Transcatheter mitral valve implantation for degenerated mitral bioprostheses or failed surgical annuloplasty rings: A systematic review and meta-analysis

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Abstract

Background: Transcatheter mitral valve-in-valve (TMVIV) and valve-in-ring (TMVIR) implantation for degenerated mitral bioprostheses and failed annuloplasty rings have recently emerged as treatment options for patients deemed unsuitable for repeat surgery.

Methods: A systematic literature review was conducted to summarize the data regarding the baseline characteristics and clinical outcomes of patients undergoing TMVIV and TMVIR procedures.

Results: A total of 245 patients (172 patients who underwent TMVIV surgery and 73 patients who underwent TMVIR surgery) were included in the study; 93.5% of patients experienced successful TMVIV or TMVIR implantation. The mortality rates at discharge, 30 days, and 6 months were 5.7%, 8.1%, and 23.4%, respectively. The transapical (TA) access route was used in most procedures (55.2%). The TA and transseptal (TS) access routes resulted in similar outcomes. No significant differences were observed in the short-term outcomes between the patients who developed mitral stenosis versus mitral regurgitation as the mode of failure.

Conclusions: TMVIV and TMVIR implantation for degenerated mitral bioprostheses and failed annuloplasty rings are safe and effective. Both procedures, via TA or TS access, can result in excellent short-term clinical outcomes in patients with mitral stenosis or regurgitation, but long-term follow-up data are currently lacking to determine the durability of these procedures.

Keywords
mitral regurgitation, mitral stenosis, TMVIR, TMVIV, transapical, transseptal

1 INTRODUCTION

Surgical mitral valve repair or replacement remains the gold standard for treating severe symptomatic mitral valve disease. Up to 35% of patients require a repeat operation during the first 10 years, and the in-hospital mortality rate may be as high as 12%.1,2 Furthermore, some patients requiring mitral valve repair/replacement are deemed to be too high risk for repeat surgery. Recently, transcatheter mitral valve
interventions have emerged as alternatives to conventional surgical valve replacement in patients requiring repeat surgery. Cheung et al\(^3\) reported the first transcatheter mitral valve-in-valve (TMVIV) implantation in humans in 2009, and the first transcatheter mitral valve-in-ring (TMVIR) implantation in humans was performed by de Weger et al in 2011.\(^4\) Since that time, additional patients have received TMVIV or TMVIR surgery.\(^5,6\) This study reviews the outcomes of TMVIV implantation for degenerated mitral bioprostheses and TMVIR implantation for failed annuloplasty rings, according to the Mitral Valve Academic Research Consortium (MVARC) criteria.\(^7\) The results are stratified according to the mitral valve failure mode and the access route. This information may aid in clinical decision making in patients with degenerated mitral bioprostheses or failed annuloplasty rings who are not candidates for repeat surgery.

2 | METHODS

2.1 | Search strategies

A comprehensive, systematic search was performed to identify all relevant articles published in the PubMed and Web of Science databases from 2000 to March 30, 2018. The following search terms were used: “transcatheter mitral valve implantation” or “transcatheter mitral valve replacement” or “TMVI” or “TMVR.” This analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.\(^8\)

2.2 | Study selection

The inclusion criteria were as follows: (1) patients received either a TMVIV or TMVIR implantation and (2) reported data necessary to assess the baseline characteristics and outcomes. Articles were excluded if any of the following criteria applied: (1) non-English article; (2) animal experiments; (3) no relevant information on TMVI implantation; (4) lack of details regarding postoperative outcomes; (4) TMVIV or TMVIR for native mitral valve; (5) insertion of a TMVIV or TMVIR during a full sternotomy under direct vision; and (6) meeting abstracts.

2.3 | Data extraction

The following information was extracted from each study: age, gender, logistic EuroSCORE, the Society of Thoracic Surgeons (STS) score, comorbidities, function of the other valves, history of heart surgery, New York Heart Association (NYHA) class, left ventricular ejection fraction, mitral regurgitation (MR) severity, mean transmural gradient, prior mitral bioprostheses, death, valve migration, access site, and vascular and other postprocedure complications. For those patients who were reported in two or more articles, we removed the duplicates by checking their age, gender, logistic EuroSCORE or STS score, prior mitral bioprostheses, and the author’s contact address. For the subgroup analysis, we recorded the mitral valve failure mode, access route, and size of the transcatheter valve. Two reviewers extracted the data independently using a predefined Excel form.

2.4 | Statistical analysis

Continuous variables are described as means and standard deviations for normally distributed data, or medians and interquartile ranges for non-normally distributed data. Differences between continuous variables were analyzed using a t-test. Categorical variables are described with absolute and relative frequencies. Differences between categorical variables were evaluated using the chi-square test or Fisher’s exact test. Survival curves were estimated by the Kaplan–Meier method. A P-value <0.05 was considered statistically significant.

3 | RESULTS

3.1 | Baseline characteristics of patients

From 2009 to March 31, 2018, 66 published reports\(^9–72\) describing 172 patients undergoing TMVIV implantation for degenerated mitral bioprostheses and 35 articles describing 73 patients undergoing TMVIR implantation\(^22,38,45,75–106\) for failed annuloplasty rings were identified (Figure 1). The patients were diagnosed with MR, MS, or mixed lesions according to the articles but the failure modes of 34 patients were unknown. The characteristics of the studies included in this meta-analysis are summarized in Table 1.

3.2 | Procedure

Transapical (TA) access was performed in 127 (55.2%) cases, and transseptal (TS) access (via a transfemoral or transjugular venous route) was performed in 91 (37.7%) patients. In addition to TA and TS access, a direct transatrial access using a sheath placed directly into the left atrium via a right anterior thoracotomy was also used in two patients.\(^67,101\) The “TA + TS” access was utilized for the Melody

![FIGURE 1](image_url) Flowchart of study selection process. TMVIR, transcatheter mitral valve-in-ring implantation; TMVIV, transcatheter mitral valve-in-valve implantation
Transcatheter valves were used in all patients and included the SAPIEN XT (n = 120, Edwards Lifesciences, Irvine, CA), SAPIEN (n = 47, Edwards Lifesciences), SAPIEN 3 (n = 26, Edwards Lifesciences), Melody (n = 18, Medtronic, Minneapolis, MN), Tiara (n = 4, Neovasc Inc, Richmond, Canada), Lotus (n = 3, Boston Scientific, Natik, MA), Tendyne (n = 1, Abbott, Abbott Park, IL), and Direct Flow Medical transcatheter valve system (DFM) (n = 9, Direct Flow Medical Inc, Santa Rosa, CA).

### 3.3 Clinical outcomes

Table 2 shows the in-hospital outcomes. The MVARC technical success rate (assessed at exit from the catheterization laboratory) was 93.5%. Five technical failures occurred in the TMVIV group and 13 occurred in the TMVIR group. Fourteen patients (5.7%) died before discharge including two intraoperative (due to left ventricular apical perforation) and 12 postoperative deaths. Thirteen patients developed access-site bleeding after TMVIV implantation. Other vascular complications occurred in two patients including one case of thrombosis on the ventricular aspect of the mitral valve prosthesis and one case of left ventricular (LV) apical pseudoaneurysm. Most patients (98.2%) were categorized as NYHA grade II or lower postprocedure. The mean transmitral gradient decreased after both procedures (P < 0.001), and the NYHA function improved significantly (Table 3). The cumulative events at 30 days and 6 months postoperatively are shown in Table 4. Three and nine additional deaths

| TABLE 1 | Baseline characteristics of all patients, TMVIV and TMVIR |
|-----------------|-----------------|-----------------|
| Clinical information | All patients | TMVIV | TMVIR |
| Total sample size, n | 245 | 172 | 73 |
| Age (years, mean ± SD) | 73.0 ± 12.1 (169) | 74.5 ± 12.5 (119) | 70.0 ± 10.8 (60) |
| Male gender, % | 50.6 (84/166) | 46.5 (53/114) | 59.6 (31/52) |
| Logistic EuroSCORE, % | 19.1 ± 12.8 (91) | 36.4 ± 17.1 (69) | 37.0 ± 21.4 (22) |
| STS score, % | 15.6 ± 13.5 (130) | 16.8 ± 15.2 (86) | 13.4 ± 9.0 (44) |
| STS score >8% | 70.8 (92/130) | 72.1 (62/86) | 68.2 (30/44) |
| Comorbidity, % | 76.0 (114/150) | 80.0 (80/100) | 68.0 (34/50) |
| PH | 35.2 (63/179) | 37.7 (46/122) | 29.8 (17/57) |
| CAD | 15.2 (29/179) | 14.8 (18/122) | 19.3 (11/57) |
| CRF | 33.0 (59/179) | 35.2 (43/122) | 28.1 (16/57) |
| Diabetes | 16.2 (29/179) | 17.2 (21/122) | 14.0 (8/57) |
| AF | 36.9 (66/179) | 41.8 (51/122) | 26.3 (15/57) |
| Other valve dysfunction, % | 32.7 (49/150) | 40.0 (40/100) | 21.4 (9/50) |
| AR | 4.4 (8/179) | 6.6 (8/122) | 0.0 (0/57) |
| AS | 10.6 (19/179) | 9.8 (12/122) | 12.3 (7/57) |
| TR | 19.0 (34/179) | 23.0 (28/122) | 10.5 (6/57) |
| TS | 0.6 (1/179) | 0.0 (0/122) | 1.8 (1/57) |
| History of heart surgery, % | 53.8 (86/160) | 51.6 (63/122) | 60.5 (23/38) |
| SAVR | 20.0 (32/160) | 20.5 (25/122) | 18.4 (7/38) |
| CABG | 27.5 (44/160) | 27.0 (33/122) | 28.9 (11/38) |
| TVR | 13.8 (22/160) | 13.9 (17/122) | 13.2 (5/38) |
| Mitral valve failure mode, % | | | |
| MR | 55.2 (116/210) | 49.3 (71/144) | 68.2 (45/66) |
| MS | 29.5 (62/210) | 31.9 (46/144) | 24.2 (16/66) |
| Mixed | 15.3 (32/210) | 18.8 (27/144) | 7.6 (5/66) |
| NYHA ≥III, % | 98.2 (165/168) | 97.3 (108/111) | 100.0 (57/57) |
| LVEF (% mean ± SD) | 46.7 ± 14.1 (106) | 51.2 ± 11.5 (73) | 36.7 ± 14.5 (33) |
| MR severe or ≥Grade 3, % | 69.4 (129/186) | 63.3 (76/120) | 80.3 (53/66) |
| Mean transmitral gradient (mmHg, mean ± SD) | 12.1 ± 5.9 (155) | 12.8 ± 5.9 (121) | 9.5 ± 5.2 (34) |

AF, atrial fibrillation; AR, aortic regurgitation; AS, aortic stenosis; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CRF, chronic renal failure; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; MS, mitral stenosis; NYHA, New York Heart Association; PH, pulmonary hypertension; SAVR, surgical aortic valve replacement; SD, standard deviation; STS, Society of Thoracic Surgeons; TMVIR, transcatheter mitral valve-in-ring implantation; TMVIV, transcatheter mitral valve-in-valve implantation; TR, tricuspid regurgitation; TS, tricuspid stenosis; TVR, tricuspid valve replacement or repair.
developed at 30 days and 6 months, respectively. Two additional pseudoaneurysms, two additional thromboses (one due to device failure: leaflet thickening and reduced leaflet motion), and two additional device migrations occurred, and two patients required an implantable defibrillator during the 30-day follow-up period. Two additional thromboses, two additional device migrations, and three additional device failures developed during the 6-month follow-up period.

### 3.4 Subgroup analysis

#### 3.4.1 Comparison of different mitral failure modes

The patients with MR or MS in the TMVIV and TMVIR groups had similar baseline characteristics, except that the MR patients had a higher mean Logistic EuroSCORE and more previous heart surgeries (65.8% vs 37.2%, \( P = 0.017 \)) in the TMVIV group and a higher percentage of the MR patients in the TMVIR group had an STS score >8% (75.0% vs 44.4%, respectively, \( P = 0.034 \)). Regarding the clinical outcomes (Table 5), no significant differences were observed between the MR and MS groups, but MS patients in the TMVIR group had a higher mean transmitral gradient (\( P = 0.002 \)). Different mitral failure modes (MR and MS) did not affect the patient’s overall survival in both the TMVIV and TMVIR procedures (\( P = 0.347 \) and 0.958, respectively) (Figure 2).

#### 3.4.2 Comparison of different access routes

Patients who underwent the TMVIV procedure via TA access had a higher incidence of concomitant aortic or tricuspid valve dysfunction.

### TABLE 2 In-hospital outcomes according to MVARC criteria

|                         | All patients | TMVIV | TMVIR |
|-------------------------|--------------|-------|-------|
| **Technical success, %**| 93.5 (229/245) | 97.1 (167/172) | 84.9 (62/73) |
| **Death, %**            | 5.7 (14/245)  | 5.2 (9/172) | 6.8 (5/73) |
| **Cardiovascular, %**   | 4.1 (10/245)  | 2.9 (5/172) | 6.8 (5/73) |
| **Valve migration, %**  | 2.9 (7/245)   | 2.3 (4/172) | 4.1 (3/73) |
| **LVOTO, %**            | 1.6 (4/245)   | 0.0 (0/172) | 5.5 (4/73) |
| **Postprocedural MR, %**|                          |       |       |
| Trace/none              | 69.3 (147/212) | 73.8 (107/145) | 59.7 (40/67) |
| Mild or grade 1         | 23.1 (49/212)  | 20.7 (30/145) | 28.3 (19/67) |
| >Mild                   | 7.6 (16/212)   | 5.5 (8/145)  | 12.0 (8/67) |
| **Access site and vascular complication, %** | | | |
| **Bleeding**            | 6.1 (15/245)  | 8.7 (15/172) | 0.0 (0/73) |
| **Thrombus**            | 0.4 (1/236)   | 0.6 (1/163) | 0.0 (0/73) |
| **Pseudoaneurysm**      | 0.4 (1/236)   | 0.0 (0/163) | 1.4 (1/73) |
| **Stroke, %**           | 1.6 (4/245)   | 1.7 (3/172) | 1.4 (1/73) |
| **MI, %**               | 0.0 (0/245)   | 0.0 (0/172) | 0.0 (0/73) |
| **New arrhythmia, %**   | 2.0 (5/245)   | 1.7 (3/172) | 2.7 (2/73) |
| **Acute kidney injury, %** | 4.5 (11/245) | 4.1 (7/172) | 5.5 (4/73) |
| **Postprocedural mean transmitral gradient, (mmHg, mean ± SD)** | | | |
|                         | 5.1 ± 2.5 (140) | 5.1 ± 2.5 (96) | 5.1 ± 2.5 (44) |
| **NYHA (at latest follow-up) ≤ II, %** | 94.0 (109/116) | 92.0 (69/75) | 97.6 (40/41) |

LVOTO, left ventricular outflow tract obstruction; MI, myocardial infarction; MR, mitral regurgitation; MVARC, Mitral Valve Academic Research Consortium; NYHA, New York Heart Association; SD, standard deviation; TMVIR, transcatheter mitral valve-in-ring implantation; TMVIV, transcatheter mitral valve-in-valve implantation.

*a*Including paravalvular leak and intervalvular regurgitation.

*b*Including 2 left ventricular apical perforations in the procedure and 13 access-site bleeding after the procedure.

### TABLE 3 Mean transmitral gradient and NYHA before and after the procedure

|                          | Mean transmitral gradient, (mmHg, mean ± SD) | NYHA ≥ III, % |
|--------------------------|---------------------------------------------|---------------|
|                          | Pre post P-value | Pre post P-value | Pre post P-value |
| All patients             | 12.1 ± 5.9 (155) | 5.1 ± 2.5 (140) | <0.001  | 98.2 (165/168) | 6.2 (7/113) | <0.001 |
| TMVIV                    | 12.8 ± 5.9 (121) | 5.1 ± 2.5 (96)  | <0.001  | 97.3 (108/111) | 8.1 (6/74)  | <0.001 |
| TMVIR                    | 9.5 ± 5.2 (34)   | 5.1 ± 2.5 (44)  | <0.001  | 100.0 (57/57)  | 3.6 (1/39)  | <0.001 |

NYHA, New York Heart Association; SD, standard deviation; TMVIR, transcatheter mitral valve-in-ring implantation; TMVIV, transcatheter mitral valve-in-valve implantation.
than those who underwent the TMVIV procedure via TS access (56.3% vs 16.7%, P = 0.001). More patients in the TA group had a previous surgical or interventional procedure (58.1% vs 34.6%, P = 0.035). Patients who underwent the TMVIR procedure via TA access had a higher mean logistic EuroSCORE, and MR was more severe in patients who underwent the procedure via TS access (93.3% vs 56.0%, P = 0.001). No significant differences were observed in clinical outcomes at discharge (Table 6). Different access routes (TA and TS) did not affect the patient’s overall survival in both the TMVIV and TMVIR procedures (P = 0.450 and 0.361, respectively) (Figure 3).

### 3.4.3 Percentage of oversized valves

We collected manufacturer inner diameter (ID) measurements for MOSAIC and HANCOCK bioprostheses and the size of the ES valve (Table 7) and compared the mean % of oversized valves (ES size-Manufacturer ID/Manufacturer ID* 100%). We excluded those undersized valves used in MR and MS patients. The mean % of oversized valves was 6.79 ± 5.37% (n = 29, range 0–20.53%) in MR patients and 4.16 ± 3.46% (n = 11, range 0–8.33%) in MS patients, but the difference was not significant (P = 0.141).

### 4 DISCUSSION

The TMVIV or TMVIR procedure for degenerated mitral bioprostheses or failed annuloplasty rings appears to be a feasible option for high-risk, inoperable patients. With the development of these techniques, an increasing number of patients can obtain good clinical outcomes, but many technical issues such as size and access route selection remain undefined. No standard guidelines exist for the TMVIV and TMVIR procedures and no long-term clinical trials (including randomized trials) have been performed to evaluate these techniques. Several ongoing trials have been designed to evaluate the safety and performance of some devices (Tiara (NCT03039855), Highlife (NCT02974881), Medtronic Intrepid (NCT03242642), Twelve (NCT02428010), and the Caisson (NCT02768402) and the effectiveness of the SAPIEN 3 (NCT03193801) valve for the TMVIR procedure, but no data have been reported to date. In our review of 245 patients using TMVIV or TMVIR, the technical success rate was 93.5% and the in-hospital mortality was 5.8%. The transmural gradient decreased and NYHA function improved significantly, with few postprocedural complications. TMVIV and TMVIR procedures are highly efficient and safe. However, in our analysis, the overall 6-month mortality was 23.4% (18.5% and 38.5% for TMVIV and TMVIR, respectively). Long-term follow-up data were limited (only 45.3% patients completed 6 months of follow-up). To date, few studies including at least 20 patients have reported long-term (with at least 1 year) mortality, and those mortalities varied as follows: 16.9% (n = 248, 1 year),107 9.6% (n = 38, more than 376 days),63 and 42.4% (n = 24, 3 years).108 Additionally, comparisons with surgical mitral valve replacement were unavailable, and only one ongoing controlled trial (NCT03242642) is currently being conducted.

Wunderlich et al96 found that the transcatheter valve could be adequately deployed within failed bioprostheses, but the failed annuloplasty ring was too oval-shaped to adapt to the configuration of the implanted valve and would be more likely to develop MR. Notably, the TMVIV procedure was associated with a higher technical success rate (97.1%) than the TMVIR procedure (84.9%, P = 0.001), and a lower postprocedural MR rate (P = 0.039) was also observed for the TMVIV procedure. This result was similar to that of Yoon et al107 (248 patients from a transcatheter mitral valve replacement multicenter registry). Of the five patients (2.9%) experiencing TMVIV failures, two were due to operative error, and three others were due to prosthesis migration: two into the left atrium and one into the left ventricle. Regarding the TMVIR procedure, technical issues caused all the failures (n = 11, 15.1%). Three of the 11 failures were due to partial ring dehiscence following prosthesis deployment, and one failure was related to incomplete ring expansion. Anatomical differences also account for the differences in the technical success rate and

### TABLE 4 Postprocedure cumulative events

|                | All patients | TMVIV | TMVIR |
|----------------|--------------|-------|-------|
|                | 30-day       | 6-month | 30-day | 6-month | 30-day | 6-month |
| Death, %       | 8.1 (17/210) | 23.4 (26/111) | 7.5 (11/147) | 18.8 (16/85) | 9.5 (6/63) | 38.5 (10/26) |
| Pseudoaneurysm, % | 2.1 (3/142) | 4.8 (3/63) | 2.1 (2/95) | 3.6 (2/55) | 2.1 (1/47) | 12.5 (1/8) |
| Stroke, %      | 2.8 (4/142) | 6.3 (4/64) | 3.2 (3/95) | 5.4 (3/56) | 2.1 (1/47) | 12.5 (1/8) |
| MI, %          | 0.0 (0/142) | 0.0 (0/60) | 0.0 (0/95) | 0.0 (0/53) | 0.0 (0/47) | 0.0 (0/7) |
| Thrombus, %    | 2.1 (3/142) | 7.5 (5/67) | 3.2 (3/95) | 8.3 (5/60) | 0.0 (0/47) | 0.0 (0/7) |
| Device migration, % | 4.9 (7/142) | 13.0 (9/69) | 5.3 (5/95) | 11.7 (7/60) | 4.3 (2/47) | 22.2 (2/9) |
| Device failure, % | 0.7 (1/142) | 6.6 (4/61) | 1.1 (1/95) | 5.6 (3/54) | 0.0 (0/47) | 14.3 (1/7) |
| ICD, %         | 1.4 (2/142) | 3.2 (2/62) | 1.1 (1/95) | 1.9 (1/54) | 2.1 (1/47) | 12.5 (1/8) |
| ASD closure, % | 6.3 (9/142) | 13.0 (9/69) | 7.4 (7/95) | 11.7 (7/60) | 4.3 (2/47) | 22.2 (2/9) |

ASD, atrial septal defect; ICD, implantable cardiac defibrillator; LVOTO, left ventricular outflow tract obstruction; MI, myocardial infarction; TMVIR, transcatheter mitral valve-in-ring implantation; TMVIV, transcatheter mitral valve-in-valve implantation.
The native mitral valve leaflets in failed rings may disrupt the valve fixation and alter motion of the transcatheter mitral leaflets and the failed ring may be deformed during deployment.

### 4.1 MR versus MS failure mode

Different mitral failure modes are associated with specific anatomic and hemodynamic characteristics. Performing a retrograde implantation in the presence of MS is more difficult than performing this procedure in the presence of MR due to the difficulty in crossing the bioprostheses with the wire and implanting the transcatheter valves. Some issues arise when the TA access route is chosen. Pagnotta et al reported that they changed to the TS access route because they were unable to cross the degenerated mitral valve bioprostheses after multiple attempts. However, no clinical data exist to address these issues at present, and almost all on-going trials are only designed for MR patients. In our analysis, both patients with MR or MS achieved a high technical success rate and good clinical outcomes, and no significant differences were observed in the early clinical outcomes for

#### TABLE 5 In-hospital outcomes of different mitral failure modes in TMVIV and TMVIR

|                | TMVIV MR | 100.0 (35/35) | 0.405 | TMVIR MR | 92.9 (13/14) | 0.837 |
|----------------|---------|---------------|-------|----------|-------------|-------|
| Technical success, % | 94.3 (50/53) | 0.0 (0/24) | 0.404 | 6.7 (3/45) | 0.0 (0/14) | >0.999 |
| Death, %       | 7.7 (3/39) | 0.0 (0/24) | 0.404 | 10.3 (3/29) | 0.0 (0/10) | 0.556 |
| Valve migration, % | 7.7 (3/39) | 0.0 (0/24) | - | 6.9 (2/29) | 10.1 (1/10) | >0.999 |
| LVOTO, % | 0.0 (0/39) | - | - | 0.0 (0/39) | - | - |

### Postprocedural MRa, %

|                | TMVIV | TMVIR | P-value |
|----------------|-------|-------|---------|
| None/trace     | 84.9 (45/53) | 77.7 (23/30) | 0.349 |
| Mild or grade 1| 11.3 (6/53) | 16.7 (5/30) | 0.724 |
| >Mild          | 3.8 (2/53) | 6.8 (2/30) | 0.954 |

### Access site and vascular complication, %

|                | TMVIV | TMVIR | P-value |
|----------------|-------|-------|---------|
| Bleeding       | 5.1 (2/39) | 4.2 (1/24) | >0.999 |
| Thrombus       | 2.6 (1/39) | 0.0 (0/24) | >0.999 |
| Pseudoaneurysm | 0.0 (0/39) | 0.0 (0/24) | - |
| Stroke, %      | 0.0 (0/39) | 0.0 (0/24) | - |
| MI, %          | 0.0 (0/39) | 0.0 (0/24) | - |
| New arrhythmia, % | 5.1 (2/39) | 0.0 (0/24) | 0.521 |
| Acute kidney injury, % | 12.8 (5/39) | 4.2 (1/24) | 0.487 |
| Postprocedural mean transmural gradient (mmHg, mean ± SD) | 5.6 ± 2.7 (45) | 5.0 ± 3.2 (28) | 0.378 |

### NYHA (at latest follow-up)

|                | TMVIV | TMVIR | P-value |
|----------------|-------|-------|---------|
| ≤II, %         | 94.3 (33/35) | 100.0 (14/14) | >0.999 |
| >II, %         | 94.7 (18/19) | 100.0 (9/9) | >0.999 |

LVOTO, left ventricular outflow tract obstruction; MI, myocardial infarction; MR, mitral regurgitation; MS, mitral stenosis; NYHA, New York Heart Association; SD, standard deviation; TMVIR, transcatheter mitral valve-in-ring implantation; TMVIV, transcatheter mitral valve-in-valve implantation.

*aIncluding paravalvular leak and intervalvular regurgitation.

FIGURE 2 Kaplan–Meier overall survival curves for patients with different mitral failure modes (MR and MS) in the TMVIV procedure (A) and the TMVIR procedure (B). MR, mitral regurgitation; MS, mitral stenosis; TMVIR, transcatheter mitral valve-in-ring implantation; TMVIV, transcatheter mitral valve-in-valve implantation.
the TMVIV and TMVIR procedures. However, the TA access was used in most MR patients (57.3%) and the TS access was chosen for most MS patients (56.9%, \( P = 0.029 \)). To determine whether the TA and TS access routes were associated with different outcomes in MS patients, we compared the outcomes between the TA (\( n = 22 \)) and TS (\( n = 26 \)) access routes, but no significant differences were found.

### 4.2 TA versus TS access

The first transcatheter mitral valve implantation in humans was performed via TS access.\(^3\) In 2013, all TMVIV procedures were successfully performed via a TA approach.\(^6\)\(^3\) The TA route was used for most procedures. The TA access has the following advantages: (1) direct and co-axial access; (2) shorter distance; and (3) better control during deployment. The TA is also the first choice for patients with peripheral vascular disease. The TS route also has several advantages, including being less invasive and can be done under local anesthesia. However, the TS access route can cause an iatrogenic atrial septal defect (ASD), and some patients (16.5%) required an ASD occluder. A study by Frerker et al showed no significant differences in clinical outcomes, especially bleeding and vascular complications between the

![FIGURE 3](image)

**FIGURE 3** Kaplan–Meier overall survival curves for patients with different access routes (TA and TS) in the TMVIV procedure (A) and the TMVIR procedure (B). TA, transapical; TMVIR, transcatheter mitral valve-in-ring implantation; TMVIV, transcatheter mitral valve-in-valve implantation; TS, transseptal.
TA and TS access route ($P = 0.35$ and $P = 0.13$, respectively); however, TS access was associated with improved survival ($P = 0.045$). In our analysis, most patients (55.2%) were treated via TA access, and no differences in clinical outcomes and survival curves were observed, especially for bleeding and vascular complications, for both the TMVIV and TMVIR procedures. Similar baseline characteristics were shared by the two procedures.

4.3 Analysis of valve migration

Valve migration was the main (37.5%) cause of technical failure for these procedures. Eight patients developed valve migration into the LA either instantly in the cath lab or delayed/after exiting from the catheterization laboratory. In the TMVIV procedure, two patients (1.2%) developed valve migration to the LA after deployment, and five patients (8.3%) developed delayed migration. We found two cases (2.7%) of instant migration to the LA, one case (1.4%) of migration to the LV and no delayed migrations in the TMVIR procedure. Although no significant differences were observed between the TMVIV and TMVIR procedures for delayed migration ($P = 0.452$), more cases of migration were associated with the TMVIR procedure.

4.4 Optimal valve positions

The optimal positions for valves for both the MIVIV and TMVIR procedures have not been determined. The SAPIEN/SAPIEN XT device should be implanted in the mitral position with 10–20% of the device located atrially. In our analysis, four patients underwent successful TMVIV surgery using the SAPIEN/SAPIEN XT valve, and the positions were as follows: 1/3 of the valves were above the annular level and 2/3 beneath this level; 30% of the new prostheses were on the atrial side, and the SAPIEN was 10% higher on the atrial end with 10% bias toward the atrial side. The 1-year follow-up results were reported in only one of the four cases. At the 6-month follow-up, one of the three pericardial leaflets was stuck in the closed position; however, the patient was in excellent clinical condition. Fluoroscopy showed an “hour-glass” shape of the SAPIEN XT valve due to a final positioning that favored the atrial side (30% to 35% on the atrial side). Unlike the TMVIV procedure, no consensus exists regarding the optimal position for the TMVIR procedure. A total of nine articles reported variable positions. The three different positions of the ES valve are as follows: (1) less atrium more ventricle: 1/3 in the atrium and 2/3 in the ventricle or 40% in the atrium and 60% in the ventricle; (2) half above and half below the mitral ring; (3) more atrium less ventricle: 40% ventricular and 60% atrial configuration. Two articles reported the position of the Melody valve as follows: 20% in the atrium and 80% in the ventricle and 40% in the atrium and 60% in the ventricle. All patients had successful TMVIR surgery and good clinical outcomes before discharge, and no migrations occurred. The position of the valve in the TMVIR procedure may be not as important as that in the TMVIV procedure. We found that the valve could be deployed more conically, and the position has little influence on valve expansion.

4.5 Sizing considerations

Currently, the ID of the valve set by the manufacturers is the most important criteria for transcatheter valve sizing for the TMVIV and TMVIR procedure. In a series by Cheung et al., the pre-existing prosthesis was oversized by a minimum of 10% according to the manufacturer’s ID. However, Seifert et al. suggested that oversizing should be limited in cases with a rigid xenograft stent because it may result in uneven stent expansion and leaflet distortion. In our study, the

| TABLE 7 | Size selection in MR and MS patients |
|----------------|----------------|----------------|----------------|----------------|----------------|
| Prior valve type | Prior valve size (mm) | Manufacture ID (mm) | Size of ES valve | No. of MR | No. of MS | No. of migration |
| MOSAIC | 23 | 20.5 | 23 | 2 | 0 | 0 |
| | 25 | 22.5 | 23 | 2 | 3 | 0 |
| | 27 | 24 | 26 | 2 | 2 | 0 |
| | 27 | 24 | 29 | 1 | 0 | 0 |
| | 29 | 26 | 26 | 2 | 1 | 0 |
| | 29 | 26 | 29 | 4 | 0 | 0 |
| | 31 | 28 | 26 | 2 | 0 | 0 |
| | 31 | 28 | 29 | 0 | 1 | 0 |
| | 33 | 30 | 29 | 3 | 0 | 0 |
| HANCOCK | 25 | 22.5 | 23 | 1 | 1 | 0 |
| | 27 | 24 | 26 | 4 | 2 | 1 |
| | 29 | 26 | 26 | 4 | 1 | 0 |
| | 29 | 26 | 29 | 3 | 0 | 0 |
| | 31 | 28 | 29 | 4 | 0 | 0 |
| | 33 | 30 | 29 | 1 | 0 | 0 |

ES, Edward SAPIEN, SAPIEN XT, and SAPIEN 3 valve; ID, internal diameter; MR, mitral regurgitation; MS, mitral stenosis.
mean extent of oversizing in MR patients was greater than that in MS patients, but both mean proportions were less than 10%, with no significant difference between groups ($P = 0.141$). Due to a lack of data regarding migration, we could not determine whether migration occurred more frequently in patients with a larger mean extent of oversizing.

4.6 Limitations

This is an observational study and all patients' data were obtained from published articles collected during a comprehensive and systematic search. Only a few articles reported long-term follow-up data; therefore, evaluation of long-term outcomes was not possible. All studies included in this study lacked control groups.

5 CONCLUSION

Use of the TMVIV or TMVIR procedure for degenerated mitral bioprostheses or failed annuloplasty rings is a highly feasible, safe, and effective technique for the treatment of either valve stenosis or regurgitation for those patients who are not candidates for repeat surgery. Both the TMVIV and TMVIR procedures are associated with excellent short-term clinical outcomes. The technical success rate of TMVIV was significantly higher than that for TMVIR, and the MR rate of TMVIV was significantly lower than that for TMVIR. No significant differences in short-term outcomes were observed between the TA and TS access groups, especially regarding vascular complications. Technical criteria, such as size selection and valve location, have not been established for transcatheter mitral valve implantation. Larger clinical trials are required to determine the durability and long-term outcomes of TMVIR and TMVIV.

CONFLICTS OF INTEREST

There are no conflicts of interest to declare.

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REFERENCES

1. Vohra HA, Whistance RN, Roubelakis A, et al. Outcome after redo-mitral valve replacement in adult patients: a 10-year single-centre experience. *Interact Cardiovasc Thorac Surg*. 2012;14:575–579.
2. Bourguignon T, Bouquiaux-Stablo A-L, Loardi C, et al. Very late outcomes for mitral valve replacement with the Carpentier-Edwards pericardial bioprosthesis: 25-year follow-up of 450 implantations. *J Thorac Cardiovasc Surg*. 2014;148:2004–2011.
3. Cheung A, Webb JG, Wong DR, et al. Transapical transcatheter mitral valve-in-valve implantation in a human. *Ann Thorac Surg*. 2009;87:E18–E20.
4. de Weger A, Ewe SH, Delgado V, et al. First-in-man implantation of a trans-catheter aortic valve in a mitral annuloplasty ring: novel treatment modality for failed mitral valve repair. *Eur J Cardiothorac Surg*. 2011;39:1054–1056.
5. Pfeiffer S, Gazdag L, Jessl J, et al. Transapical transcatheter valve-in-ring implantation following mitral annuloplasty. *J Card Surg*. 2017;32:407–409.
6. Gualis J, Estevez-Loureiro R, Alonso D, et al. Transapical mitral valve-in-valve ring implantation with the Edwards Sapien 3 prosthesis. *J Card Surg*. 2017;32:791–793.
7. Stone GW, Adams DH, Abraham WT, et al. Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: part 2: endpoint definitions: a consensus document from the mitral valve academic research consortium. *J Am Coll Cardiol*. 2015;66:308–321.
8. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol*. 2009;62:1006–1012.
9. Kaneko T, Piccirillo B, Golwala H, et al. Balloon fracture of a surgical mitral bioprosthesis during valve-in-valve transcatheter mitral valve replacement first-in-Human report. *Circ Cardiovasc Interv*. 2018;11:e006273.
10. Zanobini M, Manganiello S, Bonalumi G, et al. Emergency transapical mitral valve-in-valve implantation for bioprosthesis failure: transapical implantation of an Edwards Sapien-XT in a dysfunctional mitral bioprosthesis in a critical patient. *J Cardiothorac Surg*. 2017;12:114.
11. Tada N, Ena Y, Sakurai M, et al. Transcatheter valve-in-valve implantation for failed mitral prosthesis: the first experience in Japan. *Cardiovasc Interv Ther*. 2017;32:82–86.
12. Meduri C, Kauten J, Vannan M, et al. First report of a simultaneous transcatheter mitral valve-in-valve and aortic valve replacement in a left ventricular assist device patient. *Catheter Cardiovasc Interv*. 2017;90:526–529.
13. Herrmann HC, Sieto WY, Litt H, et al. Novel use of perfusion balloon inflation to avoid outflow tract obstruction during transcatheter mitral valve-in-valve replacement. *Catheter Cardiovasc Interv*. 2017 (in press; Epub ahead of print). https://doi.org/10.1002/ccd.27068.
14. He C, Scalia G, Walters DL, et al. Transcatheter mitral transcatheter mitral valve-in-valve implantation using an Edwards SAPIEN 3 valve. *Heart Lung Circ*. 2017;26:e19–e21.
15. Schuler A, Jones TK, Perpetua E, et al. Two-in-one using 3D: mitral paravalvular leak closure with concomitant transcatheter valve-in-valve implantation. *J Cardiothor Vasc Anesth*. 2018;32:1378–1381.
16. Schaefer U, Conradi L, Lubos E, et al. First-in-man treatment of a degenerated mitral surgical valve with the mechanical expanding Lotus valve. *EuroIntervention*. 2016;12:515–518.
17. Salau N, Aldebert P, Jaussaud N, et al. Early endocarditis and delayed left ventricular pseudoaneurysm complicating a transcatheter mitral valve-in-valve implantation percutaneous closure under local anaesthesia and echocardiographic guidance. *Circ Cardiovasc Interv*. 2016;9:e003886.
18. Rudzinski PN, Dzielenka Z, Witkowski A, et al. Transcatheter valve-in-valve implantation in a degenerated mitral bioprosthesis using a trans-septal antegrade approach and 3-D transesophageal echocardiographic guidance. *J Heart Valve Dis*. 2016;25:90–92.
19. Nejari M, Hibbert D, Brochet E, et al. First-in-man full percutaneous transfemoral valve-in-valve implantations using Edwards SAPIEN 3 prostheses to treat a patient with degenerated mitral and aortic bioprostheses. *Interact Cardiovasc Thorac Surg*. 2016;23:508–510.
20. Mick SL, Roselli EE, Kapadia S, et al. Postoperative migration of an Edwards-SAPIEN XT mitral valve-in-valve treated with direct vision implantation during beating-heart bypass. *Ann Thorac Surg*. 2016;101:1182–1185.
21. Fuchs FC, Hammerstingl C, Sinning JM, et al. Antegrade transcatheater mitral valve-in-valve implantation with combined atrial septal defect closure. Clin Res Cardiol. 2016;105:460–462.

22. Eleid MF, Cabalka AK, Williams MR, et al. Percutaneous transvenous transseptal transcatheter valve implantation in failed bioprosthetic mitral valves, ring annuloplasty, and severe mitral annular calcification. JACC Cardiovasc Interiv. 2016;9:1161–1174.

23. Cocchieri R, Koh EY, de Mol BA. Transapical mitral valve-in-valve implantation using an Edwards SAPIEN 3 prosthesis. Innovations. 2016;11:73–75.

24. Cerillo AG, Gasbarri T, Celi S, et al. Transapical transcatheter valve-in-valve implantation. Interact Cardiovasc Thorac Surg. 2016;22:501–503.

25. Bruschi G, Cannata A, Barosi A, et al. Direct Flow valve-in-valve implantation in a degenerated mitral bioprosthesis. Eurointervention. 2016;11:1549–1553.

26. Baldizion I, Espinoza A, Kuntze T, et al. Early transcatheter valve dysfunction after transapical mitral valve-in-valve implantation. Innovations. 2016;11:125–131.

27. Alli O, Booker O, Davies J. Emergent transcatheter mitral valve-in-valve implantation in a patient with cardiogenic shock secondary to a failed mitral bioprosthesis. Catheter Cardiovasc Interv. 2016;87:1342–1346.

28. Akhras N, Al Sergani H, Al Buraiki J, et al. Thrombolytic therapy as the treatment of degenerated bioprosthetic mitral regurgitation in a patient with failing mitral bioprostheses and JenaValve for the treatment of pure aortic regurgitation. Heart Surgery Forum. 2015;18:E53–EE5.

29. Worku B, de Biasi AR, Gulkarov I, et al. Transapical mitral valve-in-valve implantation for severe mitral stenosis. Clin Res Cardiol. 2015;104:1289–1295.

30. Singh GD, Smith TW, Boyd WD, et al. Complete transcatheter mitral valve-in-valve replacement of an Edwards SAPIEN aortic valve in the mitral position for severe mitral stenosis. Ann Thorac Surg. 2015;100:811–817.

31. Rossi ML, Barbaro C, Pagnotta P, et al. Transcatheter mitral valve-in-valve replacement for degenerated mitral bioprosthesis without radio-opaque indicators: the “invisible” mitral valve bioprosthesis. Heart Lung Circ. 2015;24:E19–E22.

32. Ramakrishna H, DeValeria PA, Sweeney JP, et al. Transcatheter, valve-in-valve transapical aortic and mitral valve implantation, in a high risk patient with aortic and mitral prosthetic valve stenoses. Ann Card Anaesth. 2015;18:246–251.

33. Pagnotta P, Mennuni MG, Ferrante G, et al. A hybrid double access for transcatheter mitral valve-in-valve implantation. Ann Thorac Surg. 2015;99:E149–EE50.

34. Mureretto C, Ettori F, Mazzitelli D, et al. First-in-man, mitral valve-in-valve transcatheter mitral valve implantation through an innovative minimally invasive surgical approach. Ann Thorac Surg. 2015;100:713–715.

35. Maxwell CD, Daley SM, Swaminathan M, et al. Intraoperative, real-time three-dimensional transesophageal echocardiography for the transcatheter placement of an Edwards SAPIEN aortic valve in the mitral position for severe mitral stenosis. Anesth Analg. 2015;121:1456–1459.

36. Kliger C, Angulo R, Maranan L, et al. Percutaneous complete repair of failed mitral valve prosthesis: simultaneous closure of mitral paravalvular leaks and transcatheter mitral valve implantation - single-centre experience. Eurointervention. 2015;10:1336–1345.

37. Jochheim D, Khandoga A, Bauer A, et al. Transseptal transcatheter implantation of a third-generation balloon-expandable valve in degenerated mitral bioprosthesis. JACC Cardiovasc Interv. 2015;8:E241–E243.

38. Coylewright M, Cabalka AK, Malouf JA, et al. Percutaneous mitral valve replacement using a transvenous, transseptal approach transvenous mitral valve replacement. JACC Cardiovasc Interv. 2015;8:850–857.

39. Chrissoheris M, Halapas A, Bouboulis N, et al. Treatment of a severely degenerated mitral bioprosthesis with transcatheter valve-in-valve implantation. Hellenic J Cardiol. 2015;56:347–350.

40. Chaiatriangkrai K, Goswami R, Little S, et al. Bioprosthetic mitral transcatheter transapical valve-in-valve implantation for mitral stenosis in an end-stage renal disease patient. J Cardiovasc Surg. 2015;53:697–700.

41. Berti S, Cerrillo AG, Munzi M, et al. How should I treat a severely symptomatic, high-risk female patient with degenerated mitral (Carpentier-Edwards porcine) and aortic (Sorin Mitroflow) bioprostheses? EuroIntervention. 2015;10:1250–1252.

42. Aydin U, Gul M, Aslan S, et al. Concomitant transcatheter transcatheter valve implantations: Edwards Sapien valve for severe mitral regurgitation in a patient with failing mitral bioprostheses and JenaValve for the treatment of pure aortic regurgitation. Heart Surgery Forum. 2015;18:E53–EE5.

43. Akujio AC, Delli SL, Delago AJ, et al. Transcatheter aortic and mitral valve implantation in bioprosthetic valves: when one correction is not enough. J Thorac Cardiovasc Surg. 2015;150: E15–E17.

44. Yamane K, Nazif TM, Khalique O, et al. Transcatheter valve-in-valve implantation for early prosthetic valve degeneration in aortic and mitral positions. Ann Thorac Surg. 2014;98:318–321.

45. Schafer U, Bader R, Frerker C, et al. Balloon-expandable valves for degenerated mitral xenografts or failing surgical rings. Eurointervention. 2014;10:260–268.

46. Quick S, Speiser U, Strasser RH, et al. First bioprosthesis thrombosis after transcatheter mitral valve-in-valve implantation diagnosis and treatment. J Am Coll Cardiol. 2014;63:e49.

47. Lerakis S, Hayek SS, Thoumani V, et al. Transcatheter valve-in-valve implantation for degenerated mitral valve bioprosthesis under 3D echocardiographic guidance. Expert Rev Cardiovasc Ther. 2014;12:1035–1036.

48. Kaneko T, Swain JD, Loberman D, et al. Transjugal approach in valve-in-valve transcatheter mitral valve replacement: direct route to the valve. Ann Thorac Surg. 2014;97:E161–E163.

49. Hayek SS, Babaliaros V, Thoumani V, et al. Transcatheter valve-in-valve implantation for a degenerated mitral valve bioprosthesis under echocardiographic guidance. Hellenic J Cardiol. 2014;55:338–341.

50. Duncan A, Davies S, Rosendahl U, et al. Consecutive transcatheter valve-in-valve implantations: the first in the aortic position, the second in the mitral position, in a patient with failing aortic and mitral bioprostheses. BMJ Case Rep. 2014;2014. pii: bcr2014203782.

51. D’Onofrio A, Zucchetta F, Gerosa G. Simultaneous transapical aortic and mitral valve-in-valve implantation for double prostheses dysfunction: case report and technical insights. Catheter Cardiovasc Interv. 2014;84:509–512.

52. D’Onofrio A, Gallo M, Tarantini G, et al. An unexpected finding: stuck leaflet after transcatheter mitral valve-in-valve implantation. JACC Cardiovasc Interv. 2014;7:e187–e189.

53. de Biasi AR, Wong SC, Salemi A. Reoperative “valve-in-valve” transcatheter transcatheter mitral valve replacement in a high-risk patient with a recent transcatheter transcatheter aortic valve replacement and a degenerated bioprosthetic mitral valve. J Thorac Cardiovasc Surg. 2014;148:E209–EE10.

54. Bruschi G, Botta L, Fratto P, et al. Failed valve-in-valve transcatheter mitral valve implantation. Eur J Cardiothorac Surg. 2014;45: E127–E12E.

55. Bapat VV, Khalief F, Ihleberg L. Delayed migration of Sapien valve following a transcatheter mitral valve-in-valve implantation. Catheter Cardiovasc Interv. 2014;83:E150–E154.

56. Wilbring M, Alexiou K, Tugtekin SM, et al. Transcatheter valve-in-valve implantation for deteriorated mitral valve bioprostheses. Ann Thorac Surg. 2013;95:111–118.
57. Theron A, Gariboldi V, Grisoli D, et al. Three-dimensional transesophageal echocardiography assessment of a successful transcatheter mitral valve in valve implantation for degenerated bioprostheses. Echocardiography. 2013;30:E152–E155.

58. Soon JL, Chua YL, Chao VT, et al. Asia's first successful minimally invasive transapical transcatheter mitral valve-in-valve implantation. Ann Acad Med Singapore. 2013;42:85–87.

59. Schaefer U, Frerker C, Bader R, et al. Transcatheter access route options for treatment of degenerated mitral valve prosthesis with a balloon-expandable biological valve. Catheter Cardiovasc Interv. 2013;82:999–1003.

60. Michelena HI, Alii O, Cabalka AK, et al. Successful percutaneous transvenous antegrade mitral valve-in-valve implantation. Catheter Cardiovasc Interv. 2013;81:E219–E224.

61. Fassa AA, Himbert D, Brochet E, et al. Emergency transseptal transcatheter mitral valve-in-valve implantation. Eurointervention. 2013;9:636–642.

62. Cullen MW, Cabalka AK, Alii OO, et al. Transvenous, antegrade melody valve-in-valve implantation for bioprosthetic mitral and tricuspid valve dysfunction: a case series in children and adults. JACC Cardiovasc Interv. 2013;6:598–605.

63. Cheung A, Webb JG, Barbanti M, et al. 5-Year experience with transcatheter transapical transcatheter valve-in-valve implantation for bioprosthetic valve dysfunction. J Am Coll Cardiol. 2013;61:1759–1766.

64. Seiffert M, Conradi L, Baldus S, et al. Transcatheter mitral valve-in-valve implantation in patients with degenerated bioprostheses. JACC Cardiovasc Interv. 2012;5:341–349.

65. Santarpino G, Fischlein T, Conciste G, et al. A staged approach to transcatheter aortic valve implantation and mitral valve-in-valve implantation for a degenerated bioprosthesis in a high-risk patient. Interact Cardiovasc Thorac Surg. 2012;15:764–765.

66. Poon KKC, Clarke A, Luis SA, et al. First Australian transapical mitral valve-in-valve implant for a failed mitral bioprosthesis: how to do it. Heart Lung Circ. 2012;21:737–739.

67. Bruschi G, Barosso A, Colombo P, et al. Direct transatrial transcatheter SAPIEN valve implantation through right minithoracotomy in a degenerated mitral bioprosthetic valve. Ann Thor Surg. 2012;93:1708–1710.

68. Bekeredjian R, Chorianopoulos E, Katus HA. Successful transfemoral antegrade valve-in-valve implantation of a SAPIEN XT valve into a degenerated mitral valve prosthesis. J Inv Cardiol. 2012;24:170–172.

69. Van Garsse L, Gelsomino S, Van Ommen V, et al. Emergency transthoracic transcatheter mitral valve-in-valve implantation. J Inv Cardiol. 2011;24:474–476.

70. Seiffert M, Baldus S, Conradi L, et al. Simultaneous transcatheter aortic and mitral valve-in-valve implantation in a patient with degenerated bioprostheses and high surgical risk. Thorac Cardiovasc Surg. 2011;59:490–492.

71. Nunez-Gil U, Goncalves A, Rodrigue E, et al. Transapical mitral valve-in-valve implantation: a novel approach guided by three-dimensional transesophageal echocardiography. Eur J Echocardiogr. 2011;12:335–337.

72. Montorfano M, Latib A, Chieffo A, et al. Successful percutaneous antegrade transcatheter valve-in-valve implantation in the mitral position. JACC Cardiovasc Interv. 2011;4:1246–1247.

73. Cerillo AG, Chiaramonti F, Murzi M, et al. Transcatheter valve in valve implantation for failed mitral and tricuspid bioprosthesis. Catheter Cardiovasc Interv. 2011;78:987–995.

74. de Weger A, Tavilla G, Ng ACT, et al. Successful transapical transcatheter valve implantation within a dysfunctional mitral bioprosthesis. JACC Cardiovascular Imaging. 2010;3:222–223.

75. Toutouzas K, Lozos V, Oikonomou G, et al. Reduction of para-ring regurgitation after transcatheter mitral valve replacement into a failed mitral annuloplasty ring. JACC Cardiovascular Interv. 2018;11:E17–E20.

76. Bagur R, Cheung A, Chu MWA, et al. 3-dimensional-printed model for planning transcatheter mitral-valve replacement. JACC Cardiovasc Interv. 2018;11:812–813.

77. Roy J, Eskandari M, Monaghan M, et al. Simultaneous transseptal para-ring leak closure and transcatheter mitral valve implantation for the treatment of surgical mitral repair failure. Heart Lung Circ. 2017;26:E71–E5.

78. Regazzoli D, Stella S, De Pinto S, et al. Transfemoral implantation of a balloon-expandable transcatheter valve in a rigid mitral annuloplasty ring optimized by post-dilatation. JACC Cardiovascular Interv. 2017;10:E177–E189.

79. Kamioka N, Iturbe JM, Corrigan F, et al. Grabbing the transcatheter valve skirt bail-out technique for valve embolization during valve-in-Valve transcatheter mitral valve replacement. JACC Cardiovascular Interv. 2017;10:E175.

80. Jain T, Wang DD, Eng M, et al. Transcatheter mitral valve-in-ring implantation after failure of surgical mitral ring annuloplasty. J Am Coll Cardiol. 2017;69:1262.

81. Hudec V, Bena M, Artemiou P, et al. Reversible thrombotic mitral valve stenosis after transcatheter mitral valve replacement (TMVR): Is life-long anticoagulation therapy necessary? J Card Surg. 2017;32:190–192.

82. Greenbaum AB, Condado JF, Eng M, et al. Long or redundant leaflet complicating transcatheter mitral valve replacement: case vignettes that advocate for removal or reduction of the anterior mitral leaflet. Catheter Cardiovasc Interv. 2017. (in press; Epub ahead of print). https://doi.org/10.1002/ccd.27054

83. Frisoli TM, Wang DD, Eng M, et al. Mitral annuloplasty ring fracture and annular injury during transcatheter mitral valve-in-ring intervention. JACC Cardiovascular Interv. 2017;10:E181–E184.

84. Duncan A, Daqa A, Yeh J, et al. Transcatheter mitral valve replacement: long-term outcomes of first-in-man experience with an apically tethered device—a case series from a single centre. Eurointervention. 2017;13:e1047–e1057.

85. Cheung A, Denti P, Kiiii B, et al. Mitral valve-in-ring implantation with a dedicated transcatheter mitral valve replacement system. JACC Cardiovascular Interv. 2017;10:2012–2014.

86. Said SM, Pislaru S, Kotkar KD, et al. Left ventricular outflow tract obstruction after transcatheter mitral valve-in-ring implantation: a word of caution. Ann Thorac Surg. 2016;102:E495–E497.

87. Lauterbach M, Sontag B, Parafosso A, et al. Transcatheter valve-in-ring implantation of a repositionable valve system for treatment of severe mitral regurgitation. Catheter Cardiovasc Interv. 2016;88:183–190.

88. Latib A, Ruparelia N, Bijuklic K, et al. First-in-man transcatheter mitral valve-in-ring implantation with a repositionable and retrievable aortic valve prosthesis. Eurointervention. 2016;11:1148–1152.

89. Condado JF, Babaliaros VC, Thourani VH, et al. A complex transcatheter mitral valve replacement and repair for the treatment of refractory severe mitral regurgitation. Hellenic J Cardiol. 2016;57:348–350.

90. Attizzani GF, Tam CC, Markowitz A. Transcatheter mitral valve-in-ring implantation in prohibitive surgical risk patients: single center initial experience in the United States. Catheter Cardiovasc Interv. 2016;88:E233–E248.

91. Ahn HC, Baranowski J, Dahlin L-G, et al. Transcatheter mitral valve-in-ring implantation in patients with degenerated mitral prostheses and native mitral stenosis. Ann Thorac Surg. 2016;101:2279–2284.

92. Yaryura R, Rehman A, Morsli H, et al. Transcatheter aortic and mitral valve replacement in a patient with critical aortic and mitral valve in-ring stenosis. JACC Cardiovascular Interv. 2015;8:E155–E157.
93. Wilbring M, Kappert U, Matschke K. Transapical transcatheter valve-in-ring implantation for failed mitral valve repair in the absence of radiopaque markers. J Thorac Cardiovasc Surg. 2015;149:E92–E4.
94. Latib A, Montorfano M, Agricola E, et al. First-in-human implantation of a direct flow medical valve in a radiolucent mitral annuloplasty ring. JACC Cardiovascular Interv. 2015;8:E105–E18.
95. Allende R, Doyle D, Urena M, et al. Transcatheter mitral “valve-in-ring” implantation: a word of caution. Ann Thorac Surg. 2015;99:1439–1442.
96. Wunderlich NC, Kische S, Ince H, et al. Transcatheter valve-in-ring implantation after a failed surgical mitral repair using a transseptal approach and a veno-arterial loop for valve placement. Catheter Cardiovasc Interv. 2014;84:1202–1208.
97. Neves PC, Paulo NS, Gama V, et al. Transapical aortic valve and mitral valve in ring prosthesis implantation—a new advance in transcatheter procedures. Interact Cardiovasc Thorac Surg. 2014;19:344–346.
98. Maisano F, Reser D, Pavicevic J, et al. Successful first-in-man melody transcatheter valve implant in a dehisced mitral annuloplasty ring transcatheter valve-in-ring implant. Eurointervention. 2014;10:961–967.
99. Ladeiras-Lopes R, Vouga L, Braga P, et al. Simultaneous transapical implantation of an inverted transcatheter aortic valve-in-ring in the mitral position and transcatheter aortic valve replacement first-in-human report. J Am Coll Cardiol. 2014;63:E25–E2E.
100. Kliger C, Al-Badri A, Wilson S, et al. Successful first-in-man percutaneous transapical-transseptal melody mitral valve-in-ring implantation after complicated closure of a para-annular ring leak. Eurointervention. 2014;10:968–974.
101. Mazzitelli D, Bleiziffer S, Noebauer C, et al. Transatrial antegrade approach for double mitral and tricuspid “valve-in-ring” implantation. Ann Thorac Surg. 2013;95:E25–E7E.
102. Descoutures F, Himbert D, Maisano F, et al. Transcatheter valve-in-ring implantation after failure of surgical mitral repair. Eur J Cardiothorac Surg. 2013;44:E8–E15.
103. Petronio A, Giannini C, De Carlo M, et al. Antegrade percutaneous valve implantation for mitral ring dysfunction, a challenging case. Catheter Cardiovasc Interv. 2012;80:700–703.
104. Holzhey DM, Schuler G, Mohr FW, et al. Transapical double valve implantation plus percutaneous revascularization as a bailout for a high-risk patient. J Thorac Cardiovasc Surg. 2012;144:508–510.
105. Dahle G, Fiane AE, Rein KA. Transapical 29-mm Edwards SAPIEN-XT aortic valve in a 34-mm mitral annuloplasty ring. Innovations (Phila). 2012;7:290–294.
106. Himbert D, Brochet E, Radu C, et al. Transseptal implantation of a transcatheter heart valve in a mitral annuloplasty ring to treat mitral repair failure. Circulation-Cardiovascular Interv. 2011;4:396–U164.
107. Yoon SH, Whisenant BK, Bleiziffer S, et al. Transcatheter mitral valve replacement for degenerated bioprosthetic valves and failed annuloplasty rings. J Am Coll Cardiol. 2017;70:1121–1131.
108. Frerker C, Schmidt T, Schluter M, et al. Transcatheter implantation of aortic valve prostheses into degenerated mitral valve bioprostheses and failed annuloplasty rings: outcomes according to access route and Mitral Valve Academic Research Consortium (MVARC) criteria. EurHeartJ. 2016;12:1520–1526.

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