Aortic Valvulotomy in Neonates

L. HENRY EDMUNDS, JR., M.D., HENRY R. WAGNER, M.D., AND MICHAEL A. HEYMANN, M.D.

SUMMARY Fourteen consecutive newborns, 1 month of age or younger (mean age 12 days; mean weight 3.5 kg), had aortic valvulotomy for critical life-threatening aortic stenosis. Seven infants died early and seven survived hospitalization. Clinical, laboratory, catheterization, operative and autopsy data were analyzed to determine factors relevant to success or failure.

Left ventricular chamber size and operability of the aortic valve and annulus were the most important determinants of outcome. All nonsurvivors except one had small left ventricles. All survivors had normal-sized ventricles and aortic annuli >5 mm. Left ventricular end-diastolic volumes (LVEDV) were calculated from cineangiograms in 10 infants. Six survivors and one nonsurvivor, who developed ventricular fibrillation before bypass, had LVEDV >35 ml/m². Three nonsurvivors had LVEDV <30 ml/m². Poor peripheral perfusion, severe acidosis (pH <7.25) and right ventricular hypertension (>60 torr) were significantly more common in nonsurvivors than in survivors. Seven nonsurvivors and only one survivor either required immediate operation or developed ventricular fibrillation during operation before bypass.

Two subgroups of newborns with isolated aortic stenosis are identified. Those with small left ventricular chambers represent an intermediate group between patients with "hypoplastic left-heart syndrome" and normals. Aortic valvulotomy did not save these infants. In contrast, seven of eight newborns with normal-sized left ventricles survived valvulotomy and six remain alive 1.5–6.5 years after operation.

NEWBORNS with symptomatic aortic stenosis require urgent or emergency valvulotomy, and mortality is higher than in older infants and children.1-7 Between 1973–1978, 36 children and infants older than 1 month have had operation at Children's Hospital of Philadelphia for valvar, supravalvar and subvalvar aortic stenosis, and all survived. Others also have reported low mortality.4-6 However, in newborns 1 month of age or younger, mortality was 29% and 71% in two series of seven patients each.4.6 This study was undertaken to determine factors that affect survival after aortic valvulotomy in newborns.

Methods

Between November 1970 and October 1977, 14 newborns up to 1 month of age had aortic valvulotomy consecutively by one surgeon. Five infants were operated at the Moffitt Hospital, San Francisco (University of California) and nine were operated at Children's Hospital of Philadelphia (University of Pennsylvania).

Patients with aortic atresia or associated mitral atresia, coarctation or interrupted aortic arch were excluded.

All patients had a preoperative cardiac catheterization. Cardiac output was estimated by the Fick method in 10 patients using an assumed value for oxygen consumption.10 Left ventricular angiograms were obtained retrogradely in two patients and via the mitral valve in eight. Left ventricular volumes were estimated in these 10 patients from right anterior oblique views11 or biplane posterolateral and lateral views.12 In two patients the left ventricle was not entered and in two others left ventricular angiograms were not obtained.

Cardiopulmonary bypass was planned in all patients, but could not be accomplished in two. Surface cooling to 30–32°C was used in three infants who were further cooled to 22–24°C during bypass. Moderate hypothermia to 30°C during bypass was used in nine patients. A variety of anesthetic agents was used; the most common agents were ketamine or nitrous oxide with a muscle relaxant. The valve was approached through a median sternotomy and an oblique incision in the ascending aorta. Valvulotomy was accomplished by incising stenosed commissures and occasionally by removing redundant obstructing tissue attached to thickened leaflets.

Seven infants survived hospitalization and were discharged. Six patients are alive 1.5–6 years later. One


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infant died of chronic heart failure 6 months after operation. Seven infants died early after operation. Six of these infants and the one who died late had autopsies.

For analysis, the seven hospital survivors were compared with the seven newborns who died during initial hospitalization. Variables in both groups were compared by chi-square analysis corrected for continuity.13

Results

Clinical Findings

Eleven infants were males and three were females. Ages at operation ranged from 1–34 days (mean 12 days). Weights ranged from 2.6–4.3 kg and averaged 3.5 kg. The smallest infant, a female weighing 2.6 kg, survived. Age and weight at surgery were comparable in survivors and nonsurvivors.

The clinical features of the two groups of infants are compared in table 1. All infants had systolic ejection murmurs over the left precordium; the murmurs usually extended toward the right upper sternal border. Eleven infants had signs of severe congestive heart failure and received digoxin before operation; two others, ages 1 and 4 days, had signs of early heart failure and one baby, age 33 days, was not in heart failure but had a gradient of 97 mm Hg across the aortic valve. These latter three infants did not receive digoxin preoperatively and survived. The presence of an ejection click and the absence of a right ventricular impulse, poor peripheral perfusion or severe acidosis were significantly more common in survivors than in nonsurvivors (table 1).

Laboratory Data

Chest roentgenograms showed moderate-to-marked cardiomegaly and pulmonary congestion in 11 infants with severe heart failure and mild cardiomegaly without congestion in the three newborns with clinically mild or no heart failure. The frontal QRS axes of the ECG varied from 0–120°. Left ventricular hypertrophy was present in the ECG of five survivors and two nonsurvivors. The pattern of left ventricular strain was found in four survivors and two nonsurvivors. Five nonsurvivors had R waves in V₆ of less than 5 mm and no q waves. Two survivors and four nonsurvivors had electrocardiographic evidence of right ventricular hypertrophy.

Hemoglobin varied between 7.9–18.2 g/dl and averaged 13 g/dl in each group. Arterial pH varied between 7.28–7.68 (mean 7.39) in survivors and between 6.95–7.41 (mean 7.20) before sodium bicarbonate was given in infants who died. Four nonsurvivors had an initial arterial pH below 7.25. Arterial Pco₂ was below 32 torr in seven infants and above 42 torr in two. Arterial Po₂ in room air varied widely, but only two infants, who did not survive, were hypoxemic (PaO₂ < 30 torr; Fio₂ 0.21).

Important cardiac catheterization findings are presented in table 2. Left ventricular systolic pressures ranged from 100–180 mm Hg and peak systolic pressure differences between left ventricle and ascending aorta ranged from 40–130 mm Hg. The average peak systolic gradient between the left ventricle and the ascending aorta was 79 mm Hg and equal in survivors and nonsurvivors. Right ventricular systolic pressure exceeded 60 mm Hg in two survivors and in all seven nonsurvivors (p < 0.03). Left atrial pressure exceeded 15 mm Hg in three survivors and in five nonsurvivors.

A patent ductus was demonstrated in eight infants; in two newborns, ductus shunting was right-to-left and both died. Two nonsurvivors had tricuspid insufficiency, isolated in one and associated with severe pulmonary valve stenosis in the other. Three infants had angiographic evidence of mild mitral regurgitation. Left-to-right shunting at the atrial level was present in nine infants.

Left ventricular end-diastolic volumes were estimated in six survivors and four nonsurvivors. Three nonsurvivors had estimated left ventricular volumes below 30 ml/m² body surface and three others appeared small in cineangiograms (fig. 1). In contrast, left ventricular cineangiograms appeared normal in all survivors and one nonsurvivor, and estimated left ventricular volumes were greater than 35 ml/m² (fig. 2, table 2). Left ventricular contractility and ejection fraction varied widely in both groups (table 2). Doming of the aortic valve was seen in the aortograms of five survivors but only two nonsurvivors (fig. 3). The size of the aortic annulus appeared normal in seven survivors and two nonsurvivors.

| Table 1. Clinical Observations in 14 Newborns with Symptomatic Aortic Valve Stenosis |
|----------------------------------------|----------|-----------------|
| Hospital                           | Survivors | Early deaths |
| Lethargy                           | 2         | 3               |
| Tachycardia (>150/min)              | 6         | 2               |
| Tachypneas (>50/min)                | 7         | 4               |
| Pulmonary rales                    | 2         | 2               |
| Hepatomegaly                       | 4         | 3               |
| Decreased peripheral pulses         | 7         | 6               |
| Hypertrophic left ventricular impulse | 2         | 2               |
| Gallop rhythm                      | 4         | 2               |
| Systolic ejection click             | 7         | 5               |
| Increased right ventricular impulse | 7 (p < 0.03) | 2               |
| Poor peripheral perfusion          | 7 (p < 0.03) | 2               |
| Severe acidosis (pH < 7.25)        | 4 (p < 0.1) | 0               |
| Severe heart failure               | 4         | 7               |
| Emergency operation                | 4         | 1               |
| Ventricular fibrillation before bypass | 4 (p < 0.1) | 0               |
Operative Events

Four of the seven nonsurvivors required emergency operation and one of these developed ventricular fibrillation before bypass. Only one survivor required emergency operation. Three other nonsurvivors also had ventricular fibrillation before repair—one during thoracotomy and three as the pericardium was opened. Three patients who developed ventricular fibrillation were anesthetized with ketamine and pancuronium. All had received digoxin. Nasopharyngeal temperature ranged from 32–35°C; two infants were acidotic before the arrhythmia occurred. Bypass could not be immediately started in two, and one of these patients had a normal-sized left ventricle.

Operation was carried out with cardiopulmonary bypass in 12 patients. Bypass time for the survivors ranged between 16–60 minutes (mean 32 minutes), with aortic cross-clamp times of 8–18 minutes (mean 13 minutes). In nonsurvivors, the aortic cross-clamp times ranged from 6–18 minutes (mean 13 minutes). Additional procedures were carried out in six patients: ligation of a patent ductus arteriosus in four, three of whom died; closure of an atrial septal defect in one patient who survived; and pulmonary valvotomy in one baby who died.

Four patients died in the operating room. Three patients, including one who did not have bypass, died 2–20 hours after operation.

Anatomic findings are summarized in table 3. Most of the stenotic valves were bicuspid, but one valve was unicusp with an additional subvalvar obstruction. In all survivors, but in only two nonsurvivors, both of whom required valvulotomy without cardiopulmonary bypass, the diameter of the aortic annulus was greater than 5 mm.

Hospital survivors were extubated 1–8 days after operation (mean 4 days). Discharge occurred 9–29 days after operation (mean 16 days). While three infants had smooth convalescences, four had temporary low cardiac output and required catecholamines. One developed renal failure and required peritoneal dialysis. An aortic diastolic murmur was heard in this patient after operation and the child died 6 months later.

Autopsy Data

Autopsy was performed in six patients who died early after operation. The left ventricular chamber was small and the left ventricular wall thickened in five. Three of the five patients with small left ventricles had additional severe endocardial fibroelastosis and deformed mitral valves (fig. 4). Cineangiograms showed the small, deformed mitral valves in two of these three patients. In two, fibrosis also involved the left atrium. One patient without fibroelastosis had a small ascending aorta and a small aortic annulus with microscopic calcifications. The fifth patient with a small left ventricle had a unicusp aortic valve with subvalvar obstruction. The only infant with an adequate-sized left ventricle (fig. 5) had small, probably inconsequential, foci of endocardial fibroelastosis of the left ventricle. The only nonsurvivor who was not autopsied had severe pulmonary valve stenosis and tricuspid insufficiency in addition to a small left ventricle and aortic annulus and severe stenosis of a bicuspid aortic valve.

One hospital survivor died of chronic heart failure at age 6 months. Recatheterization a few days before death showed residual or recurrent aortic stenosis (left ventricular-aortic systolic pressure difference 95 mm Hg) and insufficiency and slight mitral insufficiency. Autopsy showed moderate right ventricular hypertrophy and severe left ventricular hypertrophy with slight dilatation and endocardial fibroelastosis. The mitral valve was normal and the aortic annulus and left ventricular outflow tract were also normal. The aortic valve was bicuspid and severely dysplastic, with markedly thickened leaflets and large obstructing nodules on the ventricular surface of the valve.

Follow-up

Six patients remain alive 1.5–6.5 years (mean 3 years) after operation. All are asymptomatic and five take no medication. All have aortic systolic ejection murmurs and two have aortic diastolic murmurs. None have signs of heart failure and only one has slight cardiac enlargement by chest roentgenogram. The ECG is normal in two patients, shows mild left ventricular hypertrophy in three patients and more pronounced left ventricular hypertrophy in the sixth child. One child was recatheterized at age 15 months and was found to have a 25-mm Hg systolic pressure difference across the aortic valve, a normal left ventricular end-diastolic pressure and slight aortic insufficiency. From clinical data, only one child is considered to have moderate-to-severe residual aortic valvar disease.

Discussion

Patients with isolated aortic stenosis are easily differentiated from infants with aortic or mitral atresia, interrupted aortic arch or coarctation by catheterization and angiocraphic findings. While coarctation and valvar aortic stenosis frequently coexist, none of the newborns in this series also had coarctation. The term “hypoplastic left heart syndrome” is usually applied in newborns with tiny left ventricular chambers with either mitral or aortic atresia. Isolated aortic stenosis refers to a group of newborns in whom aortic stenosis is the predominant left-sided lesion. The term does not exclude additional right-sided lesions.

Analysis of this series defines two subgroups of aortic stenosis that can be separated on the basis of left ventricular size. One subgroup has normal left ventricular size and development. The second subgroup has small left ventricular chambers with or without hypoplastic mitral valves and endocardial fibroelasto-
### Table 2. Clinical, Laboratory, Roentgenographic and Anatomic Observations

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (days)</th>
<th>Severe heart failure</th>
<th>pH</th>
<th>Associated lesions</th>
<th>Left ventricle sys/dias (mm Hg)</th>
<th>Aortic sys/dias (mm Hg)</th>
<th>Lv-Ao pressure diff (mm Hg)</th>
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<tr>
<td>1</td>
<td>5</td>
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<td>7.28</td>
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<td>160/30</td>
<td>78/54</td>
<td>100</td>
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<td>18</td>
<td>Yes</td>
<td>7.39</td>
<td>1+ MR</td>
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<td>75/60</td>
<td>40</td>
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<td>3</td>
<td>4</td>
<td>Yes</td>
<td>7.68</td>
<td>None</td>
<td>125/20</td>
<td>65/50</td>
<td>60</td>
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<tr>
<td>4</td>
<td>33</td>
<td>No</td>
<td>7.30</td>
<td>None</td>
<td>166/1</td>
<td>69/45</td>
<td>97</td>
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<tr>
<td>5</td>
<td>30</td>
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<td>2+ MR</td>
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<td>130/5</td>
<td>65/50</td>
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<td>7.19</td>
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<td>110/26</td>
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<td>9</td>
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<td>7.34</td>
<td>PDA, 1+ TI</td>
<td>170/24</td>
<td>50/45</td>
<td>120</td>
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<tr>
<td>10</td>
<td>13</td>
<td>Yes</td>
<td>6.95</td>
<td>PDA, MS</td>
<td>—</td>
<td>75/55</td>
<td>—</td>
</tr>
<tr>
<td>11</td>
<td>19</td>
<td>Yes</td>
<td>—</td>
<td>PDA, MS</td>
<td>—</td>
<td>75/50</td>
<td>—</td>
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<td>45/30</td>
<td>50</td>
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<td>34</td>
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<td>59/45</td>
<td>95</td>
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<td>14</td>
<td>3</td>
<td>Yes</td>
<td>7.15</td>
<td>PS, TI, PDA</td>
<td>140/140</td>
<td>55/55</td>
<td>85</td>
</tr>
</tbody>
</table>

Patients 1–7 survived.

Abbreviations: LV = left ventricle; A = aortic; PDA = patent ductus arteriosus; MR = mitral regurgitation; MS = mitral stenosis; PS = pulmonary stenosis; TI = tricuspid insufficiency; sys = systolic; dias = diastolic.

**Figure 1.** End-diastolic frame of left ventricular angiogram in the posteroanterior view in case 14. Note the small, globular left ventricle and deformed, narrow aortic annulus.

**Figure 2.** End-diastolic frame of left ventricular angiogram in the posteroanterior view in case 5. The left ventricle has a normal shape and is slightly dilated. The aortic annulus is not narrowed.
s. This subgroup occupies an intermediate position between “the hypoplastic left-heart syndrome” and isolated aortic stenosis with normal ventricles.

The pathogenesis of left ventricular underdevelopment may be related to increased afterload during fetal life.9,10 Fishman et al. have shown that surgically produced aortic obstruction in late gestational fetal lambs causes hyperplasia of cardiac myocytes, increased left ventricular wall thickness and reduced left ventricular chamber volume.11 In fetal lambs, increased right ventricular inflow increases right ventricular growth.12 Lakier et al. have raised the possibility that subendocardial ischemia may cause endocardial fibrosis in newborns with aortic stenosis.9 High left ventricular pressures in young children with aortic stenosis leads to an increase in contractility and a decrease in left ventricular volume.16,17 Stewart et al., after analysis of left atrial pressure curves, concluded that impaired rates of left ventricular filling may be responsible for small left ventricular size in aortic stenosis.18 The reasons why both normal and hypoplastic left ventricles occur in association with isolated aortic stenosis are not known.

Left ventricular volumes can be measured by angiographic methods,11,12 but these measurements may be less accurate in small children and infants and in patients with abnormal orientation of the left ventricular cavity within the chest.19 In newborns and small infants, angiographic borders may be difficult to define and the applicability of standard formulas for volume measurements of small abnormal ventricles

### Table 3. Anatomic Features of the Left Ventricle, Aortic Valve and Annulus

<table>
<thead>
<tr>
<th></th>
<th>Hospital survivors</th>
<th>Early deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small left ventricle (angiogram)</td>
<td>0</td>
<td>6 (p &lt; 0.01)</td>
</tr>
<tr>
<td>Normal left ventricle (angiogram)</td>
<td>7</td>
<td>1 (p &lt; 0.01)</td>
</tr>
<tr>
<td>Calculated left ventricular volume &lt; 30 ml/m²</td>
<td>0/6</td>
<td>3/4 (p &lt; 0.1)</td>
</tr>
<tr>
<td>Aortic annulus (&lt; 5 mm)</td>
<td>0</td>
<td>5 (p &lt; 0.03)</td>
</tr>
<tr>
<td>Unicuspid aortic valve</td>
<td>0</td>
<td>1 (NS)</td>
</tr>
<tr>
<td>Bicuspid aortic valve</td>
<td>5</td>
<td>4 (NS)</td>
</tr>
<tr>
<td>Tricuspid aortic valve</td>
<td>2</td>
<td>2 (NS)</td>
</tr>
</tbody>
</table>
may be questioned. Nevertheless, Graham et al. measured left ventricular diastolic volumes in 19 infants under 2 years of age who did not have left ventricular disease, and found a mean value of $42 \pm 10 \text{ml/m}^2$. All survivors in the present series had estimated left ventricular diastolic volumes greater than 35 ml/m$^2$. Left ventricular diastolic volumes were less than 30 ml/m$^2$ in three of the four nonsurvivors in whom the measurement was made. While these data suggest that the two subgroups of neonatal, isolated aortic stenosis can be separated by angiographic measurements, the data are too few and the measurements too imprecise to define a numerical dividing line.

Left ventricular size and operability of the aortic valve as determined at operation were the most important determinants of outcome. With the exceptions of patent foramen ovale, atrial septal defect and patent ductus arteriosus, additional lesions were not common and did not directly affect outcome. All survivors had normal or nearly normal left ventricles and obstruction which could be relieved by operation. With one exception all nonsurvivors had small left ventricles with or without anatomic deformities of the aortic valve and annulus that could not be corrected (table 3). Aortic obstructions that could not be opened at operation were not encountered in patients with normal or nearly normal-sized left ventricles.

Some clinical observations correlate with early death. In general, these factors result from severe heart failure, unfavorable anatomy or both. Right ventricular hypertension, a surprising correlate, re-
reflects the severity of heart failure and degree of left-to-right shunting. All except one neonate with left atrial pressures >15 mm Hg had right ventricular hypertension, and only one infant with right ventricular hypertension did not have a high left atrial pressure.

Need for immediate operation or occurrence of ventricular fibrillation have ominous prognoses. Early operation before severe heart failure supervenes is recommended whenever possible. Furthermore, measures to avoid or reduce myocardial irritability must be taken during anesthesia and operation. The single nonsurvivor who had favorable anatomy developed ventricular fibrillation during thoracotomy and had operation without bypass.

The presence of adverse prognostic factors may deter therapeutic attempts, but two reasons argue against this conclusion. Minimal dimensions of left ventricular chamber size and aortic annular diameter necessary for survival are not known. Furthermore, growth characteristics of small left ventricles and aortic annuli are not known once the outflow tract obstruction has been partially relieved. Until more data are available we recommend aortic valvulotomy for all newborns with severe aortic stenosis regardless of left ventricular size and aortic anatomy.

Isolated aortic stenosis has been successfully treated by blind valvulotomy through the left ventricle, during inflow occlusion with or without the aid of hyperbaric oxygen and during cardiopulmonary bypass. Current bypass techniques in newborns add little morbidity. Furthermore, direct vision of the valve reduces the likelihood that the valve will be injured or that resectable obstructive nodules or subvalvular tissue will be overlooked. For these reasons we believe bypass offers the best means to obtain good early and late results in newborns with favorable anatomy. It is possible that other methods may be more suitable for some patients with unfavorable anatomy. Future reports of surgical results should include data regarding left ventricular chamber size and anatomic descriptions of the aortic valve and annulus.

Addendum

Since submission of this manuscript we have successfully operated on two newborns who did not have severe clinical heart failure but did have left ventricular-aortic pressure differences of 100 and 115 mm Hg and left ventricular end-diastolic pressures of 20 and 14 mm Hg. Anatomic features were favorable and right ventricular systolic pressures were less than 60 mm Hg. Left ventricular end-diastolic volumes were 33.5 and 37.5 ml/m².

Acknowledgment

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References

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