Severe Congenital Mitral Stenosis in Infants

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Background Despite current medical and surgical therapy, infants with symptomatic congenital mitral stenosis (CMS) continue to have high rates of morbidity and mortality. Catheter balloon dilation has been successful in relieving symptoms in a few older children with CMS but has not been evaluated in infants.

Methods and Results We reviewed the records of 85 infants with CMS to assess severity of CMS, associated cardiac lesions, echocardiographic morphological appearance of the mitral valve, treatment, and outcome. There were five valve morphologies identified: "typical" hypoplastic mitral valve with symmetric papillary muscles (SYMM, 52%), supravalvar mitral ring (SVMR, 20%), double-orifice mitral valve (DOMV, 11%), hypoplastic mitral valve with asymmetric papillary muscles (ASYMM, 8%), and parachute mitral valve (PARA, 8%). Of the 85 infants, 31 (36%) were severely symptomatic, requiring intervention within the first 2 years. Balloon dilation was performed in 18 infants (age, 8.7±5.7 months; weight, 5.9±1.9 kg) and valve surgery in 13 (age, 10.9±5.9 months; weight, 6.7±2.1 kg). Balloon dilation decreased the peak transmural gradient (LAa-LVED) >30% in 15 of 18 initial attempts, from 20.3±8.2 to 10.9±4.9 mm Hg (P<.001), and the mitral valve area increased from 0.7±0.3 to 1.0±0.5 cm²/m² (n=10, P=.01). No infants died during the initial balloon dilation, although 2 of 3 died during a repeat procedure for restenosis. Other complications included significant mitral regurgitation in 7 of 18 patients (39%), 4 of whom had SVMR. Of the 18 infants, 8 (44%) had persistent symptomatic improvement at a mean follow-up of 14 months (range, 2 to 32 months). The 2-year survival after balloon dilation was 70%; 40% remained free of repeat intervention. Mitral valve surgery in 13 infants consisted of SVMR resections in 7, mitral valve replacements in 4, and LA-to-LV aortic valved homografts in 2. The operative mortality was 30%. Sustained improvement occurred in 8 (6 with SVMR) at 11 to 62 months of follow-up (mean, 30 months), with a 2-year survival of 60%.

Conclusions Infants with severe CMS have 2-year mortality rates approaching 40% regardless of treatment modality. Balloon dilation significantly reduces the transmural gradient in the majority, but symptomatic improvement persists in only 40%. Procedure-related mortality was associated with repeat balloon dilation in patients with left ventricular hypoplasia. Balloon dilation of "typical" CMS can provide symptomatic relief in many infants, allowing postponement of valve replacement, although infants with SVMR do better with surgical management. (Circulation. 1994;89:2099-2106.)

Key Words • balloon • mitral valve • stenosis

Congenital mitral stenosis (CMS) is a very rare condition afflicting less than 4 out of 1000 infants with congenital heart disease.1 Disease severe enough to require intensive medical management or intervention during infancy is even more rare. Attempts to identify optimum management strategy are further hampered by the wide variety of anatomic type of CMS; procedures that succeed for stenotic supravalvar mitral rings may be inappropriate for parachute mitral valves. To date, analyses of various management approaches have been based on very small numbers of infants, and intensive medical management and surgical valve replacement both carry inordinately high risks when required in the first 2 years of life.2-4

The recent development of successful techniques to dilate rheumatic mitral stenosis in children5-7 prompted the extension of this technique to CMS8-10 with mixed but encouraging results.10,11 These reports and the improved results of complex open heart surgery in neonates and infants12 have resulted in the evaluation and treatment of 85 infants with CMS at our center within the last 6 years. The purpose of this report is to review the short- and intermediate-term results of treatment, with emphasis on surgical and balloon dilation management of infants with severe CMS.

Methods

Patients Between September 1987 and December 1992, 85 infants under age 2 years with CMS were diagnosed echocardiographically, excluding infants with hypoplastic left heart syndrome or atrioventricular canal defect. CMS was defined as ≥10 mm Hg peak instantaneous gradient as assessed by Doppler and or a small, abnormal-appearing mitral valve on two-dimensional echocardiogram. Due to the frequent association of atrial septal defect with CMS, transmitral gradient alone is too restrictive a criterion. These patients' medical records were reviewed to assess severity of CMS, associated cardiac lesions, echocardiographic morphological appearance of the mitral valve, treatment, and outcome. The decision for and type of treatment was solely at the discretion of the cardiologist and surgeon caring for each patient. During the first half of the study period, our institutional bias was to operate if severe growth failure or congestive heart failure was refractory to medical therapy. During the later half, balloon dilation was preferred unless significant mitral regurgitation was present.

Echocardiographic Evaluation We used parasternal and subxiphoid views to examine mitral valve morphology and associated cardiac defects. There were five valve morphologies identified in infants with CMS: (1)
"typical" symmetric hypoplastic mitral valve (SYM), defined as hypoplastic mitral valve and apparatus with short chordal attachments to small, symmetric, closely spaced papillary muscles, (2) supravalvar mitral ring (SVMR), defined as a stenotic membrane adherent to the atrial side of the mitral leaflets, (3) double-orifice mitral valve (DOMV), defined as two separate mitral valve orifices resulting from excessive valve leaflet tissue with normal chordae and papillary muscles, (4) asymmetric hypoplastic mitral valve (ASYMM), defined as hypoplastic mitral valve with short, unbalanced chordal attachments to either a predominant anterior lateral or posterior medial papillary muscle, and (5) parachute mitral valve, defined as a hypoplastic mitral valve with short chordal attachments to a single papillary muscle. Infants with SVMR were included in group 2 regardless of the morphology of the valve itself.

The maximum instantaneous and mean transmitral gradient was calculated using the Bernoulli equation with Doppler recordings of mitral inflow obtained from the apical four-chamber view. Using two-dimensional color-flow mapping from the apical and parasternal views, mitral regurgitation was graded on a scale of absent to severe, as previously described.  

Catheterization/Balloon Dilation

Informed consent was obtained before the procedure. An anesthesiologist anesthetized, paralyzed, intubated, and mechanically ventilated the patients during right and left heart cardiac catheterization, which was performed percutaneously using the femoral vein and artery. Anticoagulation with heparin (100 U/kg load) maintained an activated clotting time >200 seconds.

The technique for balloon dilation, described previously, was modified for use in infants. After measurement of cardiac index, direct transmural pressure gradient, and left ventricular angiogram to evaluate mitral regurgitation, a transatrial balloon end-hole catheter provided access to the left ventricle. A 0.035-in. or 0.038-in. stiff exchange wire (Medi-Tech Inc) was curved and placed in the left ventricular outflow tract or advanced to the descending aorta. In several infants, the guide wire had to be snared by a retrograde catheter in the descending aorta to provide enough traction to pull large balloons into these small left ventricles. The initial dilation balloon catheter (ACS, Medi-Tech Inc), chosen to be 1 to 3 mm smaller than the echocardiographically measured mitral annulus, followed the wire across the mitral valve. If transseptal puncture was required, we frequently needed to dilate the atrial septum with a 4- or 5-mm disposable balloon before balloon dilation.

The balloon was inflated by hand with dilute contrast until the "waist" disappeared or the balloon was maximally inflated. After each dilation, we measured the transmitral gradient and performed a left ventricular angiogram to assess mitral regurgitation. We repeated the procedure with progressively larger balloons until either the transmitral valve gradient decreased by >30%, the inflated balloon was 20% larger than the annulus diameter, or the degree of mitral regurgitation increased more than one grade.

Pressures are reported in millimeters of mercury except for pulmonary artery pressure, which is reported as percentage of simultaneously measured descending aortic pressure. Cardiac index was calculated using the Fick principal from measured hemoglobin concentration, oxygen saturation, and oxygen consumption. We used the formula of Gorlin and Gorlin\textsuperscript{13} to calculate the mitral valve area index.

Surgical Interventions

Surgical interventions consisted of supravalvar mitral ring resection under deep hypothermic circulatory arrest, prosthetic mitral valve replacement in the supra-annular position, and aortic homograft placed extracardiac between the left atrium and left ventricle.

Statistical Analysis

Data were reported as mean \pm SD. ANOVA is used to compare age, weight, and mean echo gradient of the three treatment groups. A paired \( t \) test was used to compare predilation and postdilation changes in the transmitral gradient, pulmonary artery and left ventricular end-diastolic pressures, cardiac index, and valve area. The Wilcoxon signed rank test was used to compare the change in mitral regurgitation before and after intervention. ANOVA was used to evaluate differences in the preintervention, postintervention, and follow-up peak and mean Doppler transmitral gradients. A life table was generated for survival and repeat intervention-free survival curves for the treatment groups.\textsuperscript{14}  

Results

Of the 85 infants, 31 (age, 9.6 \pm 5.8 months; weight, 7.2 \pm 6.5 kg) had severe stenosis defined as CMS causing growth failure <5th% and/or congestive heart failure refractory to medical management necessitating mitral valve surgery or balloon dilation within the first 2 years of life. The remaining 54 had CMS not requiring mitral valve surgery or balloon dilation. These infants were treated medically with or without surgery for associated cardiac lesions. Of the 31 infants who did require intervention on their mitral valve, 18 had balloon dilation and 13 had surgery. Mitral valve surgery consisted of SVMR resection in 7, mitral valve replacement (MVR) in 4, and left atrium–to–left ventricle (LA-to-LV) valved homografts in 2 (Fig 1). Our initial experience with balloon dilation in 5 of the 18 infants dilated has been described previously.\textsuperscript{10}  

Medical Treatment

Characteristics of infants with CMS, including those treated medically, are listed in Table 1. Infants treated medically were younger (ANOVA, \( P=.015 \)) and had a lower mean transmitral gradient (ANOVA, \( P=.001 \)) than infants who had intervention. Despite their younger age, their weight was similar to the others, suggesting less severe growth failure. Valve morphology was SYMM in 60%; the remainder were divided equally among the other morphological types. Only 3 infants had significant regurgitation associated with their CMS; all 3 had SYMM valve morphology. Associated cardiac lesions were similar in all groups, except the medical
**TABLE 1.** Characteristics of Infants With Congenital Mitral Stenosis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All</th>
<th>Medical</th>
<th>BD</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>85</td>
<td>54</td>
<td>18</td>
<td>13</td>
</tr>
<tr>
<td>Age, mo</td>
<td>7.1±6.4</td>
<td>5.7±6.4</td>
<td>8.7±5.7</td>
<td>10.9±5.9</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>5.6±2.3</td>
<td>5.2±2.5</td>
<td>5.9±1.9</td>
<td>6.7±2.1</td>
</tr>
<tr>
<td>Mean echo gradient, mm Hg</td>
<td>7.4±5.6</td>
<td>4.0±3.9</td>
<td>11.1±4.5</td>
<td>11.0±5.3</td>
</tr>
<tr>
<td>No. with moderate to severe MR</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CMS type, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SYMM</td>
<td>52</td>
<td>60</td>
<td>50</td>
<td>23</td>
</tr>
<tr>
<td>SVMR</td>
<td>20</td>
<td>9</td>
<td>22</td>
<td>61</td>
</tr>
<tr>
<td>DOMV</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>PARA</td>
<td>9</td>
<td>11</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>ASYMM</td>
<td>8</td>
<td>9</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>% With</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subaortic/valvar AS</td>
<td>55</td>
<td>44</td>
<td>78</td>
<td>69</td>
</tr>
<tr>
<td>Coarctation</td>
<td>39</td>
<td>42</td>
<td>33</td>
<td>31</td>
</tr>
<tr>
<td>VSD</td>
<td>33</td>
<td>33</td>
<td>33</td>
<td>31</td>
</tr>
<tr>
<td>PDA</td>
<td>25</td>
<td>26</td>
<td>22</td>
<td>23</td>
</tr>
<tr>
<td>ASD</td>
<td>25</td>
<td>30</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>DORV</td>
<td>18</td>
<td>22</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Small LV</td>
<td>18</td>
<td>20</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>TOF</td>
<td>6</td>
<td>7</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>No associated defect</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

BD indicates balloon dilation; MR, mitral regurgitation; CMS, congenital mitral stenosis; SYMM, typical hypoplastic symmetric mitral valve; SVMR, supravalvar mitral ring; DOMV, double-orifice mitral valve; PARA, small mitral valve with single papillary muscle; ASYM, asymmetric small mitral valve with a predominating papillary muscle; AS, aortic stenosis; VSD, ventricular septal defect; PDA, patent ductus arteriosus; ASD, atrial septal defect; DORV, double-outlet right ventricle; Small LV, <5th% for indexed echocardiographic chamber dimensions; and TOF, Fallot’s tetralogy.

The average hospital stay for the balloon dilation group was 12 days (range, 3 to 38). In 8 of the 18 infants (44%), including patients 14 and 18, who had minimal immediate reduction in transmitral gradient, sustained clinical improvement resulted, requiring reduced medical therapy to control symptoms of congestive heart failure. A successful dilation was accomplished in 15 patients with >30% decrease in left ventricular A wave–left ventricular end-diastolic pressure gradient (20.3±8.2 to 10.9±4.9 mm Hg, P<.01) (Fig 2), whereas in 2 (patients 9 and 14), only a 13% decrease resulted, without any decrease being evident in the remaining patient (patient 18). Of note, the average balloon–mitral valve annulus ratio was 0.9 in the failed dilations, identical to the average balloon size for the group as a whole. Table 2 lists the hemodynamic and Doppler measurements before and after balloon dilation. Balloon dilation increased the mitral valve area and decreased the transmitral gradient and pulmonary artery pressure without changing the cardiac index or left ventricular end-diastolic pressure. In the majority of infants after balloon dilation, the residual mitral stenosis was mild to moderate.
failure after dilation (mean follow-up, 16.1 months; range, 1 to 44) (Table 3). All eight patients manifested improved weight gain (mean percentile for weight: before, 3.0±2.2 versus 14.6±19.6 after; \( P = .16 \)). The follow-up mean Doppler transmural gradient, available in six of the eight patients, showed a persistent decrease from the predilation gradient in three and a return to the predilation value in the other three. Follow-up catheterization transmural gradient, available in three infants, showed a persistent decrease from predilation gradient in one at 17 months after balloon dilation and a return to predilation value in the others at 23 and 44 months after balloon dilation.

The remaining 10 infants had persistence or recurrence of stenosis resulting in death or the need for mitral valve replacement. The predicted survival for the infants dilated was 70\% at 24 months (Fig 3). Death related to sepsis and progressive congestive heart failure occurred in two infants within 3 months of balloon dilation. Severe tricuspid stenosis and right heart failure were evident in one and significant aortic stenosis and coarctation in the other. A repeat balloon dilation for recurrence of stenosis within 4 months of initial balloon dilation was undertaken in three infants, two of whom died within 24 hours related to complications associated with inflation of a large dilation balloon in a small left ventricle. The causes of death were left ventricular perforation and cardiac tamponade in one infant and sustained bradycardia/cardiac arrest in the other. In the third patient, a successful redilation was accomplished, and persistent clinical improvement was evident at 17 months' follow-up.

MVR was necessary in five infants within 2 months of the balloon dilation for persistent symptoms of CMS and/or iatrogenic mitral regurgitation; four of these five had associated SVMR. In another (patient 9), MVR was required 10 months after balloon dilation because of persistent mitral stenosis with progressive mitral regurgitation. Of the 6 patients who had MVR, three (patients 8, 12, and 13) were alive and asymptomatic at follow-up (10, 25, and 27 months); another (patient 9) had progressive congestive heart failure with systemic pulmonary hypertension and underwent heart/lung transplant at 20 months' follow-up; another (patient 10) died at the time of repeat MVR 2.5 years after initial replacement, and the other (patient 11) died 2 months after MVR as a result of persistent pulmonary hypertension and right ventricular failure.

Complications of Balloon Dilation

Transient hemodynamic instability, including major bradycardia and hypotension, occurred in all infants. Immediate moderate or severe mitral regurgitation appeared in 22\%, with late progression to moderate mitral regurgitation occurring in 17\%. Immediate mild regurgitation occurred in 28\%, with late progression to moderate regurgitation in one patient. In three patients (one severe, one moderate, one mild progressing to moderate regurgitation) echocardiographic evidence of a torn or flail leaflet after balloon dilation was evident. Transient second- and third-degree heart block occurred in 22\% and venous thrombosis and cardiac arrest requiring inotropic support in 6\% each.
### Table 2. Predilation and Postdilatation Hemodynamics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Before</th>
<th>After</th>
<th>% Change</th>
<th>Before</th>
<th>After</th>
<th>% Change</th>
<th>Valve Area, cm²/m²</th>
<th>PAP, % Systemic</th>
<th>B/A Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>7</td>
<td>42</td>
<td>16</td>
<td>3</td>
<td>81</td>
<td>0.61±0.94</td>
<td>0.32</td>
<td>0.70</td>
</tr>
<tr>
<td>2</td>
<td>18</td>
<td>7</td>
<td>50</td>
<td>16</td>
<td>5</td>
<td>56</td>
<td>0.28±0.32</td>
<td>0.47</td>
<td>0.49</td>
</tr>
<tr>
<td>3</td>
<td>38</td>
<td>14</td>
<td>63</td>
<td>16</td>
<td>11</td>
<td>25</td>
<td>0.89±0.69</td>
<td>0.89</td>
<td>1.00</td>
</tr>
<tr>
<td>4</td>
<td>17</td>
<td>12</td>
<td>29</td>
<td>9</td>
<td></td>
<td></td>
<td>0.34±0.04</td>
<td></td>
<td>1.09</td>
</tr>
<tr>
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<td>20</td>
<td>11</td>
<td>45</td>
<td>11</td>
<td>6</td>
<td>45</td>
<td>0.86±1.56</td>
<td>0.44</td>
<td>0.80</td>
</tr>
<tr>
<td>6</td>
<td>24</td>
<td>14</td>
<td>42</td>
<td>5</td>
<td>10</td>
<td>-100</td>
<td>1.20±1.50</td>
<td>0.83</td>
<td>0.88</td>
</tr>
<tr>
<td>7</td>
<td>15</td>
<td>8</td>
<td>47</td>
<td>12</td>
<td>6</td>
<td>50</td>
<td>1.00±0.66</td>
<td>0.78</td>
<td>0.79</td>
</tr>
<tr>
<td>8</td>
<td>20</td>
<td>4</td>
<td>80</td>
<td>6</td>
<td>4</td>
<td>33</td>
<td>0.70±1.35</td>
<td>0.78</td>
<td>1.00</td>
</tr>
<tr>
<td>9</td>
<td>16</td>
<td>14</td>
<td>13</td>
<td>16</td>
<td></td>
<td></td>
<td>0.98±0.88</td>
<td>0.40</td>
<td>0.83</td>
</tr>
<tr>
<td>10</td>
<td>21</td>
<td>11</td>
<td>48</td>
<td>6</td>
<td>8</td>
<td>30</td>
<td>0.80±1.60</td>
<td>0.59</td>
<td>0.31</td>
</tr>
<tr>
<td>11</td>
<td>18</td>
<td>12</td>
<td>33</td>
<td>13</td>
<td>22</td>
<td>-69</td>
<td>0.85±0.65</td>
<td>0.75</td>
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</tr>
<tr>
<td>12</td>
<td>21</td>
<td>12</td>
<td>43</td>
<td>16</td>
<td>10</td>
<td>38</td>
<td>0.90±0.88</td>
<td>0.51</td>
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</tr>
<tr>
<td>13</td>
<td>16</td>
<td>8</td>
<td>50</td>
<td>15</td>
<td>10</td>
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<td>1.00±0.75</td>
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</tr>
<tr>
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<td>16</td>
<td>14</td>
<td>13</td>
<td>3</td>
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<td>-100</td>
<td>0.56±0.49</td>
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</tr>
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<td>15</td>
<td>18</td>
<td>8</td>
<td>89</td>
<td>11</td>
<td>5</td>
<td>55</td>
<td>0.53±0.33</td>
<td>0.69</td>
<td>0.61</td>
</tr>
<tr>
<td>16</td>
<td>20</td>
<td>6</td>
<td>70</td>
<td>10</td>
<td>8</td>
<td>20</td>
<td>0.41±0.48</td>
<td>0.77</td>
<td>0.86</td>
</tr>
<tr>
<td>17</td>
<td>44</td>
<td>18</td>
<td>59</td>
<td>16</td>
<td>9</td>
<td>44</td>
<td>0.70±1.00</td>
<td>0.77</td>
<td>0.58</td>
</tr>
<tr>
<td>18</td>
<td>12</td>
<td>22</td>
<td>-14</td>
<td>10</td>
<td></td>
<td></td>
<td>0.57±0.49</td>
<td>0.41</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Mean±SD 20.3±8.2 10.9±4.9 44.5±24.7 11.5±4.4 8.2±4.5 17.4±57.4 0.7±0.26 1.0±0.48 0.68±0.25 0.63±0.24 0.9±0.18

P (t test) <.01 .042 .013 <.01

LAA indicates left atrial A wave; LVED, left ventricular end-diastolic pressure; PAP, pulmonary artery pressure; and B/A ratio, balloon-to-annulus ratio.

### Surgery

A total of 13 infants underwent surgery for mitral stenosis. Of these, 8 had resection of their SVMR, after which 2 developed significant regurgitation requiring MVR in the supra-annular position with a No. 16 Carbomedics valve. In 3 other infants (patients 20, 21, and 31), MVR in the supra-annular position was performed, and 2 others had an 11-mm valved aortic homograft placed between the left atrium and left ventricle (Table 4).

### Follow-up After Surgery

The average hospital stay in this group was 21 days (range, 7 to 82). Of the 13 infants, 8 (6 of whom had SVMR) had clinical improvement 11 to 62 months (mean, 30 months) after surgery. Of these 8, 1 (patient 19) developed prosthetic valve stenosis 44 months after surgery and died during repeat MVR. In the 5 with echo follow-up, the mean transmirtal gradient was 6 mm Hg.

There were five deaths in this group, with an operative mortality of 30% and 2-year survival of 55% (Fig 3). Of these, two occurred early during MVR (one with SVMR resection during the same procedure). There were three late deaths; two infants died of progressive congestive heart failure 1 and 5 months after surgery (LA-to-LV homograft in one and MVR in the other) and the other infant died suddenly 1 month after SVMR resection. Although not statistically significant, both operative (SVMR, 75% versus non-SVMR, 60%) and 2-year survival (SVMR, 75% versus non-SVMR, 40%) appear better for infants with SVMR than those with other anatomic forms of CMS.

### Complications of Surgery

Both patients who had LA-to-LV aortic homografts placed required repeat operation within 2 weeks, one for aneurysmal dilation of the original homograft and the other for homograft stenosis associated with mediastinitis. One infant developed severe mitral regurgitation 1 week after SVMR resection and required MVR. Another infant developed third-degree heart block during MVR, requiring permanent pacemaker placement. The infant with SVMR who died suddenly at home required medical treatment for significant postoperative supraventricular tachycardia, which presumably contributed to his sudden death.

### Discussion

Clearly, infants with symptomatic CMS pose a formidable therapeutic challenge. Because CMS is rare, it is difficult to generate an adequate number of patients for accurate analysis. Successful management is dependent both on anatomy and on accurate preoperative definition of the anatomic substrate. The results of intervention, that is, surgery and balloon dilation, are likely to be significantly operator dependent; therefore, results from one center may not be applicable to all other centers. For these reasons, analysis of a large series of severely
affected infants with CMS from a single center may provide important insight into management strategies.

Using echocardiography, we identified five distinct anatomic types of mitral valve abnormalities in infants with CMS. Of interest, all of the infants with SVMR in this series had associated abnormalities of the mitral apparatus, most commonly SYMM, although the asymmetric variant and parachute mitral valves did occur in some. Despite marked variability of severity within each anatomic type, infants with SVMR had a significantly higher mean Doppler transmural gradient than infants with other anatomic types. Infants with ASYMMP and parachute mitral valve had the least severe stenosis, as evidenced by the lowest mean Doppler transmural gradient. These findings are consistent with those of Ruckman et al., who showed in an autopsy series that the asymmetric variant of CMS may be a form of parachute mitral valve and is associated with the longest longevity of any anatomic type.

Significant mitral regurgitation occurred in <4% of infants with CMS and only in those with symmetric hypoplastic mitral valve. Only 3 of the 85 infants had isolated CMS, two with SYMM and the other with the asymmetric variant. Despite the strong association of left-sided obstructive lesions, subaortic stenosis and valvar aortic stenosis and coarctation, with CMS, the DOMV variant was more frequently associated with ventricular septal defect and atrial septal defect. In addition, parachute mitral valve was associated with Fallot's tetralogy and ASYMMP with DORV.

Management: Medicine

Severity of mitral stenosis and associated cardiac lesions are major determinants of treatment and eventual outcome. Among our infants with CMS, 60% had less severe stenosis requiring only medical management. Despite less severe mitral stenosis, 30% died in infancy as a result of associated cardiac lesions. Nearly 70% of the surviving infants have had follow-up Doppler evaluation of their transmural gradient, with no evidence of progression of their stenosis. Because of the variability of timing of diagnosis and the large number of patients

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**TABLE 3. Characteristics of Dilated Patients**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, mo</th>
<th>Weight, kg (%)</th>
<th>MV Morphology</th>
<th>Associated Cardiac Lesions</th>
<th>Follow-up, mo</th>
<th>Outcome</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>4.3 (50)</td>
<td>SYMM</td>
<td>AS, sub AS</td>
<td>23</td>
<td>Improved</td>
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</tr>
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<td>2</td>
<td>4</td>
<td>4.7 (5)</td>
<td>SYMM</td>
<td>sub AS, hypo LV</td>
<td>44</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>4.5 (&lt;5)</td>
<td>SYMM</td>
<td>PDA, sub AS, VSDs</td>
<td>17</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>4.8 (&lt;5)</td>
<td>SYMM</td>
<td>AS</td>
<td>3</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>6.0 (&lt;5)</td>
<td>SYMM</td>
<td>AS, ASD</td>
<td>4</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>14</td>
<td>8.3 (5)</td>
<td>SYMM</td>
<td>coarc, sub AS, VSD</td>
<td>25</td>
<td>Improved</td>
<td>MVR (1 wk)</td>
</tr>
<tr>
<td>7</td>
<td>18</td>
<td>9.6 (5)</td>
<td>SYMM</td>
<td>coarc, AS, PDA</td>
<td>3</td>
<td>Died, CHF/sep</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td>3.9 (10)</td>
<td>SYMM</td>
<td>sub AS, VSD, ASD</td>
<td>10</td>
<td>Improved</td>
<td>MVR (10 mo)</td>
</tr>
<tr>
<td>9</td>
<td>11</td>
<td>7.9 (&lt;5)</td>
<td>SYMM</td>
<td>AS, sub AS</td>
<td>20</td>
<td>Heart/lung trans</td>
<td>MVR (1 mo)</td>
</tr>
<tr>
<td>10</td>
<td>7</td>
<td>4.8 (&lt;5)</td>
<td>SVMR</td>
<td>DAA, coarc, AS, sub AS, hypo LV, VSD, PDA</td>
<td>30</td>
<td>Died at reMVR</td>
<td>MVR (1 mo)</td>
</tr>
<tr>
<td>11</td>
<td>8</td>
<td>5.6 (&lt;5)</td>
<td>SVMR</td>
<td>sub AS, PDA</td>
<td>2</td>
<td>Died</td>
<td>MVR (1 wk)</td>
</tr>
<tr>
<td>12</td>
<td>17</td>
<td>6.8 (&lt;5)</td>
<td>SVMR</td>
<td>VSD</td>
<td>37</td>
<td>Improved</td>
<td>MVR (2 mo)</td>
</tr>
<tr>
<td>13</td>
<td>19</td>
<td>8.4 (&lt;5)</td>
<td>SVMR</td>
<td>coarc, AS</td>
<td>29</td>
<td>Improved</td>
<td>MVR (1 wk)</td>
</tr>
<tr>
<td>14</td>
<td>2</td>
<td>3.6 (5)</td>
<td>DOMV</td>
<td>coarc, hypo LV, VSDs, ASD</td>
<td>23</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>4</td>
<td>3.3 (&lt;5)</td>
<td>DOMV</td>
<td>TS</td>
<td>3</td>
<td>Died, CHF/sep</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>13</td>
<td>7.1 (&lt;5)</td>
<td>PARA</td>
<td>coarc, AS, sub AS</td>
<td>4</td>
<td>Died, reedilation</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>4</td>
<td>4.5 (&lt;5)</td>
<td>ASYMMP</td>
<td>sub AS, hypo LV</td>
<td>2</td>
<td>Died</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>12</td>
<td>8.2 (&lt;5)</td>
<td>ASYMMP</td>
<td>DORV</td>
<td>1</td>
<td>Improved</td>
<td></td>
</tr>
</tbody>
</table>

MV indicates mitral valve; SYMM, typical symmetric hypoplastic mitral valve; trans, transplant; SVMR, supravalvar mitral ring; DOMV, double-orifice mitral valve; PARA, parachute mitral valve; ASYMMP, small mitral valve with predominant anterior leaflet or posterior medial papillary muscle; AS, aortic stenosis; LV, left ventricle; PDA, patent ductus arteriosus; VSD, ventricular septal defect; ASD, secundum atrial septal defect; coarc, coarctation; DAA, double aortic arch; TS, tricuspid stenosis; DORV, double-outlet right ventricle; CHF/sep, congestive heart failure with sepsis; and reMVR, repeat mitral valve replacement.
lost to follow-up in this group, we cannot develop an accurate survival curve for infants with CMS treated medically. However, our data suggest that many infants with CMS have mild stenosis that does not progress and responds favorably to medical management.

Management: Balloon Dilation

The management of infants with uncomplicated mild CMS is medical. Uncertainty arises when medical management fails in infants with severe CMS. Choices have been limited to accepting failed medical treatment or attempting surgical repair, most frequently MVR, which has a 30% to 60% operative mortality in children under 5 years and is presumably higher in infants. A recent alternative to surgical management is balloon dilation. In our series, 58% of symptomatic infants requiring immediate intervention for failure of medical therapy had balloon dilation as their initial therapy. These infants tended to be younger and smaller, with more severe growth failure than the infants who had valve surgery as their initial intervention. Balloon dilation of the mitral valve significantly decreased the transmural gradient, resulting in mild to moderate residual stenosis in most infants. Although restenosis after balloon dilation was common, symptomatic improvement persisted in 40%. Procedural mortality, absent at initial dilation, was associated with repeat dilation with large balloons in two infants with small left ventricles. Significant mitral regurgitation occurred in 39% of infants and necessitated MVR in 30%, particularly those with SVMR.

Even though dilation of infants with CMS is immediately effective in most, there is frequent inadequate persistent gradient relief or restenosis. The only infant reported by Grifka et al had immediate transmural gradient relief from balloon dilation but within 1 year required repeat balloon dilation and died at mitral valve surgery. Of the 18 infants in our series, 3 had repeat balloon dilation, with only 1 being successful. The etiology of the inadequate persistent gradient relief or restenosis is unclear. It may reflect fusion and/or scarring of torn mitral valve leaflets or simply stretching of the valve components by dilation, which causes an immediate reduction in transmural gradient but no long-term increase in mitral valve orifice size.

Predictors of successful dilation with persistent relief of symptoms remain unclear. Associated cardiac lesions, balloon-to-anulus ratio, and catheter- or Doppler-derived transmural gradients were not useful predictors. However, several important observations regarding mitral valve morphology and successful dilation can be made. First, all infants with SVMR developed significant regurgitation after dilation, necessitating MVR. Second, two of the three patients with ASSYM or parachute mitral valves developed restenosis, and the third had minimal gradient relief. Third, moderate regurgitation after balloon dilation did not necessarily indicate the need for MVR; however, echocardiographic evidence of a torn mitral leaflet did.

Management: Surgery

Our series suggests that the surgical mortality for CMS in infants under 2 years is 30%. Although the 2-year survival was 55%, repeat operation within 1 month was necessary in 30% of infants because of significant complications. Despite improved operative mortality, late morbidity continues to limit the success of surgical management in this disease. Not surprisingly, mitral valve morphology has a significant effect on surgical success. Infants with SVMR had lower operative mortality (25%) and a 2-year survival rate of 75%. All four infants with initial dilation of their SVMR

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**TABLE 4. Characteristics of Operated Patients**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, mo</th>
<th>Weight, kg (%)</th>
<th>MV Morphology</th>
<th>Associated Cardiac Lesions</th>
<th>Intervention</th>
<th>Follow-up, mo</th>
<th>Outcome</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>12</td>
<td>5.9 (&lt;5)</td>
<td>SYMM, none</td>
<td></td>
<td>homo</td>
<td>44</td>
<td>Died at MVR</td>
<td>Homo replacement (1 wk)</td>
</tr>
<tr>
<td>20</td>
<td>20</td>
<td>8.6 (&lt;5)</td>
<td>SYMM, coar, AS, VSD</td>
<td></td>
<td>MVR</td>
<td>5</td>
<td>Died, CHF</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>4</td>
<td>3.6 (&lt;5)</td>
<td>SYMM, AS, sub AS</td>
<td></td>
<td>MVR</td>
<td>0</td>
<td>Died</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>19</td>
<td>9.3 (&lt;5)</td>
<td>SVMR, coar, AS</td>
<td></td>
<td>SVMR res</td>
<td>25</td>
<td>Improved</td>
<td>MVR (1 wk)</td>
</tr>
<tr>
<td>23</td>
<td>10</td>
<td>6.6 (&lt;5)</td>
<td>SVMR, sub AS, coar, PDA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>9</td>
<td>7.5 (8)</td>
<td>SVMR, coar, VSD</td>
<td>ME</td>
<td>SVMR res</td>
<td>1</td>
<td>Died</td>
<td>SVT postop</td>
</tr>
<tr>
<td>25</td>
<td>7</td>
<td>7.6 (25)</td>
<td>SVMR, DORV, sub AS</td>
<td></td>
<td>SVMR res</td>
<td>47</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>26</td>
<td>16</td>
<td>6.5 (&lt;5)</td>
<td>SVMR, TOF, DAA</td>
<td></td>
<td>SVMR res</td>
<td>36</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>27</td>
<td>19</td>
<td>10.9 (25)</td>
<td>SVMR, DORV, sub AS</td>
<td></td>
<td>SVMR res</td>
<td>18</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>28</td>
<td>4</td>
<td>4.1 (&lt;5)</td>
<td>SVMR, VSD, sub AS</td>
<td>ME</td>
<td>SVMR res</td>
<td>11</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>10</td>
<td>6.0 (&lt;5)</td>
<td>SVMR, sub AS, PDA</td>
<td></td>
<td>SVMR res</td>
<td>62</td>
<td>Improved</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>5</td>
<td>5.0 (&lt;5)</td>
<td>DOMV, sub AS, hypo aorta, PDA, ASD</td>
<td>homo</td>
<td>13</td>
<td>Improved</td>
<td>HB, pacer (2 wk)</td>
<td></td>
</tr>
</tbody>
</table>

MV indicates mitral valve; SYMM, typical small symmetric mitral valve; SVMR res, supra valvar mitral ring resection; DOMV, double-orifice mitral valve; PARA, parachute mitral valve; ASSYM, asymmetric; AS, aortic stenosis; VSD, ventricular septal defect; PDA, patent ductus arteriosus; DORV, double-outlet right ventricle; TOF, Fallot's tetralogy; DAA, double aortic arch; ASD, secundum atrial septal defect; homo, LA-to-LV aortic homograft placement; MVR, mitral valve replacement; SVT, supraventricular tachycardia; and HB, complete heart block.
required MVR within 2 months, whereas only two of eight infants who had surgery for SVMR required MVR. Surgical repair, with MVR if necessary, is the treatment of choice for this subset of infants.

**Resource Utilization**

Our infants with CMS requiring intervention on their mitral valve averaged four echocardiograms, two catheterizations, two hospitalizations, and one surgery. In general, balloon dilation was associated with shorter hospital stays (12±11 versus 21±24 days) than mitral valve surgery. These infants required extensive medical resources, although improved patient assignment to either balloon dilation or surgery may have reduced costs.

**Study Limitations**

First, all except three infants in this study had hemodynamically significant associated cardiac defects, and over 60% had surgical or catheter interventions on those associated defects, some temporally related to their mitral valve intervention. Associated defects and their treatment confound the effects of mitral valve intervention; however, isolated CMS is too rare to accurately study. Despite this, it is precisely those infants with associated defects for whom we need to develop an effective management strategy. A second study limitation is that mean Doppler transmural gradients correlated only marginally well with both direct catheter measurements and symptomatic improvement. Mean transmural Doppler gradient increased after balloon dilation in two infants who had >30% reduction in directly measured transmural gradient and symptomatic improvement. This may be due to technical difficulties of accessing gradients in patients with associated defects and complex areas of obstruction. In addition, nonsimultaneous measurements without corrections for variations in heart rate, stroke volume, end-diastolic pressure, and contractility affect accuracy. This makes Doppler a suboptimal method of determining the severity of CMS and for evaluating long-term response to therapy; however, it is the only noninvasive quantitative tool available.

**Conclusions**

Intervention on the mitral valve is required in many infants with CMS because of failure of medical management (36% in our series). Improvements in surgical technique have reduced the operative mortality of mitral valve surgery in infants to 30%, although ongoing morbidity and mortality continue to limit the usefulness of surgical management. Balloon dilation of infants with CMS can be performed with acceptable morbidity and mortality. Balloon dilation results in immediate reduction in the transmural gradient in the majority, with persistent symptomatic improvement and gradient reduction in up to 40%. Restenosis and severe progressive regurgitation (39%) are common. Their onset may be influenced by mitral valve morphology: Restenosis is common in infants with asymmetric or parachute mitral valve (two of three), and regurgitation is common in infants with SVMR (four of four). Redilation with larger balloons after early restenosis may be associated with an increased mortality, especially in infants with left ventricular hypoplasia and asymmetric or parachute mitral valve. Because the risks of mitral valve dilation are relatively low and significant benefit occurs in many infants without SVMR, mitral valve dilation before MVR appears to be warranted in infants with symptomatic CMS if not associated with SVMR. Although results of operative management of SVMR are limited by associated valve abnormalities, initial surgical inspection and preferably valve repair or, if necessary, replacement, is the procedure of choice in this subset of infants. Accurate pretreatment anatomic definition by echocardiography and catheterization is therefore essential.

**References**

Severe congenital mitral stenosis in infants.
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