Independent Factors Associated With Outcomes of Parachute Mitral Valve in 84 Patients

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Background—Parachute mitral valve (PMV) is defined as a unifocal attachment of the mitral valve chordae to a single or dominant papillary muscle and may cause subvalvar obstruction. We sought to determine factors associated with outcomes.

Methods and Results—Patients (n=84; 64% male) who presented between 1977 and 2001 at a median age of 3 days (range, birth to 5.4 years) were assessed with PMV (without atrioventricular septal defect). Associated cardiac anomalies in 99% included aortic coarctation in 68%, atrial septal defect in 54%, ventricular septal defect in 46%, aortic valve stenosis in 32%, subaortic stenosis in 20%, and left ventricular hypoplasia in 19%, with complex anomalies in 14%. Noncardiac anomalies were noted in 32%. Survival (n=18 deaths) was 82% at 1 year and 79% at 10 years, with independent risk factors including left ventricular hypoplasia (P<0.001) and atrial septal defect (P<0.003). Freedom from surgical mitral valvotomy (n=11 patients) was 95% at age 6 months and 80% at 10 years, with independent risk factors including the absence of aortic coarctation (P<0.02) and the presence of subaortic stenosis (P<0.04). There was no significant increase in mean gradient of the PMV over time, but higher gradient was independently associated with the presence of supravalvar mitral stenosis (P<0.001), absence of atrial septal defect (P<0.04), presence of ventricular septal defect (P<0.02), and subsequent mitral valvotomy (P<0.01).

Conclusions—Outcomes for patients with PMV are dependent on the spectrum of associated cardiac lesions. The degree of mitral valve obstruction remains stable, and the majority will not require valvotomy. (Circulation. 2004;109:2309-2313.)

Key Words: mitral valve  ■  stenosis  ■  heart defects, congenital  ■  pediatrics  ■  prognosis

The prognosis and management of congenital mitral valve stenosis remains challenging in pediatric cardiology and is related in part to the high frequency of associated cardiac lesions.1-3 Parachute mitral valve (PMV) is a frequent pathological finding in the setting of congenital mitral valve stenosis, and the primary morphological feature is the unifocal attachment of chordae tendineae. Whereas true PMV is characterized by attachment of the chordae to a single or fused papillary muscle, PMV can include asymmetrical mitral valves with 2 papillary muscles, of which 1 is dominant and elongated, with its tip reaching to the valve leaflets. This dominant papillary muscle is often located higher in the left ventricle, with attachment at both its base and lateral side to the ventricular wall.4 The unifocal attachment of the chordae results in a restricted valve opening and the potential for subvalvar obstruction and, less frequently, valvar regurgitation. PMV is rarely found as an isolated lesion and may occur as part of an anomaly complex described by Shone et al5 in 1963, consisting of a PMV, supravalvular ring of the left atrium, subaortic stenosis, and coartation of the aorta, with both complete and incomplete forms having been described. The outcome of children with these multilevel left-heart obstructions and mitral valve involvement is generally poor.6,7 The contributions of these associated anomalies to outcomes for patients with PMV are incompletely defined. We sought to determine factors associated with mortality in patients with PMV, the spectrum and natural history of mitral valve obstruction, and factors associated with eventual intervention for PMV.

Methods

Study Subjects

All patients diagnosed with a PMV between 1977 and 2001 were identified from a computerized database. PMV was diagnosed when a mitral valve with unifocal attachment of the chordae to a single or dominant papillary muscle was demonstrated on 2D echocardiography, with some patients also having confirmation at surgery or autopsy. Patients with atrioventricular septal defects were excluded, but patients with complex anomalies were included.

Measurements

Demographic, anatomic, management, and outcome data were collected from the medical record, as well as serial echocardiographic measurements. The presence of left ventricular hypoplasia was defined by qualitative echocardiographic appearance.
Data Analysis
Data are described as frequencies, medians with ranges, and means with SD as appropriate. Where there are missing data, the numbers of nonmissing values are given. Kaplan-Meier analysis was used to determine time-related survival, with associated factors sought by use of Cox’s proportional-hazards modeling. To determine the prognosis of the PMV, only patients who had biventricular physiology whereby the PMV remained the systemic atrioventricular valve were included in a Kaplan-Meier analysis of time-related mitral valvotomy, with associated factors sought by use of Cox’s proportional-hazards modeling. In addition, for the biventricular patients, repeated echocardiographic measurements of mean Doppler echocardiographic diastolic gradients across the PMV during the time period preceding any mitral valve interventions were examined for trends over time and associated factors with mixed linear regression analysis for repeated measures. Repeated echocardiographic measurements of subjective grade of valvar regurgitation were likewise examined for trends over time and associated factors by use of the general estimating equation for repeated measures. All analyses were performed with SAS statistical software version 8 (SAS Institute Inc) using default settings.

Results

Patient Characteristics
The study population included 84 patients, 64% of whom were male. The mean birth weight was 3.4 kg (range, 1.6 to 7.1 kg), and the mean length of gestation was 41 weeks (range, 32 to 44 weeks).

Presentation
The median age at presentation was 3 days, with a range from birth to 5.4 years. Thirty-seven patients presented shortly after birth with congestive heart failure, and of these, 16 were found to have an arm-to-leg blood pressure gradient and a heart murmur attributable to aortic coarctation. Fourteen patients presented shortly after birth with cyanosis and were found to have congenital heart defects. Ten patients presented with a heart murmur and an arm-to-leg blood pressure gradient attributed to aortic coarctation and underwent later repair. In 7 patients, a heart murmur was the only presenting sign. Six patients had been diagnosed with congenital heart defects on prenatal ultrasound. One patient presented after investigation for recurrent pneumonias. In the remaining 9 patients, the mode of presentation was not recorded. Only 7 patients (8%) presented after 1 year of age, and none had complex lesions, although 4 had associated aortic coarctation and aortic valve stenosis, and 1 required mitral valvotomy.

Associated Cardiac and Noncardiac Lesions
Associated cardiac anomalies were found in 99% of patients, with only 1 patient having PMV as an isolated anomaly. Aortic coarctation was present in 65%, an atrial septal defect in 55%, bicuspid aortic valve in 50%, patent ductus arteriosus in 50%, ventricular septal defect in 49%, aortic valve stenosis in 32%, subaortic stenosis in 21%, hypoplasia of the left ventricle in 20%, supravalvar mitral stenosis in 7%, and supravalvar aortic stenosis in 1%, with complex anomalies, including transposition of the great arteries, double-outlet left ventricle, and double-inlet left ventricle in 14% (Table 1). Although only 3 patients (4%) had the complete form of Shone’s complex, 67 patients (80%) had at least 1 other left-heart obstructive lesion.

Extracardiac anomalies were noted in 26% of patients (Table 2).

Survival
There were 18 total deaths, with Kaplan-Meier estimates of survival from birth of 82% at 1 year, 77% at 10 years, and 73% at 20 years (Figure 1). Median age of death was 21 days (range, 1 day to 12.3 years). Independent factors associated with decreased time-related survival from birth included the presence of left ventricular hypoplasia (hazard ratio, 8.73; 95% CI, 1.26 to 9.02; P=0.006) and atrial septal defect (hazard ratio, 3.38; 95% CI, 1.89 to 40.3; P<0.02). An atrial septal defect may allow right-to-left shunting in the presence of inflow obstruction, and this may result in underfilling of the left ventricle and possibly lead to hypoplasia of left-heart structures. Further analysis of factors associated with the presence of atrial septal defect showed that it was significantly associated with more severe left-sided disease, leading to selection of a nonbiventricular repair pathway (5% of those without versus 30% of those with an atrial septal defect; P<0.004).

Causes of Death
Twelve of the deaths occurred within 2 months of birth. Eight of these patients had left ventricular hypoplasia, of whom 4 died after withdrawal of support, including 2 patients with important noncardiac anomalies (1 with trisomy 18 and imperforate anus and the other with single kidney, micrognathia, imperforate anus, and Klippel-Feil syndrome). Of the other 4 patients with left ventricular hypoplasia who died, 1 died of arrhythmias and renal failure 1 week after pulmonary...
artery banding; 1 died of respiratory syncytial virus pneumonitis, having had only balloon atrial septostomy; 1 patient with multiple severe noncardiac anomalies died 1 day after a Norwood procedure; and 1 patient died suddenly 1 week after repair of aortic coarctation. Of the remaining 4 early deaths, 1 patient had critical aortic and mitral valve stenosis with left ventricular hypoplasia and died after withdrawal of support. One patient with associated noncardiac anomaly and left ventricular hypoplasia died 1 day after repair of aortic coarctation and pulmonary artery banding at age 6 months. One late death occurred in a patient age 3.4 years who had previous repair of aortic coarctation, ventricular septal defect closure, and resection of left ventricular outflow tract obstruction. This patient died of cardiac perforation at surgical atrial septostomy in an attempt to decompress the left atrium. One patient who had previous repair of aortic coarctation and aortic valvotomy died of a viral illness at age 8.3 years. The final patient, with Williams syndrome and previous repair of supravalvar aortic obstruction, died suddenly of presumed arrhythmia at age 12.3 years.

Management
No interventions were performed in 10 patients (including the 6 patients mentioned above who died early). Ten patients (2 died) had procedures toward an eventual Fontan operation. Of the remaining 64 patients (10 died), 11 had a mitral valvotomy (1 died), with subsequent mitral valve replacement in 2 patients. Twelve patients underwent a total of 17 distinct mitral valve procedures (median age, 2.8 years; range, 0.1 to 14.2 years).

Given the high prevalence of associated cardiac anomalies, the majority of patients had 1 or more surgical or transcatheter interventions. There were a total of 112 cardiac surgeries. Forty-eight patients underwent 1 operation, 16 patients underwent 2 operations, 8 patients underwent 3 operations, and 2 patients underwent 4. There were a total of 32 interventional catheter procedures. Sixteen patients underwent 1 procedure, 5 patients underwent 2 procedures, and 2 patients underwent 3 procedures.

Morbidity
Postoperative morbidity included 2 patients with cerebral infarction and no lasting sequelae. Another patient required a placement of a permanent dual-chamber pacemaker for complete heart block. One patient developed a chylothorax after repair of aortic coarctation, and 1 patient developed a communicating hydrocephalus secondary to superior vena caval obstruction.

Factors Associated With Mitral Valvotomy
Excluding 6 patients in whom support was withdrawn and 10 patients on a single-ventricle track, 68 patients were at risk for mitral valvotomy, and this was performed in 11 patients, with 2 subsequently having mitral valve replacement. Kaplan-Meier estimates of freedom from mitral valvotomy in these patients were 95% at age 6 months, 80% at 10 years, and 72% at 20 years (Figure 2). The risk was independently increased with the absence of aortic coarctation (hazard ratio, 3).

Table 2. Associated Noncardiac Abnormalities

<table>
<thead>
<tr>
<th>Abnormality</th>
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<th>%</th>
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<tbody>
<tr>
<td>Down syndrome</td>
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<td>(4)</td>
</tr>
<tr>
<td>DiGeorge syndrome</td>
<td>2</td>
<td>(2)</td>
</tr>
<tr>
<td>Tracheoesophageal fistula</td>
<td>2</td>
<td>(2)</td>
</tr>
<tr>
<td>Horseshoe kidney</td>
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<td>(2)</td>
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<td>Cervical hemivertebrae</td>
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<td>(1)</td>
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<tr>
<td>Single kidney</td>
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<td>(1)</td>
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<tr>
<td>Double collecting system in 1 kidney</td>
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<td>(1)</td>
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<tr>
<td>Turner’s syndrome</td>
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<td>(1)</td>
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<td>Trisomy 18</td>
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<tr>
<td>Williams syndrome</td>
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<td>Klippel-Feil syndrome</td>
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<td>CHARGE syndrome</td>
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<td>Other chromosome anomalies</td>
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<td>Pyloric duplication</td>
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<td>Microcephaly</td>
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<td>Bilateral colobomata</td>
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<td>(1)</td>
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<tr>
<td>Pectus excavatum</td>
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<td>(1)</td>
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<tr>
<td>Pectus carinatum</td>
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</table>

Values are n (%).

Figure 1. Kaplan-Meier curve of survival from birth for 84 patients. Solid line represents Kaplan-Meier estimates, with dashed lines enclosing 95% confidence limits. Numbers above x axis represent number of patients at risk.
Subsequent mitral valvotomy 2.74 (1.00) 0.009

Absence of atrial septal defect 1.84 (0.68) 0.01

Associated With an Increased Echocardiographic Mean

TABLE 3. Significant Factors From Mixed Linear Regression

Factors Associated With Mean Diastolic PMV Gradient

The median initial echocardiographic Doppler mean diastolic gradient across the PMV in biventricular track patients and before any mitral valvotomy (n=45) was 5 mm Hg (range, 1 to 17 mm Hg). Repeated-measures analysis of serial echocardiographic measurements showed no significant increase in peak or mean diastolic gradient of the PMV over time, but higher mean gradient at any time during follow-up was independently associated with the presence of supravalvar mitral stenosis (P<0.001), absence of atrial septal defect (P<0.04), presence of ventricular septal defect (P<0.02), and subsequent mitral valvotomy (P<0.01) (Table 3). After adjustment for these factors, there was a nonsignificant relationship between a higher mean diastolic gradient and a lower grade of mitral valve regurgitation (P=0.13).

Factors Associated With Subjective Grade of Mitral Valve Regurgitation

The initial subjective echocardiographic grade of mitral valve regurgitation measurements in biventricular track patients and before any mitral valvotomy (n=50) was absent in 48%, trace in 12%, mild in 36%, mild to moderate in 2%, and moderate in 2%. Repeated-measures analysis of serial echocardiographic measurements showed no significant increase in subjective grade of mitral valve regurgitation over time. The only independent factor significantly associated with a higher grade of regurgitation was freedom from subsequent mitral valvotomy (P<0.03).

Discussion

Parachute mitral valve is defined as a unifocal attachment of mitral valve chordae independent of the number of papillary muscles. Oosthoek et al suggested that the valve can be distinguished on the basis of morphological features into parachute-like asymmetrical mitral valves and true PMVs. Parachute-like asymmetrical mitral valves have 2 papillary muscles, with 1 being elongated, located higher in the left ventricle with its tip reaching to the annulus, and attached at both its base and lateral side to the left ventricular wall. True PMVs have a single papillary muscle that receives all chordae. These morphologies have also been shown to differ developmentally. There is debate as to whether the asymmetrical valve can be described as a PMV and whether there is difference in surgical outcome between the true PMV and the asymmetrical valve. The PMV with a single papillary muscle is much rarer than the asymmetrical parachute-like mitral valve.

Children with multilevel left-heart obstructions and mitral valve involvement are known to have poor outcomes. The management of congenital mitral valve stenosis and associated lesions in the pediatric population is a major challenge, although several authors have reported excellent surgical results. We have noted that outcomes for patients with PMV are incompletely defined. We report factors associated with mortality in patients with PMV, the spectrum and natural history of mitral valve obstruction, and factors associated with eventual intervention for PMV.

To the best of our knowledge, this is the first study to report the natural history of the PMV using analysis of serial echocardiographic measurements. From this, we have noted that the degree of mitral valve obstruction remains stable, and the majority of patients will not require valvotomy. In addition, we have noted that for patients with PMV, the outcomes are largely dependent on the spectrum of associated cardiac lesions. The presence of left ventricular hypoplasia and atrial septal defect (markers of more severe left-heart obstruction) were independently associated with poorer survival, and the risk of mitral valvotomy was independently increased with the absence of aortic coarctation and the presence of subaortic stenosis.

In 1963, Shone et al originally described the developmental complex that included PMV, supravalvular ring of the left atrium, subaortic stenosis, and coarctation of the aorta and reported that the degree of mitral valve involvement appeared to be the main factor determining outcome in these patients. This hypothesis has been confirmed in 2 reports of the long-term surgical outcome in patients with multiple left-heart obstructions and mitral valve involvement. Bolling et al described the operative results and late outcomes of 30
patients with multiple levels of left-heart obstruction with mitral valve involvement, 26 of whom had PMV, and concluded that increasing severity of the mitral valve obstruction was associated with worsening long-term outcome and that operative mortality in patients with Shone’s anomaly is adversely affected by the degree of mitral valve disease. Brauner et al\textsuperscript{10} also reported the long-term surgical outcome of 19 patients with multiple left-heart obstructions, 12 of whom had PMV, and concluded that worsening late outcome was associated with increased mitral valve involvement and the degree of pulmonary hypertension.

Worsening outcomes after mitral valve surgery for congenital mitral stenosis are also reported to be associated with the severity of left ventricular outflow tract obstruction. Serraf et al\textsuperscript{10} reported on a series of 72 children with congenital mitral stenosis who had all undergone mitral valve surgery and at 15 years after initial surgery noted a 70% actuarial survival, a 71% freedom from reoperation, and a 69% freedom from mitral valve replacement. The study population included 32 patients who had PMV and 49 patients with multilevel left ventricular obstruction, with 25 patients categorized as having Shone’s syndrome. There were 9 early deaths. These deaths were related to associated left ventricular outflow tract obstruction and to the use of a staged approach to repair. Several other studies have also confirmed that surgical mortality for patients with Shone’s complex and severe mitral valve disease is comparable to reported experience with patients with isolated congenital mitral valve stenosis.\textsuperscript{5,10,17}

In our study, 11 patients required surgical mitral valvotomy, with 1 intraoperative death and with subsequent mitral valve replacement in 2 patients. Two patients underwent balloon dilatation of the mitral valve, both with suboptimal results and subsequently need for surgical valvotomies. This finding agrees with previous reports that the parachute deformity is not readily amenable to balloon angioplasty because of unbalanced chordal attachment.\textsuperscript{22}

### References

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