulmonary Stenosis

<table>
<thead>
<tr>
<th>Initial Interventions</th>
<th>Total Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type</td>
<td>No.</td>
</tr>
<tr>
<td>Percutaneous balloon valvotomy</td>
<td>34</td>
</tr>
<tr>
<td>Isolated</td>
<td>33</td>
</tr>
<tr>
<td>Balloon atrial septostomy</td>
<td>1</td>
</tr>
<tr>
<td>Surgical valvotomy (closed)</td>
<td>15</td>
</tr>
<tr>
<td>Isolated</td>
<td>11</td>
</tr>
<tr>
<td>and fixation of patent ductus arteriosus</td>
<td>1</td>
</tr>
<tr>
<td>and S-P shunt</td>
<td>3</td>
</tr>
<tr>
<td>Surgical valvotomy (open without inflow stasis or CPB)</td>
<td>6</td>
</tr>
<tr>
<td>Isolated</td>
<td>2</td>
</tr>
<tr>
<td>S-P shunt</td>
<td>4</td>
</tr>
<tr>
<td>Surgical valvotomy (open with inflow stasis)</td>
<td>4</td>
</tr>
<tr>
<td>Surgical valvotomy with CPB</td>
<td>17</td>
</tr>
<tr>
<td>Isolated</td>
<td>7</td>
</tr>
<tr>
<td>and patching</td>
<td>3</td>
</tr>
<tr>
<td>and atrial septal defect closure</td>
<td>4</td>
</tr>
<tr>
<td>and S-P shunt</td>
<td>36</td>
</tr>
<tr>
<td>Surgical valvotomy without CPB (details unknown)</td>
<td>2</td>
</tr>
<tr>
<td>Transannular patch</td>
<td>18</td>
</tr>
<tr>
<td>Isolated</td>
<td>8</td>
</tr>
<tr>
<td>and fixation and banding patent ductus arteriosus</td>
<td>1</td>
</tr>
<tr>
<td>and resection of right ventricular muscle</td>
<td>24</td>
</tr>
<tr>
<td>and S-P shunt</td>
<td>74</td>
</tr>
<tr>
<td>Isolated S-P shunt</td>
<td>2</td>
</tr>
<tr>
<td>No relevant procedure</td>
<td>3</td>
</tr>
<tr>
<td>None</td>
<td>1</td>
</tr>
<tr>
<td>Attempted percutaneous balloon valvotomy</td>
<td>1</td>
</tr>
<tr>
<td>Ligation of patent ductus arteriosus</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>101</td>
</tr>
</tbody>
</table>

*All procedures listed together were performed at the same time. 1Death at any time after the procedure. 2Patching of pulmonary trunk (two patients) or rightventricle (one patient) but not transannular. 3One, who lived, also had patching of pulmonary trunk. 4One, who lived, also had closure of a patent foramen ovale. 5Two, who lived, also had resection of right ventricular muscle. CPB = cardiopulmonary bypass; S-P = systemic-pulmonary artery.
Factors for Failure to Achieve Balloon Valvotomy --

(smaller) diameter (Z-value) of RV-PT junction

Procedural (earlier) date of procedure (years since 1/1/87)

Institution

Low volume institutions

Intercept

-0.8431 ± 0.36

- 1.514 ± 0.47

3.348 ± 1.10

-1.438

Nomograms of the multivariate equation showed that even very small size of the right ventricular (RV)-pulmonary trunk (PT) junction (Z value < -4) increased the risk only mildly in high volume institutions.

Appendix C

Mathematical Data

Table C-1. Details of the Multivariate Equation for Death at any Time After the Initial Accomplished Procedure (Table 2)

The shaping parametric estimates for the single phase of hazard

δ = 0, p = 1.793, ν = 1, m = 1, intercept = -2.555

Coefficients and their standard deviations and p values of the incremental risk factors

open pulmonary valvotomy without inflow stasis or cardiopulmonary bypass = 3.355 ± 0.65 (p < 0.0001)

dimension (Z value) of right ventricular-pulmonary trunk junction (signed-squared transformation) only in patients undergoing transannular patching without a concomitant systemic-pulmonary artery shunt = 0.1491 ± 0.061 (p = 0.01)

tricuspid incompetence, only in patients undergoing transannular patching without a concomitant systemic-pulmonary artery shunt = 1.324 ± 0.35 (p = 0.0002)

date of operation (years since January 1, 1987), only in patients undergoing transannular patching without a concomitant systemic-pulmonary artery shunt = -1.462 ± 0.72 (p = 0.04)

Table C-2. Details of the Multivariate Equation for the Time-Related Probability of a Two-Ventricle Repair

The shaping parametric estimates of the two phases of hazard

Early hazard phase: δ = 0, p = 0.107, ν = 0, m = -0.6432, intercept = -2.273

Constant hazard phase: intercept = -2.934. The coefficients and the standard deviations and p values for incremental risk factors

Early hazard phase: (larger) birth weight (logarithmic transformation)

2.200 ± 0.87 (p = 0.01), (larger) right ventricular cavity size (signed-squared transform of grade) 0.1964 ± 0.69 (p = 0.005)

Constant hazard phase: (larger) right ventricular cavity size (signed-squared transform of grade) 0.2147 ± 0.12 (p = 0.07)

Appendix D

Institutions Participating in the Study

This study was one of various multicenter studies carried out by the Congenital Heart Surgeons Society. The following institutions participated:

University of Michigan, Ann Arbor, Michigan; University of Alabama at Birmingham, Birmingham, Alabama; Boston Children’s Hospital, Boston, Massachusetts; Clinica Bavaria Centro Cuírrugico Cardiovascular, Buenos Aires, Argentina; Children’s Hospital, SUNY, Buffalo, New York; Medical University of South Carolina, Charleston. South Carolina; Children’s Memorial Hospital and University of Chicago/Michael Reese Hospital, Chicago, Illinois; Children’s Hospital Medical Center, Cincinnati, Ohio; Children’s Hospital of Michigan, Detroit, Michigan; Penn State University, Hershey, Pennsylvania; Indiana University Medical Center, Indianapolis, Indiana; University of Iowa, Iowa City, Iowa; Loma Linda University, Loma Linda, California; Children’s Hospital of Los Angeles and University of California, Los Angeles, Los Angeles, California; Miami Children’s Hospital and University of Miami, Miami, Florida; Montreal Children’s Hospital, Montreal, Quebec, Canada; Babies Hospital and Columbia-Presbyterian, New York, New York; University of Nebraska Medical Center, Omaha, Nebraska; Children’s Hospital of Philadelphia and Saint Christopher’s Hospital for Children, Philadelphia, Pennsylvania; Children’s Hospital of Pittsburgh, Pittsburgh, Pennsylvania; The Oregon Health Sciences University Hospital, Portland, Oregon; Saint Louis University Medical Center, Saint Louis, Missouri; All Children’s Hospital, Saint Petersburg, Florida; Heart Institute, Sao Paulo, Brazil; Primary Children’s Hospital, Salt Lake City, Utah; University of California, San Diego, San Diego, California; University of California, San Francisco, California; Hospital for Sick Children, Toronto, Ontario, Canada; British Columbia Children’s Hospital, Vancouver, British Columbia, Canada.

References


