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CONTEMPORARY REVIEW

Reoperative Mitral Surgery Versus Transcatheter Mitral Valve Replacement: A Systematic Review

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ABSTRACT: Bioprosthetic mitral structural valve degeneration and failed mitral valve repair (MVr) have traditionally been treated with reoperative mitral valve surgery. Transcatheter mitral valve-in-valve (MVIV) and valve-in-ring (MVIR) replacement are now feasible, but data comparing these approaches are lacking. We sought to compare the outcomes of (1) reoperative mitral valve replacement (redo-MVR) and MVIV for structural valve degeneration, and (2) reoperative mitral valve repair (redo-MVr) or MVR and MVIR for failed MVr. A literature search of PubMed, Embase, and the Cochrane Library was conducted up to July 31, 2020. Thirty-two studies involving 25 832 patients were included. Redo-MVR was required in ≈35% of patients after index surgery at 10 years, with 5% to 15% 30-day mortality. MVIV resulted in >95% procedural success with 30-day and 1-year mortality of 0% to 8% and 11% to 16%, respectively. Recognized complications included left ventricular outflow tract obstruction (0%–6%), valve migration (0%–9%), and residual regurgitation (0%–6%). Comparisons of redo-MVR and MVIV showed no statistically significant differences in mortality (11.3% versus 11.9% at 1 year, P=0.92), albeit higher rates of major bleeding and arrhythmias with redo-MVR. MVIR resulted in 0% to 34% mortality at 1 year, whereas both redo-MVr and MVR for failed repairs were performed with minimal mortality and durable long-term results. MVIV is therefore a viable alternative to redo-MVR for structural valve degeneration, whereas redo-MVr or redo-MVR is preferred for failed MVr given the suboptimal results with MVIR. However, not all patients will be candidates for MVIV/MVIR because anatomical restrictions may preclude transcatheter options from adequately addressing the underlying pathology.

Key Words: redo mitral valve repair ■ reoperative mitral valve replacement ■ transcatheter mitral valve replacement ■ valve-in-ring ■ valve-in-valve

Structural valve degeneration (SVD) of bioprosthetic mitral valves is common and frequently occurs after 5 or more years after initial valve replacement.[1–5] Reoperative surgical mitral valve replacement (redo-MVR) has been the gold standard treatment for bioprosthetic SVD for many years and is required in up to 35% of patients at 10 years after index surgery.[6,7] Redo-MVR is, however, associated with significant mortality and morbidities, particularly among elderly patients.[8] Similarly, mitral valve replacement (MVR) and reoperative mitral valve repair (redo-MVr) are options for patients with failed MVr, but with significant attendant risks in inexperienced centers. At the time of SVD or repair failure, patients tend to be older and hence are at a higher risk for reoperation. To meet the needs of these high-risk populations, transcatheter MVR (TMVR) using valve-in-valve (MVIV) and valve-in-ring (MVIR) techniques have emerged in the past few years. However, there have been no clinical trials comparing the aforementioned approaches, with very few

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Nonstandard Abbreviations and Acronyms

LVOTO	left ventricular outflow tract obstruction
MVIR	transcatheter mitral valve-in-ring replacement
MVIV	transcatheter mitral valve-in-valve replacement
MVr	mitral valve repair
MVR	mitral valve replacement
redo-MVr	reoperative mitral valve repair
redo-MVR	reoperative surgical mitral valve replacement
SVD	structural valve degeneration
TMVR	transcatheter mitral valve replacement

studies offering direct comparisons. Here, we critically review and assess the available data comparing the outcomes of redo-MVR and MVIV for SVD, as well as redo-MVr, MVR, and MVIR for those with failed MVrs.

METHODS

The authors declare that all supporting data, analytic methods, and study materials are available within this article (and its online supplementary files). A comprehensive search of PubMed, Embase, and the Cochrane Library was performed without any limitations to identify all studies up to July 31, 2020. The keywords "reoperative mitral valve replacement," "mitral valve replacement," "mitral valve repair," "transcatheter mitral valve replacement", "valve-in-valve", "valve-in-ring", "reoperative mitral valve repair," and "re-repair mitral valve" were indexed in all combinations for original reports and clinical work, including cross-sectional studies, observational studies, clinical trials, and reviews.

Studies evaluating (1) bioprosthetic mitral SVD, (2) reoperative mitral valve surgery, be it re-repair, MVR for a failed surgical annuloplasty, or redo-MVR, or (3) MVIV or MVIR for previous mitral valve surgery were included. Studies were excluded if they assessed outcomes not related to patients with previous mitral repairs or replacements or case reports. Throughout this process, the Cochrane methodology and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed. The Newcastle-Ottawa Scale Quality Assessment scores were used to rate all included studies (Table S1). Two independent investigators (A.S., F.Y.) assessed quality ratings, and disagreements were resolved via mutual discussion.

Primary variables of interest were short- and mid-term mortality, along with the rates of commonly recurring adverse events such as left ventricular outflow tract obstruction (LVOTO), valve thrombosis, valve migration or embolization, major vascular complication, life-threatening or major bleeding, and postprocedural mitral regurgitation.

Note that a meta-analysis was not performed for a variety of reasons. First, most of the transcatheter series included patients with relatively small sample sizes. Although small samples can still be combined with caution, we felt that this would detract from the generalizability of our results. Second, among the surgical series compiled, short-term outcomes were consistently reported, but mid- and long-term outcomes were reported on a case-by-case basis given the wide heterogeneity among these studies. Moreover, we do not have long-term data following MVIV and MVIR. Finally, although the conduct of surgical MV replacement and repair is generally well established, the technical aspects of MVIV and MVIR are evolving. Thus, earlier transcatheter series differ considerably from later series, especially with regard to the delivery technique used.

RESULTS

Our initial search identified 2123 studies, 708 of which remained after de-duplication. 79 full-text articles were assessed for eligibility and 32 were included in our qualitative synthesis (Figure 1). The vast majority of these studies were retrospective cohort and case-control studies, with 1 prospective comparative cohort trial.

Surgical and Transcatheter Options in Degenerated Bioprosthetic Mitral Valves

Reoperative Surgical Mitral Valve Replacement

Bioprosthetic mitral valves are subject to SVD because of prosthesis degeneration, thrombosis, and paravalvular leak and may lead to significant stenosis, regurgitation, or both. Rates of SVD vary widely in the literature but have been reported at ≈25% to 30% at 10 years and ≈50% to 70% at 15 years.[9] Similarly, freedom from reoperation is estimated at 96.6%, 86.6%, and 75.3% at 5, 10, and 15 years, respectively.[10]

Short- and long-term outcomes

The volume of redo-MVR has increased steadily over the past few decades, with a concomitant improvement in outcomes.[8,11,12] Mortality at 30 days following redo-MVR ranges from 5% to 15% (Figure 2).[7,8,13–21] Age, sex, preoperative New York Heart Association class, indication for reoperation, type of prosthetic valve, number of previous operations, hepatic and renal failure, and timing of reoperation have all been associated with mortality and postoperative complications after redo-MVR.[15] Preoperative diagnosis is a

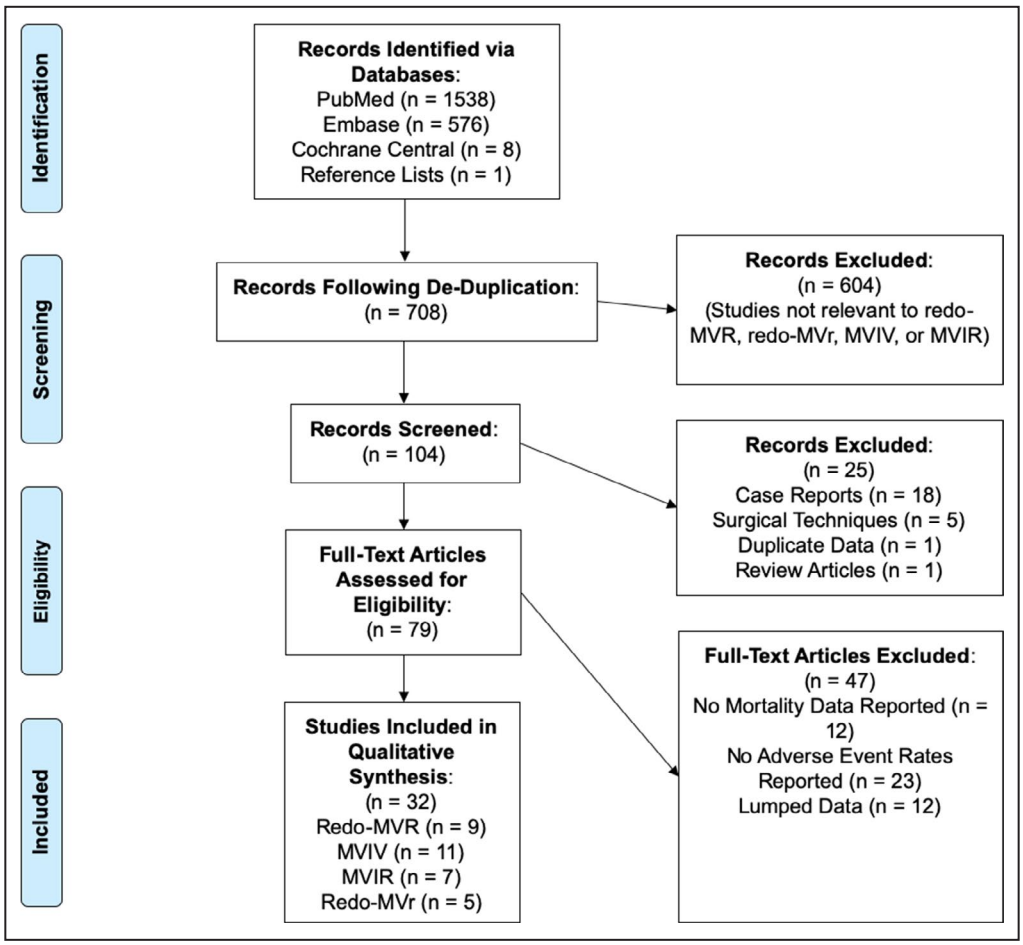

Figure 1. PRISMA diagram for study selection and identification.
PRISMA flowchart for selection of studies for eventual inclusion in the systematic review. MVIR indicates transcatheter mitral valve-in-ring replacement; MVIV, transcatheter mitral valve-in-valve replacement; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; redo-MVr, reoperative mitral valve repair; and redo-MVR, reoperative mitral valve replacement.

key driver of mortality in most series, with prosthetic valve endocarditis high in the rank list.[11] Note that because prosthetic valve endocarditis is virtually always tackled with surgery as opposed to TMVR, comparisons of the 2 techniques should exclude patients with endocarditis.

Long-term outcomes are highly variable in the literature and are not consistently reported. As an example, Vohra et al retrospectively looked at outcomes in 49 adults with bioprosthetic or mechanical valves who underwent redo-MVR between 2000 and 2010 with a mean follow-up of 47.5±37 months. Median time to reoperation was 8.2±6.6 years for first-time redo-MVR and 6.4±5.6 years for second-time redo-MVR. In-hospital mortality was 12%, and mortality rates at 1 and 5 years were 18.4% and 27.2%, respectively.[7] In another report of 347 reoperations on mitral prostheses, Bortolotti et al reported actuarial survival rates of 63±3% at 5 years, 38±4% at 10 years, and 24±5% at 15 years.[16] Note that the choice of prosthesis at the index operation has implications for potential reintervention because transcatheter approaches cannot be performed in patients with prior mechanical valves.

Transcatheter Mitral Valve-in-Valve Replacement

In the United States, the SAPIEN 3 valve (Edwards Lifesciences LLC, Irvine, CA) was approved in 2017 for MVIV by the U.S. Food and Drug Administration in high surgical-risk patients and is the only transcatheter valve that is approved for MVIV.[24,25]

Short- and midterm outcomes

Patient characteristics from the various MVIV studies are shown in Table 1. Reported outcomes of MVIV are limited to 30 days to 1 year given that this is a relatively new procedure. Mortality at 30 days and 1 year following MVIV has been reported at 0% to 8% and 11% to 16%, respectively (Figure 3), with >95% procedural success.[26–36]

Of note, Guerrero and colleagues recently reported

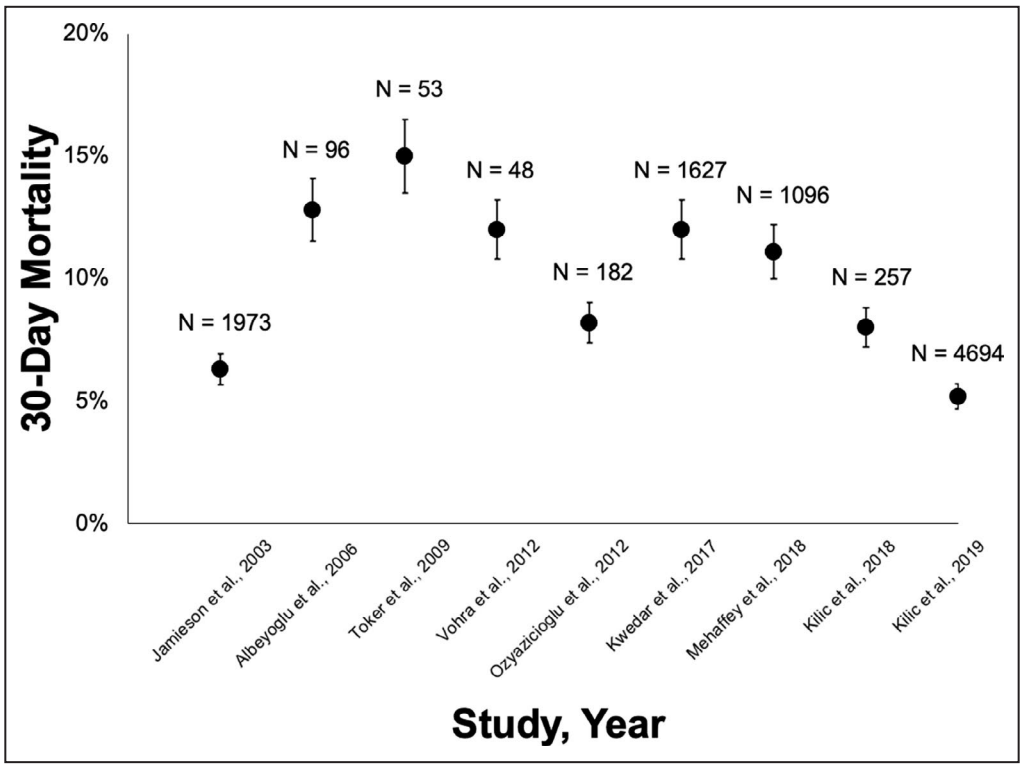

Figure 2. Thirty-day mortality following reoperative mitral valve replacement (MVR) for bioprosthetic mitral structural valve degeneration (SVD).
Shown here are the 30-day mortality rates, in ascending chronological order of year of publication, following redo-MVR for bioprosthetic mitral SVD among various surgical series. The error bars indicate the 95% CIs.[7,8,14,17,18,20,22,23]

the 1-year outcomes of 1576 patients undergoing MVIV, with either a transapical or transseptal approach, from the STS/ACC TVT (Society for Thoracic Surgeons/American College of Cardiology Transcatheter Valve) Registry. 1-year mortality was reported at 21.7% and 15.8% for the transapical and transseptal groups, respectively. Furthermore, higher complication rates (device embolization, LVOTO, and conversion to open surgery) and worse outcomes (all-cause mortality and cardiovascular death at 30 days and 1 year) were noted with the transapical approach.[37]

Direct comparison with reoperative mitral valve replacement

Few data directly comparing redo-MVR to MVIV exist in the literature.[38] Kamioka et al compared the clinical and echocardiographic outcomes of 59 patients who underwent redo-MVR with 62 who underwent MVIV (22.6% transapical; 77.4% transseptal) up to August 2017. Patients who had active endocarditis, required concomitant procedures for coronary artery disease or aortic disease, or underwent additional valve replacement were excluded. There was no statistical difference in mortality at 30 days (MVIV 3.2% versus redo-MVR 3.4%, P=1.00) and at 1 year between the 2 groups (MVIV 11.3% versus redo-MVR 11.9%, P=0.92). MVIV was associated with a much lower rate of major bleeding and atrial arrhythmias, as well as a shorter hospital stay.[31]

Complications

Reported complications of MVIV include LVOTO, valve migration or embolization, elevated postprocedural gradients, residual mitral regurgitation, and valve thrombosis (Table 2).

Surgical and Transcatheter Options in Failed Mitral Valve Repair

Patients with failed surgical MVr have historically undergone rerepair or MVR. Given the risks associated with reoperation, MVIR, although not approved by the Food and Drug Administration, has emerged as an alternative option, but robust data comparing these approaches are lacking.[39]

Mitral Valve Rerepair Following Failed Surgical Annuloplasty

Short- and long-term outcomes following redo-MVr are generally favorable in experienced mitral centers.[40,41] For instance, Kilic et al reported on 305 patients with previous repairs, 48 of whom underwent redo-MVr.

Table 1. Patient Characteristics in Studies of Transcatheter Mitral Valve-in-Valve Replacement

Study, Year[REF]	Mean Age (y)	Female (%)	NYHA Class (%)	STS-PROM (%)	DM (%)	Cr (mmol/L)	HTN (%)	PVD (%)	CVA (%)	COPD (%)	LVEF (%)	Failure Mechanism (%)
Yoon et al, 2019 (N=322)[35]	72.6±12.9	58.7	III: 87.8 IV: 32.3	9.2±7.2	23.3	130±113	69.6	11.1	17.7	28.6	55.3±11.5	MR: 36.6 MS: 40.7 B: 22.7
Guerrero et al, 2019 (N=1326)[37*]	73.4±11.9	59.2	≥III: 86.5	11.0±8.6	NA	na (5.3% on dialysis)	NA	NA	17.5	46.2	54.9±12.1	MR: 55.6 MS: 25.0 B: 19.4
Hu et al, 2018 (N=172)[30]	74.5±12.5	53.5	≥III: 97.3	16.8±15.2	17.2	NA (35.2% chronic renal failure)	NA	NA	NA	NA	51.2±11.5	MR: 49.3 MS: 31.9 B: 18.8
Urena et al, 2018 (N=34)[32]	73.0	70.6	≥III: 91.2	NA (Euro-SCORE II: 10.9	17.6	NA (67.6% eGFR <60 mL/min)	NA	NA	NA	20.6	58.0±10.0	NA
Kamioka et al, 2018 (N=62)[31]	74.9±9.4	61.3	IV: 30.7	8.7±10.1	24.2	133±133	38.7	6.5	35.5	33.9	54.6±11.9	MR: 50.0 MS: 71.0 B: 8.1
Yoon et al, 2017 (N=176)[36]	72.9±12.8	63.1	≥III: 88.1	9.3±7.0	26.1	124±98	61.9	6.3	21.0	24.4	55.3±11.1	MR: 36.4 MS: 35.8 B: 27.8
Eleid et al, 2017 (N=60)[29]	75.0±11.0	57.0	III: 45.0 IV: 55.0	12.5±7.2	22.0	115±44	85.0	17.0	8.0	35.0	57.0±11.0	MR: 63.0 MS: 32.0 B: 5.0
Eleid et al, 2016 (N=33)[28]	76.0±11.0	60.0	III: 48.0 IV: 52.0	13.2±7.4	23.0	133±80	85.0	17.0	10.0	48.0	56.0±12.0	MR: 60.6 MS: 33.3 B: 6.1
Ye et al, 2015 (N=31)[34]	78.7±8.8	58.0	≥III: 96.8	9.7 (5–16.6)	22.6	>150: 6.5%	NA	12.9	32.3	22.6	60.0 (40.0–65.0)	MR: 54.2 MS: 38.7 B: 16.1
Cheung et al, 2013 (N=23)[27]	81.1±5.8	60.9	≥III: 95.6	12.6±6.9	17.4	NA (56.5% chronic renal failure)	NA	30.4	34.8	26.1	54.5±12.3	MR: 39.1 MS: 30.4 B: 30.4
Wilbring et al, 2013 (N=7)[33]	79 (Q1–Q3: 75–81)	71.4	III: 100%	12.3±2.1	42.9	NA (42.9% chronic renal failure)	NA	NA	71.4	NA	49.3±11.8	MR: 100% MS: 0% B: 28.6%

Patient characteristics in 11 studies of transcatheter mitral valve-in-valve replacement are shown here in descending order of year of publication. B indicates both; COPD, chronic obstructive pulmonary disease; Cr, creatinine clearance; CVA, cerebrovascular accident; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; Euro-SCORE, European System for Cardiac Operative Risk Evaluation; HTN, hypertension; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; MS, mitral stenosis; NA, not available; NYHA, New York Heart Association; PVD, peripheral vascular disease; Q1, quartile 1; Q3, quartile 3; and STS-PROM, Society of Thoracic Surgeons-Predicted Risk of Mortality.

*Transseptal access only.

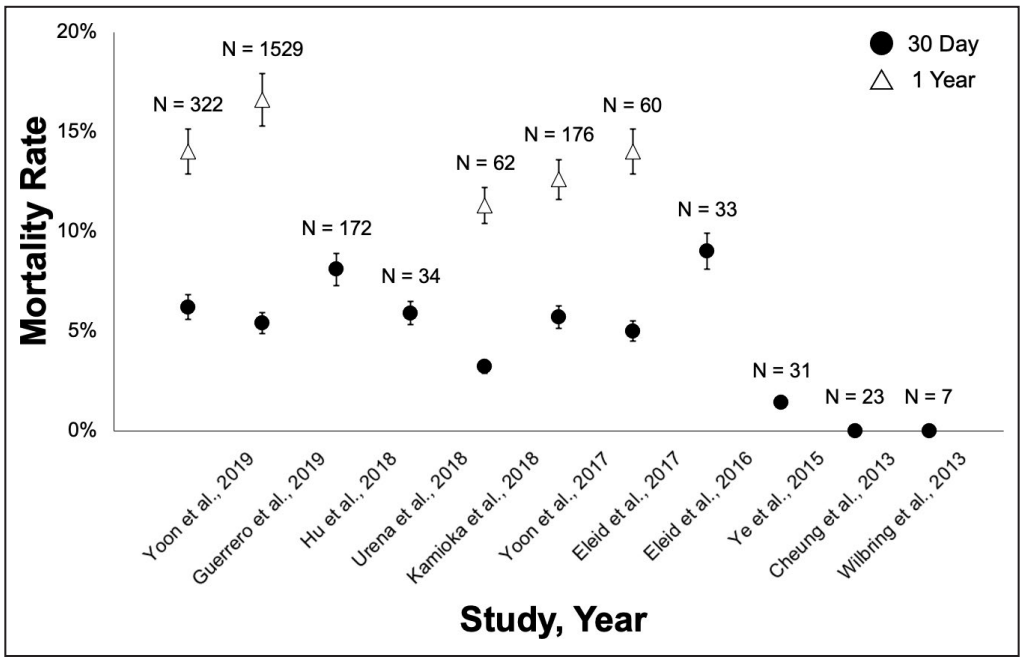

Figure 3. Thirty-day and 1-year mortality following mitral valve-in-valve (MVIV) replacement. Mortality rates at 30 days and 1 year are shown among the various MVIV series evaluated, in descending chronological order of year of publication. The error bars indicate the 95% CIs.[26–36]

There was 0% operative mortality with 96% long-term freedom from mortality at 5 years.[22]

Surgical Mitral Valve Replacement Following Failed Annuloplasty

MVR is also an option for patients with failed mitral bands or rings. Evidence suggests that, although in-hospital mortality and rates of postoperative complications may favor MVR, long-term mortality is likely similar to that of surgical rerepair.[18] In the study by Kilic et al, 257 of 305 patients underwent MVR following a previous repair. 8% operative mortality was noted, along with an increase in blood transfusion rates and duration of mechanical ventilation compared with the redo-MVr cohort. However, long-term freedom from mortality was comparable to the 48 patients who underwent rerepair (P=0.29).[22]

Multiple groups have reported on the outcomes of reoperative mitral valve surgery without making the distinction between rerepair and reoperative replacement.[8,23] In an early series, specific to reoperation in failed MVr, Cerfolio et al reported an operative mortality of 4.0%, with 87.0% of patients in New York Heart Association class I or II at 5-year follow-up.[42] A contemporary cohort of reoperation for failed MVr was recently analyzed, with a reported mortality of 6.5%. A propensity-matched cohort from that series indicated that the failed MVr itself did not affect survival compared with other reoperative procedures with normal mitral valves.[43] Other groups have reported mortality rates between 0% and 9.0%.[40,41,44,45]

Transcatheter Mitral Valve-in-Ring Replacement

In contrast to surgical reoperation, MVIR is much less invasive and avoids issues related to redo sternotomies and cardiopulmonary bypass. Several articles have reported preliminary outcomes. Patient characteristics are shown in Table 3. Thirty-day and 1-year mortality are estimated at 0% to 18% and 0% to 34%, respectively (Figure 4). Studies of MVIR have also noted several recurrent complications (Table 4).[30,35,36,46–57] Of note, only 3 of these studies reported the characteristics of the rings that had been implanted.[29,36,49]

Studies with long-term outcomes following MVIR are limited. The largest series of TMVR cases published to date by Yoon et al included 141 MVIR cases from an international registry. Procedural success was achieved in 80.9% of these cases with a 30-day mortality of 9.9% and 1-year mortality of 30.6%.[35]

DISCUSSION

Two key conclusions are evident from this systematic review: (1) given its safety profile, MVIV is a viable alternative to redo-MVR in high surgical-risk patients with bioprosthetic mitral SVD, with certain caveats;

Table 2. Short-Term Outcomes of Transcatheter Mitral Valve-in-Valve Replacement

Study, Year[REF]	30-d Mortality	Stroke	Bleeding*	MVC	Device Thrombosis	Technical Success	LVOTO	Valve Embolization	≥3+Residual MR
Yoon et al, 2019 (N=322)[35]	6.2	2.3	4.6	1.6	NA	94.4	2.2	1.7	3.3
Guerrero et al, 2019 (N=1326)[37]*	TS: 5.0 TA: 8.1	TS: 1.1 TA: 1.0	NA	TS: 1.2 TA: 2.5	TS: 0.2 TA: 0.5	TS: 97.3 TA: 94.6	TS: 0.8 TA: 2.0	TS: 0.2 TA: 0.5	NA
Hu et al, 2018 (N=172)[30]	7.5	3.2	8.7	0.0	3.2	97.1	0.0	5.3	5.5
Urena et al, 2018 (N=34)[32]	5.9	5.9	5.9	5.9	8.8	94.1	5.9	2.9	0.0
Kamioka et al, 2018 (N=62)[31]	3.2	0.0	6.5	1.6	1.9	NA	3.2	NA	3.8
Yoon et al, 2017 (N=176)[36]	5.7	2.3	2.3	1.7	NA	96.0	3.2	1.1	3.6
Eleid et al, 2017 (N=60)[29]	6.0	0.0	7.0	3.3	2.0	97.0	5.0	0.0	0.0
Eleid et al, 2016 (N=33)[28]	8.0	0.0	8.0	0.0	2.0	93.9	4.0	6.0	0.0
Ye et al, 2015 (N=31)[34]	1.0	3.2	3.2	0.0	0.0	98.6	NA	0.0	5.0
Cheung et al, 2013 (N=23)[27]	0.0	4.4	0.0	NA	0.0	100.0	NA	0.0	NA
Wilbring et al, 2013 (N=7)[33]	0.0	NA	0.0	NA	NA	100.0	NA	NA	NA

Procedural and 30-day outcomes of transcatheter mitral valve-in-valve replacement are shown. LVOTO indicates left ventricular outflow tract obstruction; MR, mitral regurgitation; MVC, major vascular complication; NA, not available; TA, transapical; and TS, transseptal.
*Life-threatening bleeding.

and (2) for those with failed surgical mitral annuloplasty, reoperative MVr or MVR is preferred to MVIR in suitable candidates. For certain high- or extreme-surgical risk patients, however, MVIR may be appropriate after a thorough assessment of all procedural risks and evaluation of the type of ring that has been implanted.

Any discussion of bioprosthetic mitral SVD and failed MVr begins with a basic understanding of the surgical principles of MVR and MVr and their relation to the technical aspects of MVIV and MVIR, respectively. In contemporary practice, when repair is not feasible, a valve replacement operation that leaves leaflets and chords intact is preferred for optimal preservation of cardiac function. During chordal-sparing valve replacement, the posterior leaflet is usually preserved, and the anterior leaflet may be divided centrally and then plicated to avoid prosthetic leaflet impingement and LVOTO.[58,59] In contrast, the anterior leaflet is almost always left intact during MVr. Thus, the anatomy after MVr is significantly different from that following MVR. As is discussed next, this has significant implications for subsequent transcatheter therapies, especially with regard to the risk of postprocedural LVOTO, and may partially explain why we observe better outcomes with MVIV than with MVIR.

Reoperative Mitral Valve Replacement and Transcatheter Mitral Valve-in-Valve Replacement

Prosthetic valve reoperations carry significant risks. Thirty-day mortality is estimated at 5% to 15% with significantly higher rates of adverse events, including major bleeding and atrial arrhythmias, when compared with MVIV. In contrast, short-term mortality for MVIV ranges from 0% to 9%, with comparable valve hemodynamics and improvements in functional status at 1 year.

There are several common themes that emerge from the literature when assessing the merits and risks of redo-MVR and MVIV. First, patients who develop SVD or require redo-MVR are generally very sick and have a high competing risk of death. Second, those who present in a higher New York Heart Association class and/or with a lower ejection fraction for redo-MVR have worse outcomes, and earlier intervention may be warranted in select cases. Third, MVIV via a transseptal approach, given its safety profile, is a reasonable alternative to redo-MVR in select high surgical-risk patients. However, redo-MVR should be performed in patients who are not high risk for surgery, those with paravalvular leak not amenable to percutaneous closure, prosthetic valve endocarditis, prosthetic valve thrombosis, patients with a high risk of LVOTO, or when concomitant cardiac surgical procedures (eg, coronary artery

Table 3. Patient Characteristics in Studies of Transcatheter Mitral Valve-in-Ring Replacement

Study, Year[REF]	Mean Age (y)	Female (%)	NYHA Class (%)	STS-PROM (%)	DM (%)	Cr (mmol/L)	HTN (%)	PVD (%)	CVA (%)	COPD (%)	LVEF (%)	Failure Mechanism (%)
Yoon et al, 2019 (N=141)[35]	71.7±9.7	36.9	III: 89.4 IV: 25.5	8.1±46.3	21.3	145±104	68.6	10.6	12.1	27.0	44.3±15.7	MR: 77.3 MS: 6.4 B: 16.3
Hu et al, 2018 (N=73)[30]	70.0±10.8	40.4	≥III: 100.0	13.4±9.0	14.0	NA (28.1% Chronic Renal Failure)	NA	NA	NA	NA	36.7±14.5	MR: 68.2 MS: 24.2 B: 7.6
Urena et al, 2018 (N=30)[32]	70.0	70.0	≥III: 80.0	NA (Euro-SCORE II: 9.6%)	13.3	NA (56.7% eGFR <60 mL/min)	NA	NA	NA	30.0	57.0±10.0	NA
Long et al, 2018 (N=8)[53]	68.7±14.2	50.0	III: 12.5 IV: 4.2	8.9±5.2	20.8	NA	NA	NA	NA	66.5	42.5±14.1	MR: 16.6 MS: 70.8 B: 12.5
Yoon et al, 2017 (N=72)[36]	71.4±10.2	41.7	≥III: 91.7	8.1±6.2	16.7	150±124	56.9	9.7	5.6	27.8	45.6±17.4	MR: 77.8 MS: 4.2 B: 18.1
Eleid et al, 2017 (N=15)[29]	72±8	60.0	III: 47.0 IV: 53.0	11.4±7.3	13.0	150±141	73.0	20.0	7.0	40.0	50.0±19.0	MR: 73.0 MS: 20.0 B: 7.0
Descoutures et al, 2013 (N=17)[49]	70.0±16.0	NA	≥III: 100.0	13.0±9.0	NA	NA	NA	NA	NA	NA	NA	MR: 70.6 MS: 29.4

Patient characteristics in 7 studies of transcatheter mitral valve-in-ring replacement are shown here in descending order of year of publication. B indicates both; COPD, chronic obstructive pulmonary disease; Cr, creatinine clearance; CVA, cerebrovascular accident; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; Euro-SCORE, European System for Cardiac Operative Risk Evaluation; HTN, hypertension; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; MS, mitral stenosis; NA, not available; NYHA, New York Heart Association; PVD, peripheral vascular disease; and STS-PROM, Society of Thoracic Surgeons-Predicted Risk of Mortality.

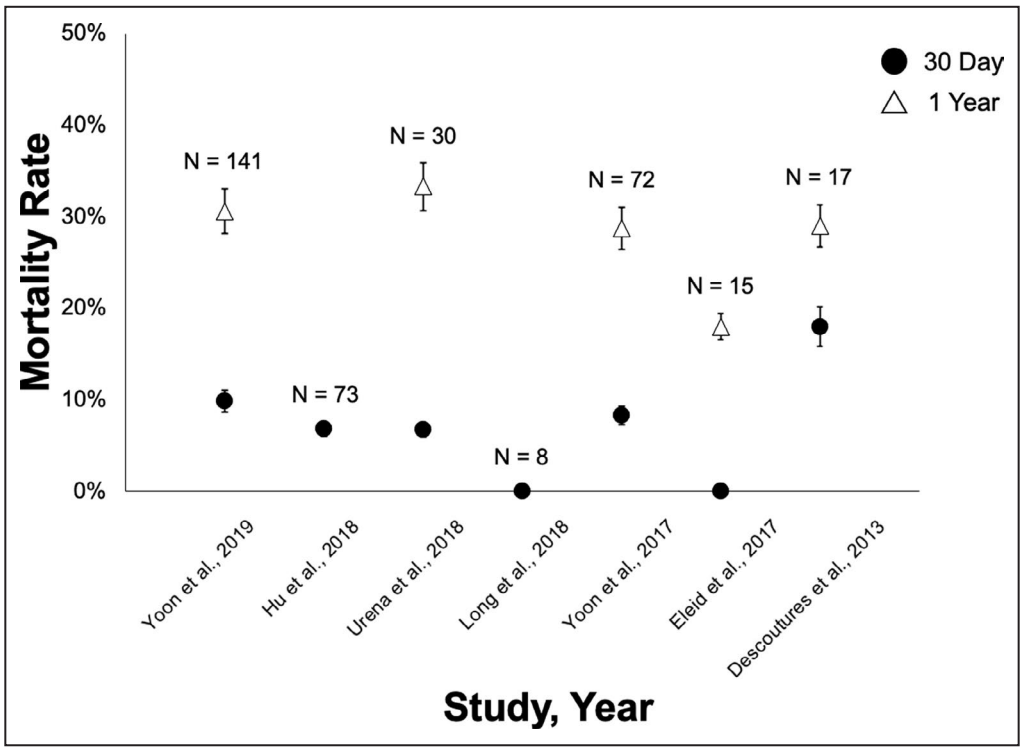

Figure 4. Thirty-day and 1-year mortality following mitral valve-in-ring (MVIR) replacement. Mortality rates at 30 days and 1 year are shown among the various MVIR series, in descending chronological order of year of publication. The error bars indicate the 95% CIs.[29,30,32,35,36,49,53]

bypass grafting, tricuspid valve repair, Maze procedure, etc) are needed. The risk of LVOTO, which can be assessed by preoperative computed tomography imaging, is a particularly important anatomical reason that precludes use of MVIV (discussed later). Finally, transapical MVIV is associated with higher mortality and morbidity as compared with transseptal MVIV, and the latter approach should be pursued whenever possible.

Comparisons of transcatheter and surgical options for patients with bioprosthetic mitral SVD have to be evaluated carefully, however, for a number of reasons. First, patients assigned to these 2 treatment modalities are generally preselected based on surgical risk, and it is difficult to directly compare outcomes with wide applicability. Given the risk of selection bias, a randomized trial comparing the safety, effectiveness, and durability of redo-MVR and MVIV is eagerly awaited. Furthermore, when comparing redo-MVR and MVIV, it is important to note whether patients in the transcatheter group underwent transapical or transseptal MVIV. Studies have shown that transapical MVIV has inferior outcomes compared with its transseptal counterpart. These 2 delivery techniques differ in numerous aspects. Transapical implantation may enable better control over the implant position given that the cardiac apex is considerably closer to the mitral valve than the peripheral veins.[60] However, the transseptal approach eliminates the need for either thoracotomy or trauma to the left ventricle and is associated with a mortality benefit and greater improvements in postprocedural functional performance.[61] Thus, although transapical MVIV may not be a viable alternative to redo-MVR, transseptal MVIV should be considered for high-risk patients with suitable anatomy, with the caveat that the transseptal approach may be more technically challenging requiring operator expertise at high-volume centers.[62]

Failed Surgical Repairs and Transcatheter Mitral Valve-in-Ring Replacement

For patients with a prior ring or band annuloplasty, MVIR seems to be inferior to both redo-MVr and MVR. As with redo-MVR/MVIV, selection bias may be at play given that patients being considered for MVIR tend to be at high or extreme risk for reoperative surgery. Mortality with MVIR at 30 days is ≈0% to 18%, and ≈0% to 34% at 1 year. In contrast, reoperative MVr can be performed with <5% mortality at most large institutions with excellent long-term outcomes. Similarly, although short-term mortality for reoperative MVR may be comparable to that of MVIR, the long-term benefits with regard to valve durability and freedom from reoperation are undeniable with the former. Thus, redo-MVr

Table 4. Short-Term Outcomes of Transcatheter Mitral Valve-in-Ring Replacement

Study, Year[REF]	30-d Mortality	Stroke	Bleeding*	MVC	Device Thrombosis	Technical Success	LVOTO	Valve Embolization	≥3+Residual MR
Yoon et al, 2019 (N=141)[35]	9.9	0.0	6.7	3.8	NA	80.9	5.0	1.4	12.6
Hu et al, 2018 (N=73)[30]	6.8	5.4	0.0	1.0	0.0	TA: 89.7 TS: 86.7	6.0	5.0	12.0
Urena et al, 2018 (N=30)[32]	6.7	0.0	3.3	6.7	6.7	80.0	0.0	3.4	NA
Long et al, 2018 (N=8)[53]	0.0	NA	NA	NA	0.0	100.0	8.3	0.0	NA
Yoon et al, 2017 (N=72)[36]	8.3	0.0	8.3	1.4	NA	83.3	2.3	2.8	13.6
Eleid et al, 2017 (N=15)[29]	0.0	NA	13.0	0.0	7.0	73.0	20.0	13.0	<10
Descoutures et al, 2013 (N=17)[49]	18.0	NA	NA	NA	NA	89.0	NA	NA	NA

Procedural and 30-day outcomes of transcatheter mitral valve-in-ring replacement are shown. LVOTO indicates left ventricular outflow tract obstruction; MR, mitral regurgitation; MVC, major vascular complication; NA, not available; TA, transapical; and TS, transseptal.
*Life-threatening bleeding.

and MVR should both be preferred to MVIR in appropriately selected patients.

A crucial consideration in preoperative planning for MVIR is assessment of the annuloplasty ring currently in place. The 3 most important characteristics to consider are ring rigidity, shape, and radio-opacity.[63]

Valves currently used for TMVR are designed to anchor and fully expand within a circular geometry. The mitral annulus, however, takes on a D-shape, and many annuloplasty rings have been designed to accommodate this. The rigidity of a ring determines its ability to conform to the circular shape upon implantation and thereby optimize valve function. Generally, rings are classified as rigid, semirigid, or flexible. Rigid rings provide the most anchoring capacity for a transcatheter valve but are the least able to conform and thus pose the greatest risk of para- and intravalvular regurgitation at the 2 corners. Semirigid rings provide an optimal balance between a solid anchor and the ability to adopt a circular shape in response to MVIR. However, smaller-sized semirigid rings tend to be more rigid and are thus less likely to fully circularize.[64]

Rings may also be incomplete or complete in shape. Flexible-incomplete rings are generally implanted in an effort to preserve the 3-dimensional saddle-geometry of the annulus. Incomplete rings have an opening at the anterior leaflet and do not provide a solid anchoring surface during MVIR procedures. Furthermore, the discontinuous portions of incomplete rings may result in significant paravalvular leak.[65] Thus, the ideal ring for MVIR appears to be a semirigid, complete annuloplasty ring with adequate radio-opacity. The "Mitral Valve-in-Valve" mobile application, developed by Dr. Vinayak Bapat, serves as a valuable reference for preprocedural planning and optimal valve positioning during the procedure.[66]

Complications of Transcatheter Mitral Valve Replacement

Left Ventricular Outflow Tract Obstruction

Previously underappreciated, LVOTO is a serious complication of TMVR that results from displacement of the native anterior mitral leaflet into the LVOT upon expansion of the transcatheter valve.[67] This occurs in ≈0% to 6% of patients following MVIV and ≈0% to 20% following MVIR. Furthermore, procedural mortality with TMVR is significantly higher among patients with LVOTO. Anatomical factors that increase the risk of LVOTO include protrusion of the device into the left ventricle, device flaring, and a shallow aortomitral angle between the plane of the aortic and mitral annuli. Device-specific preoperative assessment of the "Neo-LVOT" is useful to identify those at risk of this complication, with a sensitivity of 96.2% and specificity of 92.3%.[35,68,69]

Several risk-reduction strategies have been studied for patients at risk of LVOTO.[70,71] Laceration of the anterior mitral leaflet to prevent LVOTO is one such technique that involves splitting the anterior leaflet with an electrified wire.[72–74] In patients at risk of LVOTO owing to a prominent septum, preoperative alcohol septal ablation has also been evaluated with promising results.[75]

Other Limitations

Recognized other adverse events associated with MVIV and MVIR include (1) procedural and delayed device migration or embolization, (2) elevated postprocedural gradients, (3) residual mitral regurgitation, and (4) valve thrombosis. These complications appear to be more common in MVIR than MVIV, with small valve size (<25 mm) appearing as a consistent predictor of significantly elevated postprocedural gradients. Improvements in TMVR, including imaging and valve technology, will undoubtedly address these issues in the near future.

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Supplementary Material

Table S1

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SUPPLEMENTAL MATERIAL

Table S1. **The Newcastle-Ottawa Scale (NOS) Quality Assessment.**

			Selection of Cohorts				Comparability of Cohorts (Design, Analysis)		Outcome		
	Study[REF]	Year	Representativeness of Exposed Cohort	Selection of Non-Exposed Cohort	Ascertainment of Exposure	Demonstration that Outcome of Interest was not Initially Present	Comparability of Cohorts (Design, Analysis)	Assessment of Outcome	Appropriate Duration of Follow-Up	Follow-Up Adequacy	Total (GRADE)
MVIV	Yoon et al.[33]	2019	1	X	1	1	X	1	1	1	6/6 (A)
	Guerrero et al.[35]	2019	1	X	1	1	X	1	1	1	6/6 (A)
	Hu et al.[28]	2018	1	X	1	1	X	1	1	1	6/6 (A)
	Urena et al.[30]	2018	1	X	1	1	X	1	1	1	6/6 (A)
	Kamioka et al.[29]	2018	1	1	1	1	1	1	1	1	8/8 (A)
	Yoon et al.[34]	2017	1	X	1	1	X	1	1	1	6/6 (A)
	Eleid et al.[27]	2017	1	X	1	1	X	1	1	1	6/6 (A)
	Eleid et al.[26]	2016	1	X	1	1	X	1	1	1	6/6 (A)
	Ye et al.[32]	2015	1	X	1	1	X	1	1	1	6/6 (A)
	Cheung et al.[25]	2013	1	X	1	1	X	1	1	1	6/6 (A)

	Wilbring et al.[31]	2013	1	X	1	1	X	1	1	1	6/6 (A)
MVIR	Yoon et al.[33]	2019	1	X	1	1	X	1	1	1	6/6 (A)
	Hu et al.[28]	2018	1	X	1	1	X	1	1	1	6/6 (A)
	Urena et al.[30]	2018	1	X	1	1	X	1	1	1	6/6 (A)
	Long et al.[53]	2018	1	X	1	1	X	1	1	1	6/6 (A)
	Yoon et al.[34]	2017	1	X	1	1	X	1	1	1	6/6 (A)
	Eleid et al.[27]	2017	1	X	1	1	X	1	1	1	6/6 (A)
	Descoutures et al.[49]	2013	1	X	1	1	X	1	1	1	6/6 (A)
Redo-MVR	Kilic et al.[41]	2019	1	X	1	1	X	1	1	1	6/6 (A)
	Mehaffey et al.[8]	2018	1	1	1	1	1	1	1	1	8/8 (A)
	Kilic et al.[40]	2018	1	X	1	1	X	1	1	1	6/6 (A)
	Kwedar et al.[18]	2017	1	X	1	1	X	1	1	1	6/6 (A)
	Vohra et al.[7]	2012	1	X	1	1	X	1	1	1	6/6 (A)
	Ozyazicioglu et al.[9]	2012	1	X	1	1	X	1	1	1	6/6 (A)
	Toker et al.[20]	2009	1	X	1	1	X	1	1	1	6/6 (A)
	Albeyoglu et al.[14]	2006	1	X	1	1	X	1	1	1	6/6 (A)
	Jamieson et al.[17]	2003	1	X	1	1	X	1	1	1	6/6 (A)
Redo-MVr	Aphram et al.[39]	2018	1	X	1	1	X	1	1	1	6/6 (A)

	Kilic et al.[40]	2018	1	X	1	1	X	1	1	1	6/6 (A)
	Kwedar et al.[18]	2017	1	X	1	1	X	1	1	1	6/6 (A)
	Anyanwu et al.[38]	2014	1	X	1	1	X	1	1	1	6/6 (A)
	Shekar et al.[10]	2005	1	X	1	1	X	1	1	1	6/6 (A)