Validation and Re-Evaluation of a Discriminant Model Predicting Anatomic Suitability for Biventricular Repair in Neonates With Aortic Stenosis

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OBJECTIVES
The purpose of this study was to validate and re-evaluate our previously reported scoring systems for predicting optimal management in neonates with aortic stenosis (AS).

BACKGROUND
In 1991, we reported a multivariate discriminant equation and an ordinal scoring system for predicting which neonates with AS are suitable for biventricular repair and which are better served by single ventricle management.

METHODS
Retrospective analysis was performed to: 1) validate our scoring systems in 89 additional neonates with AS and normal mitral valve area, 2) assess the effects of 5% measurement variation on predictive scores, 3) evaluate our cohort with the Congenital Heart Surgeons’ Society scoring system, and 4) repeat the discriminant analysis on the basis of all 126 patients.

RESULTS
The original scores each predicted outcome accurately in 68 patients (77%). Minor (5%) measurement variation changed the outcome predicted by the discriminant equation in 8 patients (9%) and by the threshold system in 13 patients (15%). The most accurate model for predicting survival with a biventricular circulation among the full cohort is: 10.98 (body surface area) + 0.56 (aortic annulus z-score) + 5.89 (left ventricular to heart long-axis ratio) − 0.79 (grade 2 or 3 endocardial fibroelastosis) − 6.78. With a cutoff of −0.65, outcome was predicted accurately in 90% of patients.

CONCLUSIONS
Both of our original scoring systems are less accurate at predicting outcome than in our original analysis. Revised discriminant analysis yielded a model similar to our original equation that was 90% accurate at predicting survival with a biventricular circulation among neonates with AS and a mitral valve area z-score ≥ −2. (J Am Coll Cardiol 2006;47:1858–65) © 2006 by the American College of Cardiology Foundation

Congenital obstruction of left heart structures represents a spectrum of disease, from isolated obstruction of the aortic valve or arch to atresia of the aortic and mitral valves (MV) accompanied by extreme hypoplasia of the entire left heart. Many patients with anomalies of the left heart complex have a primary obstructive lesion (e.g., valvar aortic stenosis [AS]) in association with variable hypoplasia of other left heart structures. In some of these patients, particularly a subset with critical AS, the left heart complex is—or borders on being—insufficiently developed to support the systemic circulation in a biventricular repair. Although outcomes in newborns across the spectrum of left heart obstructive disease continue to improve, it can be challenging to predict whether patients with a “borderline” left heart are suitable candidates for biventricular repair (1−14).

In 1991, we performed a retrospective discriminant analysis in 45 patients ≤ 60 days of age with critical AS (1). Although we recognized that factors other than anatomic dimensions were likely important in determining outcome, we sought to identify anatomic features that limited the capacity of the left heart complex to support a systemic cardiac output in a biventricular circulation. We found that the multivariate equation 14.0 (body surface area [BSA]) + 0.943 (indexed aortic root diameter) + 4.78 (left ventricular [LV] long-axis to heart long-axis ratio [LAR]) + 0.157 (indexed MV area) − 12.03 (hereafter, discriminant score) successfully predicted survival with a biventricular circulation or death/conversion to a functional single ventricle (SV) circulation in 90% of patients. In addition to this discriminant score, we developed a simpler ordinal scoring system on the basis of threshold values (hereafter, threshold score), such that one point against survival was assessed for each of the following anatomic measurements below a threshold value: indexed aortic root diameter, indexed MV area, LAR, and indexed LV mass. All patients with a threshold score ≥ 2 died or underwent conversion to a functional SV circulation, and 92% of patients with a score < 2 survived.

In the 14 years since our previous study was published, we have used these scoring systems to guide therapeutic decision-making in neonates with AS. Although treatment has not been stratified strictly according to either scoring system, patients with significant hypoplasia (z-score < −2) of the MV or LV chamber have generally been referred for univentricular palliation. To assess the validity of our scoring systems, we reviewed outcomes in 89 patients ≤ 60
days of age who underwent attempted biventricular management for critical AS since our previous study was performed. We hypothesized that both scoring systems would be less accurate than in our original cohort but that an updated analysis would include similar anatomic factors in a predictive model. We also hypothesized that the threshold scoring system would be more subject to changes in predicted outcome due to small measurement errors than the discriminant scoring system.

**METHODS**

The study consisted of four components: 1) validation of the previously reported scoring systems in 89 new patients, 2) assessment of the effects of minor (5%) measurement discrepancies on predictive scores, 3) evaluation of our patient cohort according to the predictive scoring system for neonates with AS devised by the Congenital Heart Surgeons’ Society (CHSS) (5), and 4) repeat discriminant analysis including the 89 new patients along with 37 patients from our original report who underwent valvuloplasty beyond this age or patients who were thought to be “borderline” candidates for biventricular repair but ultimately underwent stage I palliation without previous valvuloplasty.

**Echocardiographic measurements.** Echocardiographic measurements were made as described in our original report (1). Structures measured included aortic valve annulus diameter, aortic root diameter, transverse arch diameter, aortic isthmus diameter, MV area, LV mass, LV end-diastolic dimension and volume, LV long-axis length, and LAR. Aortic annulus and root diameters were measured from parasternal long-axis images, with the aortic root diameter taken as the maximum dimension at the level of the sinuses. The internal dimensions of the distal transverse arch (between the left common carotid and subclavian arteries) and the aortic isthmus (immediately distal to the left subclavian artery) were measured from suprasternal notch images. Vascular diameters were measured at the maximum systolic dimensions, from inner edge to inner edge. The MV area was calculated as an ellipse from the orthogonal diameters of the MV annulus measured in early diastole from parasternal long-axis and four-chamber images. The morphology of the MV apparatus was not systematically evaluated for this study. The long axis of the heart was measured in apical four-chamber images from the plane of the MV annulus to the apical endocardium of the ventricle (left or right) that formed the apex of the heart. The LV end-diastolic and end-systolic epicardial and endocardial borders were digitized manually from subxyphoid long- and short-axis views. The LV volumes were calculated with the biplane bullet model, according to which LV volume equals five-sixths multiplied by short-axis cross-sectional area of the LV at midventricular level multiplied by the long-axis LV length. Mass was calculated as the difference between endocardial and epicardial LV volumes multiplied by the specific gravity of myocardium (1.04 g/ml). Aside from LAR, measured values were indexed to BSA, which was calculated with the method of Haycock et al. (15). For assessment of the predictive accuracy of the original discriminant and threshold scoring systems in the new patient cohort, indexed measurements were used, as they were in our original report; however, for the revised discriminant analysis, z-scores (number of standard deviations above or below the average indexed size of the structure in question, on the basis of normative data obtained at our institution from children with structurally and functionally normal hearts [16]) were used instead. On the basis of the CHSS analysis (5), LV endocardial fibroelastosis (EFE) was included in the analysis. Severity of EFE was graded separately by two echocardiographers according to the scale used in the CHSS study of neonatal
AS (5), with 0 = none, 1 = involvement of MV papillary muscles only, 2 = involvement of papillary muscles and some endocardial surface, and 3 = extensive endocardial surface involvement.

**Original threshold and discriminant scoring systems.** According to our original threshold scoring system (1), threshold values were determined for the four anatomic variables independently associated with survival or death. For each variable below the threshold value, a patient was assigned one point, such that the range of threshold scores was zero to four. The variables and threshold values included in the score were indexed aortic root diameter (\(\pm 3.5 \text{ cm/m}^2\)), indexed MV area (\(\pm 4.75 \text{ cm}^2/\text{m}^2\)), LAR (\(\pm 0.8\)), and indexed LV mass (\(\pm 35 \text{ g/m}^2\)). A threshold score <2 predicted survival with a biventricular circulation. Our original discriminant analysis yielded the equation 14.0 (BSA) + 0.943 (indexed aortic root diameter) + 4.78 (LAR) + 0.157 (indexed MV area) − 12.03, with a score of −0.35 discriminating between survival and death (\(\leq −0.35\) predicting death or conversion to SV circulation, \(> −0.35\) predicting survival with a biventricular circulation) (1).

**CHSS scoring system.** In 2001, the CHSS reported the results of a multicenter study of outcomes in 320 neonates with critical AS, over one-half of whom underwent SV palliation (5). From multivariable analyses of factors associated with outcome after stage I palliation or biventricular management, the authors derived a regression equation that can be solved for individual patients to predict the survival benefit of stage I palliation versus a biventricular repair strategy (5):

\[
\text{Survival benefit} = 30.55 \text{(inverse of age at study entry [d] + 1)} - 6.20 \text{(aortic root z-score)} + 12.14 \text{(echocardiographic grade of EFE)} + 23.33 \text{(logarithm of ascending aortic [mm])} - 28.30 \text{(presence of moderate or severe tricuspid regurgitation)} - 0.70 \text{(LV long-axis length z-score)} - 86.47
\]

The magnitude of the result indicates the predicted difference in percent survival, with a positive value indicating a survival benefit of stage I palliation and a negative value indicating a survival benefit of biventricular repair. The CHSS equation was solved for each patient using the CHSS online critical AS calculator (17).

**Data analysis.** The primary outcome was survival with a biventricular circulation. Patients who died or underwent conversion to an SV circulation were considered equally as “events.” Because all events occurred within one year and almost all occurred early (within one month of intervention), data were analyzed in a time-independent manner, as in our original report (1). Descriptive analysis was used to compute the accuracy of the original threshold and discriminant scoring systems when applied to the 89 new patients. For assessment of the effects of measurement variation on predictive accuracy, each of the measures included in the original threshold and discriminant scoring systems was increased and decreased by 5% of its measured value and reinserted into the appropriate scoring equation. For the threshold scoring system, each of the component scores was analyzed independently, and all possible permutations of the overall score were examined. For the revised discriminant analysis, statistical analysis of data from all 126 patients was performed according to the methods described in detail in our original report (1). Although indexed measurements were used in our original analysis, the updated analysis was performed with z-scores. Univariable analysis was conducted to identify variables that differed significantly between survivors and events, with separate analyses performed for patients ≤30 days of age and for patients without coarctation of the aorta (COA). Two-group linear discriminant analysis was performed with forward stepwise selection of variables for inclusion in the model. As in our original analysis, the unstandardized discriminant function was determined to optimize identification of survivors. An updated threshold scoring system was not devised. Unless otherwise specified, data are presented as mean values ± standard deviation or median (range).

**RESULTS**

**Patients.** Between 1989 and 2002, 89 patients ≤60 days of age satisfying the inclusion criteria underwent balloon aortic valvuloplasty (n = 87) or surgical aortic valvuloplasty (n = 2). The median age at valvuloplasty was 4 days (0 to 60 days), and the median weight was 3.4 kg (0.9 to 5.8 kg). Seventy-six patients (85%) were ≤30 days of age and 54 patients (61%) were ≤1 week.

Including the 37 patients from our original report whose data are included in the revised discriminant analysis, there were 126 patients. The median age at valvuloplasty was 5 days (0 to 60 days), and the median weight was 3.4 kg (0.9 to 5.8 kg). Age at valvuloplasty was ≤30 days in 104 patients (83%) and ≤1 week in 72 patients (57%). Fourteen patients (11%) underwent repair or angioplasty of COA before or within three months of aortic valvuloplasty. A patent ductus arteriosus was present in 86 patients (66%).

Outcomes (survival, conversion to an SV circulation) in the new and combined cohorts are summarized in Table 1. There was a significant reduction in mortality during the latter one-half of our experience (p = 0.005) as well as a decline in the frequency of events over time (p = 0.07) (Table 1). Moreover, all five patients who converted to an SV circulation from 1994 to 2002 survived, compared with two of nine who converted to an SV circulation before 1994 (p = 0.01). Hospital survivors were followed for a median of 5.7 years (1 month to 18 years). Intermediate outcomes in these patients have been reported separately (18).

**Validation of the original threshold and discriminant scoring systems in 89 new patients.** The distribution of ordinal threshold scores in the 89 new patients is summa-
For the discriminant scoring system, 5% variation in measurement of aortic root diameter, MV area, or LAR would change the predicted outcome in eight patients (9%), with a correct prediction made incorrect in seven (five survivors, one event), and an incorrect prediction made correct in two (both survivors).

**Predictive accuracy of the CHSS model.** For the 108 patients in our cohort who underwent pre-intervention echocardiography at \( \leq 31 \) days of age (required for entry into the CHSS study), the CHSS regression equation was solved (5). The CHSS model predicted a survival advantage with SV palliation in 63 of these 108 patients (58%), over one-half of whom (\( n = 32 \)), including 16 of 22 patients (73%) managed between 1994 and 2002, survived with a biventricular circulation. The CHSS model predicted a survival advantage with a biventricular repair strategy in the other 45 patients, 39 of whom (87%) survived with a biventricular circulation.

**Updated discriminant analysis.** Data from the 89 new patients and 37 patients in our original report were pooled and analyzed by discriminant analysis (1). An updated threshold scoring system was not derived. Differences in independent variables between survivors and events are summarized in Table 3, and selected baseline echocardiographic measurements for the entire cohort are shown in Figure 2. There was agreement about EFE grade by the two reviewing echocardiographers in 90 patients (71%), a discrepancy of one grade in 35 patients (28%), and a discrep-

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**Table 1.** Frequency of Death and Conversion to an SV Circulation

<table>
<thead>
<tr>
<th>Patient Subgroup</th>
<th>Number of Patients</th>
<th>Died</th>
<th>Converted to SV Circulation</th>
<th>Total Events*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall cohort</td>
<td>126</td>
<td>32 (25%)†</td>
<td>14 (11%) 7 survived</td>
<td>39 (31%)</td>
</tr>
<tr>
<td>New cohort</td>
<td>89</td>
<td>20 (22%)‡</td>
<td>10 (11%) 6 survived</td>
<td>26 (29%)</td>
</tr>
<tr>
<td>Year of diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before 1994</td>
<td>76</td>
<td>26 (34%)§</td>
<td>9 (12%) 2 survived</td>
<td>28 (34%)</td>
</tr>
<tr>
<td>1994–2002</td>
<td>50</td>
<td>6 (12%)¶</td>
<td>5 (10%) 5 survived</td>
<td>11 (22%)†§</td>
</tr>
</tbody>
</table>

*Total events are patients who died or survived conversion to a single ventricle (SV) circulation. †Median age 16 days (0–1 yr). ‡Median age 8 days (0–43 days). §p = 0.005 vs. pre-1994. ¶p = 0.01 vs. pre-1994. *p = 0.07 vs. pre-1994.

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**Table 2.** Distribution of Threshold Scores Among New Patients (n = 89) Who Did (Survivors) and Did Not (Events) Survive With a Biventricular Circulation

<table>
<thead>
<tr>
<th>Threshold Score</th>
<th>All Patients (n = 89)</th>
<th>Survivors (n = 64)</th>
<th>Events (n = 25)</th>
<th>Event Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>12 (13%)†</td>
<td>11† (17%)‡‡</td>
<td>1 (4%)§</td>
<td>8%</td>
</tr>
<tr>
<td>1</td>
<td>43 (48%)</td>
<td>38† (59%)‡‡</td>
<td>5 (20%)§</td>
<td>12%</td>
</tr>
<tr>
<td>2</td>
<td>22 (25%)‡</td>
<td>12 (19%)‡‡</td>
<td>10 (40%)§‡‡</td>
<td>45%</td>
</tr>
<tr>
<td>3</td>
<td>9 (10%)‡</td>
<td>3 (5%)‡</td>
<td>6 (24%)§‡‡</td>
<td>67%</td>
</tr>
<tr>
<td>4</td>
<td>3 (3%)†</td>
<td>0 (0%)‡</td>
<td>3 (12%)§‡‡</td>
<td>100%</td>
</tr>
</tbody>
</table>

*Percentage of all patients. †Accurate predictive scores. ‡Percentage of survivors. §Percentage of events.
ancy of two grades in 1 patient (1%) (kappa = 0.58). In cases with discrepant scoring, a consensus score was determined upon further review of the echocardiogram. The most accurate discriminant model for predicting survival with a biventricular circulation among the entire cohort of 126 patients is: 10.98 (BSA) + 0.56 (aortic valve annulus z-score) + 5.89 (LAR) − 0.79 (presence of grade 2 or 3 EFE) − 6.78. Taking a discriminant cutoff of −0.65, this model accurately predicted outcome in 95% of survivors and 80% of events (90% overall) (Fig. 2). Higher cutoff values

Table 3. Demographic and Anatomic Variables in Patients From the Combined Cohort (n = 126) Who Did (Survivors) and Did Not (Events) Survive With a Biventricular Circulation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Survivors (n = 88)</th>
<th>Events (n = 38)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at intervention (days)</td>
<td>9 (0 to 60)</td>
<td>2 (0 to 48)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>3.5 (0.9 to 5.8)</td>
<td>3.1 (1.3 to 4.6)</td>
<td>0.055</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>0.22 (0.09 to 0.30)</td>
<td>0.21 (0.12 to 0.27)</td>
<td>0.02</td>
</tr>
<tr>
<td>Aortic valve annulus z-score</td>
<td>-1.1 (-4.5 to 3.2)</td>
<td>-2.8 (-5.0 to -0.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Aortic root diameter z-score</td>
<td>-0.4 (-2.9 to 4.7)</td>
<td>-1.8 (-3.4 to 0.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Transverse aortic arch diameter z-score</td>
<td>-0.6 (-3.3 to 1.7)</td>
<td>-1.5 (-3.3 to 3.1)</td>
<td>0.02</td>
</tr>
<tr>
<td>LV mass z-score</td>
<td>2.1 (2.5 to 7.7)</td>
<td>1.5 (-4.1 to 6.5)</td>
<td>NS</td>
</tr>
<tr>
<td>LV end-diastolic dimension z-score</td>
<td>0.8 (-4.9 to 12.5)</td>
<td>0.9 (-3.9 to 9.3)</td>
<td>NS</td>
</tr>
<tr>
<td>LV end-diastolic volume z-score</td>
<td>1.0 (-4.8 to 8.0)</td>
<td>-0.3 (-8.1 to 5.9)</td>
<td>NS</td>
</tr>
<tr>
<td>LV long-axis to heart long-axis ratio</td>
<td>1.0 (0.7 to 1.0)</td>
<td>0.8 (0.4 to 1.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MV area z-score</td>
<td>1.3 (-1.7 to 12.2)</td>
<td>0.5 (-2.0 to 14.4)</td>
<td>NS</td>
</tr>
<tr>
<td>EFE grade 2 or 3</td>
<td>15 (17%)</td>
<td>15 (39%)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Aside from endocardial fibroelastosis (EFE) grade 2 or 3 (number of percent of patients), data are presented as median (range). Aortic valve annulus diameter z-score = aortic valve annulus diameter = (1.55 × BSA^0.5)/(0.06 + 0.083 × BSA). Aortic root diameter z-score = aortic root diameter = (2.02 × BSA^0.5)/(0.098 + 0.12 × BSA). *p values refer to comparison of means by independent samples t-test, except for data on EFE grade, which were compared using chi-square analysis.

BSA = body surface area; LV = left ventricular; MV = mitral valve.

Figure 2. Scatter plots showing pre-intervention z-scores for (A) aortic annulus diameter, (B) aortic root diameter, (C) left ventricular (LV) end-diastolic dimension (EDD), and (D) the LV long-axis to heart long-axis ratio (LAR). Survivors are depicted as solid circles and events are depicted as open symbols, with patients who died shown as open triangles and patients who survived after conversion to a functional SV circulation shown as open circles.
allowed slightly improved specificity at the expense of sensitivity. The greatest specificity while maintaining >85% sensitivity for predicting survival with a biventricular repair was at a discriminant cutoff of <−0.46, which predicted outcome accurately in 86% of survivors and 82% of events. If EFE is omitted from the analysis (owing to high interobserver variability in grading), the most accurate model for predicting survival with a biventricular circulation is: 12.16 (BSA) + 0.59 (aortic valve annulus z-score) + 5.73 (LAR) − 7.02, with a discriminant cutoff of −0.46 accurately predicting 91% of survivors and 80% of events (87% overall).

DISCUSSION
Our previously reported discriminant and threshold scoring systems accurately predicted outcomes in 75% to 78% of neonates with AS who have undergone balloon or surgical aortic valvuloplasty at our center since 1989. Both scoring systems have proven less accurate at predicting outcome than in our original retrospective analysis, in which they were >90% accurate (1), with similar decreases in accuracy among survivors and patients who died or underwent conversion to an SV circulation. In 20% of patients, one score but not the other was predictive of outcome. Although multiple factors might contribute to poorer performance of the predictive equations when they are applied to new populations, both scoring systems are susceptible to changes in predictive accuracy resulting from minor variations in echocardiographic measurements, with a 5% measurement variation altering the predicted outcome in 10% to 15% of patients. The threshold scoring system is more prone than the discriminant scoring system to changes in score and in predicted outcome due to variations in measurement, although most changes in threshold system component scores due to individual measurement variations would not have altered the overall predictive score in our patients.

When discriminant analysis was repeated with our 89 new patients and 37 patients from our original series, the resulting model predicted outcome with 90% accuracy, including correct identification in 95% of survivors. The updated model is similar to that in our original analysis, with several notable differences. Inclusion of aortic annulus z-score improved the accuracy of the revised discriminant model to a greater extent than the aortic root z-score (indexed aortic root diameter but not annulus diameter was included in the original equation), although there is a tight covariance between these measures. Also, indexed MV area, a component of our original discriminant model, did not improve the accuracy of our revised estimates. In fact, indexed MV area did not differ between survivors and events even by univariable analysis, most likely owing to the fact that patients whose MV size was the limiting factor were diverted to an SV management strategy on the basis of the discriminant score and therefore were not included in this series. All patients in this series had an MV area z-score in or above the normal range (>−2), and accordingly our findings only apply to such patients.

The predictive accuracy of both our original and modified scoring systems is greatest at the extremes and less reliable as scores approach the discriminant cutoffs. Naturally, decisions regarding the management of patients in this intermediate zone are the most challenging. In our original report, the intent of the discriminant analysis was to optimize identification of patients who would not survive with a biventricular circulation, such that no patient able to survive biventricular repair would undergo SV palliation. This approach is on the basis of the conviction that survival with a biventricular circulation is a preferable outcome to a functional SV circulation.

In 2001, the CHSS reported the results of a multicenter study of outcomes in 320 neonates with critical AS, over 50% of whom were managed with SV palliation. In contrast to our approach, the analytic strategy of the CHSS study was designed to identify factors predicting a survival benefit of either biventricular or SV management, which assumes that survival with an SV circulation is an equivalent outcome to survival with a biventricular circulation. Incremental risk factors for death after biventricular repair in the CHSS study included higher EFE grade, lower aortic root z-score, and younger age, whereas risk factors for death after stage I palliation included a smaller ascending aortic diameter and the presence of moderate or severe tricuspid regurgitation. For each patient, the multivariable hazard function equations for estimated survival after biventricular and SV management strategies were solved separately, and an estimated survival benefit of one strategy over the other was calculated as the difference between the two estimates. From these estimates, a simplified regression equation was derived that would allow for prediction of the management pathway (SV or biventricular) that provided survival benefit. Solution of the equation summarized in the CHSS report provides a weighted estimate of survival benefit of an SV versus biventricular management strategy but does not speak to the estimated survival with each strategy.

It is stated in the discussion of the CHSS study that “without the use of the equation, there is a significant error rate for each pathway, with 50% of the biventricular repair patients having better predicted survival with a Norwood approach and 20% of the Norwood patients having better predicted survival with biventricular repair” (5). Had the CHSS model been applied prospectively in their cohort, only 29% of patients would have been managed with a biventricular repair strategy; however, the two-year Kaplan-Meier survival was 71% for patients managed according to a biventricular repair strategy, in a model found to have only a single early hazard phase, suggesting that the majority of patients treated with a biventricular repair strategy against the subsequently derived model survived despite a predicted survival advantage with SV palliation. Similarly, 58% of patients in our series were predicted by the CHSS model to have a survival advantage with SV palliation, but over
one-half of those survived after biventricular repair. Thus, for a substantial proportion of patients who underwent successful biventricular repair in our series and theirs, the authors of the CHSS study propose that a Norwood procedure would have been preferable, simply because it offered a theoretical survival benefit in those patients.

Factors that must be considered in a model of this sort include not only which strategy offers a statistical survival benefit but the magnitude of the benefit (accounted for in the CHSS model) as well as the relative estimates of survival for the two strategies. For example, if the estimated survival benefit of SV palliation is small and the estimated survival with biventricular repair is high, the minor theoretical survival benefit of a Norwood procedure seems a high price to pay for the drawbacks of an SV circulation. With respect to this issue, the argument can be made that not only is the analytic strategy of the CHSS biased in favor of recommending SV palliation but the solution of the multivariable equation is as well. The only independent predictors of worse outcome after SV palliation are smaller incremental diameter of the ascending aorta (incorporated after logarithmic transformation, thus accentuating the importance of differences at the smaller end of the spectrum) and moderate or severe tricuspid regurgitation. In patients with critical AS and an adequate left heart, the ascending aorta is frequently much larger than the aortic annulus or root. Similarly, significant tricuspid regurgitation is uncommon in neonates with AS, occurring in 7% of patients managed with a biventricular strategy in the CHSS study and 3% of our patients. Accordingly, many of the best candidates for biventricular repair will also be predicted to have the best survival after stage I palliation, further complicating the prospective application of the CHSS model.

How models are derived and applied depends in part on the valuation of alternative potential outcomes. In particular, in patients with critical AS and a borderline left heart, survival with a biventricular circulation might not be considered of equivalent “value” to survival with a functional SV circulation. If not, what degree of increased early phase risk is acceptable for the potential benefit of survival with a biventricular circulation, if any? These questions, difficult to answer at best, are complicated further by the lack of knowledge about the long-term implications of early management decisions. Regardless of early survival, many patients with critical AS and a biventricular circulation will require reintervention, and data on long-term outcomes are limited (2,18). In contrast, committing a patient to a functional SV circulation necessitates staged palliation and the attendant risks of second- and third-stage operations as well as many potential late complications.

Although the initial decision to undertake a biventricular or SV management strategy is likely critical in determining outcome, such decisions are not necessarily definitive, because patients might be successfully converted from a biventricular circulation to an SV circulation and vice versa. For example, 7 of our 14 patients who converted to an SV circulation after valvuloplasty survived, including all 5 since 1994. Similarly, there are patients with a borderline left heart in whom an initial stage I palliation can be converted to a biventricular circulation (19,20).

Various factors influence a patient’s chance of survival after valvuloplasty for critical AS, including anatomic, physiologic, procedural, and other management-related variables. We propose that the predictive models presented in this and our prior report (1) be used to guide the initial management of neonates with AS but not as definitive criteria. Physiologic indicators, such as retrograde flow in the ascending aorta and transverse arch, have also been associated with outcome in neonates with AS and should be considered in the formulation of management strategy (6), as should other clinical circumstances. It should also be noted that the predictive models published in our original report and this follow-up apply only to patients with AS. As several investigators have shown, our models tend to over-predict events when applied to left heart lesions other than critical AS (7–9). In particular, our scores are not suitable for predicting outcome in patients with COA and small left heart structures who do not have AS (8,9), although they can be applied in neonates with both AS and COA (11% of patients in our series).

There are several important limitations to this study. Patients were managed over a span of almost 20 years, during which time non-anatomic factors influencing outcome might have changed. Also, because only patients who underwent attempted biventricular management were included, our analysis is likely insensitive to important anatomic factors that are used to select patients for SV management. Specifically, MV area was a component of our original scoring systems but did not improve the accuracy of our updated discriminant model. One reason for this finding might be that some patients were managed with an SV strategy at the outset because their ability to survive with a biventricular circulation was limited by a small MV, thus precluding their inclusion in the analysis. Similarly, patients with severe LV hypoplasia were unlikely to be considered for biventricular repair and are not reflected in this analysis.

The management of neonatal AS is influenced by the evolving epidemiologic and clinical landscape of this disease. As reflected in our more recent experience, outcomes have improved substantially since the inception of balloon aortic valvuloplasty. In addition, patients with critical heart disease are increasingly diagnosed in utero, which might affect prenatal management, clinical status in the newborn period, and even outcome (21). Similarly, our early experience with in utero aortic valvuloplasty for fetal AS indicates that the natural history of left heart obstructive lesions might be altered (22), resulting in an anatomically and physiologically unique pattern of left heart hypoplasia. How our discriminant model stands up to these changes remains to be seen. Ultimately, our scoring systems are not intended to provide definitive management algorithms but rather an integrated picture of the capacity of the left heart complex to
support a systemic cardiac output in a biventricular circulation and to aid in the complex task of deciding on the initial treatment course in neonates with AS and borderline left heart hypoplasia.

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