Pulmonary hypertension adversely affects short- and long-term survival after mitral valve operation for mitral regurgitation: Implications for timing of surgery

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Objective: We investigated the impact of preoperative pulmonary hypertension (PH) on early and late outcomes after mitral valve operation for mitral regurgitation.

Methods: Systolic pulmonary artery pressure (sPAP) was measured before operation in 873 consecutive patients who underwent mitral valve surgery for mitral regurgitation between January 2002 and January 2010. PH was classified as none (sPAP < 40 mm Hg), mild (40 ≤ sPAP < 50 mm Hg), moderate (50 ≤ sPAP < 60 mm Hg), or severe (sPAP ≥ 60 mm Hg).

Results: Increased preoperative sPAP was associated with greater left ventricular dysfunction and dilation, left atrial enlargement, more atrial fibrillation, and tricuspid regurgitation. Operative mortality was correlated with the degree of preoperative PH (2%, 3%, 8%, and 12% for none, mild, moderate, and severe PH, respectively, $P < .0001$). Long-term survival was related to preoperative sPAP (5-year survival: 88%, 79%, 65%, and 53% for none, mild, moderate, and severe PH, respectively; $P < .0001$). In multivariable analyses, sPAP was a predictor of both operative mortality (odds ratio, 1.023 per 1 mm Hg increase; 95% confidence interval, 1.003–1.044; $P = .0270$) and late death (hazard ratio, 1.018 per 1 mm Hg increase; 95% confidence interval, 1.007–1.028; $P = .001$). Among 284 patients with isolated degenerative mitral regurgitation due to leaflet prolapse, actuarial survival was 97.5%, 91.2%, and 80.5% for none, mild, and moderate to severe PH, respectively ($P = .0002$).

Conclusions: Preoperative sPAP is a powerful predictor of early and late survival after mitral valve operation for mitral regurgitation. Even modest increases in sPAP adversely affect outcomes. Mitral valve operation should be performed before the development of PH. (J Thorac Cardiovasc Surg 2011;142:1439-52)

Pulmonary hypertension (PH) is common among patients referred for mitral valve (MV) surgery for mitral regurgitation (MR). Although it is generally acknowledged that the presence of PH has a negative impact on operative outcomes, available data are remarkably scant and generally from small series.[1-9] Current American College of Cardiology/American Heart Association and European Society for Cardiology guidelines recommend surgery for asymptomatic patients with MR and resting systolic pulmonary artery pressure (sPAP) greater than 50 mm Hg as a class IIa recommendation based on level C evidence (expert opinion).[10,11] Pulmonary artery pressure is not included in Society of Thoracic Surgeons risk models for valve surgery.[12] The aim of the current study is to examine the impact of PH on early and long-term survival in a large cohort of patients undergoing surgery for MR.

PATIENTS AND METHODS

From January 2002 to January 2010, 953 patients underwent MV surgery for MR at the University of Maryland Medical Center. Patients were identified using the local Society of Thoracic Surgeons clinical database. This retrospective study was approved by the University of Maryland institutional review board with patient consent waived (HP-00046760). Preoperative, operative, and postoperative variables were collected. Patients with mitral stenosis, primary PH, and unrecorded sPAP (s) were excluded, leaving 873 patients for analysis (Figure 1). To assess the impact of PH on patients undergoing primary operation for isolated degenerative MR with leaflet prolapse,[13] we examined a subset of 284 patients undergoing primary isolated MV operation for leaflet prolapse (Figure 1). In cases in which preoperative right heart catheterization (RHC) was performed, the right atrial pressures, right ventricular pressures, pulmonary artery pressures (PAPs), and pulmonary capillary wedge pressures were recorded. If RHC was not performed, preoperative sPAP was measured with Doppler echocardiography (modified Bernoulli equation: 4× [tricuspid regurgitation jet velocity]^2+right atrial pressure [10 mm Hg]). sPAP was considered equal to right ventricular systolic pressure in the absence of pulmonary stenosis or right ventricular outflow tract obstruction.[14] In cases in which the sPAP was available from RHC and Doppler echocardiography, the RHC results were used. The left ventricular function and diameters and left atrial (LA) dimensions and morphology of underlying MV disease were determined using Doppler echocardiography. The severity of valvular regurgitation was assessed semiquantitatively on a scale of 0 to 4 (0 = none or trace,

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Abbreviations and Acronyms

CI = confidence interval
LA = left atrial
MR = mitral regurgitation
MV = mitral valve
NYHA = New York Heart Association
OR = odds ratio
PH = pulmonary hypertension
RHC = right heart catheterization
sBP = systolic blood pressure
sPAP = systolic pulmonary artery pressure

1 = mild, 2 = moderate, 3 = moderate to severe, 4 = severe).[15] PH was defined as sPAP 40 mm Hg or greater. Patients were categorized as follows: no PH (sPAP < 40 mm Hg), mild PH (40 mm Hg ≤ sPAP < 50 mm Hg), moderate PH (50 mm Hg ≤ sPAP < 60 mm Hg), and severe PH (sPAP ≥ 60 mm Hg). The ratio of sPAP over systemic systolic blood pressure (sBP) was also measured. The mechanism of MR was determined on the basis of preoperative echocardiography and intraoperative inspection.[16] Operative mortality was defined as in-hospital mortality or death within 30 days of operation. Predischarge echocardiography was routinely performed in a core echocardiography laboratory. Follow-up data including vital status and postoperative echocardiograms were obtained. Follow-up echocardiography was obtained at as many time points as available for each patient. A total of 1161 postoperative echocardiographic reports were obtained from our echocardiographic laboratory or the patient's referring cardiologist. sPAP data were analyzed during the following time periods: preoperatively, at discharge, during the first 2 years after surgery, and after 2 years. The Social Security Death Master File was used to determine vital status.[17] The status of all patients was assessed cross-sectionally in May 2010. The mean follow-up time was 35 ± 24 months, and the mean duration of echocardiographic follow-up was 26 ± 21 months.

The following questions were addressed:

1. What are the predictors of preoperative PH?
2. Did the presence of PH affect operative mortality and morbidity after MV operation?
3. What is the long-term survival after MV operation for MR in patients with and without preoperative PH?
4. Does PH predict adverse short- and long-term outcome after MV operation for isolated degenerative MR?
5. Did pulmonary pressures regress over time after operation?
6. What is the best systolic pulmonary pressure cutoff point to minimize early and late mortality after MV operation for MR?

Statistical Analysis

Continuous variables are expressed as the mean ± standard deviation (for reasonably symmetric variables) or median with the interquartile range (for clearly asymmetric variables). The values of categoric variables are expressed as proportions. Baseline compressions between patients' characteristics in different PH grades were performed using the chi-square test, Fisher exact test, Student *t* test, Wilcoxon rank-sum test, and 1-way analysis of variance where appropriate. In cohort 2 (patients with isolated degenerative MR), patients with moderate or severe PH were combined because of the small number of both groups. Logistic regression analysis was used (with variables listed in Appendix 1) to identify predictors of PH and operative mortality with a liberal retention criteria ($P < .10$ to enter and $P > .10$ to remove). The predicted probabilities of preoperative PH and operative mortality were identified. Long-term survival was evaluated with the Kaplan–Meier method, and the log-rank test was used to compare the groups. A Cox proportional hazard regression analysis was performed for the determination of factors independently associated with long-term survival. The odds ratio (OR) and hazard ratio (HR) for sPAP as a continuous variable are displayed for 1 mm Hg increment. Receiver operating characteristic curve analysis was performed to determine the cutoff values that best predict early and late survival. Analysis was performed using JMP 8.0 statistical software (SAS Institute Inc, Cary, NC). All statistic tests were 2-sided, with an α level less than 0.05 for statistical significance.

RESULTS

Patient Population

Between January 2002 and January 2010, 953 consecutive MV operations were performed at a single center. From this total, 888 patients met the inclusion criteria (Figure 1). sPAP was measured in 873 patients (98%) using RHC (591, 68%) and echocardiography (282, 32%). The mean patient age was 59 ± 14 years. A total of 493 patients (57%) were in New York Heart Association (NYHA) functional class III or IV, and 260 patients (30%) had atrial fibrillation (Table 1). Moderate-to-severe or severe degree of MR was present in 775 patients (89%). Right ventricular dysfunction defined as any degree of impairment in right ventricular contraction was present in 137 of 873 patients (15%).

Preoperative Characteristics and Pulmonary Artery Pressure

sPAP was determined using RHC in 591 patients (68%) (performed a mean of 29 ± 45 days before operation). Average sPAP, mean pulmonary artery pressure, right atrial pressure, right ventricular pressure, and pulmonary capillary wedge pressure measured during RHC were 43 ± 17 mm Hg, 29 ± 12 mm Hg, 9 ± 6 mm Hg, 11 ± 8 mm Hg, and 18 ± 9 mm Hg, respectively. sPAP was recorded on preoperative echocardiography in 621 patients (71%) (performed a mean of 35 ± 48 days before operation) with a mean sPAP of 46 ± 15 mm Hg. sPAP was measured in 373 patients with both echocardiography (mean ± standard deviation, 47 ± 16 mm Hg) and RHC (mean ± standard deviation, 45 ± 17 mm Hg). Measured mean sPAPs were not significantly different between these 2 modalities ($P = .9$). A linear relationship was observed between the sPAPs recorded with echocardiography and RHC ($r = 0.39$, $P < .0001$).

PH (sPAP ≥ 40 mm Hg) was present in 466 patients (53%) and was severe (sPAP ≥ 60 mm Hg) in 148 patients (17%) (Table 2). We observed a temporal trend toward a greater percentage of patients with no (sPAP < 40 mm Hg) or mild (40 ≤ sPAP < 50 mm Hg) PH undergoing surgery over the course of the study. Higher preoperative sPAPs were associated with increased age, female sex, higher NYHA function class, and a greater prevalence of comorbidities (Table 2). The mean left ventricular ejection fraction decreased as sPAP increased, whereas the mean left ventricular end-diastolic dimension was similar across

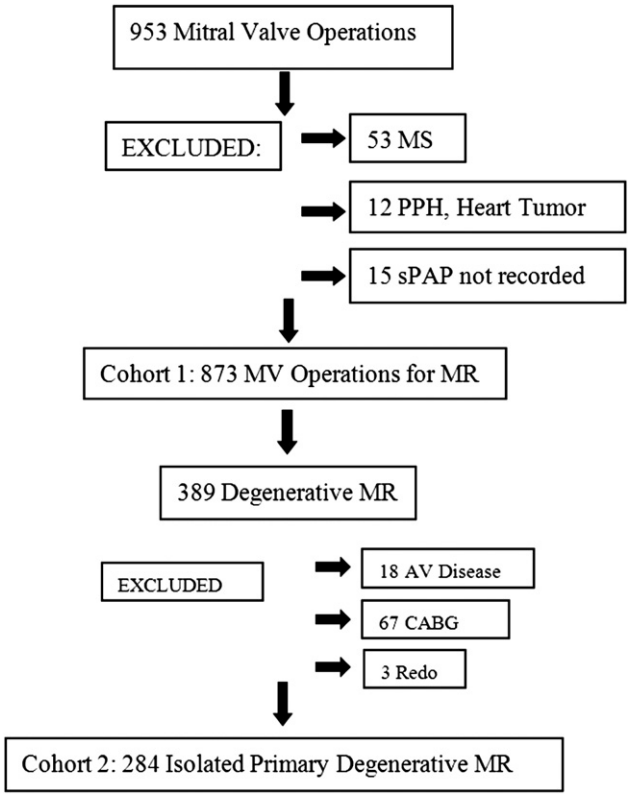

FIGURE 1. Patient population: exclusion criteria and final analysis population for cohort 1 and 2 studies. *AV,* Aortic valve; *CABG,* coronary artery bypass graft surgery; *MR,* mitral regurgitation; *MS,* mitral stenosis; *MV,* mitral valve; *PPH,* primary pulmonary hypertension; *Redo,* redo cardiac surgery; *sPAP,* systolic pulmonary artery pressure.

varying levels of sPAP. Greater degrees of LA enlargement, more atrial fibrillation, tricuspid regurgitation, systemic hypertension, and RV dysfunction were present in patients with higher preoperative sPAP. By multivariable analysis, predictors that were significantly associated with higher preoperative sPAP included female gender (OR, 2.88; 95% confidence interval [CI], 1.92–4.54; $P < .0001$), LA dimension (OR, 1.05 per 1-mm increase; 95% CI, 1.03–1.08; $P < .0001$), left ventricular end-systolic dimension (OR, 1.05 per 1-mm increase; 95% CI, 1.03–1.08; $P < .0001$), chronic lung disease (OR, 3.40; 95% CI, 1.70–7.70; $P = .0005$), dialysis (OR, 7.86; 95% CI, 3.32–33.38; $P < .0001$), previous myocardial infarction (OR, 2.37; 95% CI, 1.52–4.80; $P = .0028$), and body mass index (OR, 1.05 per 1 kg/m^2 increase; 95% CI, 1.02–1.09; $P = .0017$) (C-statistic = 0.768).

Operative Characteristics

Concomitant procedures performed included coronary artery bypass in 253 patients (29%), tricuspid valve operation in 133 patients (15%), aortic valve operation in 100 patients (11%), and CryoMaze procedure in 185 patients (21%). Sixty-one patients (7%) underwent redo operation (Table 3). MV repair was performed in 747 patients (86%), and MV replacement was performed in 126 patients (14%). Operative characteristics as a function of preoperative sPAP are summarized in Table 4. Patients with higher sPAP more commonly required concomitant procedures. MV repair was less commonly performed as the degree of PH increased (repair rate 92% for no PH, 88% for mild PH, 82% for moderate PH, and 70% for severe PH, $P < .0001$) (Table 4).

TABLE 1. Selected preoperative patient characteristics for 873 patients undergoing mitral valve operation for mitral regurgitation

Characteristic	No. (%), or mean ± SD
Age (y)	59 ± 14
Female gender	361 (41%)
BMI (kg/m^2)	27 ± 7
NYHA class III/IV	493 (57%)
Atrial fibrillation	260 (30%)
Prior cardiac surgery	61 (7%)
Prior MV surgery	22 (3%)
Chronic lung disease	115 (13%)
Hypertension	561 (64%)
Diabetes mellitus	157 (18%)
Renal failure (dialysis)	50 (6%)
Cardiac structure, function	
LV ejection fraction, mean, %	52 ± 14
LA diameter, cm	4.6 ± 0.8 (n* = 641)
LV end-diastolic diameter, cm	5.4 ± 0.8 (n = 656)
LV end-systolic diameter, cm	3.8 ± 0.9 (n = 544)
sPAP (mm Hg)	
Echocardiography	46 ± 15 (n = 621)
RHC	43 ± 17 (n = 591)
RV dysfunction	137 (15%)
MR grade	
Moderate	98 (11%)
Moderate-to-severe	210 (24%)
Severe	565 (65%)
TR grade	
None/mild	664 (76%)
Moderate	114 (13%)
Moderate-to-severe	36 (4%)
Severe	59 (7%)
AI grade	
None/mild	787 (90%)
Moderate	44 (5%)
Severe	42 (5%)
Severe AS	49 (6%)

AI, Aortic insufficiency; *AS,* aortic stenosis; *AV,* aortic valve; *BMI,* body mass index; *LA,* left atrium; *LV,* left ventricle; *MR,* mitral regurgitation; *MV,* mitral valve; *NYHA,* New York Heart Association; *RHC,* right heart catheterization; *RV,* right ventricle; *SD,* standard deviation; *TR,* tricuspid regurgitation; *sPAP,* systolic pulmonary artery pressure. *Data available.

Operative Outcomes

The operative mortality rate for the entire population was 5% (n = 43, in hospital = 40). Operative mortality was 2%

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TABLE 2. Baseline characteristics of the patient population according to degree of pulmonary hypertension*

Variable	sPAP < 40 mm Hg 407 (47%)	40 ≤ sPAP <50 mm Hg 176 (20%)	50 ≤ sPAP < 60 mm Hg 142 (16%)	sPAP ≥ 60 mm Hg 148 (17%)	*P* value
sPAP (mm Hg)					
Mean ± SD	30 ± 6	44 ± 3	53 ± 3	71 ± 10	<.00001
Median (25th–75th percentile)	30 (25–35)	44 (41–46)	53 (50–55)	69 (63–77)	
sPAP/sBP (mean ± SD)	0.24 ± 0.05	0.34 ± 0.06	0.43 ± 0.10	0.56 ± 0.12	<.0001
Age (y)	58 ± 14	61 ± 13	61 ± 15	62 ± 14	.0048
Female gender	144 (35%)	82 (47%)	78 (45%)	71 (48%)	.0008
BMI (kg/m^2, mean ± SD)	27 ± 6	28 ± 8	28 ± 6	29 ± 8	.0005
Morbid obesity†	16 (16%)	18 (31%)	8 (14%)	16 (28%)	.2274
NYHA class III/IV	188 (46%)	102 (58%)	96 (68%)	107 (72%)	.0001
Atrial fibrillation	100 (25%)	63 (36%)	51 (36%)	56 (38%)	.00034
LVEF (%)	55 ± 13	52 ± 14	47 ± 16	50 ± 14	.0001
LVEDD (cm)	5.4 ± 0.7	5.5 ± 0.9	5.5 ± 0.9	5.5 ± 0.9	.606
LVESD (cm)	3.6 ± 0.8	3.9 ± 0.1	4.1 ± 0.1	4.1 ± 0.1	.0001
LA diameter (cm)	4.4 ± 0.8	4.6 ± 0.9	4.8 ± 0.7	5.0 ± 0.8	.0001
RV dysfunction	19 (5%)	22 (13%)	43 (30%)	53 (36%)	.0001
MR grade	3.5 ± 0.7	3.2 ± 0.8	3.4 ± 0.8	3.6 ± 0.6	.0003
TR grade	0.6 ± 0.8	1.05 ± 0.9	1.4 ± 1.1	1.8 ± 1.3	<.0001
AI grade	0.2 ± 0.7	0.4 ± 1	0.5 ± 1	0.6 ± 1	.0002
Severe AS	10 (2%)	8 (5%)	16 (11%)	15 (10%)	<.0001
Chronic lung disease	36 (9%)	28 (16%)	21 (15%)	30 (21%)	.0021
Redo operation	21 (5%)	11 (6%)	12 (8%)	17 (11%)	.0625
Diabetes mellitus	45 (11%)	37 (21%)	27 (19%)	48 (32%)	.0001
Hypertension	225 (55%)	122 (69%)	100 (70%)	114 (77%)	.0001
Peripheral arterial disease	20 (5%)	8 (5%)	13 (9%)	17 (11%)	.041
History of stroke	30 (7%)	19 (11%)	21 (15%)	16 (11%)	.071
Previous MI	41 (10%)	36 (20%)	30 (21%)	31 (21%)	.0003
Cerebrovascular disease	44 (11%)	24 (14%)	25 (18%)	29 (20%)	.031
Renal failure (dialysis)	6 (1%)	6 (3%)	18 (13%)	20 (14%)	.0001
ACE inhibitors/ARB	161 (40%)	70 (40%)	76 (54%)	64 (43%)	.0284
Beta-blockers	176 (43%)	96 (56%)	85 (60%)	91 (61%)	.0009

Data presented in mean ± SD or n (%). *AI,* Aortic insufficiency; *ACE,* angiotensin-converting enzyme; *ARB,* angiotensin receptor blocker; *AS,* aortic stenosis; *BMI,* body mass index; *LA,* left atrium; *LVEF,* left ventricular ejection fraction; *LVEDD,* left ventricular end-diastolic diameter; *LVESD,* left ventricular end-diastolic diameter; *MI,* myocardial infarction; *MR,* mitral regurgitation; *NYHA,* New York Heart Association; *RV,* right ventricle; *sBP,* systemic blood pressure in systole; *SD,* standard deviation; *sPAP,* systolic pulmonary artery pressure; *TR,* tricuspid regurgitation. *PH absent: sPAP < 40 mm Hg; mild PH: 40 ≤ sPAP< 50 mm Hg; moderate PH: 50 ≤ sPAP < 60 mm Hg; severe PH: sPAP ≥ 60 mm Hg. †Morbid obesity: BMI ≥ 40 kg/m^2.

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for patients with no PH (sPAP < 40 mm Hg) compared with 3% for patients with mild PH (40 ≤ sPAP < 50 mm Hg), 8% for moderate PH (50 ≤ sPAP < 60 mm Hg), and 12% for those with severe preoperative PH (sPAP ≥ 60 mm Hg) ($P < .0001$) (Figure 2). By multivariable analysis, preoperative sPAP was a predictor associated with operative mortality (Table 5).

Major operative morbidity for the entire group included new-onset atrial fibrillation (121, 14%), dialysis (31, 3.5%), stroke (19, 2%), and sepsis (22, 2.5%). Higher preoperative sPAPs were associated with higher rates of postoperative sepsis, prolonged ventilation, and dialysis (Table 4). On comparison of patients with no PH (sPAP < 40 mm Hg) with those with mild PH (40 ≤ sPAP < 50 mm Hg), morbidity, including renal failure (dialysis) ($P = .8$), atrial fibrillation ($P = .24$), and stroke ($P = .8$), was not significantly different. However, prolonged ventilation (no PH: 43 [11%] vs mild PH: 44 [25%], $P < .0001$) and longer hospital stay (median 5 days for no PH vs 8 days for mild PH, $P < .0001$) and intensive care unit stay more than 24 hours (no PH: 13 [3%] vs mild PH 10 [6%], $P = .0244$) were more common in patients with mild PH (Table 4).

Late Survival

Actuarial survival in patients without PH (sPAP < 40 mm Hg) at 1, 3, 5, and 7 years was 96%, 92%, 86%, and 84%, respectively, compared with 83%, 73%, 67%, and 61%, respectively, for those with preoperative PH (sPAP ≥ 40 mm Hg) ($P < .00279$) (Figure 3, *A*). Long-term survival progressively decreased with increasing preoperative sPAP grade ($P < .0001$) (Figure 3, *B*). In a Cox proportional hazards analysis, increasing preoperative sPAP was associated with decreased long-term survival (Table 6). Among patients with no or minimal preoperative symptoms (380 [43%]) (NYHA class I: 88 [10%], NYHA class II: 292

TABLE 3. Operative characteristics for 873 patients undergoing mitral valve operation for mitral regurgitation

Characteristic	No. (%), or mean ± SD
MV operation	
Repair	747 (86%)
Replacement	126 (14%)
MV pathology	
Degenerative MR due to leaflet prolapse	389 (44%)
Anterior leaflet prolapse	52 (13%)
Posterior leaflet prolapse	270 (70%)
Bileaflet prolapse	67 (17%)
Isolated annular dilation (type I) or functional (type IIIb ± type I)	271 (31%)
Rheumatic	70 (8%)
Endocarditis	132 (15%)
Paravalvular leak	8 (1%)
Prosthetic valve degeneration	3 (1%)
Redo operation	61 (7%)
Concomitant procedures	
Coronary artery bypass	253 (29%)
TV operation	133 (15%)
AV operation	100 (11%)
CryoMaze procedure	185 (21%)
ASD closure	22 (3%)
Perfusion time (min)	
Mean	126 ± 49
Median	117
Crossclamp time (min)	
Mean	97 ± 37
Median	94
Operative mortality	43 (5%)

AV, Aortic valve; *ASD,* atrial septal defect; *MR,* mitral regurgitation; *MV,* mitral valve; *SD,* standard deviation; *TV,* tricuspid valve.

[33%]), even a mild increase in preoperative sPAP (40 ≤ sPAP < 50 mm Hg) compromised long-term survival (log rank, $P = .0004$). Among those 373 patients with sPAP determined with both echocardiography and RHC, we found that echocardiographic-derived sPAP was similarly predictive of late mortality as was sPAP determined by RHC (echocardiographic-derived sPAP: HR, 1.024 per 1 mm Hg increment; 95% CI, 1.011–1.034; $P = .0004$ vs RHC-derived sPAP: HR, 1.029 per 1 mm Hg increment; 95% CI, 1.0117–1.041; $P < .0001$).

Even after excluding patients with a history of myocardial infarction (n = 138), concomitant aortic valve surgery (n = 100), or coronary artery bypass surgery (n = 253), patients with sPAP 40 mm Hg or greater had higher operative mortality and long-term death (Appendix 2).

Analysis of Outcomes Based on the Ratio of Systolic Pulmonary Artery Pressure to Systemic Blood Pressure

On the basis of the ratio of systolic pulmonary to systolic systemic blood pressure, patients were categorized as having no PH (sPAP/sBP < 0.3) (n = 387, 45%), mild PH (0.3 ≤ sPAP/sBP < 0.4) (n = 200, 23%), moderate PH (0.4 ≤ sPAP < 0.5) (n = 143, 16%), and severe PH (sPAP/sBP ≥ 0.5) (n = 143, 16%). Operative mortality was 2% (n = 8) for no PH, 4% (n = 8) for mild PH, 6.3% (n = 9) for moderate PH, and 13% (n = 18) for severe PH ($P < .0001$). Long-term survival decreased significantly with increased preoperative sPAP/sBP ratio (Appendix Figure 1). These findings were nearly identical to those in which only isolated sPAP was used as a predictor.

Isolated Degenerative Mitral Regurgitation

Overall, 284 patients with isolated degenerative MR with leaflet prolapse were studied in cohort 2. The mean age was 57 ± 13 years, and the mean sPAP was 36 ± 14 mm Hg (Table 7). Preoperative sPAP was measured using RHC in 214 patients (75%). Preoperatively, 193 patients (68%) had no PH (sPAP < 40 mm Hg), 48 patients (17%) had mild PH (40 ≤ sPAP < 50 mm Hg), and 43 patients (15%) had moderate/severe PH (sPAP ≥ 50 mm Hg). Preoperative NYHA class III or IV symptoms were present in 121 patients (39%), and 173 patients (61%) had class I or II symptoms. MV repair was performed in 277 patients (98%), and MV replacement was performed in 8 patients (2%). Concomitant procedures, including tricuspid valve repair (n = 18, 6%) and CryoMaze procedure (n = 58, 20%), were more common in patients with PH (sPAP ≥ 40 mm Hg). Operative mortality was 0.8% (2/284). Kaplan–Meier analysis showed that survival decreased with increasing preoperative PH grade (Figure 4). Overall actuarial survival at 1, 3, and 5 years after MV surgery was 99.5%, 98.5%, and 97.5%, respectively, in patients with no PH (sPAP < 40 mm Hg) compared with 95.8%, 92.9%, and 91.2%, respectively, for those with mild PH (40 ≤ sPAP < 50 mm Hg) and 90.6%, 84.2%, and 80.5%, respectively, for those with moderate to severe PH (sPAP ≥ 50 mm Hg) ($P = .0002$). Compared with patients with no PH, 5-year survival decreased in patients with mild PH (98% ± 1% for no PH vs 91% ± 4% for mild PH, $P = .002$). In a Cox proportional hazards analysis, factors associated with decreased long-term survival included increasing preoperative sPAP (HR, 1.037 per 1 mm Hg increase; 95% CI, 1.004–1.066; $P = .0277$), age (HR, 1.303; 95% CI, 1.051–1.625; $P = .0277$), and left ventricular ejection fraction (HR, 0.902; 95% CI, 0.854–0.956; $P = .001$) (C-statistic for the multivariable model = 0.9).

Pulmonary Artery Pressure Changes After Operation

The mean sPAP at different time points is demonstrated in Figure 5, *A*. In the entire population, mean sPAP decreased modestly from 43 ± 16 mm Hg before operation to 39 ± 11 mm Hg before hospital discharge ($P < .0001$). Compared with the predischarge value, mean sPAP was

TABLE 4. Operative characteristics and hospital morbidity and mortality as a function of preoperative systolic pulmonary artery pressure*

Variable	sPAP < 40 mm Hg 407 (47%)	40 ≤ sPAP <50 mm Hg 176 (20%)	50 ≤ sPAP < 60 mm Hg 142 (16%)	sPAP ≥ 60 mm Hg 148 (17%)	*P* value
CVP† (mm Hg)	10 ± 5	12 ± 5	13 ± 6	15 ± 6	<.001
MV pathology					
Degenerative (leaflet prolapse)	240 (59%)	70 (40%)	36 (25%)	43 (29%)	<.0001
Isolated annular dilation (type I) or functional (type IIIb ± type I)	90 (22%)	62 (35%)	66 (46%)	53 (36%)	<.001
Rheumatic	21 (55%)	13 (7%)	13 (9%)	23 (16%)	.001
Endocarditis	51 (13%)	31 (18%)	25 (18%)	25 (17%)	.282
MV repair	373 (92%)	154 (88%)	117 (82%)	103 (70%)	<.0001
Concomitant procedure					
Coronary artery bypass	89 (22%)	51 (29%)	56 (39%)	57 (39%)	<.0001
TV operation	21 (5%)	29 (16%)	30 (21%)	50 (34%)	<.0001
AV operation	27 (7%)	22 (13%)	23 (16%)	28 (19%)	.0001
CryoMaze procedure	71 (17%)	53 (30%)	30 (21%)	31 (21%)	.0008
Operative mortality	7 (2%)	6 (3%)	12 (8%)	18 (12%)	<.0001
Morbidity					
Renal failure (dialysis)	8 (2%)	4 (2%)	9 (6%)	10 (7%)	.0094
Prolonged ventilation	43 (11%)	44 (25%)	35 (25%)	54 (36%)	<.0001
Sepsis	7 (2%)	1 (1%)	4 (3%)	10 (7%)	.0022
Atrial fibrillation	46 (11%)	26 (15%)	27 (19%)	22 (15%)	.12
Stroke	8 (2%)	3 (2%)	4 (3%)	4 (3%)	.31
Length of stay					
ICU > 24 h	13 (3%)	10 (6%)	8 (6%)	12 (8%)	.021
LOS (median [25th–75th], d)	5 (4–9)	8 (6–16)	11.5 (7–19)	12 (8–22)	<.0001

AV, Aortic valve; *CVP,* central venous pressure; *ICU,* intensive care unit; *LOS,* length of stay; *MV,* mitral valve; *sPAP,* systolic pulmonary artery pressure; *TV,* tricuspid valve. *PH absent: sPAP < 40 mm Hg; mild PH: 40 ≤ sPAP < 50 mm Hg; moderate PH: 50 ≤ sPAP < 60 mm Hg; Severe PH: sPAP ≥ 60 mm Hg. †Intraoperative, before incision.

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not markedly changed within the first 2 years (39 ± 12 mm Hg, $P = .907$) and after 2 years of follow-up (38 ± 13 mm Hg, $P = .952$) (Figure 5, *A*). Figure 5, *B*, demonstrates sPAP at different time points for each category of pulmonary artery pressure. Compared with preoperative values, sPAP decreased on predischarge echocardiography in all categories except in patients with no PH where there was a small increase. The relative decrease was most pronounced in patients with preoperative moderate (50 ≤ sPAP < 60 mm Hg) and severe PH (sPAP ≥ 60 mm Hg). On late follow-up, sPAP was similar to predischarge levels. Residual PH (sPAP ≥ 40 mm Hg) was more commonly present among patients with mild (40 ≤ sPAP < 50 mm Hg), moderate (50 ≤ sPAP < 60 mm Hg), or severe degree (sPAP ≥ 60 mm Hg) of preoperative PH (Figure 5, *B* and *C*). Of 159 patients who had preoperative sPAP 50 mm Hg or greater and follow-up echocardiographic data available, 56 (35%) still had sPAP 50 mm Hg or greater 2 years (mean, 714 ± 603 days) after surgery.

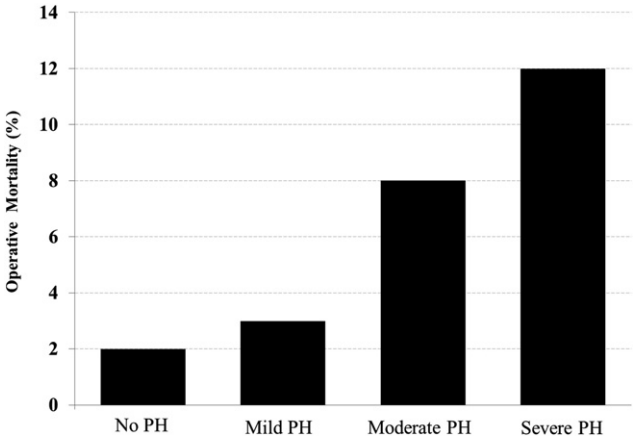

FIGURE 2. Hospital mortality according to preoperative PH grade ($P < .0001$). *PH,* Pulmonary hypertension.

DISCUSSION

Principal Findings

This article presents early and late outcomes after MV surgery in a large series of patients with MR according

TABLE 5. Predictors of operative mortality*

Variable	OR	95% CI	*P*
sPAP (per 1 mm Hg increment)	1.023	1.003–1.044	.0270
NYHA functional class III–IV	3.442	1.040–1.410	.0052
Age (per unit)	1.034	1.007–1.064	.0159
Concomitant CABG	2.133	1.041–4.464	.0395
Dialysis	4.451	1.068–1.785	.0018
IE	3.017	1.204–7.407	.0194
RV dysfunction	3.178	1.552–6.488	.0017

CABG, Coronary artery bypass graft; *CI,* confidence interval; *IE,* infective endocarditis; *NYHA,* New York Heart Association; *OR,* odds ratio; *RV,* right ventricle; *sPAP,* systolic pulmonary artery pressure. *C-statistic = 0.854.

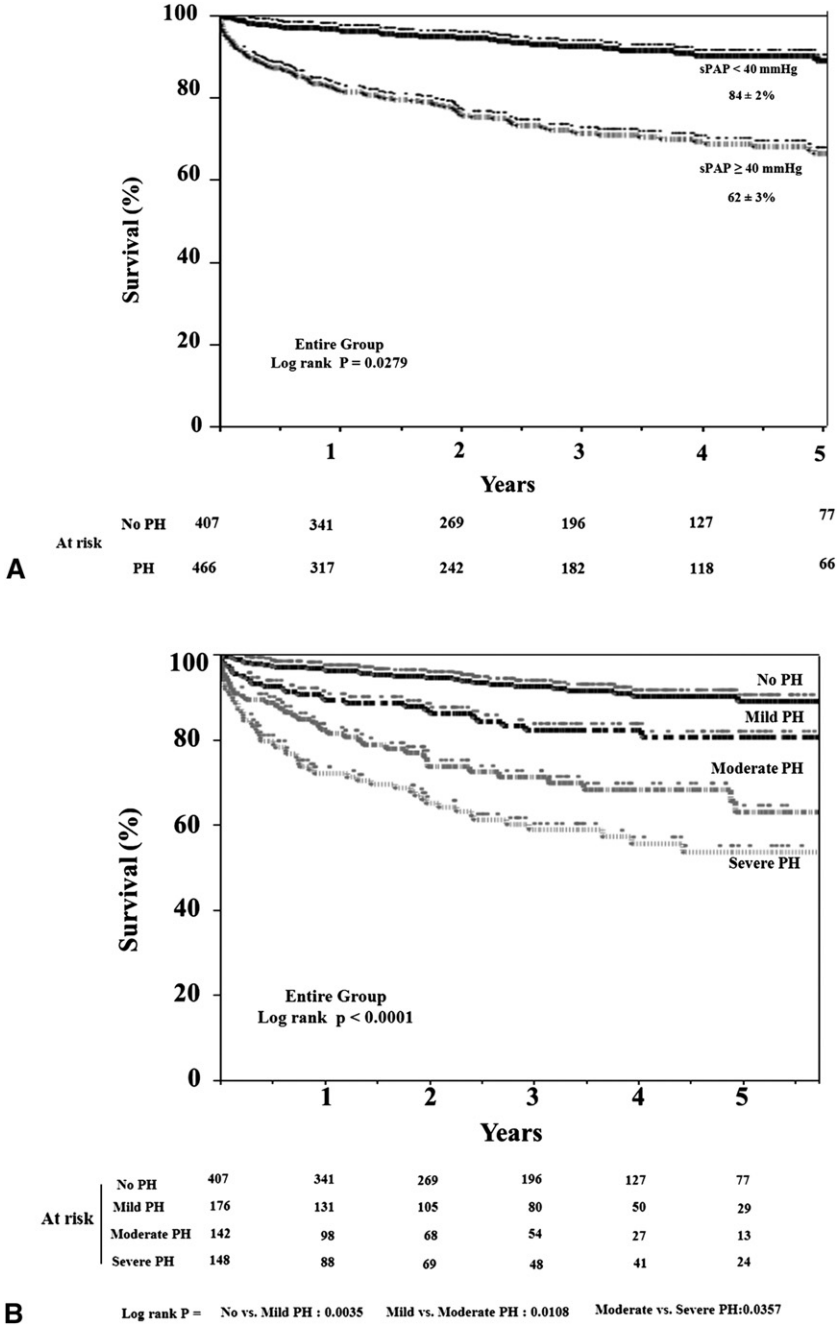

FIGURE 3. Long-term survival according to preoperative PH. A, Actuarial survival according to a cutoff value of sPAP 40 mm Hg or greater. B, Survival according to preoperative PH grade. *PH,* Pulmonary hypertension; *sPAP,* Systolic pulmonary artery pressure.

to preoperative sPAP. Pulmonary artery pressures were measured in the majority of patients with RHC. On the basis of the cutoff point of preoperative sPAP 40 mm Hg or greater, PH was observed in more than half of the population. Compared with patients with no PH (sPAP < 40 mm Hg), patients presenting with mild PH (40 ≤ sPAP < 50 mm Hg) had lower left ventricular ejection fractions, more atrial fibrillation and more tricuspid regurgitation. Operative mortality among patients with no PH (sPAP < 40 mm Hg) was low (2%). With increased sPAP 40 mm Hg or greater or sPAP/sBP 0.3 or greater, higher mortality and morbidity were observed after surgery. Long-term survival was compromised by the presence of any degree of preoperative PH, including those patients with mild PH (40 ≤ sPAP < 50 mm Hg). These findings were also evident in patients with isolated degenerative MR. Pulmonary artery pressures declined immediately after operation but not thereafter, and residual PH

TABLE 6. Predictors of long-term mortality*

Variable	HR	95% CI	*P*
sPAP (per 1 mm Hg increment)	1.018	1.007–1.028	.001
NYHA function class (III /IV vs I/II)	1.835	1.216–2.844	.0034
Age (per unit)	1.036	1.021–1.051	<.0001
Dialysis (yes vs no)	3.052	1.596–5.452	.0013
Diabetes (yes vs no)	1.826	1.222–2.688	.0037

CI, Confidence interval; *HR,* hazard ratio; *NYHA,* New York Heart Association; *sPAP,* systolic pulmonary artery pressure. *C-statistic of multivariable model: 0.764.

was observed late among all patients except those with normal preoperative sPAP(s).

The prevalence of PH in patients undergoing surgery for MR depends on the threshold of sPAP used to define PH. Although the cutoff value of sPAP to define PH (sPAP > 50 mm Hg) in current guidelines is derived from small clinical series performed on patients with systemic sclerosis,[18] various values are frequently used in practice.[8,19,20] We used a lower threshold of sPAP value (sPAP ≥ 40 mm Hg) compared with existing guidelines to identify individuals at risk for adverse outcomes after surgery. Outcomes after surgery for patients with no PH (sPAP < 40 mm Hg) were excellent. Operative mortality was 2%, and 86% survived more than 5 years after surgery. However, approximately 1 of 10 patients with severe PH (sPAP ≥ 60 mm Hg) undergoing surgery for MR died in hospital or early after surgery, and only half survived 5 years after surgery. Long-term survival in patients with isolated degenerative MR was compromised among patients with any degree of preoperative PH.

In both cohorts in this study, preoperative sPAP was an important independent predictor for long-term survival after surgery. Even the presence of mild PH (40 ≤ sPAP < 50 mm Hg) compromised long-term survival in both cohorts. These results support a management strategy of surgical intervention for MR before the sPAP reaches 50 mm Hg. Le Tourneau and colleagues[2] studied 256 patients with organic MR referred for MV surgery. Preoperative PH (sPAP ≥ 50 mm Hg) was present in 83 patients. Although PH did not significantly increase operative mortality, survival 8 years after surgery was 86% in patients with no PH compared with 58% in those with sPAP 50 mm Hg or greater. Patients with preoperative PH were more symptomatic early after surgery and had more left ventricular dysfunction compared with those with no PH. Le Tourneau and colleagues[2] found that long-term risk for mortality increased by 50% per 10 mm Hg increase in preoperative sPAP.[2] Barbieri and colleagues[7] studied 437 patients with degenerative severe MR with flail leaflet. All patients had no or minimal symptoms with normal left ventricular

TABLE 7. Baseline characteristics of the patients with isolated leaflet prolapse (n = 284) according to the degree of preoperative pulmonary hypertension*

Variable	sPAP < 40 mm Hg 193 (68%)	40 ≤ sPAP <50 mm Hg 48 (17%)	50 mm Hg ≤ sPAP 43 (15%)	*P* value
sPAP (mm Hg)				
Mean ± SD	28 ± 6	44 ± 3	63 ± 13	<.0001
Median (25th–75th percentile)	29 (25–33)	44 (40–46)	59 (51–70)	
Age (y)	55 ± 12	65 ± 14	62 ± 13	.001
Female gender	60 (31%)	19 (40%)	22 (51%)	.0370
BMI (kg/m^2, mean ± SD)	26 ± 6	27 ± 6	30 ± 8	.0045
Morbid obesity†	5 (39%)	2 (15%)	6 (46%)	.445
NYHA class III/IV	57 (30%)	27 (56%)	27 (63%)	<.0001
Atrial fibrillation	38 (20%)	19 (40%)	13 (30%)	.0109
LVEF (%)	58 ± 8	56 ± 8	55 ± 11	.0414
LVEDD (cm)	5.5 ± 0.7	5.6 ± 0.7	5.6 ± 0.8	.5551
LVESD (cm)	3.4 ± 0.7	3.7 ± 0.8	3.8 ± 0.8	.0088
LA diameter (cm)	4.5 ± 0.7	4.8 ± 0.7	4.9 ± 0.7	.0020
RV dysfunction	3 (2%)	3 (6%)	7 (16%)	.0001
MR grade	3.7 ± 0.5	3.4 ± 0.7	3.6 ± 0.5	.0207
TR grade	0.4 ± 0.6	1.0 ± 1.0	1.4 ± 1.1	<.0001
Chronic lung disease	0 (0%)	0 (0%)	0 (0%)	–
Diabetes mellitus	5 (3%)	4 (8%)	7 (16%)	.0013
Hypertension	88 (46%)	30 (63%)	27 (63%)	.0275
History of stroke	2 (1%)	0 (0%)	3 (7%)	.0149
Previous MI	1 (1%)	2 (4%)	1 (2%)	.1359
Renal failure (dialysis)	0 (0%)	0 (0%)	1 (2%)	.0601

Data presented in mean ± SD or n (%). *BMI,* Body mass index; *LA,* left atrium; *LVEF,* left ventricular ejection fraction; *LVEDD,* left ventricular end-diastolic diameter; *LVESD,* left ventricular end-diastolic diameter; *MI,* myocardial infarction; *MR,* mitral regurgitation; *NYHA,* New York Heart Association; *RV,* right ventricle; *sPAP,* systolic pulmonary artery pressure; *TR,* tricuspid regurgitation. *PH absent: sPAP < 40 mm Hg; mild PH: 40 ≤ sPAP< 50 mm Hg; moderate PH: 50 ≤ sPAP < 60 mm Hg; Severe PH: sPAP ≥ 60 mm Hg. †Morbid obesity: BMI ≥ 40 kg/m^2.

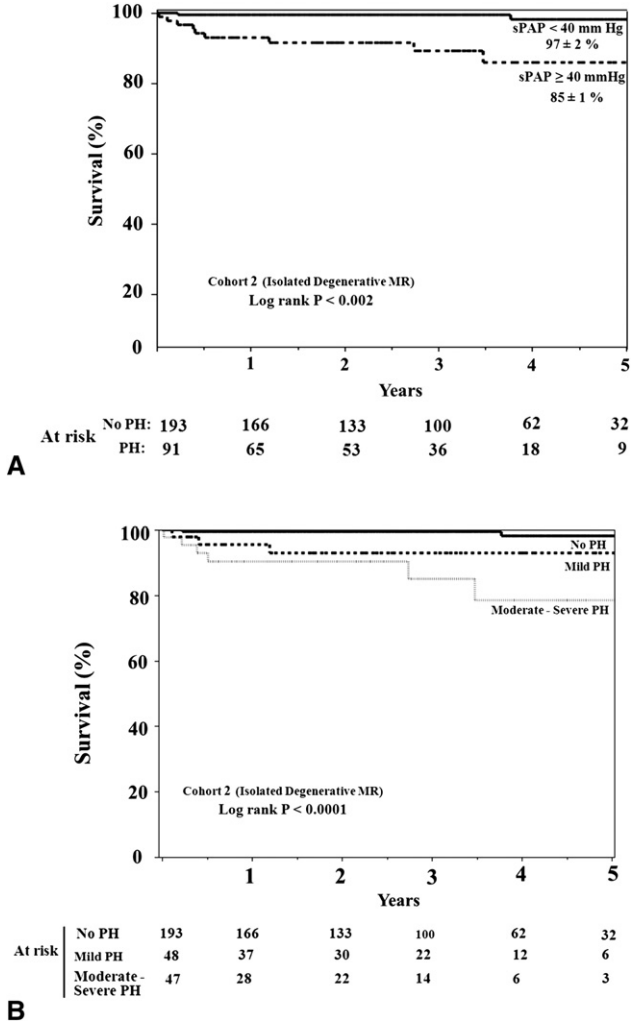

FIGURE 4. Survival curve according to preoperative PH (sPAP $\geq$ 40 mm Hg) in cohort 2 (patients with isolated degenerative MR due to flail leaflet). For all patients (A) and according to preoperative PH grade (B). *MR,* Mitral regurgitation; *PH,* pulmonary hypertension; *sPAP,* systolic pulmonary artery pressure.

function. Baseline PH (sPAP > 50 mm Hg) was present in 23% of patients. Actuarial survival 5 years after surgery was 86% in patients with no PH (sPAP < 50 mm Hg) compared with 63% in those with PH (sPAP > 50 mm Hg). MV surgery was eventually performed in 75% of patients. Postoperative survival was significantly decreased in patients with baseline sPAP 50 mm Hg or greater.[7] The authors concluded that PH (sPAP > 50 mm Hg) in patients with chronic organic MR carries an increased risk of long-term mortality, which is similar to our experience.[2] They found that MV surgery is beneficial to improve sPAP, but surgery cannot completely abolish adverse effects of PH on outcomes.[7]

Studies have shown that sustained systemic hypertension correlates with higher values of pulmonary artery pressures[21] and suggested that interpretation of sPAP in hypertensive patients should take into account sBP value.[21] We studied the pulmonary artery to systemic blood pressure in our population and found nearly identical results to our initial analysis that examined only sPAP. We found that elevated sPAP/sBP ratio (sPAP/sBP $\geq$ 0.3) compromised both early and late survival after MV surgery for MR.

No Pulmonary Hypertension Versus Mild Pulmonary Hypertension: Lessons Learned

Operative mortality and major morbidity were similar between patients with no PH (sPAP < 40 mm Hg) and those with mild PH (40 $\leq$ sPAP < 50 mm Hg). However, long-term survival was lower in patients with mild PH compared with patients with no preoperative PH in the overall study population, in the cohort with isolated leaflet prolapse, and in patients with no or minimal preoperative symptoms. Given the increased risk of adverse outcomes in patients with mild PH (40 $\leq$ sPAP < 50 mm Hg) compared with those with no PH (sPAP < 40 mm Hg), we believe that referral for MV surgery for MR should be considered before sPAP exceeds 40 mm Hg.

Regression of Pulmonary Artery Pressures After Mitral Valve Surgery

In this study, significant reduction in mean sPAP was observed early after operation. During follow-up, the mean sPAP failed to return to normal levels in patients with any degree of preoperative PH (sPAP $\geq$ 40 mm Hg). Incomplete improvement in pulmonary artery pressures after operation for MR suggests that significant pulmonary vascular disease develops early in the presence of MR, and therefore a management strategy that triggers operative intervention when the sPAP exceeds 40 mm Hg will improve long-term survival.

Study Limitations

The present study was subject to the limitations inherent in a retrospective study. We did not exclude patients with aortic valve disease or chronic obstructive pulmonary disease in the first cohort. Although we performed multivariable analysis to account for confounding factors, we cannot guarantee that unmeasured confounding factors did not influence our results. Preoperative evaluation of pulmonary pressures was comprehensive, although predischarge and follow-up echocardiographic data were incomplete. We did not have data to evaluate the impact of residual PH on other outcomes, such as freedom from heart failure, atrial fibrillation, or NYHA function class at follow-up. Medical therapy after surgery was not assessed and might affect long-term outcomes.

CONCLUSIONS

PH is a common adverse sequela of MR. Systolic pulmonary artery pressure is a predictor of operative mortality, morbidity, and long-term death. Even mild PH (40 $\leq$ sPAP < 50 mm Hg) compromises outcomes after MV

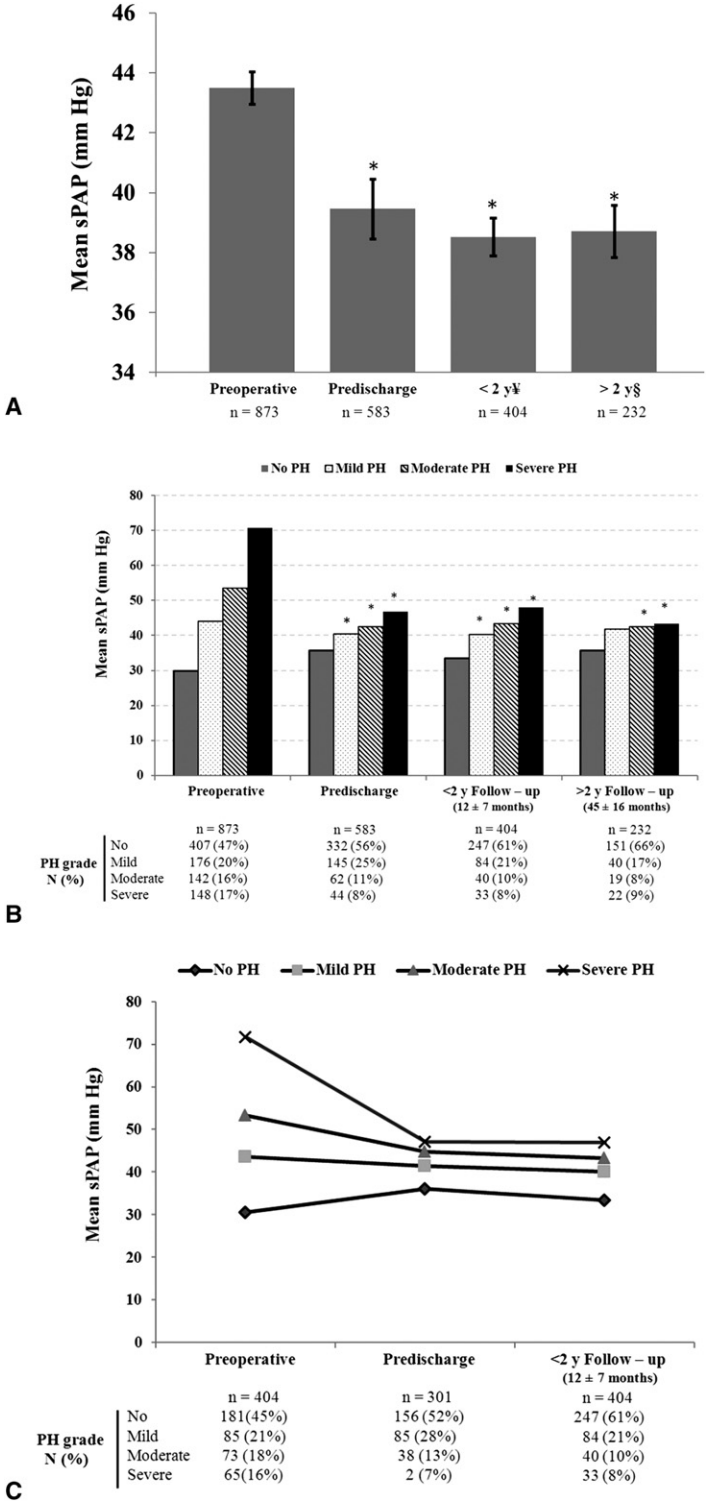

FIGURE 5. Mean sPAP at different time points. A, All patients (mean ± standard deviation sPAP at preoperative: 43 ± 16, predischarge: 39 ± 11, follow-up < 2 years: 39 ± 12, follow-up > 2 years: 38 ± 13 mm Hg). B, According to PH grade for all patients. C, For 404 patients with 2-year follow-up. Mean sPAP decreased markedly in patients with higher preoperative sPAP, but residual sPAP 40 mm Hg or greater was more common after surgery and during follow-up in these groups. Pulmonary pressures at predischarge relatively correlate with the late response of pulmonary pressure changes to surgery (no significant difference was identified in mean sPAP at predischarge and within 2 years follow-up, $P = .95$). ¥Median: 12 months (24 days to 24 months). §Median: 41 months (24–91 months). *$P < .01$ compared with preoperative value. *MR,* Mitral regurgitation; *PH,* pulmonary hypertension; *sPAP,* Systolic pulmonary artery pressure.

surgery for MR. sPAP improved early after surgery, although residual PH was commonly observed among all patients except those with normal preoperative sPAP (<40 mm Hg). Referral for MV surgery for MR should be considered in the presence of an sPAP 40 mm Hg or greater.

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APPENDIX 1. VARIABLES USED IN ANALYSIS

Demographics: age (y), gender, sex, weight (kg), height (cm), body mass index (kg/m^2), NYHA function class (I–IV), emergency operation.

Cardiac stricture and function: left ventricular ejection fraction (%), sPAP (mm Hg), left ventricular inner systolic diameter (cm), left ventricular inner diastolic diameter (cm), LA diameter (cm), right ventricular dysfunction (0 = no, 1 = yes), MV regurgitation, aortic valve regurgitation, aortic valve stenosis, tricuspid valve regurgitation.

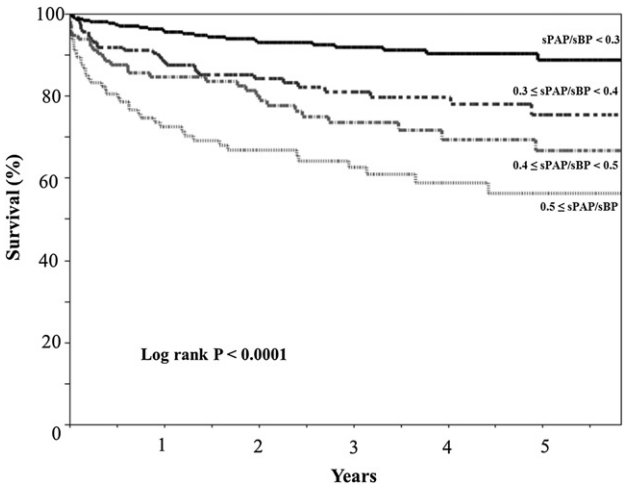
Cardiac comorbidity: number of coronary vessels with >50% stenosis, left main coronary disease ≥50% stenosis, atrial fibrillation. ventricular arrhythmia, family history of coronary artery disease, dyslipidemia, heart failure, hypertension, preoperative pacemaker, previous myocardial infarction, endocarditis.

Noncardiac morbidity: diabetes, chronic obstructive pulmonary disease, peripheral arterial disease, dialysis, stroke, smoking.

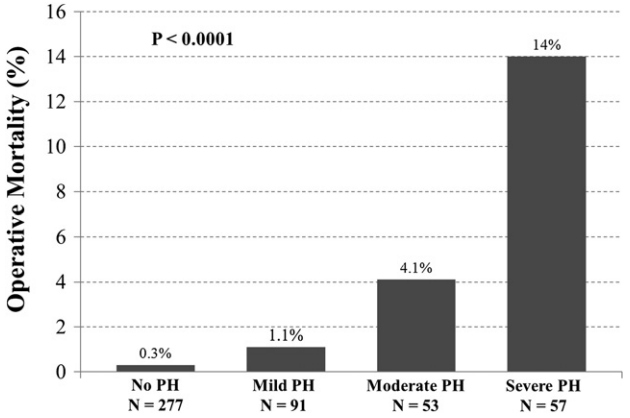
Procedures: MV repair/replacement, tricuspid valve surgery, aortic valve repair/replacement, coronary artery bypass grafting, surgical ablation for atrial fibrillation, reoperation.

APPENDIX 2. ANALYSIS OF OUTCOMES FOR ISOLATED MITRAL VALVE OPERATION FOR MITRAL REGURGITATION

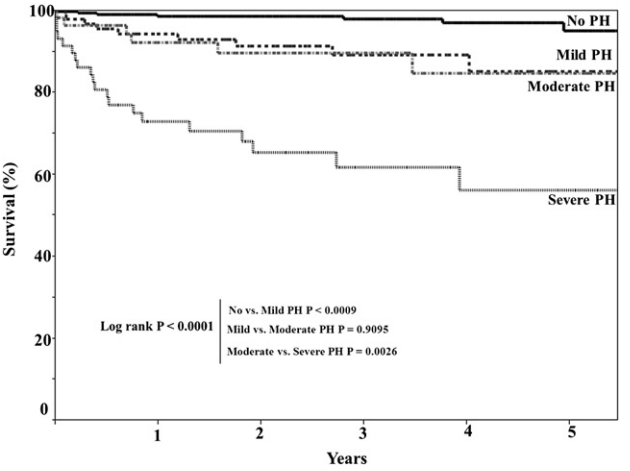
Patients with previous myocardial infarction (n = 138), concomitant aortic valve surgery (n = 100), and coronary artery bypass surgery (n = 253) were excluded, leaving



APPENDIX FIGURE 1. Kaplan–Meier survival curve according to preoperative sPAP/sBP. *sPAP,* Systolic pulmonary artery pressure; *sBP,* systolic blood pressure.



APPENDIX FIGURE 2. Hospital mortality according to preoperative PH grade among patients who underwent isolated MV operation for MR (n = 478). *PH,* Pulmonary hypertension.



APPENDIX FIGURE 3. Long-term survival according to preoperative PH among patients who underwent isolated MV operation for MR (n = 478). *PH,* Pulmonary hypertension.

478 patients for analysis. Patients were categorized as having no PH (sPAP < 40 mm Hg) (n = 277, 58%), mild PH (40 ≤ sPAP < 50 mm Hg) (n = 91, 19%), moderate PH (50 ≤ sPAP < 60 mm Hg) (n = 53, 11%), or severe PH (sPAP ≥ 60 mm Hg) (n = 57, 12%). Overall operative mortality was 2.3% (n = 11). Operative mortality (Appendix Figure 2) and long-term death (Appendix Figure 3) were significantly higher among patients with higher preoperative sPAP. Preoperative sPAP (per 1-mm increase) was an independent predictor for both operative mortality and long-term death (Appendix Table 1).

APPENDIX TABLE 1. Predictors of early and late mortality for 478 patients who underwent isolated mitral valve operation for mitral regurgitation

	Univariate analysis			Multivariate analysis		
Predictor	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Early mortality						
sPAP (per 1-mm increase)	1.063	1.0319–1.0981	.0001	1.0585	1.013–1.087	.0018
NYHA (III/IV vs I/II)	4.923	1.252–35.57	.0207			
TV surgery	4.280	1.0929–14.923	.0381			
Dialysis	19.955	4.761–76.92	.0002	10.34	2.347–41.66	.0033
History of stroke	6.099	1.545–21.141	.0124			
Late mortality	HR			HR		
sPAP (per 1-mm increase)	1.0533	1.0374–1.0687	<.0001	1.0387	1.021–1.056	<.0001
Gender (male vs female)	2.0256	1.1133–3.7900	.0206			
NYHA (III/IV vs I/II)	4.3928	2.2036–9.7415	<.0001	2.46	1.193–5.635	.0138
Age (per year)	1.0291	1.0072–1.05179	.0086	1.059	1.0327–1.0877	<.0001
LV ejection fraction	1.0345	1.0105–1.0563	.0059	1.028	1.002–1.0537	.0373
LA dimension (cm)	1.0459	1.0059–1.0855	.0242			
TR grade	1.6174	1.3124–1.9701	<.0001	1.470	1.152–1.859	.0023
MV replacement	3.2775	1.5792–6.2936	.0023			
TV surgery	2.6871	1.2953–5.1547	.0096			
RV dysfunction	3.3092	1.4909–6.6058	.0048			
Diabetes	3.0498	1.50663–5.7724	.0028			
Hypertension	2.255	1.206–4.465	.0102			
Infective endocarditis	3.3201	1.7900–6.0237	.0002	9.651	4.127–22.901	<.0001
Chronic lung disease	3.1836	14897–6.2100	.0041	2.280	1.051–4.544	.0379
Peripheral arterial disease	4.1319	1.2934–10.7091	.0211			
History of stroke	3.6746	1.809–6.979	.0006			
Atrial fibrillation	2.0265	1.0936–3.6734	.0255			
Emergency operation	6.099	1.545–21.141	.0124			

CI, Confidence interval; *LA,* left atrial; *LV,* left ventricle; *MV,* mitral valve; *NYHA,* New York Heart Association; *OR,* odds ratio; *RV,* right ventricle; *sPAP,* systolic pulmonary artery pressure; *TR,* tricuspid regurgitation; *TV,* tricuspid valve.

Discussion

Dr Gerald Lawrie *(Houston, Tex)*. This is a large series of patients, the biggest reported to date, and it also includes the broader spectrum of severity of disease of any previous report. It is also unique in that many of the patients had their PH diagnosed by RHC. Up to 40% of patients in previous studies have been excluded because insufficient tricuspid regurgitation has been present to allow them to assess pulmonary artery pressure by echocardiography.

This study has confirmed the findings of smaller earlier studies that an sPAP greater than 50 mm is a strong independent predictor of early and late survival. This study also demonstrated that in all categories of PH, regression of PH is incomplete after surgery, reaching approximately 40 mm systolic after 2 years. Despite the fact that surgery improves the prognosis at all levels of pulmonary artery pressure, regression is incomplete because the PH seen in severe MR arises not only from the MR itself but also from a series of complex changes in the left ventricle and LA morphology and their systolic and diastolic function. The pulmonary artery bed may develop increased vascular tone, and some degree of pulmonary hypertensive vasculopathy may develop as seen in mitral stenosis. Some of these changes, once present, may not regress despite relief of the MR.

These findings and those of this study suggest it may be important to pursue the issue of PH more aggressively and specifically than we have done to date.

First, these data provide further strong support for surgery early after the diagnosis of asymptomatic severe MR. Intraoperatively, improvement of LA function by atrial fibrillation ablation and volume reduction surgery could benefit, and I think we need to look more carefully at the influence of surgery on left ventricular diastolic function to try to refine our techniques to preserve left ventricular and LA function.

In patients presenting with PH in the 60 to 80 mm range, we have for many years involved our pulmonologists early preoperatively to evaluate and manage the PH and exclude other contributory causes. It is noteworthy that 21% of the patients in this study with pulmonary artery pressures greater than 60 had significant chronic obstructive pulmonary disease. It may be that this pulmonary evaluation should be extended to include RHC in all cases with drug evaluation for pulmonary artery vascular responsiveness.

Because incomplete regression of the pulmonary artery pressure was still present 2 years after surgery, it also may be that these patients should be followed long-term by a pulmonologist, something we have not done, and a cardiologist. Long-term pulmonary artery drug therapy could be beneficial in some cases.

Thank you for this excellent presentation, which I think has brought a neglected topic to our attention. I do have 2 questions for the presenter.

What proportion of the patients with no tricuspid regurgitation on echo had RHC showing significant PH? Do you think that all patients undergoing mitral repair with no TR should have RHC to assess their pulmonary artery pressure before they go to surgery? The second question relates to the fact that you agree we have a big problem here that we have neglected and that the approach to the care of these patients with persistent significant PH should involve long-term follow-up with a pulmonologist with active treatment to moderate their PH.

Dr Ghoreishi. To respond to your first question, we could not assess the sPAP based on echocardiography because of an absent tricuspid regurgitation jet velocity in 15% of patients. Among these patients, sPAPs were greater than 40 in 37% as measured on RHC. In 373 patients who were studied with both echocardiography and RHC, we found a reasonably good correlation between the results of echo and RHC, although there was significant variability. We expect some discrepancies between measurement of sPAP with RHC and echocardiography. Pulmonary artery pressures are dynamic, and the echocardiography and RHC were performed at different times.

We believe that the current recommendation to operate after the sPAP exceeds 50 mm Hg is associated with compromised early and late outcomes, and therefore we are recommending moving that threshold back to 40 mm Hg.

We advocate RHC for patients with asymptomatic severe MR who are managed nonsurgically to make sure that PH (sPAP $\geq$ 40 mm Hg) is not present.

To respond to your second question, we currently do not have any therapeutic protocols directed at residual PH. We found that during follow-up, sPAP in patients with preoperative PH (sPAP $\geq$ 40 mm Hg) never decreased to normal after surgery. We agree with you that these patients may benefit from long-term pharmacologic treatment after surgery and follow-up with a multidisciplinary team including a pulmonologist, but currently we don't have a protocol for these patients.

Dr Thierry Mesana *(Ottawa, Ontario, Canada)*. Congratulations for this large and interesting study. I noticed you had 12% mortality in those with high severe PH, and you basically had almost no mortality in the patients with leaflet prolapse. Does this mean that most of your mortality was in the patients without organic disease, such as ischemic patients?

Dr Ghoreishi. The number of patients with severe PH was low in patients with degenerative MR. In the entire group, more than 30% of patients had moderate or severe PH, and patients with higher degrees of preoperative PH were more likely to have functional and rheumatic MV disease.

Dr Mesana. Patients with severe PH may not have the same level of PH at the time of operation. So when did you take your measurements to consider the patient as having severe PH? You can have a patient with a pulmonary systolic pressure of 60 before surgery, going down to 40 during anesthesia, and it is the same patient. So when did you qualify the patient with severe PH?

Dr Ghoreishi. Determination of the presence and degree of PH in this study was based completely on preoperative evaluation, not intraoperative assessment.

Dr Chitwood. No Swan–Ganz?

Dr Ghoreishi. No.

Dr Mesana. No Swan–Ganz in the operating room?

Dr Ghoreishi. We routinely measure the pulmonary artery pressure intraoperatively, but the results in this study are based on catheterization-derived SPAP performed preoperatively.

Dr Chaw-Chi Chiu *(Kaohsiung, Taiwan)*. You didn't mention the diastolic pulmonary artery pressure in your presentation. As we know, elevated diastolic pulmonary artery pressure is important to evaluate the reversibility of PH after the operation.

Usually, if the differences between the diastolic pulmonary artery and the left ventricular end-diastolic pressures are more than 10 mm Hg, it would mean irreversibility of the PH even after the operation. I would like to suggest measuring the diastolic pulmonary pressure before operation to evaluate if the PH will decrease after operation.

Dr Dan Lindblom *(Stockholm, Sweden)*. I am currently working in Africa on different humanitarian projects, mainly in Sudan on a big project where we are doing a lot of valve surgery. Last year, we performed more than 600 MV procedures, obviously mainly for mitral stenosis in young patients. More than half of our patients came to surgery with a pulmonary pressure more than 60 mm Hg, and supersystemic pulmonary pressures were not uncommon.

In your experience, do you have any cutoff line where you would refuse the patient for surgery because of extreme PH? What precautions would you take if you have a patient with very high pulmonary pressures?

Dr Ghoreishi. Twenty-five patients in this study had an sPAP greater than 80 mm Hg, and operative mortality was significantly higher (17%) among those patients. However, we do not have any absolute cutoff point to refuse surgery because a good number of patients with significant PH can expect some symptomatic benefit from operation.