Outcomes of repeat mitral valve replacement in patients with prior mitral surgery: A benchmark for transcatheter approaches

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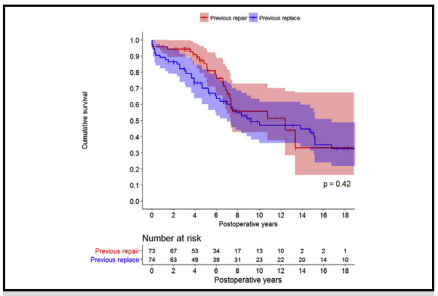
ABSTRACT

Objectives: With the emergence of transcatheter mitral valve-in-valve/ring replacement for deteriorated bioprostheses or failed repair, comparative clinical benchmarks for surgical repeat mitral valve replacement (re-MVR) are needed. We present in-hospital and survival outcomes of a 24-year experience with re-MVR.

Methods: From January 1992 to June 2015, 520 adult patients underwent re-MVR; 273 had undergone prior mitral valve repair (pMVP) and 247 had undergone prior MVR (pMVR). A benchmark cohort of isolated re-MVR was defined based on potential eligibility for transcatheter mitral valve-in-valve/ring replacement, resulting in 73 pMVPs with previous annuloplasty rings and 74 pMVRs with previous bioprosthetic valves for comparison.

Results: For the entire cohort, mean age was 64 ± 12 years for pMVP patients and 63 ± 15 years for pMVR patients ($P = .281$), which was similar for the benchmark cohort. Overall operative mortality was 14 out of 273 (5%) for pMVP versus 23 out of 247 (9%) for pMVR ($P = .087$). There were 3 operative deaths (4.1%) in both groups of the benchmark cohort ($P = 1.0$). For the benchmark cohort, median time to reoperation was 9.8 years for pMVP and 9.1 years for pMVR. Cox proportional hazard analysis showed that chronic kidney disease (hazard ratio [HR], 2.47; 95% CI, 1.77-3.44), endocarditis (HR, 1.49; 95% CI, 1.07-2.07), pMVR (HR, 1.45; 95% CI, 1.12-1.89), early reoperation ≤ 1 year (HR, 1.49; 95% CI, 1.02-2.17), and age (HR, 1.04/y; 95% CI, 1.03-1.05) were associated with decreased survival after re-MVR.

Conclusions: A re-MVR is a high-risk operation, but in carefully selected patients such as our benchmark population, it can be performed with acceptable results. Patients undergoing pMVP also have better long-term survival compared with patients undergoing pMVR. These results will serve as a benchmark for transcatheter mitral valve-in-valve/ring replacement. (J Thorac Cardiovasc Surg 2018;156:619-27)



Kaplan-Meier survival curve for isolated reoperative-mitral valve replacement (re-MVR) in the benchmark cohort (subgroup).

Central Message

Repeat MVR in patients with prior MV procedures is a high-risk operation, but in carefully selected patients such as our benchmark population, it can be performed with acceptable result.

Perspective

With the emergence of transcatheter mitral valve-in-valve/ring (TMVIV/R) replacement for deteriorated bioprostheses, comparative clinical benchmarks for surgical repeat mitral valve replacement (re-MVR) are needed. In this study, outcomes of an entire re-MVR cohort, as well as a benchmark cohort of patients undergoing isolated re-MVR, defined based on potential eligibility for TMVIV/R are reported.

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Mitral valve repair (MVP) remains the preferred treatment strategy for a variety of mitral valve pathologies, with the evidence strongest for myxomatous degeneration.[1,2] The

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Abbreviations and Acronyms

CABG = coronary artery bypass graft
CKD = chronic kidney disease
MVP = mitral valve repair
MVR = mitral valve replacement
pMVP = prior mitral valve repair
pMVR = prior mitral valve replacement
PROM = predicted risk of mortality
re-MVR = repeat mitral valve replacement
STS = Society of Thoracic Surgeons
TMVIV/R = transcatheter mitral valve-in-valve/ring

durability of MVP in this disease population is also excellent, reportedly with an 80% to 95% freedom from reoperation 10 to 20 years after surgery.[1,3-6] According to the Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database summary, there were 12,792 MVPs and 4548 mitral valve replacements (MVRs) performed in the United States during 2015.[7]

Overall, 4% to 10% of patients who undergo MVP will require a second intervention, most frequently a repeat MVR (re-MVR).[1,3,4,6,8] Although the advantages of mitral valve re-repair over replacement may persist at reoperation,[8] re-repair is only feasible in 36% to 85% of these patients.[8-11] Re-repair is also not always feasible in the setting of endocarditis, mitral stenosis, bileaflet prolapse, or severe degenerative progression of native disease. For patients who undergo MVR, the increasing use of bioprosthetic valves[12,13] and the desire to avoid lifelong anticoagulation[2] has resulted in increasing number of structural valve deterioration and subsequent re-MVR.[14] Previous reports suggest that re-MVR is a high-risk procedure with a 5% to 12% operative mortality[15-17] and a 7-year survival of 69%.[18] This has largely been attributed to the increased technical difficulty inherent to reoperations, greater frailty of the reoperative patients, and the fact that prosthetic valve endocarditis is a common indication for reoperation.[19]

Transcatheter valve technology provides a minimally invasive alternative to open cardiac valve replacement in high-risk patients. The existing transcatheter aortic valve has also been creatively utilized in deteriorated mitral valve bioprosthesis or in previous annuloplasty ring as transcatheter mitral valve-in-valve or ring replacement (TMVIV/R).[20,21] The reported outcomes have been favorable and the Food and Drug Administration recently approved the use of TMVIV/R for high risk-patients.[22-28] However, with the emergence of TMVIV/R for failed mitral valve rings/bioprostheses, comparative clinical benchmarks for surgical re-MVR are needed to assess their efficacy, safety, and durability, and determine their role in the therapeutic arsenal for MVR.

Furthermore, the majority of previous reports of reoperative MVR include patients with previous coronary artery bypass grafting (CABG) or nonmitral valve cardiac surgery.[14,16,29,30] Very few studies have actually examined outcomes of patients undergoing re-MVR prior MVP (pMVP) or replacement (pMVR). These studies were limited by small cohorts, older series, and did not stratify outcomes by type of prior mitral valve prosthesis.[6,14,15,29,31-33] We report the contemporary outcomes of a 24-year experience with re-MVR in a cohort of pMVP and pMVR patients. Our study had 2 aims: to report the postoperative outcomes of all patients (ie, entire cohort) undergoing re-MVR and to define a benchmark cohort of re-MVR eligible for TMVIV/R (ie, isolated from the entire cohort), and to provide this cohort's outcomes for TMVIV/R comparisons.

METHODS

Patient Selection

All adult patients aged 18 years or older who underwent re-MVR after pMVP or pMVR between January 1992 and May 30, 2015, at Brigham and Women's Hospital, were identified from our prospective cardiac surgery database and retrospectively reviewed. Patients with a history of any previous cardiac surgery or those undergoing concomitant cardiac surgery procedures were also included in our cohort. This study was approved by the Partners Healthcare Institutional Review Board and informed consent was waived.

Data Collection

Patient characteristics, medications, laboratory values, and in-hospital outcomes of the index surgery were extracted from our institutions electronic medical record. Follow-up data were aggregated from our electronic medical record as well as the patients' primary care physicians or cardiologists. Type of pMVP technique, and the use of ring annuloplasty, bioprosthetic replacement, or mechanical valve replacement was obtained from individual chart review of operative report (if available), preoperative echocardiogram, and pathology reports of the explanted device, if relevant. Long-term survival data were obtained from routine institutional follow-up protocols, our internal research data repository, and the Massachusetts Department of Public Health (Dorchester, Mass). We had 100% follow-up at 30 days and 95% long-term follow-up using our various sources. Patient demographic characteristics and hospital outcomes were coded and defined according to the STS Adult Cardiac Surgery database (version 2.52) specifications. Chronic kidney disease (CKD) was defined a priori as a preoperative creatinine $\geq$2.0 mm/dL or most recent clinical documentation of renal disease. Postoperative stroke was defined as the presence of a central neurologic deficit persisting postoperatively for more than 72 hours. Our primary outcomes of interest were 30-day mortality, postoperative morbidity, and long-term survival, both overall and in the benchmark cohort. Observed-to-expected operative mortality was calculated by dividing the observed mortality by the mean STS predicted risk of mortality (PROM) score for that cohort.

Benchmark Cohort

Because TMVIV/R can only be performed in a subset of pMVP and pMVR patients, a benchmark cohort was defined for comparison. TMVIV/R can be performed in patients with failed bioprosthetic valves and annuloplasty rings. They are contraindicated in the setting of endocarditis, or in patients with multivalve disease, and are seldom used in emergency settings. We excluded patients with endocarditis, concomitant

procedures (ie, CABG and/or aortic surgery), and those undergoing multivalve procedures (eg, double or triple valve replacements). Thus, our benchmark cohort consisted of comparable patients undergoing elective, isolated re-MVR after pMVP with ring annuloplasty or pMVR with bioprosthetic valves (Figure 1).

Statistical Analysis

Continuous variables were examined visually with histograms and with the Shapiro-Wilks test for normality. Normally distributed variables were expressed as a mean with standard deviation, and compared using Student *t* tests with Levene test for homogeneity for variance. Nonnormally distributed variables were expressed as median with interquartile range (IQR), and were compared using Mann-Whitney *U* tests. On the other hand, categorical variables were presented as number and percentages, and were compared using χ^2 or Fisher exact tests. Time to a long-term event was calculated in months from date of surgery to the first documented qualifying event, or if none occurred, to June 30, 2016 (observation end). Survival and time-to-events were examined by Kaplan-Meier estimation. A forward stepwise Cox proportional hazards model was used to evaluate adjusted survival. Variables selected included those found to be significantly different between groups on univariate analyses (Table 1), variables known to be contributors to all-cause mortality, and those deemed clinically meaningful in the context of valve surgery; final variables tested included age (in years), CKD, type of previous surgery, concomitant procedures, infectious endocarditis, New York Heart Association functional class, peripheral vascular disease, cerebrovascular disease, operative status, and hypertension. Full-factorial interaction terms were examined and a $P \leq .05$ retention threshold was used. All analyses were conducted using IBM-SPSS Statistics version 23.0 (IBM-SPSS Inc, Armonk, NY) and $P \leq .05$ was the criterion for significance.

RESULTS

Entire Cohort

During the study observation period, a total of 7226 mitral valve operations were performed, which included 4687 MVP and 2539 MVR procedures. Overall, 520 patients underwent re-MVR, which comprised 273 pMVP and 247 pMVR patients. Of our 520 re-MVR patients, 121 (23.3%) had their original mitral valve operation done at our institution (75 MVP and 46 MVR), resulting in an unadjusted institutional rate for re-MVR of 1.7%.

Baseline patient characteristics for the entire cohort are summarized in Table 1. The mean age was 64 ± 12 years for pMVP and 63 ± 15 years for pMVR patients ($P = .281$), with 60% being women in both groups. The 2 groups were otherwise similar in baseline comorbidities except that the pMVR group had higher prevalence of cerebrovascular disease (24.7% vs 16.1%; $P < .001$) and higher median left ventricular ejection fraction (60% vs 58%; $P < .039$). The mean STS PROM in patients after 2002 was 5.4% ± 2% and 6.7% ± 3% for pMVP and pMVR, respectively ($P = .241$). Patients before 2002 had no STS PROM estimates. Although details of pMVP technique were missing for the majority of patients, ring annuloplasty was used in 146 out of 273 patients (53.5%). For patients with pMVR, 161 out of 247 (65.2%) had prior bioprosthetic valves placed and 86 (34.8%) had mechanical valves placed. The median duration from pMVP to re-MVR was 9.8 years (IQR, 4.1-15.5), whereas the median duration from pMVR to re-MVR was 10.7 years (IQR, 6.7-20.1). Likewise, in patients undergoing pMVR, the median duration to re-MVR was 9.6 years (IQR, 3.8-14.2) and 12.8 years (IQR, 7-21.6) for bioprosthetic valves and mechanical valves, respectively.

The most common indications for valve replacement in the pMVP group were recurrent regurgitation in 134 out of 273 patients (49%), stenosis in 105 patients (38.5%), mixed in 19 patients (7%), and endocarditis in 24 patients (8.8%)—not mutually exclusive. For patients with prior

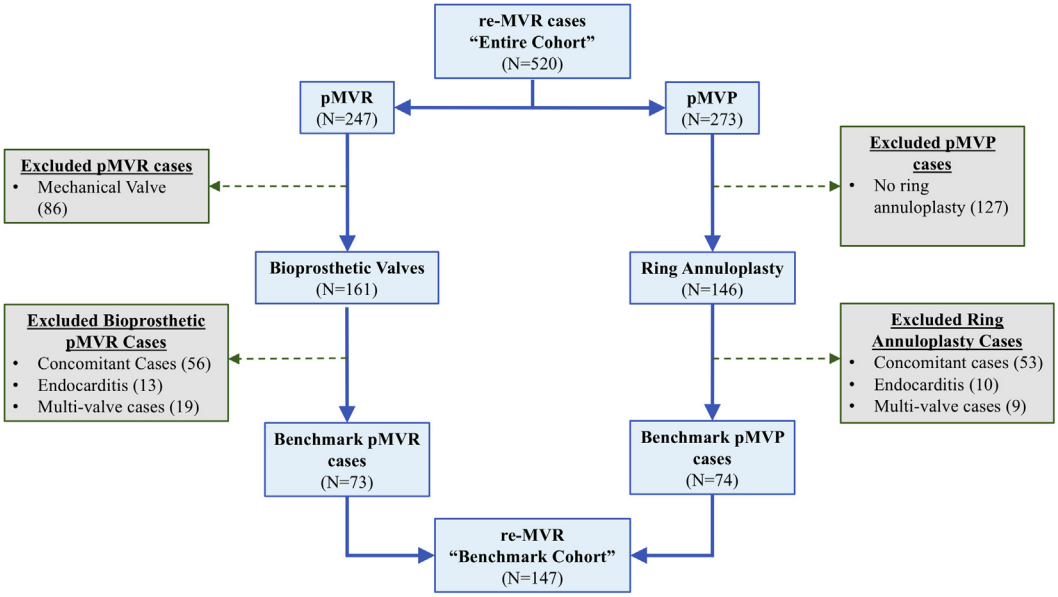


FIGURE 1. Flow diagram showing isolation of the benchmark cohort (subgroup) from the entire cohort. *re-MVR*, Repeat mitral valve replacement; *pMVR*, prior mitral valve replacement; *pMVP*, prior mitral valve repair.

TABLE 1. Baseline patient characteristics for the entire cohort (ie, those with prior mitral valve repair [pMVP] and prior mitral valve replacement [pMVR])

Characteristic	All (N = 520)	pMVP (n = 273)	pMVR (n = 247)	*P* value
Age, y	63.3 ± 13.5	63.9 (12.2)	62.7 (14.9)	≤.281
Women	311 (59.8)	165 (60.4)	146 (59.1)	≤.788
Hypertension	230 (44.3)	137 (50.2)	93 (37.7)	≤.005*
Chronic kidney disease	64 (12.3)	29 (10.6)	35 (14.2)	≤.231
Preoperative creatinine	1.21 ± 0.63	1.16 (0.66)	1.26 (0.58)	≤.096
Ejection fraction (%)	60 (50-65)	58 (50-61)	60 (52-65)	≤.039*
New York Heart Association functional class III or IV	319 (61.4)	160 (58.5)	159 (64.3)	≤.207
Peripheral vascular disease	44 (8.5)	27 (9.9)	17 (6.9)	≤.270
Cerebrovascular disease	105 (20.2)	44 (16.1)	61 (24.7)	≤.016*
Emergent procedure	91 (17.5)	5 (1.8)	9 (3.6)	≤.279
Society of Thoracic Surgeons predicted risk of mortality†	6.12 ± 6.53	5.54 (5.81)	6.7 (7.1)	≤.241
Duration from prior surgery, y	8.1 (3.1-14.3)	9.8 (4.1-15.5)	10.7 (6.7-20.1)	–
Prior bioprosthetic MVR			9.6 (3.8-14.2)	
Prior mechanical MVR			12.8 (7-21.6)	
Reasons for reoperation after pMVP				–
Recurrent mitral regurgitation		134 (49.1)		
Recurrent mitral stenosis		105 (38.5)		
Mixed mitral regurgitation and mitral stenosis		19 (10.6)		
Endocarditis		24 (8.8)	67 (27.1)	≤.001*
Reasons for reoperation after pMVR				–
Bioprosthetic valves (n = 161)				
Structural valve deterioration			135 (83.9)	
Endocarditis			37 (23.0)	
Paravalvular leak			11 (6.8)	
Mechanical valves (n = 86)				
Paravalvular leak			44 (51.2)	
Endocarditis			30 (34.9)	
Thrombosis/dehiscence			18 (11.2)	

Continuous variables are presented as mean ± standard deviation or median (interquartile range). Categorical variables are summarized as n (%). All variables were coded according to the Society of Thoracic Surgeons Adult Cardiac Surgery database (version 2.52). *pMVP*, Prior mitral valve repair; *pMVR*, prior mitral valve replacement; *MVR*, mitral valve replacement. **P* value ≤ .05 was considered statistically significant. †Only available on patients from 2002 when risk score was developed.

bioprosthetic MVR, the most common reasons for reoperations were structural valve deterioration in 135 out of 161 patients (83.9%), endocarditis in 37 patients (23%), and paravalvular leak in 11 patients (6.8%). In patients with prior mechanical valves, the most common reasons for reoperation were paravalvular leak in 44 out of 86 patients (51.2%), endocarditis in 30 patients (34%), and valve thrombosis/dehiscence in 18 patients (21%). There were also only 5 right lateral thoracotomies and 20 hemisternotomies performed, whereas all others were full sternotomies. These numbers were too small to determine the influence of surgical access.

Table 2 shows the operative and in-hospital outcomes for the entire cohort. Patients undergoing pMVR were more likely to have concomitant CABG and valve procedures (50.2% vs 46.2%; $P < .014$), with longer median perfusion (180 vs 160 minutes; $P < .001$) and crossclamp times (118 vs 100 minutes; $P < .005$). Overall, operative mortality for the entire cohort was 7%, but similar between pMVP and pMVR patients, respectively (5% vs 9%; $P = .087$).

The unadjusted 5- and 10-year survival rates were 79% versus 71%, and 60% versus 48% for pMVP and pMVR, respectively ($P = .001$) with a total follow-up time of 3777 patient-years (range, 0- 24.4 years) (Figure 2). Cox proportional hazard analysis showed that CKD (hazard ratio [HR], 2.47; 95% confidence interval [CI], 1.77-3.44), endocarditis (HR, 1.49; 95% CI, 1.07-2.07), pMVR (HR, 1.45; 95% CI, 1.12-1.89), early reoperation within 1 year (HR, 1.49; 95% CI, 1.02-2.17), and age (HR, 1.04/y; 95% CI, 1.03-1.05) were associated with decreased survival after re-MVR (Table 3) (–2 Log likelihood = 2724.45, $\chi^2 = 102$; $df = 4$; $P < .001$). No interaction terms were found to be significantly contributory.

TABLE 2. Operative and in-hospital outcomes for the entire cohort (ie, those with prior mitral valve repair [pMVP] and prior mitral valve replacement [pMVR])

Outcome	All (N = 520)	pMVP (n = 273)	pMVR (n = 247)	*P* value
Operative outcomes				
Procedure				
Isolated MV	270 (51.9)	147 (53.8)	123 (49.8)	≤.014*
MV + CABG	40 (7.7)	16 (5.9)	24 (9.7)	
MV + AV	66 (12.7)	27 (9.9)	39 (15.8)	
MV + TV	101 (19.4)	64 (23.4)	37 (15.0)	
Complex other†	43 (8.3)	19 (7.0)	24 (9.7)	
Perfusion time, min, median (IQR)	166 (129-224)	160 (124-206)	180 (140-242)	≤.001*
Crossclamp time, min, median (IQR)	103 (78-144)	100 (76-132)	118 (81-164)	≤.005*
Type of valve implanted				≤.042*
Bioprosthetic valve	203 (39.0)	117 (42.8)	86 (34.8)	
Mechanical valve	317 (61.0)	156 (57.1)	161 (65.2)	
Postoperative outcomes				
Reoperation for bleeding	21 (4)	8 (2.9)	13 (5.3)	≤.189
Redo valve	4 (0.7)	2 (0.7)	2 (0.8)	≤1.000
Permanent stroke	27 (5.2)	14 (5.1)	13 (5.3)	≤1.000
New onset atrial fibrillation	23.1 (120)	57 (20.9)	63 (25.5)	≤.213
New permanent pacemaker	43 (8.3)	22 (8.1)	21 (8.5)	≤.875
ICU LOS, h, median (IQR)	67 (31-120)	50 (27-106)	72 (43-130)	≤.001*
LOS, d, median (IQR)	9 (7-14)	9 (7-12)	11 (8-17)	≤.001*
Operative mortality	37 (7.1)	14 (5.1)	23 (9.3)	≤.087
Observed/expected mortality	1.16	0.92	1.38	
Unadjusted mean survival, y, mean ± 0.47	12.1 (0.47)	13.0 (0.63)	10.7 (0.63)	≤.001*
Median follow-up, y, median (IQR)	6.4 (3.1-11.0)	6.8 (3.3-11.1)	6.0 (2.3-10.9)	

Continuous variables are presented as mean ± standard deviation or median (interquartile range); categorical variables are summarized as n (%). All variables were coded according to the Society of Thoracic Surgeons Adult Cardiac Surgery database (version 2.52). *pMVP*, Prior mitral valve repair; *pMVR*, prior mitral valve replacement; *MV*, mitral valve; *CABG*, coronary artery bypass grafting; *AV*, aortic valve; *TV*, tricuspid valve; *ICU*, intensive care unit; *LOS*, length of stay. *P value ≤ .05 was considered statistically significant. †Complete other included 22 patients with triple valve surgery, 4 patients with triple valve surgery undergoing concurrent CABG surgery, 16 patients with aortic valve, mitral valve, and CABG surgery, and 1 patient with mitral valve, pulmonary valve, and aortic surgery.

Benchmark Cohort

From the entire cohort, we isolated the benchmark cohort, consisting of 73 pMVP patients with ring annuloplasty, and 74 pMVR patients with prior bioprosthetic MVR (Figure 1). Mean age was 61 ± 12 years for pMVP and 63 ± 15 years for patients undergoing pMVR (P = .240), with women being 50.7% and 39.2%, respectively (P = .186). The mean STS PROM was 5.0% ± 2% and 6.8% ± 3% for pMVP and pMVR, respectively (P = .158). Median duration from pMVP to re-MVR was 9.8 years (IQR, 4.1-15.5) and from pMVR to re-MVR was 9.1 years (IQR, 2.9-14.2) (Table 4). There was no difference in operative mortality between the 2 groups within the benchmark cohort (4.1% vs 4.1%; P = 1.00). The 2 groups also had comparable rates of postoperative stroke, reoperation rates for bleeding, new onset atrial fibrillation, or median hospital length of stay (all P values > .05). After stratifying the benchmark cohort into low (≤4.0%), medium (4.1%-8.0%), and high (>8.0%) operative risk based on STS PROM, observed-to-expected operative mortality ratios of 0.97 (2.4/2.47), 1.61 (9.5/5.9), and 0.49 (6.7/13.8), respectively (Table E1). Notably, patients with pMVP had a higher survival at 5 years compared with pMVR (85% vs 70%; P = .0467), but no survival difference by 10 years (56% vs 49%; P = .419), respectively, as demonstrated in the Kaplan-Meier survival curves for the benchmark cohort (Figure 3). A parsimonious Cox proportional hazards model showed no differences between the 2 groups in adjusted survival (residual χ^2 for pMVP vs pMVR = 0.08; df = 1; P = .78).

DISCUSSION

This contemporary study of 520 re-MVR patients is among the largest series to date and is the first to compare outcomes of patients undergoing re-MVR after pMVP or pMVR using our institutions, robust 24-year experience. We had several noteworthy findings (Video 1). Firstly, operative mortality was 7.1% in the entire cohort, confirming that re-MVR is a high-risk operation. Patients undergoing pMVP had a higher long-term survival by Cox adjusted analysis compared to patients undergoing pMVR. Secondly, we defined a benchmark cohort of isolated re-MVR

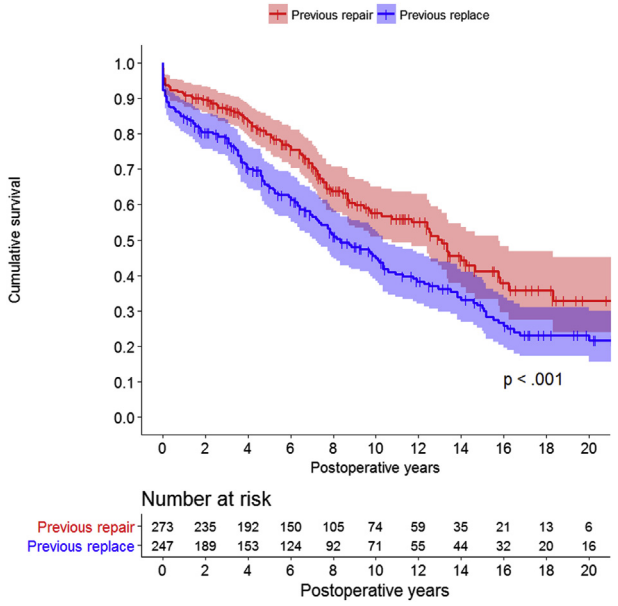


FIGURE 2. Kaplan-Meier survival curve for the entire cohort of patients undergoing reoperative mitral valve replacement (comparing those with prior mitral valve repair with prior mitral valve replacement).

that excluded mechanical prosthesis, emergency cases, and endocarditis patients, for TMVIV/R comparison. In this selective population, operative mortality was lower at 4.1%. We believe it was important to include both the entire and benchmark cohort, because the large entire cohort provides the outcome for re-MVR that all cardiac surgeons need to perform for different indications, whereas the benchmark results will provide the basis for direct comparison to TMVIV/R.

Notably, our operative mortality for the entire cohort was 7.1%, but had a trend toward lower mortality in patients undergoing pMVP (5.1%) compared with patients undergoing pMVR (9.3%) ($P = .087$). These findings are within the ranges reported in previous literature.[14-17,30,31] Akay and colleagues[31] reported a reoperative mortality of 6.4% in cohort of 62 patients, Borger and colleagues[14] reported a 9% rate, and Vohra and colleagues[17] reported a 12% rate in a cohort of 49 patients over a 10-year experience. These results have been attributed largely to the increased technical difficulty inherent to reoperations, greater frailty of the reoperative patients, and the fact that prosthetic valve endocarditis is a common indication for reoperation.[19] In our cohort, the slightly higher operative mortality and lower long-term survival in patients undergoing pMVR may likely have been due to the higher proportion of patients with endocarditis and concomitant coronary/valve procedures.

Moreover, in patients undergoing pMVP, the main indications for reoperation were mainly valve stenosis or regurgitation. Re-repair is not always feasible in the setting of stenosis, endocarditis, bileaflet prolapse, or degenerative progression of native disease. For patients with failed MVP, the decision between re-MVP versus re-MVR is

TABLE 3. Predictors of poor long-term survival following reoperative mitral valve replacement by Cox regression

Contributing factor*	Hazard ratio	*P* value	95% Confidence interval
Age, y	1.039	≤.001	1.028-1.050
Previous mitral valve replacement	1.453	≤.001	1.119-1.887
Chronic kidney disease	2.468	≤.001	1.770-3.440
Endocarditis	1.490	≤.017	1.073-2.067
Reoperation ≤ 1 y from previous	1.490	≤.038	1.022-2.174

*Noncontributory variables: gender, peripheral vascular disease, cerebrovascular disease, New York Heart Association functional class, and concomitant procedures.

TABLE 4. Baseline characteristics and in-hospital outcomes for the benchmark cohort (ie, those with prior mitral valve repair [pMVP] and prior mitral valve replacement [pMVR]). Benchmark cohort was isolated from the entire cohort (see Figure 1)

Variable	pMVP (n = 73)	pMVR (n = 74)	*P* value
Baseline characteristic			
Age	61.1 ± 11.9	63.7 (15.3)	≤.240
Woman	37 (50.7)	29 (39.2)	≤.186
Hypertension	42 (57.5)	24 (32.4)	≤.003
Chronic kidney disease	7 (9.6)	6 (8.1)	≤.780
Preoperative creatinine	1.16 ± 0.45	1.16 (0.37)	≤.485
Ejection fraction (%), median (IQR)	60 (55-60)	58 (50-65)	≤.648
NYHA class III or IV	40 (54.8)	49 (65.8)	≤.179
Peripheral vascular disease	7 (9.6)	2 (2.7)	≤.097
Cerebrovascular disease	7 (9.6)	15 (20.3)	≤.104
STS PROM*	5.03 ± 2.1	6.82 (3.0)	≤.158
Duration from prior MVP, y, median (IQR)	9.8 (4.1-15.5)		–
Duration from prior MVR, y, median (IQR)		9.1 (2.9-14.2)	–
Postoperative outcomes			
Reoperation for bleeding	2 (2.7)	2 (2.7)	≤ 1.000
Redo valve	1 (1.4)	1 (1.4)	≤ 1.000
Permanent stroke	4 (5.5)	2 (2.7)	≤.442
New onset atrial fibrillation	20 (27.4)	14 (18.9)	≤.246
New permanent pacemaker	3 (4.1)	3 (4.1)	≤ 1.000
ICU LOS, h, median (IQR)	49 (30-89)	46 (24-72)	≤.275
LOS, d, median (IQR)	8 (6-10)	9 (7-12)	≤.125
Operative mortality	3 (4.1)	3 (4.1)	≤ 1.000

Continuous variables are presented as mean ± standard deviation or median (interquartile range). Categorical variables are summarized as n (%). All variables were coded according to the Society of Thoracic Surgeons Adult Cardiac Surgery database (version 2.52). *pMVP*, Prior mitral valve repair; *pMVR*, prior mitral valve replacement; *NYHA*, New York heart association; *STS PROM*, Society of Thoracic Surgeons predicted risk of mortality; *MVP*, mitral valve repair; *MVR*, mitral valve replacement; *LOS*, length of stay; *ICU*, intensive care unit. *STS PROM only available on patients from 2002 when risk score was developed.

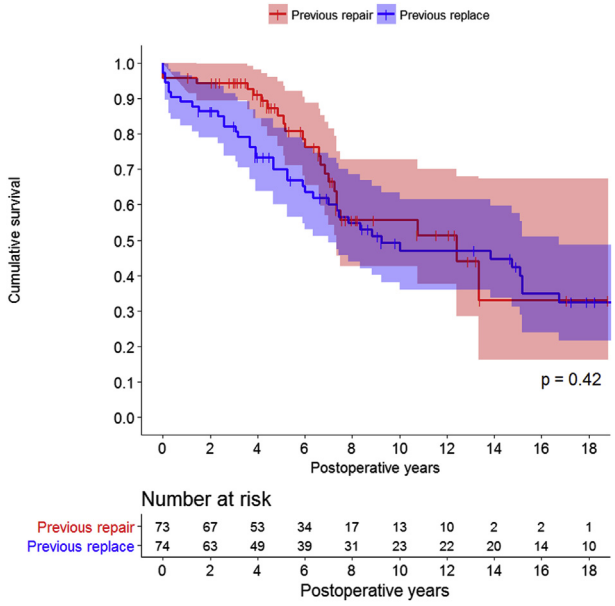
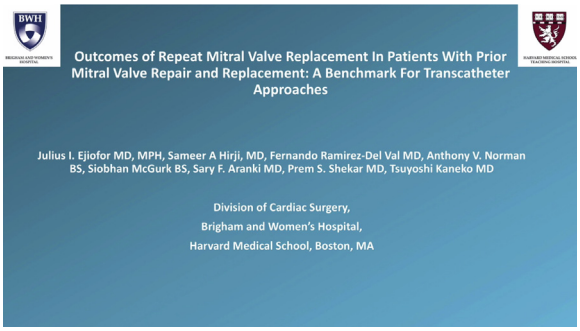


FIGURE 3. Kaplan-Meier survival curve for the isolated reoperative mitral valve replacement in the benchmark cohort (subgroup).

complex, and challenging, especially with limited contemporary data to guide clinical decisions. In our institution, patients with failed pMVP are thoroughly assessed with transthoracic echocardiography and transesophageal echocardiography. If the mechanism for recurrence appears simple, such as single posterior leaflet prolapses, inadequate annuloplasty ring size, we attempt re-MVP. However, we believe that complex re-MVP is a strong risk factor for re-recurrence, and to avoid third time reoperation, we have a low threshold for performing re-MVR.

For patients with pMVR, the indication for reoperation differed depending on valve type. Structural valve deterioration was the most common indication for reoperation in 84% of patients with bioprosthetic valves, whereas paravalvular leak and valve thrombosis or dehiscence were the main reasons in patients with prior mechanical valves.



VIDEO 1. Dr Tsuyoshi Kaneko discussing the essence of our study on the outcomes of repeat mitral valve replacement in patients with prior mitral valve repair and replacement: A benchmark for transcatheter approaches. Video available at: https://www.jtcvs.org/article/S0022-5223(18)30909-7/fulltext.

The median time to reoperation for bioprosthetic valves was significantly shorter at 9.6 years compared with 12.75 years for mechanical valves. Moreover, the mean age for pMVR was 62.7 years, indicating that the majority of these bioprosthetic valves were implanted before age 60 years. It has been well established that structural valve deterioration occurs faster in bioprostheses in the mitral position versus in the aortic position because it is exposed to relatively higher pressures.[32,34,35] Additionally, we previously showed the superiority of mechanical mitral valves in this younger population.[13] Because of these reasons, the majority (61.3%) of our patients, whose average age was younger than 65 years, received mechanical valves during re-MVR.

Furthermore, in our Cox regression analysis, increased age, renal impairment, endocarditis and previous mitral valve replacement were significant predictors of poor long-term survival. These findings are also consistent with prior studies.[15,17,31] However, New York Heart Association functional class was not predictive in our study, as shown by Vohra and colleagues.[17] This may be due to the preserved left ventricular ejection fraction in our patient cohort, which had a mean of 60%. Patients undergoing pMVP also had better long-term survival compared with patients undergoing pMVR (median survival, 13.7 years vs 8.3 years; $P = .001$). By Cox regression, the HR of long-term survival in patients with pMVR was 1.4 (95% CI, 1.07-1.8; $P < .013$) compared with pMVP.

The emergence of TMVIV has rekindled the excitement toward the use of bioprosthetic valves in younger patients. The promise of TMVIV/R is to use bioprosthetic valves in younger patients who wish to avoid lifelong anticoagulation, and when their valves eventually fail, minimally invasive TMVIV/R can be performed. However, caution is warranted with this management strategy because the durability of these transcatheter valves in the mitral position are unknown and there is risk of left ventricular outflow tract obstruction. Early results of TMVIV/R are promising, and show low periprocedural mortality, but with some potential problems such device embolization, paravalvular leaks (especially with C- or D-shaped rings) and left ventricular outflow tract obstruction.[21-28,36,37] TMVIV/R has also mainly been performed via the transapical approach, although recent series have shown the feasibility of transvenous transseptal implantation.[25,38] More recently, Yoon and colleagues[39] examined midterm outcomes of TMVIV/R in 248 high-risk patients with degenerated mitral bioprostheses: valve-in-valve was performed in 176 patients with failed mitral bioprothesis and valve-in-ring was performed in 72 patients with prior ring annuloplasty—and also found that mitral valve-in-ring was associated with higher rates of procedural complications (ie, technical success of 83.3% vs 96%; $P = .001$) and midterm (1-year) mortality (28.7% vs 12.6%; $P = .01$) compared with mitral valve-in-valve. Furthermore, failed annuloplasty ring was independently

associated with all-cause mortality on multivariable analysis (HR, 2.7; 95% CI, 1.34-5.43; $P = .005$).[39] Although TMVIV/R has now been approved by the Food and Drug Administration in high-risk patients, comparable surgical re-MVR outcomes are also needed to assess its safety and indications, especially in lower-risk patients. Nonetheless, with these results in the benchmark cohort, TMVIV/R will likely be competitive and perhaps maybe favorable. On the other hand, valve-in-ring will still remain challenging given its worse outcomes compared with TMVIV/R and the issue of paravalvular leak. In this population, we foresee re-MVR being performed more commonly. Moreover, future benchmarking to TMVIV/R may be limited by a relatively young age of these patient populations, especially in the era when this procedure is only indicated for high-risk patients. The ongoing Mitral Implantation of Transcatheter Valves trial (NCT02370511) may also provide further insight to TMVIV/R, although this registry lacks a surgical re-MVR arm for comparison.

Our study is subject to the limitations inherent in a single-center retrospective cohort design and our findings may not be generalized to other hospitals or patients. We were not able to obtain all the detailed operative techniques that were used at the time of original mitral valve procedure, or patient echocardiographic data, because 76% of the patient cohort were referrals from other centers within New England. Additionally, we unable to quantify patients who were offered re-MVP but received re-MVR due to nonfeasibility of re-MVP.

CONCLUSIONS

Although open re-MVR after pMVP or pMVR remains the standard of care, it is a high-risk operation with an operative mortality of 7.1%. Despite the encouraging results of TMVIV/R, an in-depth assessment of this technology is extremely crucial, especially in the context of limited long-term data. Re-MVR could be performed safely especially in the isolated MVR benchmark cohort, and should be the golden standard approach in the current era. However, further studies or registries are needed to directly compare these 2 interventions, especially in lower-risk patients.

Conflicts of Interest Statement

Dr Kaneko is a member of the speaker's bureau for Edwards LifeSciences, Irvine, Calif. All other authors have nothing to disclose with regard to commercial support.

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Key Words: mitral valve replacement, mitral valve repair, repeat mitral valve replacement, transcatheter mitral valve-in-valve replacement

TABLE E1. Operative mortality of the benchmark cohort, stratified by Society of Thoracic Surgeons predicted risk of mortality (STS PROM). Benchmark cohort was isolated from the entire cohort (see Figure 1)*

	Valid, n†	Mean STS PROM	Operative mortality	Observed to expected ratio
STS PROM ≤ 4.0				
Overall	90	2.39	4.4	1.84
Iso re-MVR Benchmark	42	2.47	2.4	0.97
STS PROM 4.1-8.0				
Overall	46	5.76	6.5	1.13
Iso re-MVR Benchmark	21	5.89	9.5	1.61
STS PROM > 8.0				
Overall	36	15.04	8.3	0.55
Iso re-MVR Benchmark	15	13.80	6.7	0.49

STS PROM, Society of Thoracic Surgeons predicted risk of mortality; *re-MVR*, repeat mitral valve replacement. *Patients with STS PROM scores. Patients before 2002 had no STS scores. †For the benchmark cohort, our observed to expected ratio was < 1 except for intermediate-risk patients. The exact reason for this discrepancy between intermediate risk and other patients are unclear, but may be due to risks not captured by the STS PROM score such as pulmonary hypertension, liver disease, or frailty.