Characteristics and longer-term outcomes of paravalvular leak after aortic and mitral valve surgery

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ABSTRACT

Background: Paravalvular leak (PVL) is often seen after aortic (AV) and mitral valve (MV) surgery, either due to infection or valve dehiscence. We sought to describe predictors of longer-term outcomes in patients who developed PVL after AV and MV surgery and were considered eligible for reoperative cardiac surgery (RCS).

Methods: We studied 495 such patients (65 ± 14 years, 65% men, 47% with MV PVL) who presented at our center between January 2003 and December 2011. Patients with severe mitral/aortic stenosis, patients with less than mild PVL, and those with prohibitive risk precluding RCS were excluded. Society of Thoracic Surgeons (STS) score was calculated. Primary endpoint was mortality.

Results: At baseline, mean STS score and left ventricular ejection fraction were $5.8 \pm 4\%$ and $52 \pm 12\%$, respectively. In total, 105 (21%) had infective PVL and 72% had moderate or greater PVL. At a median of 8 days, 351 (71%) patients underwent RCS to repair PVL (3% in-hospital postoperative mortality), and at 6.6 ± 4 years, 230 (47%) patients died. On multivariable Cox survival analysis, greater STS score (hazard ratio or HR 1.35), mitral versus aortic PVL (HR 1.66), infectious etiology (HR 2.05), and greater right ventricular systolic pressure (HR 1.09) were associated with greater longer-term mortality, whereas surgery (HR 0.58) was associated with improved longer-term survival (all $P < .05$).

Conclusions: Patients who develop mild or greater PVL after AV/MV surgery have a high rate of longer-term mortality, despite excellent perioperative outcomes. Greater STS score, right ventricular systolic pressure, infectious etiology, and MV (vs AV) involvement were all independently associated with long-term mortality, whereas RCS for PVL closure was associated with improved longer-term survival. (J Thorac Cardiovasc Surg 2019;157:1785-92)

Imaging example of a paravalvular leak.

Central Message

In a study of 495 patients, we demonstrate that patients who develop mild PVL or greater following aortic/mitral valve surgery have a high rate of longer-term mortality, despite excellent perioperative outcomes. Greater STS score, right ventricular systolic pressure, infectious etiology and mitral (vs aortic valve) involvement were all independently associated with long-term mortality whereas surgery for PVL closure was associated with improved longer-term survival.

Perspective

In a study of 495 patients, we demonstrate that patients who develop mild PVL or greater following aortic/mitral valve surgery have a high rate of longer-term mortality. Greater STS score, RVSP < infectious etiology, and mitral (vs aortic valve) involvement were all independently associated with long-term mortality whereas surgery for PVL closure was associated with improved longer-term survival.

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Dr Desai is supported by the Haslam Family endowed chair in cardiovascular medicine. Drs Shah and Alashi contributed equally to this article.

Received for publication Feb 5, 2018; revisions received July 19, 2018; accepted for publication Aug 11, 2018; available ahead of print Nov 7, 2018.

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0022-5223/\$36.00

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<https://doi.org/10.1016/j.jtcvs.2018.08.096>

Paravalvular leak (PVL) is a potentially serious complication that is frequently observed after circumferentially sutured surgical valve replacement, resulting in an abnormal communication between cardiac chambers separated by

Scanning this QR code will take you to the article title page to access supplementary information.

Abbreviations and Acronyms

AV	= aortic valve
CI	= confidence interval
IE	= infective endocarditis
MV	= mitral valve
NRI	= net reclassification improvement
PVL	= paravalvular leak
RCS	= reoperative cardiac surgery
RH	= hazard ratio
RVSP	= right ventricular systolic pressure
sHR	= subdistribution hazard ratio
STS	= Society of Thoracic Surgeons
TTE	= transthoracic echocardiogram

the valve prosthesis,¹ with an associated increased morbidity and mortality²⁻⁷ (Figure 1 and Video 1). In older reports, surgical aortic valve (AV) replacement has a reported PVL incidence of 2% to 17% and 7% to 22% after surgical mitral valve (MV) replacement⁸⁻¹²; however, in a recent report, mild or greater PVL occurred in 2.2% of aortic and 2.9% of mitral cases.¹³ Although 74% of PVL occurs within first year,¹⁴ PVLs that occur as the result of prosthesis dehiscence or endocarditis occur late.^{1,6} Clinically relevant PVL, which occurs in 2% to 5% of cases, can potentially cause symptomatic hemolytic anemia, congestive heart failure, and, if left untreated, death (often due to sepsis).

Reoperative cardiac surgery (RCS) remains the definitive standard of care in patients with PVL in the setting of intractable hemolytic anemia or heart failure symptoms^{1-6,8,13}; however, with advancement in technology, percutaneous PVL closure has emerged as a potential alternative, especially in high-risk patients (without endocarditis).^{6,15,16} Hence, there is a potential need to establish a benchmark for outcomes in patients with significant PVL undergoing RCS, as it could identify those patients who may most benefit from less-invasive percutaneous PVL closure. Previous data detailing the predictors of outcomes in patients undergoing PVL closure are limited by small sample size and relatively short-term follow-up.^{1-6,8,13,15,16} We sought to describe the characteristics and predictors of longer-term outcomes in a large group of patients who developed PVL after AV/MV surgery and were considered eligible for RCS.

METHODS**Study Population**

This was an observational study of 495 consecutive patients diagnosed with at least mild PVL after MV/AV surgery at outside institutions who presented to our institution between January 2003 and December 2011 for evaluation and management. All patients had a comprehensive transthoracic echocardiogram (TTE) and transesophageal echocardiogram at the time of initial assessment. Patients in whom infective endocarditis (IE) was suspected were also evaluated by an infectious disease specialist.

We excluded patients who developed PVL post-transcatheter valve replacement. We also excluded patients who were considered high risk for RCS due to prohibitive comorbidities ($n = 108$, Table E1). The investigators performed manual extraction of data before analysis. Society of Thoracic Surgeons (STS) score was calculated. Etiology of PVL (infectious vs suture dehiscence) was ascertained. Hemolytic anemia was defined as a combination of abnormal peripheral blood smear and abnormalities in serum lactate dehydrogenase and bilirubin. This study was approved by the institutional review board.

Imaging Data

All patients underwent baseline TTE using commercial instruments (Philips, Bothell, Wash; Siemens, Malvern, Pa; and General Electric, Milwaukee, Wis). Left ventricular ejection fraction, indexed left ventricular dimensions, and left atrial area were measured at rest on TTE.¹⁷ Right ventricular systolic pressure (RVSP) was measured at rest. Multiplane transesophageal echocardiogram was performed with the patient under conscious sedation.¹⁸ The use of 3-dimensional echocardiography was at the discretion of the attending cardiologist. Severity of PVL was classified on a 4-class grading scheme (mild, moderate, moderate severe, and severe).^{19,20} In addition, contrast-enhanced computed tomography (Philips NL, Amsterdam, the Netherlands, or Siemens, München, Germany) of the chest was performed using electrocardiographic gated protocols in a standard fashion.^{21,22}

Surgery During Follow-up

All patients who underwent RCS were symptomatic due to either hemolytic anemia, infection, or volume overload related to significant PVL. The decision to refer a patient for PVL closure was made after a consensus opinion between attending cardiologists and cardiac surgeons. We recorded the RCS for PVL closure during follow-up (including the type of valve surgeries, type of prostheses, and concomitant procedures).²²⁻²⁴ In infectious cases, we typically performed an extensive RCS for infection source control.

Outcomes

The date of baseline TTE at our institution was defined as the beginning of the observational period. Periprocedural outcomes were recorded. Long-term all-cause mortality (primary endpoint) was recorded from chart review and state/nationally available databases, including the National Death Index (last query in December 2016). In addition, where feasible, cause of death was ascertained (including malignancy and liver/pulmonary/neurologic disease).

Statistical Analysis

Continuous variables are expressed as mean $\pm$ standard deviation and/or median with interquartile range (25th and 75th percentile) and compared using Student *t* test or Mann-Whitney *U* test, as appropriate. Categorical data are expressed as percentage and compared using χ^2 . To assess all-cause mortality, Cox proportional hazards analysis was performed. The proportional hazards assumption was examined through inspection of Schoenfeld residuals plotted against time. A parsimonious multivariable survival analysis was performed using relevant variables known to be associated with outcomes in these patients. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. For secondary outcomes analysis, since longer-term cardiac and noncardiac deaths were competing risks, multivariable survival analysis was performed by competing risk regression analysis using the Fine-Gray proportional subhazards model, and subdistribution hazard ratios (sHRs) were calculated, along with 95% CI. Cumulative proportion of patients with events as a function over time was obtained by Kaplan-Meier method, and event curves of different outcomes were compared using the log-rank test or Generalized Wilcoxon test, as appropriate. The discriminative ability of various survival models was compared using the c-statistic and the classification of risk was

FIGURE 1. A patient with a history of previous bioprosthetic aortic valve replacement presented with infectious endocarditis. A, Transesophageal echocardiogram demonstrates a bioprosthetic aortic valve with aortic root abscess and a paravalvular leak (arrows). B, Contrast-enhanced computed tomography confirms a large contrast filled cavity adjacent to the aortic valve suggestive of an abscess (arrows).

assessed using net reclassification improvement (NRI). STS score + RVSP (clinical model) were considered as starting points for incremental survival analyses, as these are a composite of various individual predictors associated with longer-term outcomes in patients undergoing cardiac surgery. Statistical analysis was performed using SPSS, version 11.5 (SPSS Inc, Chicago, Ill) and R 3.0.3 (R foundation for Statistical Computing, Vienna, Austria). A *P* value of $<.05$ was considered significant.

RESULTS

Baseline data are shown in Tables 1 and 2. In total, 276 patients had previous MV surgery (162 mechanical,

69 bioprosthesis, and 45 repairs), whereas 331 had previous AV surgery (214 mechanical and 117 bioprosthesis). In addition, 105 (21%) patients had evidence of IE, with the breakdown of organisms as follows: 18 negative blood culture (due to antibiotics before presentation), 17 *Staphylococcus aureus*, 16 coagulase-negative *Staphylococcus*, 10 *Enterococcus*, 10 *Streptococcus viridans*, 1 *Escherichia coli*, 2 *Propionibacterium*, 2 *Klebsiella*, 2 *Serratia*, 2 *Pseudomonas*, 3 *Lactobacillus*, 3 *Candida*, 2 *Enterobacter*, 1 *Corynebacterium*, and 16 cases with polymicrobial organisms.

Procedural Details

After a confirmed diagnosis of PVL, 351 (71%) patients underwent RCS at a median of 8 days [4, 31 days]. All patients were symptomatic with New York Heart Association Class $\geq$ II, whereas 21% had an evidence of recent IE. In total, 144 (29%) patients were not offered surgery due to mild PVL and lack of symptoms (including perceived infection control in endocarditis cases), after shared decision-making between cardiologists, cardiac surgeons, and infectious disease specialists, as appropriate. Various AV/MV operations were as follows: (1) AV (total $n = 142$); (2) MV ($n = 157$); and (3) combined AV/MV ($n = 52$). Within AV operations, 30 were mechanical, 69 bioprostheses, and 74 were homografts. Within MV operations, 31 were mechanical, 102 were bioprosthesis, and 45 underwent repair with a ring/patch/suture. The following concomitant operations were also performed: (1) coronary bypass grafting ($n = 76$); (2) tricuspid valve repair ($n = 86$); (3) ascending aortic surgery ($n = 104$); and (4) left atrial appendage ligation +/- maze ($n = 45$).

Periprocedural Outcomes

The average in-hospital length of stay following RCS was 18 ± 16 days (median 19, interquartile range 12,

VIDEO 1. Transesophageal echocardiogram demonstrating a bioprosthetic aortic valve with aortic root abscess and a paravalvular leak (PVL). The relevant data on 108 patients with significant PVL that were not offered cardiac reoperation (of whom 37 underwent percutaneous PVL closure) due to prohibitive perioperative risk are shown in Table E1. The reasons for these patients being deemed high risk were as follows: (1) severe systemic infection with valvular abscess ($n = 27$); (2) very high STS score ($>10\%$, $n = 66$); and (3) advanced age (>85 years, $n = 15$). STS, Society of Thoracic Surgeons. Video available at: [https://www.jtcvs.org/article/S0022-5223\(18\)32491-7/fulltext](https://www.jtcvs.org/article/S0022-5223(18)32491-7/fulltext).

TABLE 1. Baseline characteristics of the study sample (n = 495)

Variable	Total (n = 495)	Conservative therapy (n = 144)	Reoperative cardiac surgery (n = 351)	P value
Age, y	63 ± 14 (median 65 [IQR 56, 74])	64 ± 14 (median 65 [IQR 56, 74])	63 ± 14 (median 65 [IQR 56, 74])	.19
Male sex	323 (65%)	99 (69%)	224 (64%)	.17
Body surface area, kg/m ²	1.9 ± 0.2	1.9 ± 0.3	1.9 ± 0.2	.32
Hypertension	317 (64%)	94 (65%)	223 (64%)	.71
Diabetes mellitus	93 (19%)	28 (19%)	65 (19%)	.45
Coronary artery disease	227 (46%)	69 (48%)	158 (45%)	.31
Atrial fibrillation	245 (50%)	75 (52%)	170 (48%)	.26
Stroke	82 (17%)	21 (15%)	61 (17%)	.27
Chronic kidney disease on dialysis	19 (4%)	4 (3%)	15 (4%)	.31
Smoker	113 (23%)	32 (22%)	81 (23%)	.81
Documented hemolytic anemia	86 (17%)	4 (3%)	82 (23%)	<.001
Pacemaker/defibrillator	116 (23%)	40 (28%)	76 (22%)	.12
Society of Thoracic Surgeons score	5.8 ± 4 (median 5.7 [IQR 3.2, 8.9])	5.9 ± 3 (median 5.8 [IQR 3.0, 9.3])	5.8 ± 4 (median 5.7 [IQR 2.8, 8.3])	.25
Aspirin	134 (27%)	38 (27%)	96 (27%)	.83
Statins	163 (33%)	46 (32%)	117 (33%)	.77
Warfarin	183 (37%)	55 (38%)	128 (36%)	.72
Number of previous CV surgeries				.18
1	288 (59%)	89 (62%)	199 (57%)	
2	142 (29%)	45 (31%)	97 (28%)	
≥3	65 (13%)	10 (7%)	55 (15%)	
Time from previous CV surgery to current clinical evaluation, y	6.4 ± 7 (median 5.9 [IQR 2.3, 8.5])	6.3 ± 7 (median 6 [IQR 2.1, 7.7])	6.4 ± 7 (median 6.1 [IQR 2, 8.7])	.81
Type of previous valve surgery*				
Mitral valve repair/replacement	276 (56%)	71 (49%)	205 (58%)	.06
Aortic valve replacement	331 (67%)	100 (69%)	231 (66%)	.43
Hemoglobin, mg/dL	11.6 ± 2.2	12.1 ± 2	11.4 ± 2.2	.001
Serum creatinine, mg/dL	1.4 ± 1	1.5 ± 1.2	1.4 ± 1.3	.26
Serum lactate dehydrogenase, mg/dL	722 ± 907 (median 408 [IQR 276, 756])	370 ± 247 (median 213 [IQR 124, 432])	803 ± 98 (median 786 [IQR 535, 973])	.001
Serum total bilirubin, mg/dL	1.5 ± 0.5 [median IQR 0.6, 2.3]	1.3 ± 0.2 [median IQR 0.3, 1.7]	1.8 ± 1 [median IQR 1.2, 2.9]	.001

IQR, Interquartile range; CV, cardiovascular. *A total of 112 patients had more than 1 valve repaired/replaced previously.

25 days). In the RCS subgroup, the rates of perioperative 30-day/in-hospital adverse events were as follows: 10 (3%) deaths (3 in mitral, 5 aortic, and 2 combined aortic and mitral PVL), 11 (3%) strokes, 55 (16%) shock requiring vasopressor support lasting >24 hours, 115 (33%) transient postoperative atrial fibrillation, 29 (8%) renal failure requiring dialysis, 60 (17%) in-hospital postoperative blood transfusion within 30 days, 58 (17%) advanced heart block requiring permanent pacemaker, and 9 (3%) readmission within 30 days. At the time of discharge, all living patients with an infectious PVL were

on appropriate antibiotics, based on culture sensitivity (lasting for at least 1 week).

Longer-Term Outcomes

Over 6.6 ± 4 years, there were 230 (47%) deaths. The results of multivariable Cox Proportional survival analysis for all-cause mortality are shown in Table 3. Also, within the RCS group (n = 351), 7 patients underwent subsequent downstream RCS (8 MV replacement, 6 AV replacement and 3 requiring both AV/MV replacement) during longer-term follow-up at our institution.

TABLE 2. Echocardiographic data of the study sample (n = 495)

Variable	Total (n = 495)	Conservative therapy (n = 144)	Reoperative cardiac surgery (n = 351)	P value
Left ventricular ejection fraction, %	52 ± 12	51 ± 11	52 ± 11	.18
Indexed left atrial diameter, cm/m ²	2.2 ± 0.5	2.3 ± 0.5	2.2 ± 0.5	.54
Indexed left ventricular end-diastolic dimension, cm/m ²	2.5 ± 0.6	2.6 ± 0.4	2.5 ± 0.6	.43
Mean aortic valve gradient, mm Hg	19 ± 11	16 ± 8	21 ± 12	<.001
Mean mitral gradient, mm Hg	7 ± 4	6 ± 3	8 ± 4	.002
Valve associated with PVL				.007
Mitral	233 (47%)	55 (38%)	178 (51%)	
Aortic	262 (53%)	89 (62%)	173 (49%)	
Degree of PVL				<.001
Mild	140 (28%)	94 (65%)	46 (13%)	
Moderate	120 (24%)	50 (35%)	70 (20%)	
Moderate-severe	160 (32%)	0	160 (46%)	
Severe	75 (15%)	0	75 (21%)	
Etiology of PVL				<.001
Infective endocarditis	105 (21%)	11 (8%)	94 (27%)	
Suture dehiscence	390 (79%)	133 (92%)	257 (73%)	
Moderate tricuspid regurgitation or greater	183 (37%)	22 (15%)	161 (46%)	<.001
Right ventricular systolic pressure, mm Hg	44 ± 19	40 ± 20	47 ± 20	.001

PVL, Paravalvular leak.

Addition of PVL location, etiology, and RCS to the clinical model (STS score + resting RVSP) provided incremental prognostic value for longer-term mortality. With sequential addition of PVL location (mitral vs aortic), etiology (infectious vs not), and RCS (vs conservative therapy), the c-statistic for longer-term mortality increased from 0.63

TABLE 3. Multivariable Cox proportional hazards survival analysis for all-cause mortality

Variable	Hazard ratio [95% CI]	P value
Society of Thoracic Surgeons score (for 1% absolute increase)	1.35 [1.02-1.79]	.03
Primary valvular involvement (mitral vs aortic)	1.66 [1.25-2.20]	<.001
Etiology of paravalvular leak (infectious vs not)	2.05 [1.49-2.83]	<.001
Baseline RVSP (for 10-mm Hg increase)	1.09 [1.01-1.19]	.03
Reoperative cardiac surgery during follow-up	0.58 [0.43-0.78]	<.001

The following additional variables were considered but not significant: time from previous surgery, previous mechanical versus bioprostheses, paravalvular leak (moderate or greater vs less), aortic and mitral valve gradients, tricuspid regurgitation, number of reoperations, concomitant cardiac surgery (ie, coronary bypass grafting, tricuspid valve, or aortic surgery), type of valve prosthesis (mechanical vs bioprosthesis vs homograft), antibiotics, serum hemoglobin, lactate dehydrogenase, and bilirubin. Variables included in the Society of Thoracic Surgeons score were not individually considered. The interaction term between etiology of paravalvular leak (infectious vs noninfectious) and location (aortic vs mitral valve) was not significant when entered into multivariable analysis. CI, Confidence interval; RVSP, right ventricular systolic pressure.

(95% CI, 0.53-0.71) for the clinical model (STS score + RVSP) to 0.67 (95% CI, 0.61-0.77), to 0.76 (95% CI, 0.63-0.85) and 0.84 (95% CI, 0.77-0.93), respectively (all $P < .01$ for sequential increase). Similarly, sequential addition of PVL location (mitral vs aortic), etiology (infectious vs not), and RCS (vs conservative therapy) significantly improved reclassification for longer-term mortality (all $P < .01$): clinical model + PVL location (categorical NRI 0.26; 95% CI, 0.09-0.42), clinical model + PVL location + etiology of PVL (categorical NRI 0.22; 95% CI, 0.11-0.39), and clinical model + PVL location + PVL etiology + cardiovascular surgery (categorical NRI 0.33; 95% CI, 0.17-0.48).

The proportion of longer-term deaths were significantly greater in MV versus AV PVL: 126 of 233 (54%) versus 104 of 262 (40%), Log-rank statistic $P < .001$, Figure 2. Similarly, the proportion of longer-term deaths were significantly greater in infectious versus noninfectious cases: 59 of 105 (56%) versus 171 of 390 (44%), Log-rank statistic $P < .01$, Figure 3. The proportion of longer-term deaths was significantly lower in RCS versus conservative subgroups: 155 of 351 (44%) versus 75 of 144 (52%), Generalized Wilcoxon statistic $P = .04$, Figure 4. The shorter-term outcomes in the RCS group were worse than in the conservatively managed group, as would be expected due to increased perioperative morbidity and mortality.

We further performed survival analysis only in patients who underwent RCS (n = 351, number of deaths = 155), excluding conservatively treated patients. The results of multivariable Cox proportional hazard survival analysis

Numbers at risk

Infectious PVL	105	64	50	25	8
Noninfectious PVL	390	318	241	123	31

FIGURE 2. Kaplan-Meier survival curves separated on basis of infectious versus noninfectious etiology of PVL. PVL, Paravalvular leak.

are as follows (all $P < .05$): greater STS score (HR 1.49 [95% CI, 1.03-2.22]), mitral versus AV PVL (HR 1.38 [95% CI, 1.04-1.82]), infectious versus not (HR 1.67 [95% CI, 1.17-2.38]), and greater resting RVSP (HR 1.04 [95% CI, 1.01-1.12]) remained independent predictors of mortality.

The data on multivariable competing risk regression analysis based on Fine-Gray proportional subhazards model for longer-term cardiac deaths (cardiac deaths = 220, documented noncardiac deaths = 10) were similar (all $P < .05$): greater STS score (sHR, 1.29; 95% CI, 1.03-1.84), mitral versus aortic PVL (sHR, 1.61; 95% CI, 1.21-2.27), infectious versus noninfectious etiology HR (sHR, 1.99; 95% CI, 1.43-2.80) and greater RVSP (sHR, 1.08; 95% CI 1.01-1.23) were associated with increased longer-term events and RCS was associated with significantly lower events (sHR, 0.52; 95% CI, 0.40-0.76). The outcomes of 108 patients turned down for RCS are shown in Table E1.

DISCUSSION

The current study demonstrates our experience in managing patients with mild PVL or greater considered eligible for RCS, along with their longer-term prognosis. Despite good in-hospital outcomes, the longer-term mortality was high. Infectious PVL or PVL in mitral position was associated with a greater longer-term mortality; whereas RCS, performed in appropriately selected patients, was associated with improved longer-term survival (vs conservative management). To avoid the bias of advanced comorbidities

Numbers at risk

Mitral PVL	233	169	127	58	21
Aortic PVL	262	213	164	90	18

FIGURE 3. Kaplan-Meier survival curves separated on basis of mitral versus aortic PVL. PVL, Paravalvular leak.

and prohibitive operative risk, such patients were excluded. Also, patients undergoing percutaneous PVL closure were not included (as they were offered only in high-risk nonendocarditis patients turned down for RCS). As would be

Numbers at risk

Conservative therapy	144	106	77	27	6
Reoperative cardiac surgery	351	276	214	121	33

FIGURE 4. Kaplan-Meier survival curves separated on basis of conservative versus reoperative cardiac surgery to treat paravalvular leak.

expected from this relatively sick population, the postoperative length of in-hospital stay was long and, despite an expected in-hospital postoperative mortality of 6% based on STS score, the observed mortality was only 3%. This is in contrast to previous studies, which have reported much greater operative mortality rates ($\geq 7\%$).^{1-6,8,13} To the best of our knowledge, this is one of the largest studies describing outcomes in patients who develop PVL after AV/MV surgery, with a large proportion of patients undergoing RCS at an experienced center.

Managing patients with PVL is often challenging because there is no effective medical therapy, thus making invasive therapy the only option. RCS remains the definitive treatment for significant PVL. However, previous studies demonstrated that RCS was associated with a high operative mortality, although long-term outcomes seem to be better versus those treated conservatively.^{1-6,8,13,25} Indeed, our study demonstrated that in an experienced center, despite low operative mortality, the longer-term survival of the RCS group is still relatively high, albeit slightly better in the RCS versus the conservative group.

The current study also demonstrates that patients with mitral PVL have worse longer-term survival versus those with aortic PVL. Previous studies have demonstrated operative mortality ranging from 3% to 7% for aortic and 7% to 13% for mitral PVL surgery, respectively.^{2,4,5} However, these were limited by small cohort size and a relatively short follow-up period. Another study demonstrated no significant differences in outcomes between aortic and mitral PVL, but the authors excluded patients with endocarditis.³ These survival differences between aortic and mitral PVL could potentially be due to differences in hemodynamics, as mitral PVL occurs during systole whereas aortic PVL occurs during diastole. Additional factors could also be greater proportion of atrial fibrillation, pulmonary hypertension associated with mitral PVL, and the greater difficulty in debriding the mitral versus aortic annulus. Furthermore, in the presence of an infection, a subsequent homograft provides a readily available prosthetic substitute at the aortic position that is associated with potentially decreased risk of reinfection.²⁶⁻²⁸

Another factor appears to be the etiology behind PVL. Although valve dehiscence is a very common etiology of PVL, endocarditis is also a frequent cause of PVL. It was observed in 21% patients, predominantly due to gram-positive organisms. Previous studies have suggested that poor prognosis of prosthetic valve endocarditis might be partially reversed by the survival impact of valve replacement surgery, which is consistent with the results of the current study.^{22,29}

Because of the increased complexity and morbidity of RCS, there has been an evolution of percutaneous techniques to close PVL. Typically, percutaneous PVL closure has been carried out in high-risk populations as an

alternative, less-invasive treatment.^{7,16-18} In our practice, percutaneous PVL is performed in patients without infection who are turned down for RCS due to prohibitive risk. Further prospective multicenter studies are necessary to confirm the improved survival of PVL closure following invasive therapies, especially prospective head-to-head comparison of percutaneous versus open closure.¹⁹ The results of the current study could potentially serve as a benchmark for future trials comparing different strategies for managing PVL (conservative vs RCS vs percutaneous).

Limitations

This was an observational study from a large tertiary center, which has its own inherent biases, including hidden differences between 2 groups compared, selection, and referral biases. The current study only reports associations, not causality. The study was not designed to prospectively test the natural history of PVL or head-to-head comparison of invasive techniques (percutaneous vs RCS). Because percutaneous PVL closure (during the study time frame) was only performed in patients turned down for RCS due to prohibitive perioperative risk, they were not included in the current analysis. However, because of a small sample size, propensity matching could not be performed. Also, because of very different follow-up schedules (and in turn, natural history), patients operated on at our center who developed subsequent PVL that was recognized soon after surgery were not studied. Our center is well experienced in complex valvular surgeries, and results may not be generalizable across lesser experienced centers. However, the current results also underscore the importance of a multidisciplinary approach at an experienced center for managing this high-risk cohort. A sizable proportion of patients with PVL have an infectious etiology, and the outcomes in these patients are more a reflection of the broader endocarditis milieu. However, not all patients have an infection related PVL. Hence, it is crucial to ascertain the etiology of PVL. We report a 4-class grading scheme for PVL, as not all patients underwent advanced imaging currently available (including 3-dimensional echocardiography and cardiac magnetic resonance).¹⁹ This increases the potential for misclassification of PVL severity. In addition, we report all-cause mortality as primary endpoint, as opposed to cardiac mortality. However, on secondary outcomes analysis using competing risk regression, the basic results were similar.

CONCLUSIONS

Patients who develop PVL after aortic or mitral surgery have a high rate of longer-term mortality, which is associated with mitral PVL and an infectious etiology. At a high-volume experienced center, despite excellent operative outcomes, the longer-term mortality of appropriately selected patients with PVL remains high, albeit better in the RCS group versus the conservative group. These findings need prospective validation.

Conflict of Interest Statement

Dr Marc Gillinov is on speakers' bureau for Atricure, Edwards, Medtronic, and St Jude's Medical and has an equity stake in Pleuraflow. All other authors have nothing to disclose with regard to commercial support.

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Key Words: paravalvular leak, aortic valve, mitral valve, surgery, reoperative cardiac surgery

TABLE E1. Outcomes of 108 patients turned down for RCS

Variable	N = 108
Age, y	66 ± 11
Male sex	57 (53%)
Hypertension	94 (89%)
Diabetes mellitus	32 (30%)
Hyperlipidemia	75 (69%)
Coronary artery disease	54 (50%)
Atrial fibrillation	69 (64%)
Hemolytic anemia	40 (37%)
Society of Thoracic Surgeons score	7.3 ± 4
>1 previous CV surgery	57 (53%)
Left ventricular ejection fraction, %	48 ± 11
Mean gradient across aortic valve, mm Hg	19 ± 12
Mean gradient across mitral valve, mm Hg	7 ± 4
Valve associated with PVL	
Mitral	71 (66%)
Aortic	37 (34%)
Degree of PVL	
Mild	12 (11%)
Moderate or greater	96 (89%)
Etiology of PVL	
Infective endocarditis	27 (25%)
Suture dehiscence	81 (75%)
Right ventricular systolic pressure, mm Hg	47 ± 18

During follow-up, 85 (79%) patients died, of which 56 deaths (66%) occurred within the first year. The 30-day and 1-year survival in this group was significantly lower than the main study sample at 76% and 52%, respectively. CV, Cardiovascular; PVL, paravalvular leak.