Parachute mitral valve: Morphologic descriptors, associated lesions, and outcomes after biventricular repair

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Objective: In “true” parachute mitral valve, mitral valve chordae insert into one papillary muscle. In parachute-like asymmetric mitral valve, most or all chordal attachments are to one papillary muscle. This study compared morphologic features, associated lesions, and palliation strategies of the two parachute mitral valve and dominant papillary muscle types and examined interventions and midterm outcomes in patients with biventricular circulation.

Methods: Echocardiography and autopsy databases were reviewed to identify patients with “true” parachute mitral valve or parachute-like asymmetric mitral valve from January 1987 to January 2006. Predictors of palliation strategy in the entire cohort, mitral stenosis on initial echocardiogram, and mortality in the biventricular cohort were determined with logistic regression.

Results: Eighty-six patients with “true” parachute mitral valve ($n = 49$) or parachute-like asymmetric mitral valve ($n = 37$) were identified. Chordal attachments to the posteromedial papillary muscle were more common (73%). The presence “true” parachute mitral valve ($P = .008$), hypoplastic left ventricle ($P < .001$), and two or more left-sided obstructive lesions ($P = .002$) predicted univentricular palliation. Among 49 patients maintaining biventricular circulation at follow-up, 8 died median follow-up 6.4 years (7 days–17.8 years). Multivariate analysis revealed that “true” parachute mitral valve was associated with mitral stenosis on initial echocardiogram ($P = .03$), and “true” parachute mitral valve ($P = .04$) and conotruncal anomalies ($P = .0003$) were associated with mortality. Progressive mitral stenosis was found in 11 patients; 2 underwent mitral valve interventions, and 1 died.

Conclusion: Nearly two thirds of this parachute mitral valve cohort underwent biventricular palliation. Some progression of mitral stenosis occurred, although mitral valve intervention was rare. “True” parachute mitral valve was associated with mitral stenosis on initial echocardiogram. “True” parachute mitral valve and conotruncal anomalies were associated with mortality in the biventricular population.

Supplemental material is available online.

Congenital mitral stenosis (MS) results from a variety of anatomic anomalies in the pediatric population, and it is commonly associated with parachute mitral valve (PMV),^{1,2} an abnormality in which the mitral valve (MV) chordae insert into a single papillary muscle (anterolateral papillary muscle [ALPM] or posteromedial papillary muscle [PMPM]).³

Parachute-like asymmetric mitral valve (PLAMV)⁴ is a similar anomaly in which chordae are distributed unequally between two identifiable papillary muscles. Usually the dominant papillary muscle is normal and the other is elongated and displaced toward the mitral valve annulus. Although both mitral valve anomalies have predominant unifocalization of chordae, “true” PMV has only one papillary muscle to which all chordae are attached. When both types of PMV occur, the chordae are short and thickened, limiting movement of normal mitral valve leaflets³ and resulting in functional and hemodynamic abnormalities.⁵ Although clinical presentations may be similar, “true” PMV and PLAMV are defined separately, because the valves originate and develop in different ways morphogenetically.⁶

PMV is associated with other cardiac anomalies,⁷ which significantly affect patient outcome.⁸ These associations may determine whether a patient requires univentricular palliation, in which an atrial septectomy is performed, making the tricuspid valve the systemic atrioventricular valve and thus rendering the functional outcome of the PMV less important. In patients with “true” PMV or PLAMV and a biventricular circulation, the degree of MS or mitral regurgitation (MR) is of paramount importance.

Historically, “true” PMV and PLAMV have been grouped together and analyzed as a single lesion. The

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Abbreviations and Acronyms

ALPM	= anterolateral papillary muscle
MR	= mitral regurgitation
MS	= mitral stenosis
MV	= mitral valve
PLAMV	= parachutelike asymmetric mitral valve
PMPM	= posteromedial papillary muscle
PMV	= parachute mitral valve

influence of PMV type and dominant papillary muscle on associated lesions, palliation strategies, and outcomes in patients who maintain a biventricular circulation has not been previously analyzed. The objectives of this study were as follows: (1) to describe and compare the morphologic features and associated lesions of the two PMV and dominant papillary muscle types, (2) to assess for predictors of univentricular palliation in the entire PMV cohort, (3) to describe the interventions and midterm outcomes of patients who maintained biventricular circulation, and (4) to assess for predictors of MS on initial echocardiogram, progressive MS and MR, and mortality in the biventricular cohort.

METHODS

Study Design

This study was a retrospective case series including all patients with the diagnosis of “true” PMV or PLAMV from January 1, 1987, to January 1, 2006, at The Children’s Hospital of Philadelphia. The study was approved by the institutional review board (IRB #2006-3-4758).

Patient Data

Patients were identified through the echocardiography laboratory database and Cardiac Registry via autopsy specimen at The Children’s Hospital of Philadelphia. Demographic information, echocardiography, and surgical and catheter-based intervention data were collected from patient charts, echocardiography laboratory, and cardiology databases at The Children’s Hospital of Philadelphia. Most autopsy reports identified through the Cardiac Registry did not specify PMV type or dominant papillary muscle, necessitating specimen examination. If disagreement was noted between echocardiogram and autopsy specimen, autopsy data were used. Patients were separated into univentricular and biventricular categories according to palliation strategy. Patients with biventricular circulation who were unavailable for follow-up were excluded from outcome analysis. Patients with common atrioventricular canal were excluded.

Echocardiographic Data

The images from the initial echocardiogram were reviewed for papillary muscle anatomy, original anatomic diagnoses, associated cardiac lesions, and the presence of MS and MR. When all pertinent echocardiographic information was not present, additional echocardiograms were reviewed to complete data acquisition.

“True” PMV was diagnosed when a mitral valve with unifocal attachment to a single papillary muscle was identified with 2-dimensional echocardiography (Figure 1, A). PLAMV was diagnosed when two papillary muscles were identified, with one papillary muscle receiving most or all of the chordae from the mitral valve leaflets (Figure 1, B). Normal mitral valve anatomy features bifocal attachment of chordae distributed equally

between two distinct papillary muscles (Figure 1, C). These definitions are those described by Oosthoek and colleagues.⁴

The levels of left-sided obstruction were identified at the mitral valve (supravalvular mitral ring, MS), aortic valve (subaortic stenosis, aortic stenosis, aortic atresia, supravalvular aortic stenosis), and aortic arch (aortic arch hypoplasia, coarctation of the aorta, interrupted aortic arch). MS was defined as mild (mean Doppler gradient 3–5 mm Hg or peak Doppler gradient 5–8 mm Hg) or moderate or greater (mean Doppler gradient >5 mm Hg or peak Doppler gradient >8 mm Hg). Aortic stenosis was defined as a peak instantaneous pressure gradient across the aortic valve of at least 20 mm Hg, an aortic valve annulus with a *z* score less than –2.0, or both. Aortic arch obstruction was defined as an adjusted peak instantaneous pressure gradient of greater than 10 mm Hg or a *z* score less than –2.0 for the ascending, transverse, or isthmus regions of the aorta. The left ventricle was considered hypoplastic when the length of the left ventricle was less than 80% of the distance from the atrioventricular groove to the apex of the heart. According to the regurgitant jet area relative to the left atrial area, MR was defined as none, trivial or mild (<30%), moderate (30%–50%), or severe (>50%).⁹

Follow-up data and most recent echocardiogram were obtained for patients with a biventricular circulation. Most recent echocardiographic results were obtained before any mitral valve intervention, if applicable. The follow-up echocardiogram and data for biventricular patients no longer followed up at our institution were obtained from each patient’s cardiologist with permission. Presence, degree, and progression of MS and MR were assessed. Progressive MS was defined as any increase in mean gradient at least 2 mm Hg, an increase in peak gradient greater than 3 mm Hg, or by an increase from no MS to the presence of MS relative to the initial echocardiogram. Progressive MR was defined by any increase in category of regurgitation relative to initial echocardiogram. Patients with only one echocardiogram before death or mitral valve intervention were excluded from analysis of progressive MS or MR.

Statistical Methods

Nonparametric data were expressed as median and range, and parametric data were expressed as mean $\pm$ SD. Dichotomous variables were tabulated.

The Fisher exact test was used to assess for associations between PMV type, dominant papillary muscle, and associated lesions, as well as associations between palliative strategy and PMV type, dominant papillary muscle, associated lesions, and increasing levels of left-sided obstruction. Logistic regression with multiple predictors and backward model selection was then used to identify predictors of palliation strategy.

After the biventricular cohort was identified, associations between PMV type, dominant papillary muscle, and surgical and catheter-based interventions were assessed with the Fisher exact test. Logistic regression was used to assess for predictors of MS at initial echocardiogram. Predictors of mortality in the biventricular group were identified by logistic regression and Cox proportional hazard regression analysis. Kaplan–Meier curves for time to death were computed and plotted, and variables that showed an association with mortality were stratified. The log-rank test was used to assess for differences in survival between stratified groups. Multivariate analysis was not used to predict progressive MS, because only two echocardiograms (initial and most recent) were used for analysis, and the exact time after initial echocardiogram at which the MS progressed was not known. Echocardiographic changes in MS and MR were assessed with the McNemar test for correlated proportions. Statistical analysis was performed with R version 2.2.0 (<http://www.r-project.org>) and STATA 10.0 (StataCorp LP, College Station, Tex).

A sequential Bonferroni correction (Holm method) was used to correct for multiple comparisons.¹⁰ A *P* value at least .025 but less than .05 was considered to represent a trend toward significance when multiple comparisons were performed. A *P* value at least .05 but less than .10 was considered a trend toward significance when performing the McNemar test for correlated proportions.

FIGURE 1. Mitral valve anatomy. Schematic drawings of true parachute mitral valve, with all chordae attached to a single papillary muscle (A); parachute-like asymmetric mitral valve, with chordae attached to two papillary muscles, one being elongated and displaced toward mitral valve annulus (B); and normal mitral valve, with chordae distributed equally between two distinct papillary muscles (C). Reproduced with permission from: Oosthoek PW, Wenink AC, Macedo AJ, Gittenberger-de Groot AC. The parachute-like asymmetric mitral valve and its two papillary muscles. *J Thorac Cardiovasc Surg.* 1997;114:9-15.

RESULTS

Patient Population

A total of 86 patients with “true” PMV ($n = 49$) or PLAMV ($n = 37$) were identified. Eighty-one patients were identified in the echocardiography database, and 5 additional patients were identified solely in the Cardiac Registry from autopsy reports; all of the latter had univentricular circulation. The patients identified solely in the Cardiac Registry all predated the echocardiography database, and echocardiogram reports were not available for review. Most of the patients ($n = 54$, 63%) were male, and the median age at initial echocardiogram was 11 days (range 1 day–16.8 years). In 86% of the patients, the initial echocardiogram revealed all the echocardiographic data points, whereas 8% required evaluation of a second echocardiogram. Six percent of the cohort had anatomic details obtained from autopsy specimen inspection. Chordal attachments were more common to the PMPM ($n = 63$, 73%). One or more associated cardiac lesions were found in 85 of 86 patients and are listed in Table 1. Sixty-two patients (72%) in the cohort had at least one level of left-sided obstruction, 40 patients (47%) had two or more levels of left-sided obstruction, and 18 patients (21%) had three or more levels of left-sided obstruction. Eleven patients (12%) had conotruncal anomalies (interrupted aortic arch, tetralogy of Fallot, double-outlet right ventricle, dextrotransposition of the great arteries) and had right and/or left-sided obstructive lesions. Associated genetic defects, noncardiac anomalies, or syndromes were found in 13 patients (15%) and are described in Table

E1; the most commonly identified noncardiac abnormality was 22q11 microdeletion ($n = 4$, 4.7%).

A comparison of patient demographic characteristics and associated cardiac lesions by PMV type and dominant papillary muscle is shown in Table 1. For both types of PMV, PMPM was the dominant papillary muscle ($n = 36$ in “true” PMV, 73%, $n = 27$ in PLAMV, 73%). There were no statistically significant associations noted among PMV type, dominant papillary muscle, associated cardiac lesions, and levels of left-sided obstruction.

Management

Three patients in the cohort (3.5%) did not undergo any surgical or catheter-based intervention and proceeded down a biventricular management pathway. Biventricular palliation was pursued in 58.1% of the patients ($n = 50$), and univentricular palliation was undertaken in 38.4% ($n = 33$). Patient demographic characteristics and associated cardiac lesions by palliation strategy are noted in Table 2. There was an association between an increasing number of levels of left-sided obstruction and univentricular palliation ($P < .001$). When stratifying by number of levels of obstruction, the presence of two or more levels of left-sided obstruction was strongly associated with univentricular palliation ($P < .001$). One level of left-sided obstruction was not statistically significantly associated with univentricular palliation.

Multivariate analysis of lesions associated with univentricular palliation revealed “true” PMV ($P = .008$), the

TABLE 1. Patient demographic data and associated cardiac lesions by parachute mitral valve type and dominant papillary muscle anatomy

	Total	PMV type		Dominant papillary muscle	
		“True” PMV	PLAMV	ALPM	PMPM
Total	86	49	37	23	63
Male		30 (61%)	24 (65%)	16 (70%)	38 (60%)
ALPM		13 (27%)	10 (27%)		
PMPM		36 (73%)	27 (73%)		
Associated lesions					
Ventricular septal defect	44 (52%)	28 (57%)	16 (43%)	13 (57%)	31 (49%)
Conoventricular		18 (37%)	11 (30%)	9 (39%)	20 (32%)
Malalignment		5 (10%)	3 (8%)	3 (13%)	5 (8%)
Muscular		8 (16%)	5 (16%)	2 (9%)	11 (17%)
Inlet		1 (2%)	1 (3%)	1 (4%)	1 (2%)
Atrial septal defect	11 (13%)	9 (18%)	2 (5%)	4 (17%)	7 (11%)
Hypoplastic left ventricle	29 (34%)	19 (39%)	10 (27%)	6 (26%)	23 (37%)
Aortic stenosis	21 (24%)	12 (24%)	9 (24%)	7 (30%)	14 (22%)
Aortic atresia	4 (5%)	4 (8%)	0	1 (4%)	3 (5%)
Bicuspid aortic valve	35 (41%)	16 (33%)	19 (51%)	7 (30%)	28 (44%)
Subaortic stenosis	12 (14%)	6 (12%)	6 (16%)	4 (17%)	8 (13%)
Aortic arch hypoplasia	35 (41%)	22 (45%)	13 (35%)	7 (30%)	28 (44%)
Supravalvular mitral ring	5 (6%)	2 (4%)	3 (8%)	2 (9%)	3 (5%)
Coarctation of aorta	48 (56%)	23 (47%)	25 (68%)	12 (52%)	36 (57%)
Interrupted aortic arch	2 (2%)	1 (2%)	1 (3%)	0	2 (3%)
Tetralogy of Fallot*	6 (7%)	5 (10%)	1 (3%)	2 (9%)	4 (6%)
Double-outlet right ventricle	2 (2%)	2 (4%)	0	1 (4%)	1 (2%)
Dextrotransposition of great arteries	1 (1%)	1 (2%)	0	0	1 (2%)
Initial mitral stenosis		22 (45%)	15 (41%)	11 (48%)	26 (41%)
Left superior vena cava to coronary sinus	15 (17%)	8 (16%)	7 (19%)	5 (22%)	10 (16%)
Left-sided obstructive lesions					
0	24 (28%)	15 (31%)	9 (24%)	7 (30%)	17 (27%)
≥1	62 (72%)	34 (69%)	28 (76%)	16 (70%)	46 (73%)
≥2	40 (47%)	22 (45%)	18 (49%)	10 (43%)	30 (48%)
3	18 (21%)	10 (20%)	8 (22%)	5 (22%)	13 (21%)

Values are numbers of patients with percentages of total population, parachute mitral valve type, or dominant papillary muscle with each characteristic, as applicable. There were no statistically significant associations noted among parachute mitral valve type, dominant papillary muscle, and associated cardiac lesions. PMV, Parachute mitral valve; PLAMV, parachutelike asymmetric mitral valve; ALPM, anterolateral papillary muscle; PMPM, posteromedial papillary muscle. *Tetralogy of Fallot alone, with absent pulmonary valve, or with pulmonary atresia.

presence of a hypoplastic left ventricle ($P < .001$), and two or more levels of left-sided obstruction ($P = .002$) as the strongest predictors of univentricular palliation. There was a trend toward an association between univentricular palliation and the presence of a muscular ventricular septal defect ($P = .033$). No lesions predicted biventricular palliation, and there was no association between dominant papillary muscle and palliation strategy.

Most patients with “true” PMV and PLAMV who underwent univentricular palliation had a Norwood procedure performed as the initial operation ($n = 31$, 94%). Two patients had pulmonary artery banding performed at the neonatal palliation. Both of these patients later underwent a hemi-Fontan procedure in combination with a Damus–Kaye–Stansel procedure. Initial neonatal palliation procedures for the univentricular group are noted in Table 3.

Biventricular circulation was maintained in 53 of 86 patients (62%, “true” PMV $n = 25$, 47%, PLAMV $n = 28$,

53%), 38 of whom (72%) had the PMPM as the dominant papillary muscle. Ninety-two percent of the patients with biventricular circulation (49/53) had follow-up data and were included in analysis. Only 3 patients in the biventricular group (6%) remained free of cardiac intervention; the remaining 46 patients underwent a total of 68 operations and catheter-based interventions. Surgical and catheter-based interventions for the biventricular cohort are delineated in Table 3. There were no statistically significant associations noted between PMV type, dominant papillary muscle, and surgical and catheter-based interventions for the biventricular cohort.

Two patients (2/49, 4%) underwent a total of 3 mitral valve surgeries or catheter-based interventions. One patient underwent mitral valvotomy; the other underwent mitral valvotomy followed by mitral valve replacement and died 4 months later. Too few patients underwent mitral valve intervention to analyze for predictors of MV intervention.

TABLE 2. Patient demographic data and associated cardiac lesions by palliation strategy

	Palliation strategy		P value	
	Biventricular	Univentricular	Univariate	Multivariate
Total	53	33		
Male	35 (66%)	19 (58%)	NS	NS
PMV type			.026	.008
True PMV	25 (47%)	24 (73%)		
PLAMV	28 (53%)	9 (27%)		
Dominant papillary muscle			NS	NS
ALPM	15 (28%)	8 (24%)		
PMPM	38 (72%)	25 (76%)		
Associated lesions				
Ventricular septal defect	24 (45%)	20 (61%)	.06	NS
Conoventricular	16 (30%)	13 (40%)	NS	NS
Malalignment	6 (11%)	2 (6%)	NS	NS
Muscular	4 (8%)	9 (27%)	.027	.033
Inlet	0	2 (6%)	NS	NS
Atrial septal defect	5 (9%)	6 (18%)	NS	NS
Hypoplastic left ventricle	4 (8%)	25 (76%)	<.001	<.001
Aortic stenosis	7 (13%)	14 (42%)	.004	NS
Aortic atresia	0	4 (12%)	.019	NS
Bicuspid aortic valve	20 (38%)	15 (45%)	NS	NS
Subaortic stenosis	4 (8%)	8 (24%)	.052	NS
Aortic arch hypoplasia	12 (23%)	23 (70%)	<.001	NS
Supravalvular mitral ring	4 (8%)	1 (3%)	NS	NS
Coarctation of aorta	29 (55%)	19 (58%)	NS	NS
Interrupted aortic arch	2 (4%)	0	NS	NS
Tetralogy of Fallot*	6 (11%)	0	NS	NS
Double-outlet right ventricle	0	2 (6%)	NS	NS
Dextrotransposition of great arteries	1 (2%)	0	NS	NS
Initial mitral stenosis	16 (30%)	21 (58%)	NS	NS
Left superior vena cava to coronary sinus	4 (8%)	11 (33%)	.003	NS
Left-sided obstructive lesions				
0	19 (36%)	2 (15%)	NS	NS
≥1	34 (64%)	28 (85%)	NS	NS
≥2	17 (32%)	23 (70%)	<.001	.002
3	4 (8%)	14 (42%)	<.001	NS

Values are numbers of patients with percentages of palliation type with each characteristic. NS, Not significant; PMV, parachute mitral valve; PLAMV, parachuteline asymmetric mitral valve; ALPM, anterolateral papillary muscle; PMPM, posteromedial papillary muscle. *Tetralogy of Fallot alone, with absent pulmonary valve, or with pulmonary atresia.

Biventricular Group Follow-up

Echocardiographic data. Of the 49 patients in the biventricular follow-up group, 1 (2%) had a single echocardiogram before death and was therefore not included in MS or MR analysis because progressive MS and progressive MR analysis required serial echocardiograms. The 48 remaining patients had a median follow-up of 6.4 years (7 days–17.8 years).

Sixteen (33%) patients had MS at initial echocardiogram (Figures 2 and E1). The initial median peak gradient in patients with MS was 14 mm Hg (6–20 mm Hg), with a median mean gradient of 6 mm Hg (5–13 mm Hg). On the most recent echocardiogram, 22 of the patients in the biventricular group (46%) had MS. The median peak gradient at follow-up was 15 mm Hg (9–29 mm Hg), with a median mean gradient of 6 mm Hg (4–14 mmHg). Eleven of the 22 patients (50%) had progressive MS. Although there

was a trend toward progression of MS from initial to most recent echocardiogram ($P = .07$), 5 of 16 patients with initial MS had a decrease in level of MS from initial to most recent echocardiogram. Two of the 5 patients with a decrease in MS from initial to most recent echocardiogram had undergone ventricular septal defect closure during the interim period.

Six (13%) of the patients in the biventricular follow-up group had trivial or mild MR on initial echocardiogram, and no patients had moderate or severe MR (Figures 2 and E2). Fourteen patients (29%) had MR noted on the most recent echocardiogram; 2 of them had hemodynamically significant MR. Eleven of the 14 patients (79%) had progressive MR. There was statistically significant progression of MR from initial to most recent echocardiogram ($P = .003$).

Predictors of mortality. Within the biventricular cohort, 8 patients (16%) died (Table E2). Three of these 8 patients

TABLE 3. Surgical and catheter-based interventions by parachute mitral valve type and dominant papillary muscle anatomy

	PMV type		Dominant papillary muscle	
	"True" PMV	PLAMV	ALPM	PMPM
Total	47	35	23	59
Univentricular group (n = 33)	24	9	8	25
Stage 1	23 (96%)	8 (89%)	7 (88%)	24 (96%)
Pulmonary arterial band	1 (4%)	1 (11%)	1 (12%)	1 (4%)
Biventricular group (n = 53)	25	28	15	38
Ventricular septal defect repair	10 (40%)	9 (32%)	6 (40%)	13 (34%)
Atrial septal defect repair	2 (8%)	1 (4%)	2 (13%)	1 (3%)
Pulmonary arterial banding	1 (4%)	0	0	1 (3%)
Aortic arch repair	13 (52%)	18 (64%)	7 (47%)	24 (63%)
Balloon dilation angioplasty for recoarctation	2 (8%)	4 (14%)	4 (27%)	2 (5%)
Aortic valve procedure*	0	5 (18%)	3 (20%)	2 (5%)
Subaortic membrane resection	0	3 (11%)	1 (7%)	2 (5%)

Values are numbers of patients with percentages of parachute mitral valve type or dominant papillary muscle with each intervention, depending on palliation group. Univentricular group interventions listed are only the initial intervention these patients received; biventricular group interventions listed are all the cardiac interventions these patients received during the study. There were no significant associations noted between parachute mitral valve type, dominant papillary muscle, and surgical and catheter-based interventions for the biventricular cohort. PMV, Parachute mitral valve; PLAMV, parachute-like asymmetric mitral valve; ALPM, anterolateral papillary muscle; PMPM, posteromedial papillary muscle. *Aortic valve procedures included aortic valvotomy and aortic valvuloplasty.

were known to have a primary left-sided obstructive lesion and died as a direct result of the consequences of long-standing moderate or greater MS and pulmonary hypertension. One of the patients had pulmonary hemorrhage that was worsened by moderate MS and elevated pulmonary arterial pressures. Two died of respiratory failure unrelated to the presence of the PMV. Mortality did not statistically differ by sex, presence of MS or MR at initial echocardiogram, or presence of progressive MS or MR at most recent echocardiogram.

Among the 8 patients who died in the biventricular group, 7 patients (88%) had "true" PMV, whereas 1 had PLAMV. Mortality was associated with having "true" PMV ($P = .02$) but was not statistically significantly related to a dominant papillary muscle. All 8 patients who died had a ventricular septal defect, and 6 of 8 had a conotruncal anomaly (tetralogy of Fallot, interrupted aortic arch, aortic arch hypoplasia with ventricular septal defect); both malalignment ventricular septal defect ($P = .004$) and conotruncal anomaly ($P < .001$) were associated with mortality by univariate analysis. In addition, surgical repair of ventricular septal defect was associated with mortality ($P = .02$).

Freedoms from mortality for the entire biventricular cohort at 1, 5, and 10 years after initial diagnosis are shown in Figure 3 (A). The 1-, 5-, and 10-year survivals after stratification by "true" PMV and conotruncal anomalies are

plotted in Figure 3 (B and C). After stratification, the log-rank test for the Kaplan–Meier curves was significant for both "true" PMV ($P = .02$) and conotruncal anomaly ($P < .001$). When Cox proportional hazard regression analysis was used, only conotruncal anomaly was a significant predictor of mortality ($P = .002$).

Predictors of MS and MR. Multivariate analysis revealed predictors of MS at initial echocardiogram to include "true" PMV ($P = .024$). There was no association between progressive MS and PMV type, dominant papillary muscle, sex, or any surgical or catheter-based interventions. Because only 2 patients had hemodynamically significant MR on the most recent echocardiogram, multivariate modeling for predictors of progressive MR was not performed.

DISCUSSION

In the past, "true" PMV and PLAMV have been grouped together under the single anomaly of PMV. This study further confirms that PMV is not an isolated cardiac anomaly. Only 1 patient in the cohort had PMV without an associated cardiac defect. The most commonly associated cardiac lesions on initial echocardiogram were patent ductus arteriosus, coarctation of the aorta, and ventricular septal defect. As in other studies describing the lesions associated with PMV, left-sided obstructive cardiac lesions and ventricular septal defects were common in our cohort.^{3-5,7-8,11-13} There was no association noted between the number of levels of obstruction and PMV type. Interestingly, conotruncal anomalies accounted for 13% of our PMV cohort. Similarly, Tandon and associates¹³ reported that 26% of the specimens in a pathologic analysis of 52 cases of PMV had conotruncal anomalies.

To our knowledge, this is the first study to examine associated cardiac lesions by PMV type and dominant papillary muscle, although no statistically significant associations were noted. There was no association between PMV type or dominant papillary muscle and hypoplastic left ventricle, aortic stenosis or atresia, or subaortic stenosis as single entities. This may have resulted from the smaller sample size used for subgroup analyses.

Because "true" PMV and PLAMV are not isolated lesions, it is not surprising that the vast majority of patients underwent at least one surgical or catheter-based intervention separate from the PMV. We believe this to be the first study to evaluate palliation strategy according to PMV type and dominant papillary muscle. Univentricular palliation was elected in 38% of patients. Almost three fourths of the patients in our study who required univentricular palliation had "true" PMV. In multivariate analysis, "true" PMV was associated with univentricular palliation, along with hypoplastic left ventricle and the presence of two or more levels of left-sided obstruction. We speculate that "true" PMV may result in reduced left ventricular inflow relative to PLAMV and may result in left ventricular hypoplasia,

FIGURE 2. Mitral stenosis and mitral regurgitation at initial and most recent echocardiograms in patients with biventricular circulation. Percentages of patients in biventricular cohort with mitral stenosis and mitral regurgitation at initial and most recent echocardiogram.

aortic stenosis, arch hypoplasia, or all three. Excluding patients in which support was withdrawn, Schaverien and coworkers⁸ showed that 13% of their patients underwent univentricular palliation, but they did not differentiate by PMV type or dominant papillary muscle.

Among patients who underwent biventricular palliation, patients with “true” PMV had a greater risk for mortality than did patients with PLAMV. Mortality in the biventricular cohort was also associated with conotruncal anomaly. Of the 8 patients who died in the biventricular group, 6 (75%) had conotruncal anomaly, and 5 of these 6 had “true” PMV. This differs considerably from the findings of Oosthoek and associates,⁴ whose patients with conotruncal anomaly had PLAMV almost exclusively. Both the higher incidence of conotruncal anomaly in Oosthoek and associates’ autopsy cohort⁴ and the deaths in our study cohort may potentially have resulted from right- and left-sided obstructive disease. Schaverien and coworkers⁸ found the presence of hypoplastic left ventricle and atrial septal defect to be associated with mortality in patients with PMV. The mortality analysis performed by Schaverien and coworkers⁸ included patients from their PMV cohort both biventricular and univentricular palliation. Because atrial septal defect and left ventricular hypoplasia are markers for severe left-sided heart obstruction, which would likely be associated with univentricular palliation or higher-risk biventricular palliation, it is not surprising that these markers were associated with death. All patients in our cohort who had severe left-sided obstruction underwent univentricular palliation and thus were not included in our biventricular mortality analysis.

In our biventricular cohort, we found a significant association between “true” PMV and the presence of MS at initial echocardiogram according to multivariate analysis. Although we found a trend toward progressive MS from initial to most recent echocardiogram in our study, the analysis was complicated because the group had both progression and

regression. In the vast majority of cases in which MS progressed, MS was not noted at initial echocardiogram. Among those patients with MS on initial echocardiogram, most remained at the same level from initial to follow-up echocardiogram. In the minority of patients in whom the gradient of MS fell from initial to most recent echocardiogram, ventricular septal defect closure had occurred in the interim, thereby reducing the preload on the left atrium.

In our study, we found a significant increase in MR from initial to most recent echocardiogram. Of note, most patients with progressive MR did not have MR at initial echocardiogram, and only a small number of patients had progression to hemodynamically significant MR. Despite the rarity of patients with moderate or greater MR at most recent echocardiogram, we believe that patients with PMV may be at risk for progressive MR and should be followed up long-term for hemodynamically significant MR.

Only 4% of the patients in our biventricular cohort (2/49) underwent mitral valve interventions. This incidence is lower than that reported by Schaverien and coworkers,⁸ who reported mitral valve intervention in 19% of their cohort. This may have been because more patients underwent univentricular palliation in our cohort, or there may have been a difference in institutional biases regarding when to perform mitral valve intervention for MS.

Study Limitations

This study has several potential limitations. It is a retrospective study, and therefore information bias may exist. The follow-up period between first and last echocardiogram differed between patients and may not have provided the long-term follow-up required to assess the effects on mortality of PMV type, dominant papillary muscle, associated cardiac lesions, multiple levels of left-sided obstruction, and progressive MS and MR. Because of the prevalence of ventricular septal defect and patent ductus arteriosus as

FIGURE 3. Kaplan-Meier survival curves. Freedoms from mortality for entire biventricular cohort (A), and stratified for parachute mitral valve type (B) and presence of conotruncal anomaly (C).

associated lesions, some patients may have had the gradient across the mitral valve overestimated as a consequence of an increased left atrial preload. Additionally, the prevalence of ventricular septal defect as an associated lesion may have affected the ability to assess reliably obstructive lesions of the aortic valve or aortic arch in some patients because of left-to-right shunting at the ventricular level. Because of different biases toward univentricular and biventricular palliation strategies among centers, the patients in our biventricular cohort may differ from other biventricular cohorts at other centers, where more patients might undergo biventricular palliation and therefore undergo more frequent mitral valve interventions. Although all echocardiograms at our institution were reviewed by a single cardiologist for anatomy and associated lesions, follow-up data for patients no longer at our institution were obtained from outside echocardiogram reports. Additionally, only 2 echocardiograms per

patient were reviewed, which may have limited the sensitivity of the progressive MS and MR analyses.

CONCLUSIONS

Both “true” PMV and PLAMV have a broad spectrum of associated lesions, both of which have PMPM as the dominant papillary muscle. “True” PMV, hypoplastic left ventricle, and the presence of two or more left-sided obstructive lesions were predictors of univentricular palliation in our center, and in patients with biventricular palliation, “true” PMV and conotruncal anomalies were associated with mortality. At midterm follow-up, among patients who underwent biventricular palliation, progressive MS as seen on echocardiogram was not uncommon, but mitral valve intervention was rare. MR in this group was progressive but hemodynamically insignificant. Although progressive MS has not been associated with mitral valve intervention or mortality in our study to

date, progression of MS should be followed carefully in patients with “true” PMV and PLAMV in this high-risk population.

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FIGURE E1. Progression of mitral stenosis in patients with biventricular circulation. Mitral stenosis status at initial and most recent echocardiogram (*Echo*).

FIGURE E2. Progression of mitral regurgitation in patients with biventricular circulation. Mitral regurgitation status at initial and most recent echocardiogram (*Echo*).

TABLE E1. Associated noncardiac abnormalities

	No.	%
22q11 Microdeletion disorders	4	4.7%
9p Syndrome mosaic	1	1.2%
Trisomy 21 mosaic	1	1.2%
Turner mosaic	1	1.2%
Trisomy 18	1	1.2%
Trisomy 8	1	1.2%
Partial trisomy 6	1	1.2%
6q Deletion	1	1.2%
Jobert syndrome	1	1.2%
Goldenhar syndrome	1	1.2%
Noonan syndrome	1	1.2%
Microcephaly	1	1.2%
Dysplastic kidneys	1	1.2%
Duodenal atresia	1	1.2%
Hemorrhagic gastritis	1	1.2%
Malrotation of intestine	1	1.2%

TABLE E2. Mortality in the biventricular group

Patient	PMV type	Dominant PM	Original diagnosis	Procedures	Cause of death
1	PLAMV	ALPM	TOF	TOF repair, PDA ligation	Unknown
2	True PMV	ALPM	Arch hypoplasia, VSD	Coarctation repair, VSD repair	Pulmonary hypertension
3	True PMV	PMPM	TOF and PA with MAPCAs	Unifocalization, RV–pulmonary artery conduit, LPA/RPA balloon dilation angioplasty and stenting, resection of RV pseudoaneurysm, coil embolization of collaterals	Pulmonary hemorrhage followed by cardiac arrest
4	True PMV	ALPM	MS, VSD	VSD repair, mitral valvuloplasty, MVR	Pulmonary hypertension
5	True PMV	PMPM	TOF and PA with confluent pulmonary arteries	RV to pulmonary artery conduit placement, VSD closure	Unknown
6	True PMV	PMPM	Trisomy 18, VSD, ASD, PDA, dysplastic PV	No procedures	Respiratory failure
7	True PMV	PMPM	IAA	Aortic arch repair, PAB (×2), debanding, VSD closure, residual VSD closure, RVOT reconstruction, arch patch augmentation for recoarctation, pacemaker for resynchronization therapy	DCM, cardiac arrest while awaiting heart transplant
8	True PMV	PMPM	TOF with absent PV	TOF repair with plication of pulmonary arteries	Respiratory failure

PMV, Parachute mitral valve; PM, papillary muscle; PLAMV, parachuteline asymmetric mitral valve; ALPM, anterolateral papillary muscle; TOF, Tetralogy of Fallot; PDA, patent ductus arteriosus; VSD, ventricular septal defect; PMPM, posteromedial papillary muscle; PA, pulmonary atresia; MAPCA, major aortopulmonary collateral artery; RV, right ventricle; LPA, left pulmonary artery; RPA, right pulmonary artery; MS, mitral stenosis; MVR, mitral valve replacement; ASD, atrial septal defect; PV, pulmonary valve; IAA, interrupted aortic arch; PAB, pulmonary arterial banding; RVOT, right ventricular outflow tract; DCM, dilated cardiomyopathy.