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## Clinical Research

# Outcome of Patients Undergoing Transcatheter Implantation of Aortic Valve With Previous Mitral Valve Prosthesis (OPTIMAL) Study

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***See editorial Salaun and Pibarot, pages 805–808 of this issue.***


## ABSTRACT

**Background:** Transcatheter aortic valve replacement (TAVR) is the gold standard for severe valvular aortic stenosis in patients at high/prohibitive surgical risk. This procedure has also been used in patients with previous mitral valve (MV) prostheses, with contrasting outcomes reported. The aim of this study is to describe procedural and early outcomes of patients with previous MV prostheses undergoing TAVR.

**Methods:** This is a retrospective registry of 154 patients with previous MV prostheses who underwent TAVR across high-volume medical centres at a mean of 11.7 ± 8.4 years after mitral surgery.

**Results:** Mean mitroaortic distance at computed tomography was 9.7 ± 4.8 mm. Procedural success was achieved in 150 (97.4%) patients, with reduction of aortic gradients (42.6 ± 14.2 to 10.0 ± 7.0 mm Hg; $P < 0.001$). Device success was achieved in 133 (86.3%) patients. MV prosthesis interference by the TAVR device was observed in 2 patients; in both, the mitroaortic distance was <5 mm, with 1 complicated by TAVR prosthesis embolization. Periprocedural compli-

## RÉSUMÉ

**Contexte :** Le remplacement valvulaire aortique par cathéter (RVAC) est le traitement de référence de la sténose valvulaire aortique grave pour les patients qui présentent un risque chirurgical élevé ou prohibitif. Cette intervention a également été utilisée, avec des résultats rapportés très variables, chez des patients ayant reçu précédemment une prothèse valvulaire mitrale. L'objectif de cette étude était d'évaluer l'efficacité de l'intervention et de décrire les premiers résultats chez des patients ayant déjà reçu une prothèse valvulaire mitrale qui subissent un RVAC.

**Méthodologie :** Il s'agit d'une étude rétrospective d'un registre de 154 patients ayant subi un RVAC après une période moyenne de 11,7 ± 8,4 années depuis l'implantation chirurgicale d'une prothèse de valve mitrale, dans des centres médicaux traitant des volumes élevés de patients.

**Résultats :** La distance mitro-aortique moyenne évaluée par tomodensitométrie était de 9,7 ± 4,8 mm. La réussite sur le plan de


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See page 873 for disclosure information.

Transcatheter aortic valve replacement (TAVR) is an established therapeutic option in patients with severe aortic stenosis (AS) at increased surgical risk.[1-4] In this context, advances in device technology, the use of computed tomography (CT) for procedural planning and more appropriate application of TAVR have reduced complications limiting previous

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cations included 4 (2.6%) cerebrovascular accidents, 10 (6.6%) major vascular complications, 22 (14.4%) severe bleedings, 1 (0.7%) myocardial infarction, and 5 (3.2%) in-hospital deaths (all cases cardiovascular or procedure related). At a median follow-up of 13.5 (interquartile range 1.0 to 36.0) months, 26 (16.9%) deaths occurred; 15 (9.7%) were cardiac related. Late fatal mitral prosthesis thromboses occurred in 2 patients. We recorded a case of fatal hemorrhagic stroke; hospital readmission was observed in 25 (16.2%) patients due to worsening heart failure.

**Conclusions:** TAVR in patients with previous mitral prostheses appears to be safe and feasible, with good hemodynamic results at 30-day and at longer-term follow-up.

l'intervention a été obtenue chez 150 (97,4 %) patients et était accompagnée d'une réduction du gradient aortique (de 42,6 ± 14.2 à 10,0 ± 7,0 mm Hg; $p < 0{,}001$). La réussite sur le plan du dispositif a été obtenue chez 133 (86,3 %) patients. Une interférence du dispositif de RVAC sur la prothèse valvulaire mitrale a été observée chez 2 patients; dans les deux cas, la distance micro-aortique était < 5 mm et 1 cas était compliqué par une embolisation de la prothèse de RVAC. Parmi les complications peropératoires, on a relevé 4 (2,6 %) accidents vasculaires cérébraux, 10 (6,6 %) complications vasculaires majeures, 22 (14,4 %) hémorragies graves, 1 (0,7 %) infarctus du myocarde et 5 (3,2 %) décès à l'hôpital (d'origine cardiovasculaire ou en lien avec l'intervention). Après une période de suivi médiane de 13,5 (intervalle interquartile, de 1,0 à 36,0) mois, 26 (16,9 %) décès étaient survenus, dont 15 (9,7 %) d'origine cardiaque. Des thromboses de prothèse mitrale fatales tardives sont survenues chez 2 patients. Nous avons noté un cas fatal d'accident vasculaire cérébral hémorragique; 25 (16,2 %) patients ont été réhospitalisés à cause d'une aggravation de leur insuffisance cardiaque.

**Conclusions :** Chez les patients ayant reçu antérieurement une prothèse mitrale, le RVAC semble être une intervention sûre et réalisable, et donne de bons résultats hémodynamiques selon un suivi à 30 jours et à plus long terme.

iterations and therefore maximized the likelihood of positive outcomes. However, several subgroups of patients are still at a higher risk owing to both procedural and clinical factors.

Recently, TAVR in patients with surgical mitral valve (MV) prostheses has been identified as a subgroup at potentially increased risk.[5] This may be due to the potential interference between the prostheses and the increased risk that reoperation has *per se*. Nonetheless, robust clinical data regarding this patient subset are limited to a single recent study showing similar mortality and higher bleeding risk in patients with TAVR and previous MV prostheses compared with those without.[6] The aim of this study is to describe real-world procedural and early outcomes of patients with previous MV prostheses undergoing TAVR at high-volume centres.

## Methods and Endpoints

### Patient population

All patients with surgical MV prostheses who underwent TAVR were included in the **O**utcome of **P**atients Undergoing **T**ranscatheter **Im**plantation of **A**ortic Valve With Previous Mitra**l** Valve Prosthesis (OPTIMAL) study. This is an international multicenter retrospective registry involving 12 high-volume TAVR centres conducted between March 2008 and August 2017.

Severe AS was defined by echocardiographic criteria including an aortic valve area (AVA) of $<1\text{cm}^2$ or an indexed AVA of $<0.6\ \text{cm}^2/\text{m}^2$ in combination with clinical symptoms.[7,8] All patients were at intermediate or high surgical risk defined as a Society of Thoracic Surgeons (STS) score of $\geq$4%, a logistic **Euro**pean **S**ystem for **C**ardiac **O**perative **R**isk **E**valuation (EuroSCORE) $\geq$ 10%, or had relevant risk factor(s) for surgery not included in these scores. The decision to perform TAVR was made by a multidisciplinary heart team including an interventional cardiologist, a cardiothoracic surgeon, an imaging cardiologist, and an anesthesiologist.[8]

Before the procedure, all patients underwent multimodality cardiovascular imaging including transthoracic and/or transesophageal echocardiography; cardiac CT angiography; and, when required, invasive cardiac catheterization.[9,10] On echocardiography, valvular regurgitation was assessed by current guideline recommendations[11] and graded on a semiquantitative scale ranging from 0 to 4. Cardiac CT was used for the accurate assessment of aortic valve anatomy, associated calcification, aortic root size, height of coronary ostia from the aortic annular plane, mitroaortic distance, and valve sizing. Mitroaortic distance was calculated as the perpendicular distance between the virtual basal ring and the closest point of the MV prosthesis cage. Examples of preprocedural imaging are reported in Figures 1 and 2.

Transthoracic or transesophageal echocardiographic assessment, according to Valve Academic Research Consortium (VARC-2) criteria,[12] was used to determine the presence (and severity) of postprocedural aortic insufficiency and the transvalvular mean and peak gradients immediately following valve implantation, at hospital discharge, and at follow-up.

In general, the choice of device used was left to the discretion and preference of the operator. Aortic devices used in the study are summarized in Figure 3.

### Study endpoints

Safety and efficacy endpoints were defined according to the VARC-2 consensus document.[12] The primary endpoint of device success was the composite of absence of procedural mortality and correct positioning of a single transcatheter aortic valve prosthesis into the proper anatomical location with subsequent mean aortic valve gradient < 20 mm Hg and no moderate or severe prosthetic valve regurgitation. Secondary endpoints were the VARC-2-defined 30-day early safety composite endpoint and the clinical efficacy (after 30

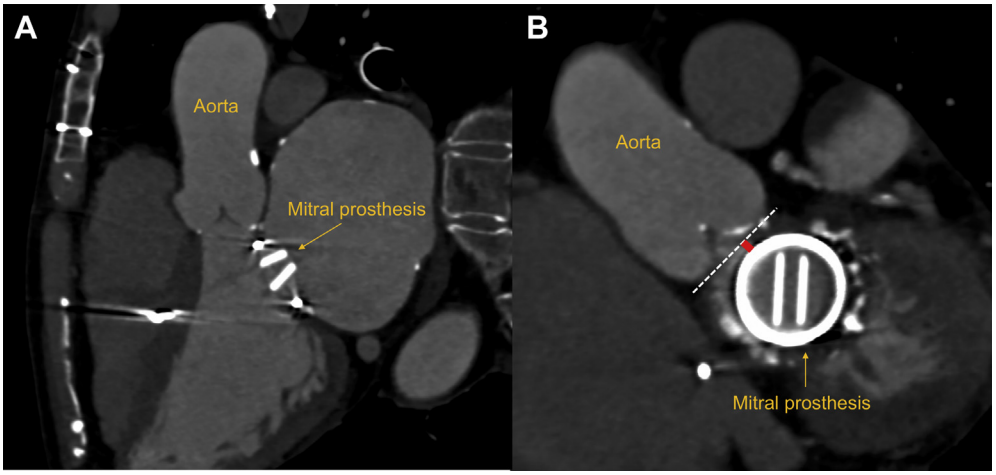


**Figure 1.** Mitroaortic distance. The virtual basal ring is identified by multiplane reconstruction (**A, B**). Then, the mitroaortic distance (**red line**) is calculated as the perpendicular segment between the virtual basal ring plane (**white dashed line**) and the closest point of the MV prosthesis cage (**B**).

days) composite endpoint. For each patient, the longest follow-up available was recorded.

### Statistical analysis

Continuous variables are described as means and standard deviations or as medians and interquartile (IQR) ranges, as appropriate. Normality was checked by the Kolmogorov–Smirnov test. Categorical variables are expressed as proportions and compared with $\chi^2$ test with Yates correction for continuity or the Fisher exact test as appropriate for the available data. Comparison of independent groups was performed either with an unpaired Students' *t*-test, the Mann–Whitney U test, the sign-test, or a Kruskal–Wallis H test, as appropriate. The baseline and follow-up measurements were compared using a paired Students' *t*-test or the Wilcoxon signed rank test, as appropriate; $P < 0.05$ was considered statistically significant. To explore predictors of relevant outcomes, a binomial logistic regression was performed. To avoid multicollinearity, a "low-noise model" has been researched, in which each predictor variable correlates at most only minimally with the other. Selection of the variables included in the multivariate model was done with backward elimination, based on covariates that were significantly associated ($P < 0.10$) with the risk of cardiac death at univariate analysis. All analyses were performed using SPSS software (SPSS, v 24, IBM Corporation, Armonk, NY).

## Results

### Study population

Between March 2008 and August 2017, a total of 154 patients with a surgical MV prostheses underwent TAVR in

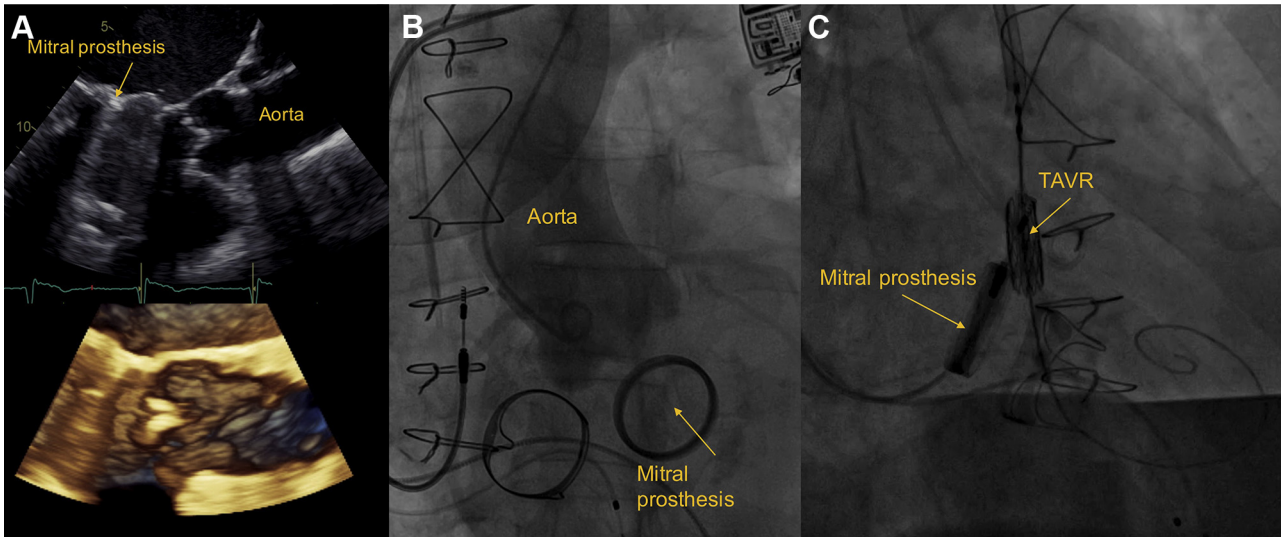


**Figure 2.** Multimodality imaging to assess mitroaortic spatial relationship. At transesophageal 2D (**upper A**) and 3D (**lower A**) echocardiography midesophageal 120° scan visualizes the MV prosthesis and the left ventricular outflow tract (LVOT). At fluoroscopy, a left anterior oblique projection shows an *en-face* view of the MV prosthesis (**B**); (**C**) right anterior oblique projection.

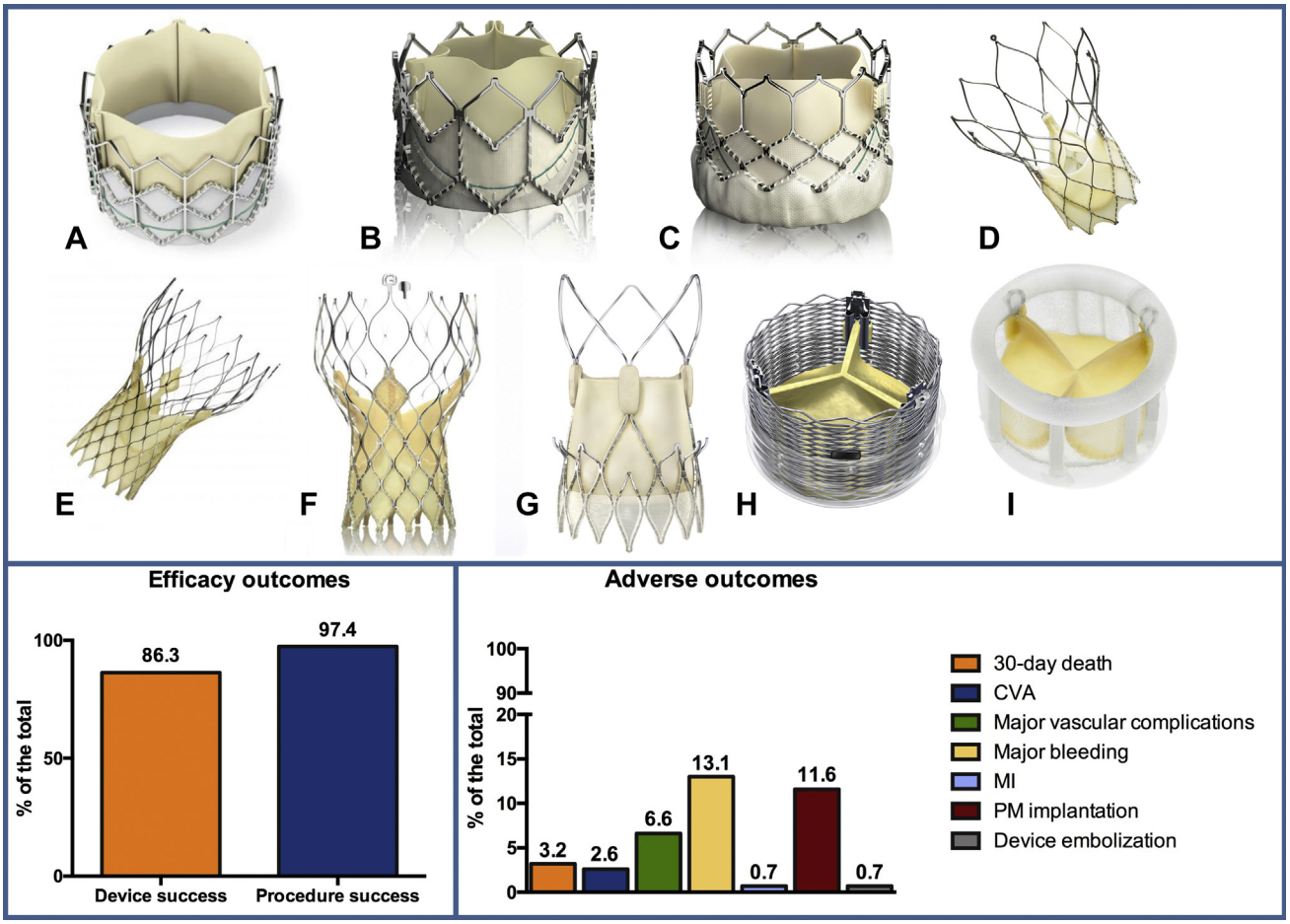


**Figure 3.** (**Upper panel**) Overview of transcatheter aortic prostheses implanted in this study (**left panel**) and relevant design characteristics (**right panel**). (**A**) Edwards Sapien prosthesis (Edwards Lifesciences Corp, Irvine, CA); (**B**) Edwards Sapien XT prosthesis; (**C**) Edwards Sapien 3 prosthesis; (**D**) Portico prosthesis (St Jude Medical, St Paul, MN); (**E**) CoreValve prosthesis (Medtronic, Minneapolis, MN); (**F**) CoreValve Evolut R prosthesis (Medtronic); (**G**) ACURATE neo prosthesis (Boston Scientific, Marlborough, MA); (**H**) Lotus prosthesis (Boston Scientific); and (**I**) DirectFlow prosthesis (Direct Flow Medical Inc, Santa Rosa, CA). (**Lower left panel**) Efficacy outcomes. (**Lower right panel**) Safety outcomes. CVA, cerebrovascular accidents; MI, myocardial infarction; PM, pacemaker. (**A-C**) Reproduced with permission from Edwards Lifesciences Corp. (**D**) Reproduced with permission from St Jude Medical. (**E, F**) Reproduced with permission from Medtronic. (**H**) Material provided courtesy of Boston Scientific. Copyright 2019 © Boston Scientific Corporation or its affiliates. All rights reserved.

12 centres and were included in the OPTIMAL registry; these patients represent the study population (mean age was 77.2 ± 8.6 years, 79.9% were female, STS score 8.7% ± 8.0%). Baseline population characteristics are summarized in Table 1.

All patients had previously undergone surgical MV replacements, with a mean time from MV surgery to TAVR procedure of 11.9 ± 8.4 years. Previous cardiac surgery included 128 (83.1%) isolated MV surgeries; 3 (1.9%) MV plus aortic valve surgeries; 20 (13.0%) MV plus tricuspid valve surgeries; and 3 (1.9%) MV, aortic valve, and tricuspid valve surgeries.

Our population included a total of 107 (69.5%) mechanical MV prostheses and 47 (30.5%) biologic MV prostheses. The mean mitral prostheses annular size was 26.4 ± 2.2 mm (range 23 to 31 mm). Baseline antithrombotic medication data were available for 113 (73.4%) patients; the majority (75 of 113; 66.4%) of patients were on oral anticoagulation therapy (OAC), followed by single antiplatelet therapy (SAPT) in 15 of 113 (13.3%) patients.

## Preprocedural assessment

At echocardiographic assessment, the mean aortic gradient was 42.6 ± 14.2 mm Hg, and mean AVA was 0.74 ± 0.22 $cm^2$. Eleven (7.1%) patients had concomitant severe aortic regurgitation. Left ventricular ejection fraction (LVEF) was 46.6 ± 16.8%. Ten (6.5%) patients had moderate to severe mitral regurgitation, and 2 (1.3%) patients had severe mitral regurgitation.

Preprocedural CT studies were performed in all the patients, but data were available only for 105 (68.2%) patients. Mean aortic annular area was 4.0 ± 1.1 $cm^2$, mean aortic annular perimeter was 71.0 ± 15.1 mm, and the mean aortic diameter was 23.7 ± 2.6 mm. Distance of left main coronary artery ostium to annulus was 13.2 ± 3.3 mm, and distance of right coronary artery ostium to annulus was 14.7 ± 3.6 mm. Mitroaortic distance calculation was available for 45 (29.2%) patients only. Mean mitroaortic distance was 9.7 ± 4.8 mm (range 1 to 20 mm). In 14 of the 45 patients, the mitroaortic distance was ≤ 7 mm. One of these patients was implanted

**Table 1.** Baseline clinical characterics and preprocedural echocardiogaphic and cardiac computed-tomograpy data of the study population

| | |
|---|---|
| Clinical characteristics (n = 154) | |
| Age (years) | 77.2 ± 8.6 |
| Female patients, n (%) | 123 (79.9) |
| Hypertension, n (%) | 105 (68.2) |
| Diabetes, n (%) | 33 (21.4) |
| NYHA class | 3.01 ± 0.56 |
| History of CAD, n (%) | 53 (34.4) |
| Previous MI, n (%) | 15 (9.7) |
| Previous CABG, n (%) | 28 (18.2) |
| History of AF, n (%) | 105 (68.2) |
| Peripheral vascular disease, n (%) | 23 (14.9) |
| Cerebrovascular disease, n (%) | 34 (22.1) |
| Chronic obstructive pulmonary disease, n (%) | 29 (19.5) |
| Creatinine (mg/dL) | 1.22 ± 0.59 |
| eGFR (mL/min/1.73m$^2$) | 52.5 ± 21.4 |
| Logistic EuroScore (%) | 26.4 ± 15.8 |
| STS mortality score (%) | 8.7 ± 8.0 |
| Mitral prosthesis | |
| Time from MV surgery to TAVR (years) | 11.7 ± 8.4 |
| Mechanical, n (%) | 107 (69.5) |
| Biological, n (%) | 47 (30.5) |
| Mean prosthetic annular size (mm) | 26.4 ± 2.2 |
| MV prosthesis mean gradient (mm Hg) | 6.6 ± 2.7 |
| Electrocardiographic baseline | |
| Sinus rhythm, n (%) | 42 (27.3) |
| Atrial arrhythmia, n (%) | 83 (53.9) |
| Left bundle branch block, n (%) | 19 (12.3) |
| Right bundle branch block, n (%) | 7 (4.5) |
| Left anterior fascicular block, n (%) | 7 (4.5) |
| Previous PM, n (%) | 41 (26.6) |
| Echocardiographic data | |
| LVEF (%) | 46.6 ± 16.8 |
| AVA (cm$^2$) | 0.74 ± 0.22 |
| Mean aortic gradient (mm Hg) | 42.6 ± 14.2 |
| Moderate-severe AR, n (%) | 23 (14.9) |
| Severe AR, n (%) | 11 (7.1) |
| Moderate-severe MR, n (%) | 10 (6.5) |
| Severe MR, n (%) | 2 (1.3) |
| Moderate-severe TR, n (%) | 28 (18.2) |
| Severe TR, n (%) | 25 (16.2) |
| Computed tomography characteristics | |
| Aortic annular area (cm$^2$) | 4.0 ± 1.1 |
| Aortic perimeter (mm) | 71.4 ± 15.1 |
| Aortic mean diameter (mm) | 23.7 ± 2.6 |
| Distance LM ostium to annulus (mm) | 13.2 ± 3.3 |
| Distance RCA ostium to annulus (mm) | 14.7 ± 3.6 |
| Mitroaortic distance (mm) | 9.7 ± 4.8 |
| Porcelain aorta, n (%) | 7 (4.5) |

AF, atrial fibrillation; AR, aortic regurgitation; AVA, aortic valve area; CABG, coronary artery bypass grafting; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; LM, left main; LVEF, left ventricle ejection fraction; MI, myocardial infarction; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association; PM, pacemaker; RCA, right coronary artery; STS, Society of Thoracic Surgeons; TAVR, transcatheter aortic valve replacement.

with an Edwards-Sapien (Edwards Lifesciences Corp, Irvine, CA), 6 with Edwards-Sapien XT valves, 1 with a Edwards-Sapien 3, 2 with CoreValve prostheses (Medtronic, Minneapolis, MN), 1 with a CoreValve Evolut R, and 3 with Portico valves (St. Jude Medical, St Paul, MN). Porcelain aorta was evident in 7 (4.5%) patients. Preprocedural imaging assessment is summarized in Table 1.

## TAVR procedure and in-hospital outcomes

All patients underwent TAVR procedures. Transfemoral access was chosen in 120 (77.9%) patients, transapical in 24 (15.7%), trans-subclavian in 3 (2.0%), direct transaortic in 6 (3.9%), and a transcaval in 1 (0.7%) patient. Balloon predilatation was performed in 73 (47.7%) patients, with a median balloon size of 22 mm (range: 18 to 25 mm).

**Table 2.** Choice of transcatheter aortic valve prostheses in our study registry

| Transcatheter aortic valves implanted (n = 153) | |
|---|---|
| Balloon-expandable | |
| Edwards Sapien (Edwards Lifesciences Corp, Irvine, CA)* | 11 (7.2%) |
| Edwards Sapien XT* | 40 (26.1%) |
| Edwards Sapien 3† | 22 (14.4%) |
| Total | 73 (47.7%) |
| Self-expanding | |
| Portico (St Jude Medical, St Paul, Minnesota)† | 4 (2.6%) |
| CoreValve (Medtronic, Minneapolis, Minnesota)* | 45 (29.4%) |
| CoreValve Evolut R† | 24 (15.7%) |
| ACURATE neo (Boston Scientific, Marlborough, MA)† | 2 (1.3%) |
| Total | 75 (49.0%) |
| Mechanically expandable | |
| Lotus (Boston Scientific, Marlborough, MA)† | 4 (2.6%) |
| Other design | |
| DirectFlow (Direct Flow Medical Inc, Santa Rosa, CA)† | 1 (0.7%) |
| *First-generation devices | 96 (62.7%) |
| †Second-generation devices | 57 (37.3%) |
| Total | 153 (100%) |

* First-generation devices.
† Second-generation devices.

A total of 155 prostheses were implanted (153 patients implanted with single TAVR devices and 2 patients requiring second valves). An overview of the devices employed in this registry is given in Figure 3, and their use is summarized in Table 2. A total of 96 (62.7%) patients were implanted with first-generation devices and 57 (37.3%) with second-generation devices. A balloon-expandable (BE) device was chosen for 73 (47.7%) patients, a self-expanding (SE) device for 75 (49.0%) patients, and a device with other deployment systems was used in 5 (3.3%) patients. Compared with patients who had mechanical mitral prostheses, a significantly higher proportion of patients with biologic mitral prostheses were implanted with BE prostheses (63.0% vs 43.1%; $P = 0.039$). An aortic valve-in-valve procedure was performed in 21 (13.7%) patients. Median aortic prosthesis size was 26 mm (range: 23 to 31 mm). Balloon postdilatation was performed in 25 (16.3%) patients, and median balloon size was 25 mm (range: 22 to 29 mm); procedural fluoroscopy time was 73.7±50.2 minutes and mean contrast medium volume used was 143.7 ± 74.0 mL.

VARC-2-defined device success was achieved in 133 (86.3%) patients. Procedure success, defined as the implantation at the desired site of a single prosthesis with no procedural mortality and no surgical conversion, was achieved in 150 (97.4%) patients. One patient was not implanted because of fatal refractory hypotension during induction of anesthesia. Two patients (1.3%) required implantation of second TAVR prostheses. Both cases were related to device malpositioning: 1 was caused by high implantation of an Edwards-Sapien S3 23-mm valve, causing moderate paravalvular leak (PVL) and the second to a high implantation of a CoreValve 29-mm device.

There were 2 cases of TAVR interference with the mitral prosthesis. In 1 case, embolization in ascending aorta of a CoreValve 29-mm device, which was released in a high

position because of low mitroaortic distance (4.6 mm), required full valve retrieval and repositioning. In the other case, impingement with the mobile elements of a mechanical mitral prosthesis of a Portico 27-mm device was resolved with full valve retrieval and repositioning, achieving complete restoration of normal mitral tilting disk excursion. This patient had a very low mitroaortic distance (2 mm). In addition, we recorded 5 (3.3%) cases of partial aortic prosthesis retrieval, all related to low implant of TAVR prostheses. No cases of surgical conversion were observed.

In-hospital and 30-day endpoint adverse outcomes for the 153 patients who survived included 4 (2.6%) cerebrovascular accidents (1 transient ischemic attack and 3 strokes) and 10 (6.5%) major vascular complications (in 6 patients associated with major bleeding and in 2 patients complicated with fatal bleeding). Overall, 22 (14.4%) patients had severe bleeding, 2 resulting in patient death (see above), and 1 causing hypovolemic shock due to bleeding from the abdominal rectus muscle. Antithrombotic regimens after TAVR were available for 124 patients (81.0%); the majority of patients received OAC (51 of 124; 41.1%), OAC plus SAPT (47 of 124; 37.9%), or dual antiplatelet therapy (DAPT) (11 of 124; 8.9%). Of the 2 patients with available data regarding antithrombotic treatment who had fatal or life-threatening bleeding, 1 was on OAC plus SAPT and the other on OAC plus DAPT.

The only myocardial infarction recorded (0.7%) occurred in a patient with previously known coronary artery disease complicated by a major bleeding, subsequently resulting in in-hospital death. At 30-day follow-up, a total of 5 (3.2%) in-hospital deaths were observed; all events were cardiovascular or procedure related. No differences were recorded in VARC-2-defined success according to the TAVR access route ($P = 0.781$), between BE or SE valves ($P = 0.709$), between first- or second-generation TAVR devices ($P = 0.665$), or between mechanical or biologic surgical MV prostheses ($P = 0.861$).

New permanent pacemaker (PMM) implantation was required in 13 patients (11.6% of 112 patients without previously implanted PPM), new-onset left bundle branch block (LBBB) occurred in 22 patients (16.4% of 134 without baseline LBBB) and in 8 (6.0%) patients persisted at discharge. A significant rise in creatinine from baseline was seen after TAVR (1.43 ± 0.91 vs 1.26 ± 0.64; $P = 0.001$); this rise was, however, transient, as discharge creatinine was not significantly different from baseline (1.22 ± 0.77 vs 1.26 ± 0.64; $P = 0.430$). Median hospital stay was 9 days (IQR: 7 to 14 days).

Overall, a significant reduction in aortic mean gradient (10.0 ± 7.0 vs 42.6 ± 14.2 mm Hg; $P < 0.001$) and a significant increase in AVA (1.87 ± 0.55 vs 0.72 ± 0.24 $cm^2$; $P < 0.001$), were observed. Of the 153 patients who underwent TAVR, 9 (5.9%) had at least moderate aortic regurgitation (all except 1 due to PVL), but no cases of postprocedural severe aortic regurgitation were recorded. No differences were recorded in mean aortic gradient ($P = 0.360$) or degree of aortic regurgitation ($P = 0.805$) according to the TAVR access route chosen. No differences were recorded in mean aortic gradient ($P = 0.240$) according to whether a BE or SE prosthesis was chosen. The degree of aortic regurgitation at discharge, based on a semiquantitative scale, was significantly higher in the SE devices cohort ($P = 0.006$). However, no significant difference was found in the proportion of patients with more than mild aortic regurgitation between the BE or SE cohorts (6.8% vs 5.3%; $P = 0.967$). Compared with baseline, there was no statistically significant difference in terms of mitral ($P = 0.590$) regurgitation, but there was a tendency toward tricuspid regurgitation reduction ($P = 0.056$) after TAVR. No cases of MV stenosis or dysfunction caused by interference of the implanted aortic prosthesis were reported before discharge. These results are summarized in Figure 4 and Table 3.

At univariate analysis, significant predictors of 30-day device failure were MV prosthesis size, TAVR device size, and CT mean aortic annular perimeter. After adjustment at multivariate analysis, none of these factors was significantly associated with study outcome (Supplemental Table S1).

Observed clinical outcomes were comparable with those of similar real-world TAVR studies (Table 4). In addition to all-comers real-word experiences,[13,14] we compared our experience with studies limited to patients with previous nonvalvular cardiac surgery[15] and to female patients[16] to better match our registry population clinical profile.

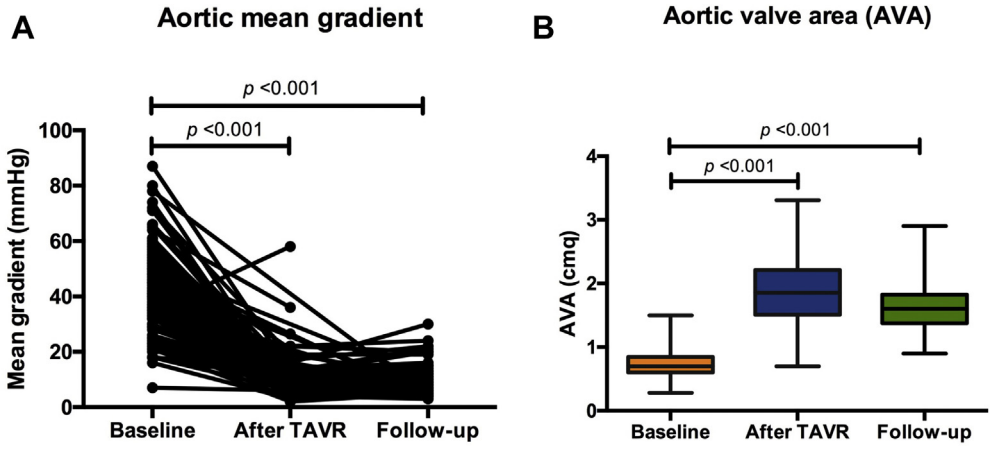


**Figure 4.** TAVR performance at follow-up. Mean aortic gradient (**A**) and AVA (**B**): the favourable hemodynamic profile after TAVR was maintained at long-term follow-up.

**Table 3.** Study endpoints, clinical efficacy, and safety outcomes

| | |
|---|---|
| Study endpoints | |
| VARC-2 Device success, n (%) | 133 (86.3%) |
| Procedural death, n (%) | 1 (0.6%) |
| Second valve implanted, n (%) | 2 (1.3%) |
| Valve embolization, n (%) | 1 (0.6%) |
| Mean aortic gradient ≥ 20 mm Hg, n (%) | 8 (5.2%) |
| Aortic regurgitation ≥ moderate, n (%) | 9 (5.8%) |
| Procedure success, n (%) | 150 (97.4%) |
| In-hospital outcomes | |
| 30-day/in-hospital death, n (%) | 5 (3.2%) |
| Cerebrovascular accident, n (%) | 4 (2.6%) |
| Major vascular complication, n (%) | 10 (6.6%) |
| Bleeding,n (%) | 22 (14.4%) |
| Major bleeding, n (%) | 20 (13.1%) |
| Life-threatening bleeding, n (%) | 1 (0.7%) |
| Fatal bleeding, n (%) | 2 (1.3%) |
| Myocardial infarction, n (%) | 1 (0.7%) |
| In-hospital death, n (%) | 5 (3.3%) |
| PM implantation, n (%) | 13/112 (11.6%) |
| New-onset LBBB, n (%) | 22/134 (16.4%) |
| Median in-hospital stay (days) | 9 (7-14) |
| Periprocedural outcomes | |
| Second valve implanted, n (%) | 2 (1.3%) |
| Partial retrieval, n (%) | 5 (3.3%) |
| Full retrieval, n (%) | 2 (1.3%) |
| Mitral prosthesis impingement, n (%) | 2 (1.4%) |
| TAVR embolization, n (%) | 1 (0.7%) |
| Procedure duration (min) | 73.7 ± 50.2 |
| Contrast medium volume (mL) | 143.7 ± 74.0 |
| Follow-up outcomes | |
| Median (IQR) follow-up length (months) | 13.5 (1.0-36.0) |
| Death, n (%) | 26 (16.9%) |
| Cardiac death, n (%) | 15 (9.7%) |
| Hospitalization due to heart failure, n (%) | 25 (16.2%) |

IQR, interquartile range; LBBB, left bundle branch block; PM, pacemaker; TAVR, transcatheter aortic valve replacement; VARC-2, Valve Academic Research Consortium-2.

### Late outcomes

The median clinical follow-up was 13.5 (IQR: 1.0 to 36.0) months. A total of 26 (16.9%) deaths occurred, and the median time to death was 19.0 (IQR: 11.0 to 49.8) months. Fifteen (9.7%) deaths were cardiac related; of note, 2 cases were related to fatal mitral prosthesis thrombosis (in 1 case, the patient autonomously dropped anticoagulant therapy after receiving a diagnosis of malignancy). Overall, no significant variation was noted in mean MV prostheses gradients after TAVR (6.5 ± 2.8 vs 6.6 ± 2.7 mm Hg; $P = 0.333$). At follow-up, we recorded a single case of fatal hemorrhagic stroke due to intracranial bleeding. There were no new cases of myocardial infarction. Rehospitalization due to worsening heart failure was observed in 25 (16.2%) patients. The population showed an overall improvement in heart failure symptoms, with a mean New York Heart Association (NYHA) class at follow-up of 2.1 ± 0.8 vs 3.0 ± 0.6 ($P < 0.001$). These results are summarized in Table 3.

Echocardiographic evaluation at follow-up demonstrated improvement in LVEF from 46.4 ± 17.0 to 51.9 ± 10.8% ($P < 0.001$), mean aortic gradient from 44.5 ± 14.3 to 9.5 ± 5.0 mm Hg ($P < 0.001$) and mean AVA from 0.70 ± 0.21 to 1.71 ± 0.43 $cm^2$ ($P < 0.001$) (Fig. 4). Of note, no significant differences between mean aortic gradient and mean AVA were observed between hospital discharge and follow-up ($P$ = ns for all).

## Discussion

Several aspects of performing TAVR in the setting of previously implanted mitral prostheses raise specific safety and efficacy concerns. Possible pitfalls include higher risk of bleeding due to concomitant anticoagulation therapy for MV prostheses, risk of interference of TAVR valve with MV prosthesis stent or mobile elements and *vice versa*, choice of ideal access route for TAVR deployment, choices between BE or SE TAVR devices, and choices between older vs newer retrievable/repositionable devices.

In this study, we report on 154 cases performed across high-volume centres in real-world settings. The high rate of procedural success observed in our paper (97.4%) supports the notion of the feasibility of TAVR in this specific subset of patients.

Recently, Amat-Santos et al. compared TAVR outcomes in patients with (n = 91) or without (n = 2323) previous MV prostheses,[6] reporting procedural success rate (98.6%) similar to that recorded in our registry, although our device success rate was somewhat higher (86.3% vs 72.2%). Clinical characteristics of our study population are in line with that of Amat-Santos et al.: relatively young patients, a clear female prevalence, and a wider proportion of mechanical MV prostheses. In both studies, TAVR was performed after approximately 12 to 14 years from MV surgery. The rates of periprocedural complications are similar in both studies: major bleeding 13.1% vs 15.4%; periprocedural stroke/transient ischemic attack 2.6% vs 2.5%; periprocedural myocardial infarction 0.7% vs 0.0%; and in-hospital death 3.2% vs 5.5% in our experience vs Amat-Santos et al., respectively. The observation that 2 out of 3 patients with fatal or life-threatening complications were on combined OAC and antiplatelet therapy is hypothesis generating and raises the question of optimal antithrombotic regimens after TAVR in this setting. Although the presence of mechanical prostheses mandates OAC, addition of antiplatelet drugs may be associated with excess bleeding. Further studies are warranted to define the best antithrombotic treatment in such patients.

In this study, the access route and the choice between BE and SE valve was left to physician discretion; therefore, we included a variety of different accesses and TAVR devices. Overall, no significant differences were found in terms of TAVR hemodynamics and safety outcomes comparing different access routes, BE vs SE devices, and first- vs second-generation valves. Of note, there was a higher proportion of BE valves implanted in the cohort of patients with biologic mitral prostheses. This may reflect the preference for a device with lower stent height to avoid interference with the biologic MV prostheses, which usually have higher commissural stent struts profiles.

TAVR requiring repositioning or retrieval was observed in 7 (4.6%) patients. In 1 case of interference of the TAVR device with the MV prosthesis, multiple retrievals were necessary to restore a normal MV valve function and a proper TAVR positioning. It is conceivable that new, repositionable, or completely retrievable devices could be particularly suitable for this particular clinical setting.

Compared with Amat-Santos et al., we observed a substantially lower rate of TAVR device embolization (0.7% vs 6.7%). The only case recorded was in a patient with a biologic mitral prosthesis at a very low mitroaortic distance (4.6 mm),

**Table 4.** Comparison of study outcomes with other real-world clinical TAVR experiences

| | OPTIMAL study N = 154 | Reino et al. (2016)[15] N = 4194 | WIN-TAVI registry[16] N = 1019 | GARY registry[13] N = 15964 | TVT registry[14] N = 26414 |
|---|---|---|---|---|---|
| Baseline characteristics | | | | | |
| Age, years | 77.2 ± 8.6 | 79 ± 6 | 82.5 ± 6.3 | 80.9 ± 6.1 | 82 |
| Female patients, % | 79.9 | 27 | 100 | 54.1 | 49.5 |
| Logistic EuroScore, % | 26.4 ± 15.8 | 33.1 | - | 18.3 (11.0-30.5) | - |
| STS mortality score, % | 8.7 ± 8.0 | - | 8.3 ± 7.4 | 5.0 (3.4-7.7) | 6.5 |
| Previous CABG, % | 18.2 | 100 | 6.2 | - | 31.4 |
| COPD, % | 19.5 | 14 | 18.5 | 14.2 | - |
| Atrial fibrillation, % | 68.2 | 42 | 19.6 | - | 40.8 |
| Study endpoints | | | | | |
| VARC-2 Device success, % | 86.3 | - | 86.0 | - | 92.7 |
| Second valve implanted, % | 1.3 | - | 1.7 | - | - |
| Valve embolization , % | 0.6 | - | 1.1 | - | 0.6 |
| Aortic regurgitation ≥ 2, % | 5.8 | - | 14.1 | 5.2 | 5.1 |
| Procedure success, % | 97.4 | - | - | - | 97.3 |
| Early outcomes | | | | | |
| 30-day/in-hospital death, % | 3.2 | 7.6 | 3.4 | 5.2 | 5.7 |
| Cerebrovascular accident, % | 2.6 | 2.1 | 1.3 | 1.2 | 2.2 |
| Major vascular complication, % | 6.6 | - | 7.7 | 4.1 | 4.9 |
| Bleeding, % | 14.4 | 7.3 | - | - | - |
| Major bleeding, % | 13.1 | - | - | 26.3 | 4.9 |
| Life-threatening bleeding, % | 0.7 | - | 4.4 | - | 5.4 |
| Fatal bleeding, % | 1.3 | 2.4 | - | - | - |
| Myocardial infarction, % | 0.7 | - | 0.2 | - | 0.5 |
| In-hospital death, % | 3.3 | - | - | - | 4.9 |
| PM implantation, % | 11.6 | 15.3 | 11.6 | 17.5 | 10.0 |
| New-onset LBBB, % | 16.4 | - | 10.1 | - | - |
| Median in-hospital stay (days) | 9 (7-14) | 17 ± 12 | 11.8 ± 8.0 | - | - |

CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; IQR, interquartile range; LBBB, left bundle branch block; PM, pacemaker; STS, Society of Thoracic Surgeons; TAVR, transcatheter aortic valve replacement; VARC-2, Valve Academic Research Consortium-2.

where the TAVR valve was released in a high position to avoid interference with the MV prosthesis.

A safe mitroaortic distance cut-off of 7 to 8 mm has traditionally been proposed to identify high-risk anatomies. Of note, in the experience of Amat-Santos et al., all patients with TAVR embolization had CT-measured mitroaortic distances < 7 mm.

Although our work supports this notion—as the cases of interference between TAVR device and MV prosthesis were observed in patients with very narrow mitroaortic distance—it is noteworthy that the TAVR procedure was nonetheless safe and feasible in other patients with low or very low mitroaortic distances, given a careful preprocedural assessment. In patients with mitroaortic distances < 7 mm, implantation of BE or SE devices performed equally. However, interference or embolization during deployment were observed only in patients with SE devices; it is conceivable that the lower stent profile of BE valves might be preferred to reduce the risk of interference with MV prostheses in very low mitroaortic distances.

Taken together, these findings highlight the role of preprocedural CT imaging for intervention planning and risk stratification.

Finally, safety and efficacy of TAVR procedures in the population of patients with previous MV prostheses were confirmed; at follow-up, the good hemodynamic performance of TAVR devices was maintained, and no cases of TAVR-related MV dysfunction were observed.

## Limitations

The main limitation of this study is its retrospective design and the lack of a control group. Moreover, there are substantial missing data regarding preprocedural CT studies, and antithrombotic regimen details were not available. In addition, despite being the largest group of patients treated with TAVR in the setting of previous MV prostheses in the literature to date, larger numbers are needed to draw definitive conclusions about the safety and efficacy of TAVR in this setting.

## Conclusions

In summary, our experience confirms the feasibility of TAVR in patients with previously implanted MV prostheses. This was demonstrated throughout a wide range of TAVR devices and MV prostheses. The procedure appears safe; however, more caution is needed in cases with very narrow mitroaortic distances, given the possibility of TAVR interference with the MV prostheses and *vice versa*.

## Disclosures

The authors have no conflicts of interest to disclose.

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## Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi/org/10.1016/j.cjca.2019.03.028.