Successful Percutaneous Mitral Paravalvular Leak Closure Is Associated With Improved Midterm Survival

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Background—Percutaneous closure of prosthetic mitral valve paravalvular leak (PVL) has emerged as an alternative to surgical treatment in high-risk patients. Limited data exist on the impact of successful percutaneous PVL closure on midterm outcomes.

Methods and Results—We examined consecutive patients who underwent percutaneous mitral PVL closure at Mayo Clinic, Rochester, MN, between January 2006 and January 2017. Procedural success, in-hospital outcomes, and midterm mortality were assessed. A total of 231 patients underwent percutaneous mitral PVL repair at a mean age of 67±12 years. Mean time from mitral valve replacement to percutaneous PVL repair was 1.25 (0.31–7.25) years. One hundred sixty-two patients (70%) had ≤mild PVL after the procedure. Compared with those who had >mild residual PVL, patients with ≤mild residual PVL had lower rates of repeat surgical interventions (6% versus 17%; P=0.004) and lower all-cause mortality at 30 days (1% versus 14%; P<0.001) and 1 year (15% versus 39%; P<0.001). Survival at 3 years was 61% in patients who had ≤mild residual leak and 47% in patients with higher grade of residual PVL (P=0.002).

Conclusions—In a large consecutive cohort of patients undergoing percutaneous mitral PVL closure, successful percutaneous reduction of the PVL to mild or less was associated with significant midterm survival benefit. **(*Circ Cardiovasc Interv*. 2017;10:e005730. DOI: 10.1161/CIRCINTERVENTIONS.117.005730.)**

Key Words: mitral valve ■ paravalvular leak ■ percutaneous closure ■ reoperation ■ survival

Paravalvular leak (PVL) is a challenging complication of mitral valve replacement that is associated with significant morbidity and mortality.[1–3] Although most PVLs are subclinical with unknown clinical significance, ≈3% of patients develop severe heart failure, hemolysis, or a combination of both, necessitating intervention.[4–6] Surgical patch repair and valve rereplacement have been the historical gold-standard treatment for severe symptomatic mitral PVL but are associated with significant operative risk and high recurrence rates.[3,6–8] Novel percutaneous techniques to treat mitral PVL were introduced in the early 2000s as less-invasive alternatives to surgery and have demonstrated safety and efficacy during short-term follow-up.[9–12] Despite increasing interest and published investigations, the current literature is limited by (1) the combined reporting of the outcomes of percutaneous closure of mitral and aortic PVL. Percutaneous treatment of mitral PVL is intricate with techniques and risks distinct from aortic PVL closure.[13] (2) The variability in closure techniques and plugs used in the paravalvular space. To date, the largest reported series of mitral PVL closure come from Canadian and European centers where many procedures are performed using closure devices that are unavailable in the United States.[14–16] In addition, these are compositions of heterogeneous experiences without a unified approach.[14,15] We report the largest experience of percutaneous mitral PVL closure from a single high-volume center with uniform assessment and closure techniques. This article aims to describe the risk profiles, procedural characteristics, and impact of percutaneous mitral PVL reduction on midterm survival.

Methods

Study Population

The data and study materials will not be publically available to other researchers for purposes of reproducing the results. We retrospectively identified patients who underwent percutaneous closure of mitral PVL at Mayo Clinic (Rochester, MN) between January 2006 and January 2017. The Mayo Clinic Institutional Review Board approved the study. Clinical indications for mitral PVL closure were severe dyspnea with moderate or severe PVL or clinically significant hemolytic anemia. Clinically significant hemolytic anemia was defined as symptomatic anemia (hemoglobin <11 g/dL in women or <12.5 g/dL in men) with laboratory evidence of intravascular hemolysis. Patients who had one of the following findings were referred to a surgical

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WHAT IS KNOWN

- Percutaneous closure of mitral paravalvular leak (PVL) is effective in improving symptoms and reducing the need for mitral valve reoperation.

WHAT THE STUDY ADDS

- In patients undergoing percutaneous mitral PVL closure, successful reduction of the PVL to mild or less is associated with significant improvement in short- and mid-term survival.
- Longer time from mitral valve replacement surgery to PVL closure, severe pulmonary hypertension, and the presence of multiple leaks predict inadequate PVL reduction with percutaneous techniques.

valve reoperation rather than percutaneous closure: active endocarditis, PVL involving more than one-half of the circumference of the sewing ring, evidence of valve dehiscence, or need for concomitant cardiac surgical intervention. Patients who did not meet one of the abovementioned criteria and those who deemed at high risk for reoperation were referred for percutaneous closure.

PVL Closure Techniques

Percutaneous Techniques

All procedures were performed with transesophageal echo guidance under general anesthesia except for one in which intracardiac echo was used because of esophageal pathology. An antegrade transseptal approach was used to cannulate the PVL in 91.8% of patients. An AMPLATZER Vascular Plug II (AVP-II; St. Jude Medical, St. Paul, MN) was used for PVL closure in most patients. The remainder of used devices included the AMPLATZER Duct Occluder, AMPLATZER Septal Occluder, and AMPLATZER Muscular VSD Occluder (St. Jude Medical), which were used rarely and early in our experience. Oval and oblong devices are used frequently abroad but are not available in the United States[14,15,17] Several percutaneous techniques were used including single device placement, simultaneous (double wire) deployment, sequential (anchor wire) deployment, and sequential deployment using an arteriovenous rail as previously described.[18,19] The procedural approach was determined by the size, number, and location of the PVL(s). Transapical access was used in the minority of cases to create an arteriovenous rail.

Definitions and Study End Points

Patients were divided into 2 groups according to the degree of residual PVL immediately post-procedure with successful closure defined as ≤mild residual leak and failure defined as >mild residual PVL. Recently, achieving mild or less residual PVL with percutaneous closure has been suggested to improve clinical outcomes.[14,20] The severity of the mitral PVL, before and immediately after the procedure, was graded semi-quantitatively using Doppler echocardiography and color-flow imaging by echocardiographers experienced in the intraoperative assessment of prosthetic mitral valves. Grading of the mitral PVL used the unifying 5-class grading scheme suggested by the PVL Academic Research Consortium.[20] Doppler parameters for ≤mild residual leak included small color Doppler jet area (<4 cm^2 or <20% of left atrial area), vena contracta width <2 mm, normal mean transmitral gradient, absence of dense continuous-wave Doppler jet, diastolic pressure half-time <130 ms, circumferential extent of the PVL of <5% with color Doppler, and regurgitant volume of <15 mL/beat.

Events classified as major adverse cardiovascular events were vascular complications requiring intervention or blood transfusion, acute kidney injury, stroke or transient ischemic attack, cardiac tamponade, device embolization requiring surgical intervention, and other complications requiring surgical interventions. The primary end point was the occurrence of all-cause mortality at maximum follow-up between the 2 groups. The secondary end points were all-cause mortality at 30 days and 1 year in addition to major adverse cardiovascular events at 30 days.

Data Analysis

Procedural, in-hospital, and 30-day outcomes were assessed by retrospective chart review. Patient's vital status (dead versus alive) was obtained from Mayo Clinic electronic medical records and by contacting patients via phone if the vital status is not available in electronic medical record or if the last contact with the clinic was older than 6 months. Normally distributed continuous parameters are reported as means and SDs were compared using a Student *t* test. Continuous variables that were not normally distributed are reported as medians and interquartile range and were compared using a Mann–Whitney *U* test. Categorical data are reported as frequencies and percentages and were compared using a χ^2 test or Fisher exact test where appropriate.

Risk factors for procedural failure (>mild residual PVL) were assessed using univariable and multivariable logistic regression to estimate odds ratios and their associated 95% confidence intervals (CI). We examined all variables described in the univariable assessment in for all multivariable assessments. If a factor had a *P* value <0.1, it was examined in the multivariable model. These variables were manually assessed in a bidirectional stepwise fashion. Factors with a *P* value <0.1 were kept in the model. We also included variables that we felt were clinically relevant such as patient age at the time of PVL closure, history of treated endocarditis, and the presence of a mechanical prosthetic valve given its impact on the technical performance on a percutaneous PVL closure.

Factors found to have a *P* value <0.1 in the univariable analysis or those felt to be clinically relevant were included in the multivariable model and assessed in a stepwise fashion.

Overall survival was estimated and compared between patients with successful versus unsuccessful PVL closure using the Kaplan–Meier method. We estimated the association of procedural success of mitral PVL closure (≤mild versus >mild residual PVL) and mortality using a Cox proportional hazards model to estimate hazard ratios (HRs) and 95% CI. Person-time was calculated from the date of PVL treatment to either death or the last date of available follow-up. The HR was stratified by procedural success and adjusted for baseline characteristics including age, chronic obstructive pulmonary disease, severe mitral annular calcification, chronic kidney disease, and left ventricular ejection fraction <50%. All time-to-event outcomes were determined using a survival table. All analyses were performed with SPSS software version 22 (IBM corporation). Statistical significance was inferred at $P \leq 0.05$.

Results

A total of 231 patients underwent percutaneous treatment of mitral PVL during the study period. Median length of follow-up was 2.04 (0.7–4.9) years. Follow-up data were available for 96% of patients. Overall mean age was 67.4±12.2 years, 44% of patients were females, 61% had a mechanical mitral valve, and 21 (9%) had >3 prior sternotomies (Table 1). The AVP-II device was used for PVL closure in the majority (73%) of cases. Arteriovenous rail was used in 45% of patients overall but in 67% of patients in the latter half of the study period. Percutaneous PVL closure was successful in 162 patients (70%). Patients with failed PVL closure had a later presentation after their index surgery, were more likely to be in class III–IV congestive heart failure, and have a mechanical mitral valve (Table 1). This group also had a higher incidence of prior endocarditis and a higher mean estimated right ventricular

Table 1. Characteristics of Patients Undergoing Mitral PVL Closure

Characteristic	All Patients (n=231)	≤Mild Residual PVL (n=162)	>Mild Residual PVL (n=69)	*P* Value
Age, mean±SD, y	67.4±12.2	67.4±12.2	67.3±12.2	0.97
Female n (%)	102 (44)	68 (42)	34 (49)	0.31
Presenting symptoms, n (%)				
Heart failure class NYHA III/IV	184 (80)	123 (76)	61 (88)	0.031
Hemolysis	106 (46)	70 (43)	36 (54)	0.12
Both	80 (35)	50 (31)	30 (45)	0.036
Mitral valve surgery				
Surgery to repair time, IQR, y	1.25 (0.3–7.3)	1.17 (0.3–6.2)	2.08 (0.3–12.4)	0.135
Bioprosthetic valve, n (%)	89 (38)	69 (43)	20 (29)	0.052
Number of sternotomies, IQR, y	2 (1–2)	2 (1–2)	2 (1–3)	0.029
Medical comorbidity, n (%)				
Chronic pulmonary disease	48 (21)	39 (24)	9 (13)	0.059
Atrial fibrillation/flutter	168 (73)	113 (70)	55 (80)	0.12
Chronic renal insufficiency (stage 3–5)	80 (35)	50 (31)	30 (43)	0.065
Coronary artery disease	129 (56)	95 (59)	34 (49)	0.19
Previous CABG	63 (27)	50 (31)	13 (19)	0.060
Previous endocarditis	50 (22)	29 (18)	21 (30)	0.034
Chronic steroid	14 (6)	13 (8)	1 (1)	0.055
Rheumatic heart disease	54 (23)	33 (20)	21 (31)	0.086
Prior chest radiation	15 (6)	14 (9)	1 (1)	0.042
Prior permanent pacemaker	80 (35)	56 (35)	24 (35)	0.98
Prior implantable defibrillator	12 (5)	7 (4)	5 (7)	0.35

CABG indicates coronary artery bypass graft surgery; IQR, interquartile range; NYHA, New York Heart Association; and PVL, paravalvular leak.

systolic pressure (Tables 1 and 2). Procedural techniques were similar in both groups. However, patients with >mild residual PVL had longer fluoroscopy time and longer hospitalizations (Table 3).

Eleven patients (5%) died within 30 days of the procedure (1% versus 14% in the successful versus failed PVL closure groups, respectively; $P<0.001$). Among these patients, 11 (100%) presented with class III–IV heart failure, 6 (55%) were referred because of decompensated heart failure within 3 months of the index valve surgery, 8 (73%) had stage III-V chronic renal insufficiency, 7 (64%) had severe pulmonary hypertension, and 2 (18%) had 5 prior sternotomies. Notably, out of these 11 patients, only 2 (18%) had major adverse events after PVL closure, and none underwent redo surgery during the 30-day period.

A total of 22 acute procedural complications occurred in 21 patients (9%), without a significant difference between the 2 study groups (Table 3). Two patients (1%) developed ventilation-dependent respiratory failure after the procedure: 1 was an 82-year-old female with a 27-year-old mechanical valve, who was admitted with class IV heart failure, and 1 was a 68-year-old female with severe pulmonary hypertension who was admitted with class III heart failure 3 months after a redo mechanical mitral valve replacement. Both of these patients had failed percutaneous closure and died during the hospitalization. Vascular complications requiring intervention occurred in 5 patients (2%); of those, 2 were femoral artery pseudoaneurysms requiring thrombin injection, 2 were large hematomas necessitating blood transfusion, and 1 was a retroperitoneal bleed also needing blood transfusion. Stroke occurred in 2 patients (1%), at days 1 and 11 post-procedure, respectively. Hemothorax related to apical access occurred in 3 patients (1%); all were successfully treated with chest tube placement±blood transfusion. Device embolization ensued in 4 patients (2%); successful percutaneous snaring was performed in 3 patients, whereas 1 patient had to undergo surgical retrieval. Two patients (1%) developed left ventricular pseudoaneurysms, both of which were treated with percutaneous closure. Interestingly, these patients did not undergo an apical puncture. The pseudoaneurysms were rather attributed to wire-related injury during arteriovenous rail establishment. Acute kidney injury occurred in 2 patients (1%), but none required hemodialysis. Leaflet impingement after device release occurred in 1 patient, requiring urgent cardiac surgery. One patient had bronchial bleeding after the procedure necessitating prolonged ventilation.

Successful PVL reduction to mild or less was associated with significantly lower all-cause midterm morality. In the

Table 2. Baseline Echocardiographic Findings in Patients Undergoing Mitral PVL Closure

	All Patients (n=231)	≤Mild Residual PVL (n=162)	>Mild Residual PVL (n=69)	*P* Value
PVL grade, n (%)				0.17
Mild (grade I)	1 (0)	1 (0)	0 (0.0)	
Moderate (grade II)	39 (17)	32 (20)	7 (10)	
Severe (grade III)	190 (82)	129 (80)	61 (90)	
No. of mitral PVL, n (%)				0.13
1 leak	157 (68)	113 (70)	44 (64)	
2 leaks	59 (25)	42 (26)	17 (25)	
>2 leaks	15 (7)	7 (4)	8 (12)	
Location of the leak, n (%)				0.45
Medial	60 (26)	41 (26)	19 (27)	
Lateral	39 (17)	27 (17)	12 (17)	
Anterior	46 (20)	37 (23)	9 (13)	
Posterior	20 (9)	14 (9)	6 (9)	
Multiple jets	63 (27)	40 (25)	23 (33)	
Severe mitral annular calcification, n (%)	47 (20)	33 (20)	14 (20)	
Left ventricular ejection fraction, mean±SD	60.4±12.2	59.4±12.9	62.8±9.8	0.03
Left ventricular ejection fraction <50%, n (%)	34 (15)	28 (17)	6 (9)	0.092
Left ventricular end-diastolic dimension, mean±SD	52.2±7.9	52.2±8.0	52.0±7.6	0.83
Left ventricular end-systolic dimension, mean±SD	35.2±8.8	35.6±9.3	34.2±7.5	0.29
Right ventricular systolic pressure, mean±SD	58.3±18.8	55.0±18.7	65.9±16.7	<0.001
Severe pulmonary hypertension, n (%)	112 (48)	66 (45)	46 (72)	<0.001

PVL indicates paravalvular leak.

adjusted Cox model assessing overall mortality, patients with a failed percutaneous closure were more likely to die (adjusted HR, 2.02; 95% CI, 1.34–3.03; *P*<0.001) than those with successful closure. The majority of the survival benefit of successful PVL closure in the adjusted Cox model was seen within the first 30 days of the procedure. However, there was a nonstatistically significant trend toward continuous improvement in survival among patients with <mild residual PVL beyond 30 days (adjusted HR, 1.24; 95% CI, 0.84–1.99; *P*=0.24; Figure I in the Data Supplement). The cumulative probability of freedom from death at 3 years was 61% in patients who had ≤mild residual leak compared with 47% in patients with higher grade of residual PVL (*P*=0.009; Figure). Patients who underwent a failed percutaneous closure were more likely to require repeat surgical intervention (17% versus 6%; *P*<0.001) than those who had ≤mild residual PVL.

In a univariable logistic regression model, the presence of >2 PVLs, severe pulmonary hypertension, time from index surgery to PVL closure, class III/IV heart failure, history of infective endocarditis, and mechanical mitral prostheses were predictive of >mild residual leak after percutaneous closure. However, in the multivariable logistic regression model, the presence of >2 PVLs, severe pulmonary hypertension, and time from index surgery to closure procedure were the only predictors of >mild residual leak after PVL closure (Tables 4 and 5).

Discussion

Successful reduction of mitral PVL to mild or less with percutaneous closure is associated with a significant improvement in short-term and midterm survival. Delayed presentation, severe pulmonary hypertension, and the presence of >2 PVLs were predictive of failed percutaneous PVL closure.

The effectiveness of percutaneous closure techniques in reducing mitral PVL has been demonstrated in multiple studies.[10,11,14,16,21,22] Patients who had successful percutaneous PVL closure had significant improvement in their symptoms, a reduction in heart failure–related hospitalization, and lower rates of mitral valve reoperation. However, the impact of successful percutaneous mitral PVL closure on midterm outcomes has not been well described. To our knowledge, only 1 study has shown a survival benefit of successful mitral PVL closure.[14] In this study, Calvert et al reported the outcomes of 115 patients with mitral PVL closure who underwent percutaneous closure in the United Kingdom and Ireland. The authors found that patients who had >mild residual PVL after percutaneous PVL closure had a 2-fold increase in all-cause mortality at 3 years compared with those who had successful percutaneous closure. Similarly, our findings suggest a significant mortality reduction in midterm mortality after successful percutaneous PVL closure. It is worth noting, however, that despite the association between successful PVL closure and improved

Table 3. Procedural Details and Clinical Outcomes in Patients Undergoing Mitral PVL Closure

	All Patients (n=231)	≤Mild Residual PVL (n=162)	>Mild Residual PVL (n=69)	*P* Value
Closure technique, n (%)				
Arteriovenous rail	103 (45)	64 (40)	39 (56)	0.21
Apical puncture	19 (8)	11 (7)	8 (12)	0.22
Closure device, n (%)				
AMPLATZER Vascular Plug II	168 (73)	128 (84)	40 (77)	0.28
Procedural details				
No. of device placed, n (%)				<0.001
No device	19 (8)	0 (0)	19 (27)	
Single device	109 (47)	91 (56)	18 (26)	
2 devices	62 (27)	48 (30)	14 (20)	
3 devices	25 (11)	13 (8)	12 (17)	
4 devices	16 (7)	10 (6)	6.(9)	
Fluoroscopy time, IQR, min	53 (38–78)	47 (31–65)	74 (54–93)	<0.001
Contrast load, IQR, mL	10 (5–25)	10 (5–20)	10 (5–30)	0.26
Residual PVL grade, IQR	1 (0–2)	1 (1–2)	2 (2–3)	<0.001
MACE at 30 d, n (%)	30 (13)	16 (10)	15 (22)	0.03
Death	11 (5)	1 (1)	10 (14)	<0.001
Major complications	21 (10)*	15 (9)	7 (10)	0.83
Hemothorax	3 (1)	3 (2)	0 (0)	
VDRF	1 (0)	0 (0)	1 (1)	
Vascular complication	5 (2)	5 (3)	0 (0)	
Stroke	2 (1)	2 (1)	0 (0)	
Device embolization retrieved percutaneously	3 (1)	1 (1)	2 (3)	
Device embolization requiring surgery	2 (1)	0 (0)	2 (3)	
Leaflet impingement requiring surgery	1 (1)	0 (0)	1 (1)	
Acute kidney injury	2 (1)	2 (1)	0 (0)	
Bronchial bleeding	1 (1)	0 (0)	1 (1)	
Left ventricular pseudoaneurysm	2 (1)	2 (1)	0 (0)	
Hospital length of stay, mean±SD, d	3 (1–7)	3 (1–5)	5 (2–13)	<0.001
Length of follow-up, mean±SD, y	2.04 (0.7–4.9)	2.43 (0.88–3.29)	1.15 (0.27–3.0)	0.001
All-cause mortality at 1 y, n (%)	48 (21)	22 (15)	26 (39)	<0.001
Needed redo intervention for PVL, n (%)				
Percutaneous redo	10 (4)	5 (3)	5 (7)	0.16
Surgical redo	21 (9)	9 (6)	12 (17)	0.004

IQR, interquartile range; MACE, major adverse cardiovascular event; PVL, paravalvular leak; and VDRF, ventilator-dependent respiratory failure.
*A total of 22 complications occurred in 21 patients

survival, mortality remained high in these patients suggesting a residual negative impact to mitral PVL despite successful treatment.[23–25] These data call for collaborative efforts to investigate the incidences, causes, and predictors of PVL so improved surveillance and preventative measures can be developed.

An intriguing finding in our study that warrants further discussion is the association between successful PVL reduction and a lower 30-day mortality rate. This unexpected difference in short-term mortality is likely multifactorial and merits more scrutiny:

1. The higher mortality rate in patients with >mild residual mitral regurgitation may be related to the higher severity of illness at presentation in these patients; the prevalence of class III/IV heart failure, advanced renal insufficiency, and severe pulmonary hypertension was 100%, 73%, and 64% in patients with >mild residual mitral regurgitation, compared with 80%, 35%, and 49% in the overall cohort,

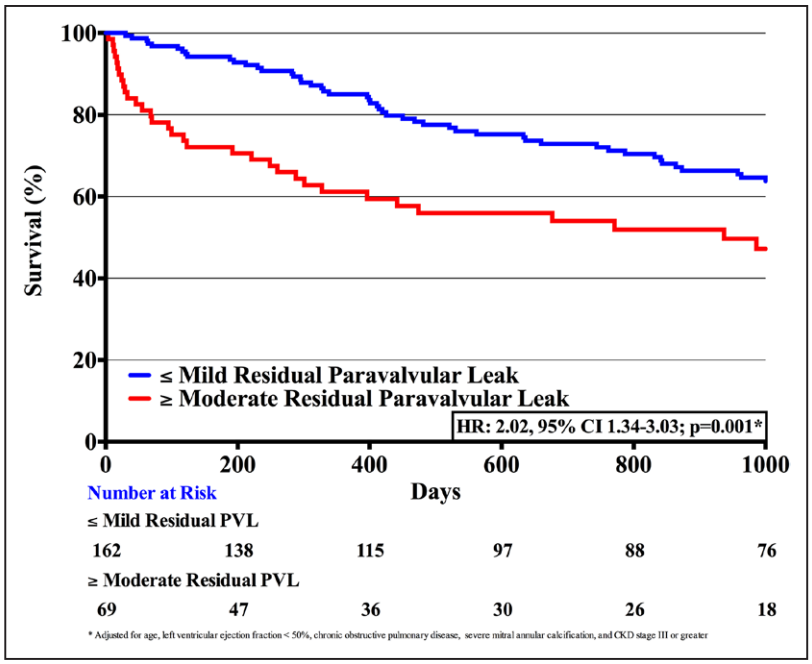

Figure. Impact of successful percutaneous mitral paravalvular leak (PVL) closure on midterm mortality. CI indicates confidence interval; and HR, hazard ratio.

respectively. Also, none of these patients underwent redo valve surgery after a failed percutaneous closure, suggesting that this cohort represents a sicker group of patients, in whom surgical repair was not a feasible option even after a failed percutaneous closure attempt.

2. Procedural complications and the need for redo valve surgery in patients with failed PVL closure do not explain the short-term mortality differences, as among patients who died within 30 days, only 2 had experienced a procedural complication, and none died because of redo surgery. When a landmark survival analysis excluding the first 30 days was performed, an incremental separation in the survival curves between patients who had successful versus failed PVL closure was noted. However, this was not statistically significant likely because of the underpowering of the study given its modest size. Similar, albeit less pronounced, early excess mortality in patients with >mild residual leak was observed by Calvert et al.[14]

Our study also identifies several predictors of significant residual leak: (1) Delayed presentation: the time from index surgery to percutaneous closure was longer in patients who had >mild residual leak versus those who had <mild residual leak. The prolonged time lag from index mitral valve surgery to percutaneous PVL closure is consistent in the literature, 4.7±4.1 and 8.5±7.8 years in the largest registries from the United Kingdom

Table 4. Univariable Predictors of Moderate or Greater Residual Leak in Patients Undergoing Percutaneous PVL Closure

	Odds Ratio	95% CI	*P* Value
Age	1.00	0.98–1.02	0.97
Female	1.34	0.76–2.37	0.31
Time to PVL repair	1.06	1.02–1.10	0.004
NYHA class III/IV heart failure	2.42	1.07–5.49	0.04
Hemolysis	1.58	0.89–2.81	0.12
Severe pulmonary hypertension	3.14	1.66–5.92	<0.001
Chronic renal insufficiency	1.72	0.96–3.08	0.07
History of infective endocarditis	2.01	1.05–3.85	0.04
Severe mitral annular calcification	1.00	0.49–2.00	0.99
Atrial fibrillation\flutter	1.70	0.87–3.35	0.12
Mechanical mitral valve	1.82	0.99–3.33	0.05
Coronary artery disease	0.69	0.39–1.21	0.19
Chronic steroid use	0.17	0.02–1.32	0.09
PVL closure via apical puncture	1.80	0.69–4.69	0.23
Greater than 2 PVL	2.90	1.01–8.36	0.048
First 50 percutaneous PVL closures	0.60	0.29–1.25	0.17
Greater than 3 prior sternotomies	1.50	0.59–3.81	0.39

CI indicates confidence interval; NYHA, New York Heart Association; and PVL, paravalvular leak.

Table 5. Multivariable Predictors of Moderate or Greater Residual Leak in Patients Undergoing Percutaneous PVL Closure*

	Odds Ratio	95% CI	*P* Value
Age, y	1.01	0.98–1.04	0.37
Time to PVL repair	1.07	1.02–1.12	0.003
NYHA class III/IV heart failure	2.08	0.80–5.43	0.13
Severe pulmonary hypertension	2.31	1.16–4.60	0.02
Chronic renal insufficiency	1.78	0.91–3.51	0.09
History of infective endocarditis	1.94	0.87–4.30	0.10
Mechanical mitral valve	1.69	0.79–3.65	0.18
Greater than 2 PVL	3.84	1.11–13.30	0.03

*Model included age, time to PVL repair, NYHA class III/IV heart failure, severe pulmonary hypertension, chronic renal insufficiency, history of infective endocarditis, mechanical mitral valve, and greater than 2 PVL. CI indicates confidence interval; NYHA, New York Heart Association; and PVL, paravalvular leak.

and Spain, respectively.[14,15] This may not be entirely related to under-recognition of this entity or late referral for treatment but can also be because of delayed development of PVL.[26] (2) Multiple PVLs: our study included higher proportions of patients with multiple PVLs compared with other reports (6% versus 2% in the UK registry).[14] The presence of >2 PVL jets was a strong predictor of a significant residual leak (HR, 3.84; 95% CI, 1.11–13.30; *P*=0.03). This finding has important implications on patient's risk stratification. Patients with several mitral PVL jets need to be informed about the lower chances of adequate PVL reduction compared with those who had 1 to 2 leaks. (3) Pulmonary hypertension: although the presence of significant pulmonary hypertension in patients with mitral PVL can be linked to the larger number of PVL jets or the longer surgery to closure time, the presence of severe pulmonary hypertension was an independent predictor of >mild residual leak (HR, 2.31; 95% CI, 1.16–4.60; *P*=0.02).

Other predictors of procedural success versus failure that have been identified in the literature include annual procedural volume and the type of device used.[14,15,27] This later variable deserves special emphasis: García et al[15] found that the use of oblong devices such as the AMPLATZER vascular plug III (AVP-III; St. Jude Medical) versus other circular occluders was associated with a significantly higher chance of procedural success (HR, 2.68; 95% CI, 1.29–5.54; *P*=0.008). Calvert et al[14] also found a trend toward an additional incremental benefit of using a purpose-specific device (PLD; Occlutech GmbH, Jena, Germany) over the AVP-III device (HR, 1.37; 95% CI, 0.96–1.96; *P*=0.079) in patients with mitral PVL. Unfortunately, neither the AVP-III nor the Occlutech device is available in the United States. The majority of mitral PVL closure procedures in the United States are performed off-label with the AVP-II device. Nevertheless, successful reduction in PVL to mild or less occurred in comparable rates in our study to what has been reported in the European registries mainly using oblong and purpose-built devices.[14,15] The unavailability of these devices at our center was possibly offset by the concentrated high-volume experience compared with other low-volume centers.

Advances in transcatheter valve therapies have fueled a growing interest in percutaneous PVL treatment modalities.[18] However, randomized trials in the PVL field are extremely unlikely because of the borderline patient cohort size and the high associated cost of bringing novel devices into the market. Nevertheless, our findings serve to narrow the knowledge gap in the PVL field and aid in patient selection and risk stratification.

Limitations

Our study has several limitations. (1) The study is retrospective and observational in nature. Therefore, our results should be interpreted with caution. Procedural success is higher in patients with smaller round-shaped leaks and possibly the improved survival in these patients was causal and a marker of less illness at baseline. Nevertheless, the mortality benefit seen in our study is similar to what has recently been observed in the large published experience from the United Kingdom and Ireland.[14] (2) Data presented in this study are from a tertiary referral center in the United States with a large experience with percutaneous PVL closure. Several factors have to be accounted for when generalizing these results including the learning curve of the procedure, the maturation of the percutaneous technique, referral biases, and the unavailability of purpose-specific occluder devices. (3) Certain pertinent data (eg, postprocedural hemolysis indices) were not uniformly collected because of the retrospective design of the study and the tertiary nature of the study's institution. (4) Grading of mitral PVL can be challenging. Echocardiographic measures used to grade PVL are semi-quantitative and have limited validation. This could lead to interpretation variability, which may affect the results of this study.

Conclusions

In patients with significant symptomatic mitral PVL, successful percutaneous reduction of the PVL to mild or less is associated with significant improvement in short-term and midterm survival. Delayed presentation, severe pulmonary hypertension, and the presence of multiple PVLs predict >mild residual leak after percutaneous closure. In light of these findings, attempts should be made to reduce PVL as much as possible. Future research in the field is warranted to assess the role of purpose-specific devices in further improving the outcomes on percutaneous PVL closure.

Disclosures

None.

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Successful Percutaneous Mitral Paravalvular Leak Closure Is Associated With Improved Midterm Survival

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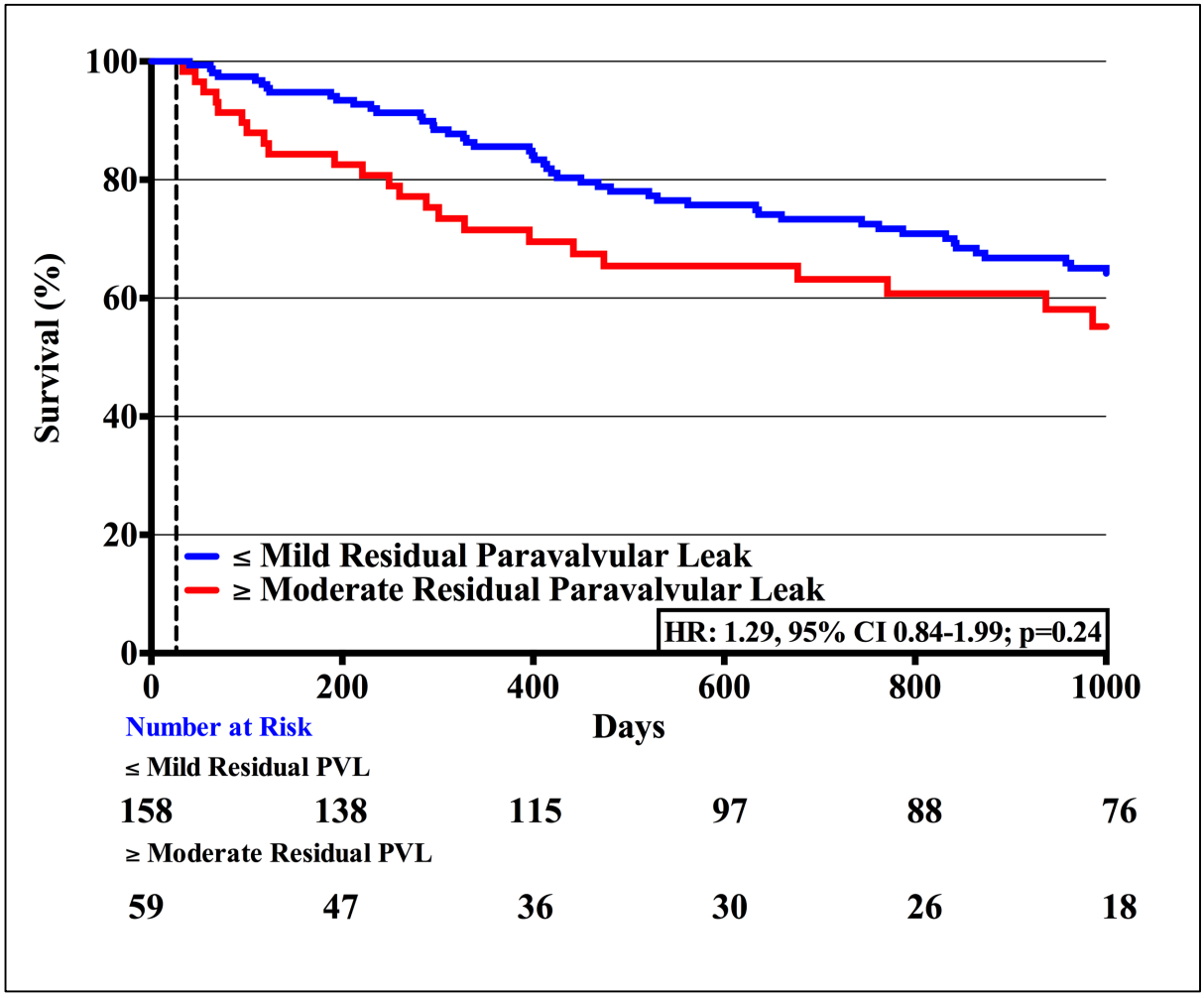

e-Figure (1):

Landmark Survival Analysis Illustrating the Impact of Successful Paravalvular Leak Closure on Patient's Mid-Term Survival Beyond 30 days