Predictors of Survival in Neonates With Critical Aortic Stenosis

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Background. Failure of infants with critical aortic stenosis to survive after adequate valvotomy despite a left ventricular size that appears to be adequate indicates that additional preoperative anatomic features may contribute to mortality.

Methods and Results. Discriminant analysis was used to determine which of several echocardiographically measured left heart structures were independent predictors of survival after valvotomy for neonatal critical aortic stenosis. It was possible to predict outcome after classic valvotomy (two-ventricle-type repair) with 95% accuracy based on mitral valve area, long-axis dimension of the left ventricle relative to the long-axis dimension of the heart, diameter of the aortic root, and body surface area. Left ventricular volume was not a major determinant in this study, in part because patients who had initial valvotomy had been preselected in favor of an adequately sized left ventricle. Patients with multiple small left ventricular structures were found to have significantly improved survival after initial Norwood operation. In contrast, balloon valvotomy with subsequent Norwood procedure was usually unsuccessful.

Conclusions. The adverse effects of small inflow, outflow, and/or cavity size of the left ventricle are cumulative. The accuracy of prediction of outcome based only on preoperative anatomy indicates that adequacy of valvotomy is not generally a limiting factor for survival in this group of patients. It is possible to identify subjects whose chance of survival is better after a Norwood procedure rather than valvotomy, even if left ventricular volume is not critically small. (Circulation 1991;84:2325–2335)

Recent advances in the palliation of infants with critical aortic stenosis, with or without left ventricular hypoplasia, have improved the outlook for these patients. The alternatives to valvotomy resulting in a two-ventricle repair include cardiac transplantation or a Norwood procedure,1 a two-stage single-ventricle repair in which the main pulmonary artery is anastomosed to the aorta with creation of a systemic-to-pulmonary shunt, followed later by construction of an atropulmonary connection (Fontan-type operation). The latter option results in the right ventricle supporting the systemic circulation, absence of a pulmonary ventricle, and the functional sacrifice of the left ventricle. Generally, the decision as to which approach to take must be made within the first hours or days of life. Investigators have attempted to define the lower limits of left ventricular size that can successfully support a classic valvotomy (two-ventricle repair), and most clinical decisions are currently based on left ventricular size alone. It is likely that the size of other left heart structures such as the mitral or aortic valve and the aortic arch are important in determining survival in these subjects as well. Therefore, we examined a number of additional parameters of left heart size and function in patients with critical aortic stenosis in an attempt to define other potential determinants of morbidity and mortality after attempted two-ventricle repair.

Methods

Patient Selection

Study inclusion criteria consisted of 1) an echocardiographic diagnosis of aortic stenosis made at The Children's Hospital, Boston, within the first 2 months of life in subjects with left ventricular dysfunction on echocardiography and the clinical syndrome of congestive heart failure; 2) normally related great arteries; 3) patency of the aortic and mitral valves; and 4) absence of subvalvular or supravalvular aortic stenosis or ventricular septal defect. Case finding was accomplished by review of the computerized cardiology data base.
Data Collection and Analysis

The medical record of each patient was reviewed retrospectively. The catheterization reports were reviewed to determine the age at time of the procedure, left ventricular end-diastolic pressure, peak systolic ejection gradient across the aortic valve, presence and significance of mitral regurgitation, and left ventricular volume (if measured). The surgical reports were reviewed for intraoperative findings and the surgical procedures performed.

The two-dimensional echocardiograms for each patient were reviewed, and selected images were digitized using a microcomputer-based video image capture and analysis work station (Dextra Medical Systems, Inc.). Measurements were performed on the digitized images with the use of an electronic caliper system. Aortic annulus size was measured from parasternal long-axis images. Aortic root dimension was taken as the maximum dimension at the level of the sinuses of Valsalva, obtained from the parasternal long-axis view (Figure 1). The internal dimensions of the transverse arch between the innominate and left carotid and of the aortic isthmus just distal to the left subclavian were taken from suprasternal images. The antero-posterior and lateral early diastolic dimensions of the mitral and tricuspid annuli were taken from long-axis parasternal and apical four-chamber images, respectively. The mitral and tricuspid valve areas were calculated directly from the orthogonal diameters (D1 and D2) by using the formula for an ellipse (area = π[(D1×D2)/2]). The relative mitral valve area was then calculated as the ratio of the two atrioventricular valve areas. Left ventricular end-diastolic and end-systolic epicardial and endocardial borders were hand digitized from subxyphoid long- and short-axis views, and the volume, mass, and ejection fraction were calculated using the biplane bullet model. In this model, the short-axis area enclosed by the endocardium at midventricular level is measured by planimetry, and the long-axis length of the left ventricle (LV) is measured as the distance from the plane of the mitral valve annulus to the apex of the ventricle. Left ventricular volume is then calculated as % multiplied by short-axis area multiplied by long-axis length. Mass was obtained as the difference between epicardial and endocardial volume multiplied by the specific gravity of myocardium (1.04 g/ml). The long axis of the heart was measured from the apical four-chamber view as the distance from the crux of the heart to the apical endocardium (either right or left ventricle, whichever formed the apex of the heart). The relative LV length was calculated as the ratio of the LV long-axis length to the long-axis length of the heart. The aortic annulus, root, arch, and isthmus, the LV long-axis dimension, end-diastolic and end-systolic dimensions, and mass, and the mitral valve area were divided by body surface area (BSA) to adjust for differences in body size. This method of normalization erroneously assumes a linear relation between BSA and each of the variables. However, the deviation of each of the relations from linear is insignificant over the narrow range of BSA values encountered in this patient population, allowing this simplified method of normalization to be used without the introduction of significant error.

Statistical Analysis

The relation between survival after initial two-ventricle repair (aortic valvotomy and/or coarctation repair) to age at presentation, BSA, and each of the echocardiographic measurements was examined by univariate analysis of variance. To evaluate the potential confounding effect of including the subjects who did not have an intervention within the first month of life, we performed the univariate analysis first including all subjects and then excluding patients over 33 days of age at the time of the first intervention. We selected this time period because there was

FIGURE 1. Image of the mode of measurement of aortic root dimension (Ao Root) from long-axis parasternal views. RV, right ventricle; LV, left ventricle.
a natural breaking point in the data (no subjects with
time of first intervention between 33 and 45 days).
Similarly, the presence of an aortic coarctation could
also confound the analysis by including subjects with
less severe aortic stenosis. We evaluated this possi-
bility by performing the univariate analysis with and
without the patients who had repair of coarctation.

The univariate analysis identifies variables that
differ significantly between survivors and nonsur-
vivors but does not allow prediction of outcome for
new cases. In addition, it is possible that the presence
of multiple left-heart structures that are small may
independently contribute to mortality. To this end,
multivariate analysis was performed using a two-
group linear discriminant analysis with stepwise vari-
able selection (SPSS, SPSS Inc.). The unstandard-
ized discriminant function was determined for
optimal group classification with respect to survival,
first including all subjects and then limiting analysis
to those patients who underwent an intervention at
33 days of age or less. Standardized discriminant
function coefficients and the correlations between
the discriminant function and the values of the
discriminating variables were used to rank the rela-
tive importance of the variables to the discriminant
function.

Discriminant analysis weighs the variables in a
linear fashion. From a physiological point of view, it
is more likely that these anatomic variables contrib-
ute to survival in a nonlinear, sigmoid-shaped fash-
ion. That is, once a structure such as the mitral valve
is above a certain size, it completely ceases to be a
contributing factor to outcome, and conversely, if the
size is below a certain limit, it will be an absolute
determinant of survival. This can be most simply
modeled as a threshold phenomenon. Based on the
rank order of importance of the anatomic variables as
determined in the discriminant analysis, the four
structures found to be most closely related to survival
were used to devise a simplified risk scoring system.
This scoring system was optimized to predict failures
of two-ventricle repair, based on the assumption that
it is preferable to perform an aortic valvotomy if
there is any chance of survival because the surgical
alternatives are either cardiac transplantation or
single-ventricle repair. The scoring system was there-
fore optimized to identify only those subjects who
would not survive after a two-ventricle repair (that is,
there were no patients who were predicted not to
survive but in fact did survive after a two-ventricle
repair). For each anatomic variable, subjects were
assigned one point if the size of that structure was
below a defined threshold value. Each variable was
weighted equally and the total risk score for each
individual was determined as the simple sum of the
assigned points. The threshold values that gave opti-
mum separation of survivors from nonsurvivors were
then determined by a computerized iterative search
procedure that systematically examined all possible
values for all variables to determine which threshold
values predicted the maximum number of deaths.

Using these criteria, all subjects were stratified for
the total number of structures below the threshold
size for that structure, and survival was compared
according to the type of initial procedure (single or
bi-ventricular repair) by using a Fisher’s exact test.

Results
A total of 65 patients were identified, 46 males and
19 females (Table 1). The patients were grouped
according to the initial procedure performed (Figure
2). In three patients (cases 1 through 3, Table 1),
death occurred before any intervention could be
undertaken. They are not included in the analysis.
Sixteen patients were considered to be poor candi-
dates for two-ventricle repair; therefore, a Norwood
procedure was performed. This decision was made by
the responsible clinicians and was not based on
predefined anatomic criteria. In 14 of 16 patients, the
echocardiogram was adequate for quantitative analy-
sis of morphological variables, and these patients
(cases 6 through 19, Table 1) comprise the single-
ventricle repair group.

The left ventricular cavity size had been consid-
ered potentially capable of supporting the systemic
circulation in the other 46 patients. The initial pro-
cedure in these patients consisted of either no inter-
vention (n=1), balloon dilation of the aortic valve
(n=36), surgical aortic valvotomy (n=4), or repair of
aortic coarctation (n=5). Nineteen of these patients
had a second intervention. Of the 36 patients who
had balloon dilation as the primary procedure, 15
had second procedures that consisted of repeat dil-
ation (n=7), coarctation repair (n=2), or Norwood
procedure (n=6). One of the four patients who had
surgical valvotomy as the initial procedure subse-
quently had balloon dilation of the mitral valve. Of
the five patients whose initial surgery was repair of
aortic coarctation alone, two had subsequent balloon
dilation of the aortic valve and one had a Norwood
procedure. The echocardiograms were inadequate
for quantitative analysis in three of these patients
(cases 21, 57, and 58). The remaining 43 patients
comprised the two-ventricle repair group. There
were a total of 26 deaths (three patients who had no
intervention, nine after a single-ventricle repair, and
14 after a two-ventricle repair). For those patients
who died after an initial two-ventricle repair, the age
at death and the cause of death are given in Table 2.

Comparison of patients in the two-ventricle repair
group who survived with those who died disclosed
that several morphometric features were significantly
associated with death (Table 3). The indexed diam-
eter of the aortic annulus, root, arch, and isthmus
were significantly smaller in the patients who died.
The indexed left ventricular long-axis dimension and
the long-axis dimension relative to the long axis of
the heart, the left ventricular end-diastolic and end-
systolic volumes indexed for BSA, and the left ven-
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tricuspid mass index were all significantly smaller in the patients who died. The indexed mitral valve area and the mitral valve area relative to the tricuspid valve area were also significantly smaller in the patients who died. There was no significant difference between survivors and nonsurvivors with respect to age at presentation, BSA, ejection fraction, or Doppler gradient. There were absolute lower limits of size for several anatomic structures below which no patients survived. All eight patients with an indexed mitral valve area of less than 3.1 cm²/m² died, and all four subjects with an LV mass index of less than 35 g/m² died. However, for the other nine variables, only zero to two deaths were predicted by using an absolute lower limit criterion because there was considerable overlap of values between survivors and nonsurvivors for each of the measurements. The spread of data for six of the most important variables is illustrated in Figure 3. A maximum of eight of the 14 deaths could be predicted on the basis of a single criterion.

When the univariate analysis was restricted to the subgroup of patients who had an intervention at 33 days of life or less, the findings were similar to the group as a whole (Table 3), although LV mass index, the indexed aortic isthmus dimension, and the mitral valve parameters no longer attained significance. Exclusion of patients who had coarctation repair did not alter the results with the exception of the aortic isthmus diameter, which no longer differed between survivors and nonsurvivors.

Discriminant analysis for survival indicated that multivariate analysis considerably improved predictive capacity for survival. The best predictive equa-
tion for survival included BSA, aortic root dimension indexed to body surface area (ROOT), the ratio of the long-axis dimension of the LV to the long-axis dimension of the heart (LAR), and the indexed mitral valve area (MVA). The equation for the discriminating score for survival was

\[
\text{Score} = 14.0 (\text{BSA}) + 0.943 (\text{ROOT})_t + 4.78 (\text{LAR}) + 0.157 (\text{MVA}) - 12.03
\]

with a discriminating score of less than \(-0.35\) predictive of death after a two-ventricle repair. When this equation was applied to the 43 patients in this study, outcome was correctly predicted in 88\%, with four survivors and one nonsurvivor misclassified. When applied to the 32 patients with interventions at 33 days of age or less, 91\% were correctly classified, with two survivors and one nonsurvivor misclassified. There was a single patient who was initially managed with valvotomy but later underwent a Norwood-type procedure and survived. If this patient was considered a death, that is, a failure of the two-ventricle repair, then the performance of this equation was improved to 90\% in the overall group and 94\% in the group with an intervention at 33 days of age or less. The coefficients of the variables in this equation do not give an indication of the relative importance of the variables in determining the discriminating score because the units, means, and variance for the variables are different. However, the relative sizes of the correlations between the discriminating variable and the values of the discriminant function do provide a measure of the independent contribution of each variable.

**Table 2. Age at Time of Norwood Procedure and at Time of Death and Cause of Death in Patients Who Died After Initial Two-Ventricle Repair**

<table>
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<td>56</td>
<td>10</td>
<td>30</td>
<td>59</td>
<td>Staphylococcal and fungal sepsis</td>
</tr>
<tr>
<td>64</td>
<td>3</td>
<td></td>
<td>93</td>
<td>Sudden death</td>
</tr>
<tr>
<td>65</td>
<td>6</td>
<td>33</td>
<td>33</td>
<td>Intraoperative death</td>
</tr>
</tbody>
</table>

Initial, age in days at time of first procedure; Norwood, age in days at time of Norwood procedure; Death, age in days at time of death; LAD, left anterior descending coronary artery; Sub-AS, subaortic stenosis; EFE, endocardial fibroelastosis; DIC, disseminated intravascular coagulation.

**Table 3. Comparison of Anatomic Measurements in Survivors and Nonsurvivors for Patients With Two-Ventricle Repair**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>All two-ventricle repair subjects</th>
<th>Intervention ≤33 days</th>
<th>Norwood group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dead (n=14)</td>
<td>Alive (n=29)</td>
<td>p</td>
</tr>
<tr>
<td>Body surface area</td>
<td>0.21±0.03</td>
<td>0.22±0.05</td>
<td>0.442</td>
</tr>
<tr>
<td>Indexed LV EDV</td>
<td>44.1±17.9</td>
<td>80.8±45.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Indexed LV ESV</td>
<td>26.8±15.0</td>
<td>51.1±39.9</td>
<td>0.007</td>
</tr>
<tr>
<td>Indexed LV mass</td>
<td>63.7±30.1</td>
<td>111.9±66.2</td>
<td>0.002</td>
</tr>
<tr>
<td>Indexed aortic annulus</td>
<td>2.41±0.51</td>
<td>3.15±0.65</td>
<td>0.000</td>
</tr>
<tr>
<td>Indexed aortic root</td>
<td>3.35±0.64</td>
<td>4.27±0.86</td>
<td>0.000</td>
</tr>
<tr>
<td>Indexed aortic arch</td>
<td>2.78±0.80</td>
<td>3.58±0.86</td>
<td>0.006</td>
</tr>
<tr>
<td>Indexed aortic isthmus</td>
<td>2.50±0.62</td>
<td>3.04±0.77</td>
<td>0.021</td>
</tr>
<tr>
<td>Indexed LV long axis</td>
<td>13.2±2.56</td>
<td>16.7±3.41</td>
<td>0.001</td>
</tr>
<tr>
<td>Relative LV long axis</td>
<td>0.82±0.12</td>
<td>0.94±0.09</td>
<td>0.003</td>
</tr>
<tr>
<td>Indexed mitral area</td>
<td>4.03±2.87</td>
<td>7.17±3.18</td>
<td>0.003</td>
</tr>
<tr>
<td>Relative mitral area</td>
<td>0.49±0.20</td>
<td>0.68±0.30</td>
<td>0.022</td>
</tr>
<tr>
<td>Doppler gradient</td>
<td>41.7±27.5</td>
<td>58.6±24.8</td>
<td>0.076</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>37.3±11.5</td>
<td>40.6±19.5</td>
<td>0.499</td>
</tr>
</tbody>
</table>

LV, left ventricle; EDV, end-diastolic volume; ESV, end-systolic volume; NA, not applicable.
variable, and these are presented in order of magnitude as determined by the adjusted F ratio in Table 4. This table presents the rank order for the entire group and for the 33-day-or-less subgroup. The predictive capacity of nonindexed variables was also tested by performing the discriminant analysis by using nonindexed echocardiographic measurements. The predictive ability of discriminatory function was considerably degraded, with only 72% of cases correctly predicted as to outcome. Thus, adjustment of these measurements for BSA is necessary.

Due to the multifactorial nature of the mortality-related risk factors in infants in whom aortic valvotomy had been performed, a simplified scoring system was constructed based on the four anatomic factors that were found to have the most significant independent relation to survival in this group. The critical value for each variable was determined by an iterative process with end-point criteria of 1) maximum group separation and 2) no patient who survived being predicted to die. For the four risk factors identified, the critical levels were 1) a left ventricular long axis to heart long-axis ratio of 0.8 or less; 2) an indexed aortic root diameter of 3.5 cm/m² or less; 3) an indexed mitral valve area of 4.75 cm²/m² or less; and 4) an LV mass index of 35 g/m² or less. The results of applying this scoring system are given in Table 5. The mortality was 100% in the 12 patients with two or more risk factors and 8% in the 31 patients with one or fewer risk factors. Similar results
were obtained when these criteria were applied after exclusion of subjects who had no intervention before 33 days of age (Table 5). In both groups, 86% of deaths were successfully separated from survivors based on these anatomic criteria.

Discriminant analysis indicated that of the four variables, LV mass contributed the least to differentiating the two groups. In addition, of the variables included in the risk scoring system, only LV mass requires off-line analysis with a video digitizing system. Finally, it is our impression that LV mass is subject to the greatest measurement error among these variables. Therefore, we examined the results of a scoring system based solely on the above threshold values for the relative LV long-axis length, the indexed aortic root dimension, and the indexed mitral valve area, excluding LV mass. Exclusion of LV mass as a factor resulted in only a small reduction in predictive capacity (Table 5), with 79% of patients who died correctly identified.

Among the 14 patients who had single-ventricle repair as the initial procedure, there were seven deaths (50% mortality rate). The decision to proceed directly to single-ventricle repair was based in part on left ventricular size. However, the left ventricular volume constitutes only one risk factor. One patient had only one anatomic risk factor by using the above criteria but the remainder had two or more. For those subjects with two or more risk factors, survival after single-ventricle type repair was improved compared with valvotomy (42% versus 0%, p<0.01, Table 5).

Discussion

Critical valvar aortic stenosis is generally a lethal condition in the neonatal period if left untreated. The therapeutic options that have been used are valvotomy (surgical or transcatheter), a Norwood operation, or cardiac transplantation. The decision as to which of these approaches to take is often irreversible and must be made emergently during the newborn period. Consequently, it is essential to define which approach has the best chance of success for any given patient before the initial intervention. Prediction of outcome from preintervention anatomic features may be possible, based on the hypothesis that an LV that is adequate to function as a systemic ventricle must have an adequately sized inflow orifice, pumping chamber volume and mass, and outflow orifice, and that the functional consequences of abnormalities in any of these areas are likely to be additive.

In this retrospective study, we examined the predictive capacity of 11 separate measurements of left ventricular inflow, outflow, volume, mass, and arch size for outcome after an attempted two-ventricle repair. Nine of the 11 parameters were found to be significantly smaller in the group who died. Nonetheless, there was significant overlap between groups for

Table 4. Correlations Between Discriminating Variables and Discriminant Function for Alive Versus Dead With Variables Ordered by Size of Correlation for the Entire Group

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients</th>
<th>Intervention≤33 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indexed aortic root</td>
<td>0.60612</td>
<td>0.58926</td>
</tr>
<tr>
<td>Relative LV long axis</td>
<td>0.55516</td>
<td>0.52853</td>
</tr>
<tr>
<td>Indexed aortic annulus</td>
<td>0.52894</td>
<td>0.68381</td>
</tr>
<tr>
<td>Indexed aortic arch</td>
<td>0.48906</td>
<td>0.42148</td>
</tr>
<tr>
<td>Indexed mitral area</td>
<td>0.46246</td>
<td>0.13203</td>
</tr>
<tr>
<td>Indexed LV mass</td>
<td>0.43613</td>
<td>0.23065</td>
</tr>
<tr>
<td>Relative mitral area</td>
<td>0.43141</td>
<td>0.19289</td>
</tr>
<tr>
<td>Indexed LV EDV</td>
<td>0.40445</td>
<td>0.27463</td>
</tr>
<tr>
<td>Indexed LV long axis</td>
<td>0.40211</td>
<td>0.37058</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>0.14379</td>
<td>0.04227</td>
</tr>
<tr>
<td>Body surface area</td>
<td>0.12136</td>
<td>0.03074</td>
</tr>
</tbody>
</table>

LV, left ventricle; EDV, end-diastolic volume.

Table 5. Results of Simplified Scoring System for Anatomic Risk Factors

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Biventricular</th>
<th>Intervention≤33 days</th>
<th>Norwood</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>deaths</td>
<td>%</td>
</tr>
<tr>
<td>0</td>
<td>16</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>1</td>
<td>15</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>7</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>3</td>
<td>100</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>Totals</td>
<td>43</td>
<td>14</td>
<td>33</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Biventricular</th>
<th>Intervention≤33 days</th>
<th>Norwood</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>deaths</td>
<td>%</td>
</tr>
<tr>
<td>0</td>
<td>16</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>1</td>
<td>16</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>7</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>4</td>
<td>100</td>
</tr>
<tr>
<td>Totals</td>
<td>43</td>
<td>14</td>
<td>33</td>
</tr>
</tbody>
</table>

Including left ventricular mass as a risk factor criterion

Excluding left ventricular mass as a risk factor criterion
each parameter, precluding identification of a useful lower limit below which a two-ventricle repair should not be attempted. The potential cumulative adverse effect of multiple small left heart structures was explored with linear discriminant analysis, which indicated that survival can be predicted with almost 90% accuracy based on the mitral valve area, the LV long axis relative to total length of the heart, and aortic root size. It should be noted that the best discriminating function included a measure of the size of the LV inflow, the LV chamber, and the LV outflow. There was a small decrease in discriminatory capability when alternative measures of LV chamber size (mass or volume) or LV outflow size (aortic annulus, aortic arch) were substituted. An incremental scoring system based on threshold values for these variables was devised to permit identification of subjects with no chance of survival after two-ventricle repair. In those patients undergoing valvotomy, it was found that additional anatomic measurements below the threshold values incurred an increased risk of death such that in patients with two or more risk factors, there was 100% mortality. This simplified scoring system correctly classified subjects as to outcome in 95% of cases.

The ability to predict which patients would have a successful outcome after a two-ventricle repair based on preoperative anatomy was substantially improved by incorporation of multiple left-heart structures into the predictive equation. In fact, threshold values of individual structures were poorly predictive of outcome. For the patients who had a two-ventricle repair in this study, the patient with the smallest LV volume survived, although the LV volume was below the commonly accepted threshold value. In fact, if the value of 20 mL/m² had been used as the sole selection criterion, one of the 29 survivors would not have had a two-ventricle repair and only one of the 14 deaths would have been predicted. Although there is clearly a lower limit of LV size that is capable of functioning as a systemic ventricle, this was not tested in the present study because many of the patients with the smallest ventricles had a single-ventricle repair as their first procedure. For those subjects with a ventricular size above the absolute minimum, inclusion of other morphological variables improves the predictive capacity. It is of interest that the values for mitral valve size and aortic root size, which provide an incremental risk in subjects with critical aortic stenosis, are just below what would otherwise be considered the normal range. The mitral valve area of 4.75 cm²/m² is in the normal range for a neonate, representing a dimension of 1.1 cm in an infant with a BSA of 0.2 m², and as an isolated finding is perfectly compatible with survival. In fact, eight of the 29 survivors in this study had an indexed mitral annulus smaller than this value. Similarly, the aortic root cutoff value of 3.5 cm²/m² is equivalent to an aortic root dimension of 0.95 cm in a 0.2 m² infant, and five of 29 survivors had an indexed aortic root diameter below this value. This points out the cumulative impact of these abnormalities. An anatomic feature that may represent little risk in isolation represents a substantial risk in the presence of associated abnormalities. Thus, it appears that in the presence of severe aortic stenosis with root hypoplasia, even mild degrees of mitral hypoplasia are poorly tolerated.

Attempts have been made to identify predictors of mortality and morbidity after valvotomy for critical aortic stenosis in the neonate and infant.6–13 Although several features have been found to be significant predictors of mortality (aortic annulus size,8,13 ejection fraction,6,8,9 end-diastolic pressure,8,9 mean left atrial pressure,8 presence of endocardial fibroelastosis,6,9 most studies have focused on defining the minimum left ventricular volume that can support the systemic circulation.6 Left ventricular size alone is not fully predictive of outcome. Most studies in infants with critical aortic stenosis have included only patients who had an aortic valvotomy, and did not attempt to include the entire spectrum of the disease. Because patients judged to have unfavorable anatomy would have been excluded, many of the potential anatomic factors contributing to adverse outcome were not tested. This almost certainly accounts for the fact that several studies did not find LV size to be associated with survival.8,9

A recent study by Hammon et al12 looked at six variables measured at the time of cardiac catheterization as potential predictors of survival in infants with critical aortic stenosis. These included mean pulmonary artery pressure, left ventricular peak systolic pressure, left ventricular end-diastolic pressure, peak transaortic valve gradient, left ventricular end-diastolic volume, and ejection fraction. The only two variables with a significant relation to survival were end-diastolic volume and mean pulmonary artery pressure. These results are similar to ours with respect to the lack of an association between survival and ejection fraction and a significant predictive value for end-diastolic volume. We found that the subjects who died tended to have a lower transvalvar gradient although this did not attain statistical significance (p=0.076). This tendency reflects the fact that most of these patients have severely impaired ventricular function at the time of presentation and limited antegrade flow across the aortic valve. Consequently, transaortic gradient would not be expected to reflect the severity of stenosis, and the lack of an association between gradient and outcome is not surprising.

This series includes analysis of 14 patients without aortic or mitral atresia who had a Norwood type of palliation as a primary procedure. The range of LV cavity size in these patients was 5.2–28.2 mL/m² (mean±SD, 16.7±6.8 mL/m²). It is, of course, not possible to know with certainty if the LV would have been an adequate systemic ventricle for any of these patients, but in six of 14 the LV size was in the range of survivors of a two-ventricle repair (18 mL/m² or greater). When the proposed scoring system was
applied to the preoperative status for the group of 14
patients who had a single-ventricle repair as a first
procedure, 13 were found to have two or more risk
factors. Survival in this group was significantly better
(six of 13) than for the group of patients with two or
more risk factors who had a valvotomy (none of 12),
indicating that the single-ventricle repair as a first
procedure would be preferable in patients in this
category regardless of absolute LV size.

Transcatheter palliation of critical aortic stenosis
in neonates enables the decision concerning a single-
ventricle repair to be delayed in some instances. That
is, in patients with a borderline LV size, a possible
approach is to perform an initial balloon dilation of
the aortic valve with the expectation that some
patients will still require a single-ventricle repair.
Although, as seen in this series, it is possible in some
instances to resort to the single-ventricle approach
after failure of a valvotomy, second procedures are
generally unsuccessful or are precluded by severe
clinical compromise or death. For the patients in this
series who died after two-ventricle repair, eight did
not have an attempt at a single-ventricle repair either
because of sudden death or because they were con-
sidered to be too ill to survive surgery. Only one of
the seven cases in whom a Norwood was attempted
after initial two-ventricle repair survived. The deci-
sion to resort to a single-ventricle repair after failure
of an initial two-ventricle repair is difficult and is
generally made only if the patient is doing quite
poorly. For the patients in this series in whom a
single-ventricle repair was attempted after failure of
a two-ventricle repair, four of seven died intraopera-
tively and two of seven died of sepsis postoperatively,
indicative of their poor clinical status. In addition,
survival was better after single-ventricle repair as a
primary procedure, indicating that this mortality rate
is not simply the result of the risks inherent in the
Norwood operation but reflects in part the hazards of
attempting this operation in subjects with severe
hemodynamic compromise. This experience indicates
that in those subjects for whom the two-ventricle
palliation is unlikely to succeed, it is preferable to
proceed directly to a Norwood procedure.

There are factors other than preoperative anatomy
that may affect outcome, including the degree to
which LV outflow obstruction is relieved. Pelech et
al.8 found no significant difference in mortality be-
tween closed versus open valvotomy. Recently, Zeevi
et al.14 reported a series from this hospital that
included many of the patients in this study and
showed no significant difference between balloon and
surgical valvotomy. Thus, it is unlikely that the results
of this study would have been different if a higher
percentage of these patients had undergone surgical
valvotomy. More importantly, the results of this study
indicate that inadequate relief of valvar stenosis is
doi.

Quantification of the severity of aortic stenosis in
neonates is problematic. As noted above, the trans-
valvar pressure drop or Doppler velocity does not
provide an accurate index of valve orifice size be-
cause of the variable transvalvar flow. Quantification
of LV output is difficult because the ductus arteriosus
remains patent in most patients and mitral regurgi-
tation may be present. In general, markedly abnor-
mal valve morphology with associated ventricular
dysfunction and clinical congestive heart failure are
the diagnostic findings, and these were the entrance
criteria used in this study. However, coarctation of
the aorta occurs commonly in association with aortic
stenosis in neonates and may compound the hemo-
dynamic abnormalities. Because the clinical status of
the patient was used in part to judge the severity of
the lesion, an associated coarctation could result in
overestimate of the severity of aortic stenosis. There
were two subjects in the current study who became
asymptomatic after coarctation repair without valvot-
y, and a single subject who survived with no
procedure. Although both appear to have severe
aortic stenosis at present, it is possible that the
severity of aortic stenosis in these subjects was less
than in the subjects who underwent aortic valvotomy.
We examined the potential confounding effects of
these subjects by performing the data analysis both
with and without inclusion of the subjects who did
don't have a valvotomy and the subjects who had a
coarctation repair. With the exception of the finding
that aortic isthmus size was no longer significantly
associated with mortality or morbidity after exclusion
of the coarctation patients, there was no change in
any of the other results, indicating that these subjects
did not distort our findings.

Although neonates are of greatest interest, we chose
to not to use valvotomy at less than 1 month of age as a
study entrance criterion for two reasons: 1) the timing
of intervention was not exclusively based on objective
criteria, rendering this an unreliable index of disease
severity (some patients who had early intervention
might have survived beyond 1 month without interven-
tion), and 2) inclusion of subjects who survive to an
older age before intervention is undertaken provides
additional data concerning those anatomic variables
that do or do not limit survival.

Conclusions

Critical valvar aortic stenosis in the neonatal pe-
riod requires the physician and family to make deci-
sions about treatment in a timely fashion. We have
examined which of the many potential parameters
are important in deciding whether to proceed to
either a two-ventricular repair or a Norwood pro-
dure. This retrospective study has identified a scoring
system based on the size of multiple left-sided struc-
tures that may help in making this decision. The
results indicate that patients with multiple small left-heart structures may have improved survival after a Norwood procedure compared with valvotomy, even if no single feature is too small to preclude survival if it were an isolated abnormality. The strength of the conclusions is limited by the fact that this is a retrospective study on a limited number of patients. However, the results are significant enough that this method deserves to be tested in other series and, more importantly, in a prospective fashion.

Addendum

Since completion of this study, eight additional patients with critical aortic stenosis have undergone transcatheter balloon valvotomy at our institution. The age at procedure was 1–29 days (median, 4 days). For the group, the indexed LV end-diastolic volume was 49±23, indexed LV mass was 55±9, indexed aortic root dimension was 3.8±0.6, LV long-axis ratio was 0.94±0.10, and indexed mitral valve area was 4.0±1.46. Thus, for most parameters this group tended to have as small or smaller values than our previous experience. There were two deaths, and six of eight survived. Applying the discriminant equation derived above to this group of patients correctly classified seven of eight, with a single survivor misclassified. Using the scoring system based on threshold values for mass, mitral valve area, relative long-axis dimension, and aortic root, all eight subjects were correctly classified based on preintervention anatomy. There were two patients meeting no criteria and four subjects with one risk factor, and these were the six survivors. The two patients who died had below-threshold values for two of four and three of four variables, respectively.

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KEY WORDS • aortic stenosis • neonates • Norwood procedure • valvotomy
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