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ORIGINAL RESEARCH

# Transcatheter Aortic Valve Replacement With Self-Expandable Supra-Annular Valves for Degenerated Surgical Bioprostheses: Insights From Transcatheter Valve Therapy Registry

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**BACKGROUND:** Transcatheter aortic valve replacement with supra-annular transcatheter heart valves has been adopted in patients with degenerated surgical aortic valves. The next generation self-expanding Evolut PRO valve has not been evaluated in patients with surgical valve failure.

**METHODS AND RESULTS:** Patients undergoing transcatheter aortic valve replacement in degenerated surgical aortic valve procedures using the Evolut R or Evolut PRO transcatheter heart valves in the Society of Thoracic Surgeons and American College of Cardiology Transcatheter Valve Therapy Registry between April 2015 and June 2019 were evaluated. Transcatheter valve performance was evaluated by clinical site echocardiography. In-hospital, 30-day, and 1-year clinical outcomes were based on the Society of Thoracic Surgeons-American College of Cardiology-Transcatheter Valve Therapy registry definitions. Transcatheter aortic valve replacement in degenerated surgical aortic valve was performed in 5897 patients (5061 [85.8%] patients received the Evolut R valve and 836 [14.2%] received the Evolut PRO valve). Thirty-day transcatheter heart valves hemodynamic performance was excellent in both groups (mean gradient: Evolut PRO: 13.8±7.5 mm Hg; Evolut R: 14.5±8.1 mm Hg), while paravalvular regurgitation was significantly different between valve types ($P$=0.02). Clinical events were low at 30 days (Evolut PRO: for the all-cause mortality, 2.8%, any stroke was 1.8%, new pacemaker implantation, 3.0%: Evolut R:all-cause mortality, 2.5%, any stroke was 2.2%, new pacemaker implantation, 5.3%) and 1 year (Evolut PRO: all-cause mortality, 9.2%; any stroke, 3.1%; Evolut R: all-cause mortality, 9.8%; any stroke, 2.9%).

**CONCLUSIONS:** Transcatheter aortic valve replacement in degenerated surgical aortic valve with self-expandable supra-annular transcatheter heart valves is associated with excellent clinical outcomes and valve hemodynamics. Additional reductions in residual paravalvular regurgitation were obtained with the next generation Evolut PRO.

**Key Words:** surgical aortic valve replacement ■ transcatheter aortic valve replacement in degenerated surgical aortic valve ■ transcatheter aortic valve replacement ■ valve-in-valve

Many patients with severe aortic stenosis who have received a surgical aortic bioprosthetic valve replacement will present with structural valve degeneration at some point in their lifetime.[1,2] Reoperation for failed surgical valves in high-risk patients can carry considerable risks.[3–6] More recently,

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## CLINICAL PERSPECTIVE

### What Is New?

- This is the largest study to date assessing the safety and efficacy of Evolut R and Evolut PRO devices for transcatheter aortic valve replacement in degenerated surgical aortic valves.
- The results of this multicenter real-world experience were robust and consistent with low rates of complications and permanent pacemaker implantation.
- Furthermore, we observed excellent valve performance with a slight advantage of Evolut PRO through 1-year follow-up.

### What Are the Clinical Implications?

- Transcatheter aortic valve replacement in degenerated surgical aortic valve with self-expandable supra-annular transcatheter heart valves is associated with excellent clinical outcomes and valve hemodynamics.
- Additional reductions in residual paravalvular regurgitation were obtained with the next-generation Evolut PRO.
- Although we observed excellent overall performance of self-expandable valves at 1 year, longer follow-up periods will be warranted to determine the best treatment strategy in this setting.

### Nonstandard Abbreviations and Acronyms

| | |
|---|---|
| **EOA** | effective orifice area |
| **EOAi** | effective orifice area index |
| **PPI** | permanent pacemaker implantation |
| **PPM** | patient prosthesis mismatch |
| **PVR** | paravalvular regurgitation |
| **TAV-in-SAV** | transcatheter aortic valve replacement in degenerated surgical aortic valve |
| **TAVR** | transcatheter aortic valve replacement |
| **TVT** | Transcatheter Valve Therapy |

transcatheter aortic valve replacement (TAVR) in a degenerated surgical aortic valve (TAV-in-SAV) has emerged as a less invasive alternative to surgical reoperation for these patients.[6–8]

Early global registries showed that treating such patients by TAV-in-SAV is feasible and safe.[9] The self-expandable, recapturable Evolut R bioprosthesis (Medtronic, Minneapolis, MN) and the next-generation Evolut PRO bioprosthesis (Medtronic, Minneapolis, MN), which contains a thin pericardial wrap outside of the frame to reduce paravalvular regurgitation, deliver excellent acute valve performance because of their unique supra-annular design. These hemodynamic benefits are most pronounced in patients with smaller annulus sizes, which makes them a particularly attractive alternative to repeat surgery by using a TAV-in-SAV procedure.[10–12] While self-expandable supra-annular valves have been widely adopted for TAV-in-SAV to treat degenerated surgical bioprostheses, a comprehensive understanding of the procedural and clinical outcomes is lacking, especially with the most recent iteration of the Evolut PRO bioprosthesis.

The purpose of this study was to evaluate in-hospital, 30-day and 1-year procedural and clinical outcomes of a large current practice cohort following TAV-in-SAV with self-expandable valves and to compare echocardiographic and clinical outcomes in patients treated with Evolut PRO and Evolut R bioprostheses.

## METHODS

### TVT Registry and Study Population

The Transcatheter Valve Therapy (TVT) Registry, jointly operated and managed by the Society of Thoracic Surgeons and American College of Cardiology, includes a vast majority of patients treated with a commercially available TAVR device in the United States. We analyzed data entered in the TVT Registry from patients who underwent a TAV-in-SAV procedure using an Evolut R or Evolut PRO valve between April 2015 and June 2019. The Chesapeake Research Review Incorporated, a central institutional review board, reviews and approves the activity of the TVT Registry and has waived patient informed consent for analyses of TVT Registry data. The authors requested data analyses from Medtronic, who has obtained Medtronic TAVR product-specific data from the TVT Registry. The raw data and statistical codes are controlled by Medtronic and will not be shared for purposes of reproducing the results or replicating the procedure. The authors and F.L. had full access to the data, and F.L. performed all statistical analyses.

### Study End Points and Definitions

We evaluated clinical outcomes at 30 days and 1 year including all-cause mortality, the rate of stroke, major vascular complications, major bleeding, reinterventions, and permanent pacemaker implantation (PPI). Transcatheter device success was defined according to the original Valve Academic Research Consortium.[13]

Site-reported echocardiographic measures were recorded postprocedure, at 30 days and 1 year,

including mean aortic valve gradient, total aortic regurgitation (AR), and the presence and severity of paravalvular regurgitation (PVR). Effective orifice area (EOA) was only available at baseline and postprocedure. For the present analysis, patient prosthesis mismatch (PPM) based on the effective orifice area index (EOAi) was determined for each patient using the Valve Academic Research Consortium II definition.[14] For patients with body mass index <30, severe PPM was defined as EOAi ≤ 0.65 $cm^2/m^2$, moderate PPM as 0.65 $cm^2/m^2$ ≤ EOAi ≤ 0.85 $cm^2/m^2$, and no PPM was EOAi > 0.85 $cm^2/m^2$. For patients with body mass index ≥30, severe PPM was defined as EOAi < 0.60 $cm^2/m^2$, moderate PPM as 0.60 $cm^2/m^2$ ≤ EOAi ≤ 0.70 $cm^2/m^2$, and no PPM as EOAi > 0.70 $cm^2/m^2$.

## Statistical Analysis

For this post hoc analysis, patients were stratified according to use of the Evolut R and Evolut PRO valves in TAV-in-SAV procedures. Data are reported for all patients and separately by valve type (Evolut R or Evolut PRO). Categorical variables are summarized as numbers and percentages and compared using the $\chi^2$ test or Fisher exact test for nominal categorical variables and using Cochran–Mantel–Haenszel test with the use of modified ridit scores for ordinal variables. Continuous variables are summarized as mean±SD, median, minimum, maximum, and first and third quartiles (Q1, Q3). Clinical outcomes are reported as Kaplan–Meier estimates in time-to-event analyses and compared with the log-rank test. When estimating the Kaplan–Meier rates of each 30-day and 1-year outcomes, patients without an event were censored at last known date of follow-up, including death where the event is not known. Comparison between groups was performed using 2-sample Student *t* test if distributions were approximately normal or Wilcoxon rank-sum test otherwise. All *P* values reported are 2-sided, with $P<0.05$ considered to indicate statistical significance. No adjustments for multiple comparisons were made. All statistical analyses were performed with the use of SAS, version 9.4 (SAS Institute, Cary, NC).

# RESULTS

The TAV-in-SAV procedure was performed in 5897 patients; the Evolut R valve was implanted in 5061 (85.8%) patients and the Evolut PRO valve was implanted in 836 (14.2%) patients. Baseline characteristics are shown in Table 1. Overall, patients were mostly male (58.7%) and had a mean age of 75.1±10.5 years. The mean Society of Thoracic Surgery Predicted Risk of Mortality score was 7.7±6.6%, and most patients were in New York Heart Association functional class III or IV (80.3%). The most prominent comorbidities were hypertension (89.4%) and chronic obstructive pulmonary disease (44.1%).

Procedural data are shown in Table 2. The valves were successfully implanted in 98.4% of patients and 49.2% of patients received a 23 mm valve. Most

**Table 1. Demographics and Baseline Characteristics**

| Characteristics | All patients (N=5897) | Evolut R (N=5061) | Evolut PRO (N=836) | *P* value (EVR vs PRO) |
|---|---|---|---|---|
| Age, y | 75.1±10.5 | 75.2±10.5 | 74.6±10.3 | 0.110 |
| BSA, $m^2$ | 1.92±0.25 | 1.91±0.25 | 1.93±0.27 | 0.041 |
| Male | 3462 (58.7) | 2974 (58.8) | 488 (58.4) | 0.832 |
| STS-PROM, % | 7.7±6.6 | 7.7±6.5 | 7.2±7.1 | 0.074 |
| Diabetes | 2012/5888 (34.2) | 1743/5055 (34.5) | 269/833 (32.3) | 0.217 |
| History of hypertension | 5270/5894 (89.4) | 4518/5058 (89.3) | 752/836 (90.0) | 0.584 |
| Peripheral vascular disease | 1589/5890 (27.0) | 1380/5056 (27.3) | 209/834 (25.1) | 0.178 |
| Previous stroke | 756/5894 (12.8) | 657/5059 (13.0) | 99/835 (11.9) | 0.365 |
| Previous TIA | 480/5885 (8.2) | 423/5053 (8.4) | 57/832 (6.9) | 0.138 |
| Chronic lung disease/COPD | 2584/5861 (44.1) | 2213/5031 (44.0) | 371/830 (44.7) | 0.702 |
| Previous MI | 1214/5879 (20.6) | 1067/5046 (21.1) | 147/833 (17.6) | 0.021 |
| NYHA | | | | 0.717 |
| I | 109/5853 (1.9) | 89/5022 (1.8) | 20/831 (2.4) | |
| II | 1044/5853 (17.8) | 895/5022 (17.8) | 149/831 (17.9) | |
| III | 3392/5853 (58.0) | 2928/5022 (58.3) | 464/831 (55.8) | |
| IV | 1308/5853 (22.3) | 1110/5022 (22.1) | 198/831 (23.8) | |
| III/IV | 4700/5853 (80.3) | 4038/5022 (80.4) | 662/831 (79.7) | 0.618 |

Data are presented as mean±SD or no./total no. (percentage). BSA indicates body surface area; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; NYHA, New York Heart Association; STS-PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; and TIA, transient ischemic attack.

**Table 2. Procedural Characteristics**

| | All patients (N=5897) | Evolut R (N=5061) | Evolut PRO (N=836) | *P* value (EVR vs PRO) |
|---|---|---|---|---|
| Hybrid cath lab or cath lab | 2404/5894 (40.8) | 2090/5059 (41.4) | 314/835 (37.6) | 0.043 |
| General anesthesia | 3468/5883 (58.9) | 3022/5049 (59.9) | 446/834 (53.5) | <0.001 |
| Femoral/iliac | 5602/5895 (95.0) | 4806/5061 (95.0) | 796/834 (95.4) | 0.553 |
| Device implanted successfully | 5778/5873 (98.4) | 4959/5039 (98.4) | 819/834 (98.2) | 0.655 |
| Device success | 5411/5839 (92.7) | 4643/5006 (92.7) | 768/833 (92.2) | 0.572 |
| Procedure time, min | 110.2±57.6 | 110.1±57.5 | 110.7±58.5 | 0.775 |
| Valve size implanted | | | | |
| 23 mm | 2871/5830 (49.2) | 2534/5002 (50.7) | 337/828 (40.7) | <0.001 |
| 26 mm | 1985/5830 (34.0) | 1671/5002 (33.4) | 314/828 (37.9) | 0.011 |
| 29 mm | 808/5830 (13.9) | 631/5002 (12.6) | 177/828 (21.4) | <0.001 |
| 34 mm | 166/5830 (2.8) | 166/5002 (3.3) | 0/828 (0.0) | <0.001 |
| Length of hospital stay postprocedure, d | 2 (1.0, 3.0) | 2 (1.0, 4.0) | 2 (1.0, 3.0) | <0.001 |
| Discharge alive | 5791/5897 (98.2) | 4974/5061 (98.3) | 817/836 (97.7) | 0.264 |
| Home discharge | 5135/5790 (88.7) | 4409/4973 (88.7) | 726/817 (88.9) | 0.865 |

Data presented as no./total no. (percentage) or mean±SD or median (Q1, Q3).

procedures were transfemoral (95%) and performed with patients under general anesthesia (58.9%). The median total length of stay after the procedure was 2.0 (Q1, Q3; 1.0, 3.0) days, and 98.2% patients left the hospital alive with 88.7% being discharged home.

In-hospital mortality was 1.8%. Patients had low rates of coronary obstruction (0.5%) and myocardial infarction (0.3%). Major vascular complications were rarely observed (1.1%). Importantly, only 4.2% of the patients required a new permanent pacemaker/implantable cardioverter defibrillator implantation during hospitalization (Table 3). At 30 days, the rate of all-cause mortality was 2.5%, while stroke was observed in 2.2% of the patients.

Echocardiographic findings through 1 year are shown in Table 4. Importantly, low gradients and low rates of moderate/severe total AR and PVR were observed postprocedure and sustained at 30 days and 1 year (Table 4, Figure).

## Evolut PRO versus Evolut R

We also performed a subanalysis comparing Evolut PRO versus Evolut R. Moderate and severe PPM postprocedure were comparable between groups and observed in 25.3% and 28.3% of patients in the Evolut PRO group and in 24.7% and 31.4% of patients in the Evolut R group, respectively (*P*=0.11). Clinical outcomes for the combined cohort of patients receiving the Evolut R and Evolut PRO devices stratified by postprocedural moderate and severe PPM are shown in Table S1. There were no significant differences between all-cause mortality or rehospitalization in patients with no PPM and those with moderate PPM or severe PPM through 1 year (Table S1).

There were no significant differences in all-cause mortality (2.8% versus 2.5%, *P*=0.52), stroke (1.8% versus 2.2%, *P*=0.48), aortic valve re-intervention (0.1% versus 0.6%, *P*=0.10), and valve-related readmissions (0.2% versus 0.4%, *P*=0.47) for patients with the Evolut PRO versus the Evolut R valve, respectively, at 30 days. Rates of new PPI/implantable cardioverter defibrillator implantation (3.0% versus 5.3%, *P*=0.01) were lower in patients who received Evolut PRO compared with Evolut R valves at 30 days and these differences were sustained at 1-year follow-up (Table 3).

The mean gradient across the aortic valve was significantly lower at 30 days and 1 year in those implanted with the Evolut PRO valve compared with the Evolut R valve. Likewise, total AR and PVR were also less frequently observed in those implanted with the Evolut PRO at postprocedure and 30 days (Table 4, Figure). Clinical and echocardiographic findings comparing Evolut PRO and Evolut R valves by valve size are shown in Tables S2, S3, and S4.

# DISCUSSION

This study is the largest analysis to date evaluating the utilization of self-expandable supra-annular valves for TAV-in-SAV to provide a better understanding of their safety and efficacy profile as they emerge as a less invasive option compared with re-do surgical aortic valve replacement. Importantly, we studied patients from a large nationwide database, which minimizes selection bias and ultimately delivers a more comprehensive

**Table 3. Clinical Outcomes for All Patients and by Valve Type Over Time**

| Events | All patients (N=5897) | Evolut R (N=5061) | Evolut PRO (N=836) | *P* value (EVR vs PRO) |
|---|---|---|---|---|
| In-hospital | | | | |
| All-cause mortality | 106 (1.8) | 87 (1.7) | 19 (2.3) | 0.264 |
| Any stroke | 109 (1.8) | 95 (1.9) | 14 (1.7) | 0.687 |
| Myocardial infarction | 16 (0.3) | 12 (0.2) | 4 (0.5) | 0.268 |
| Endocarditis | 0 (0.0) | 0 (0.0) | 0 (0) | NA |
| Major or life-threatening bleeding event | 317 (5.4) | 269 (5.3) | 48 (5.7) | 0.613 |
| Major vascular complication | 63 (1.1) | 51 (1.0) | 12 (1.4) | 0.265 |
| Pacemaker or ICD* | 206 (3.5) | 189 (3.7) | 17 (2.0) | 0.013 |
| Pacemaker or ICD† | 200 (4.2) | 183 (4.5) | 17 (2.5) | 0.012 |
| Aortic valve re-intervention | 21 (0.4) | 20 (0.4) | 1 (0.1) | 0.347 |
| 30-D | | | | |
| All-cause mortality | 145 (2.5) | 122 (2.5) | 23 (2.8) | 0.524 |
| Any stroke | 126 (2.2) | 111 (2.2) | 15 (1.8) | 0.481 |
| Myocardial infarction | 19 (0.3) | 14 (0.3) | 5 (0.6) | 0.126 |
| Endocarditis | 2 (0.0) | 1 (0.0) | 1 (0.1) | 0.138 |
| Major or life-threatening bleeding event | 343 (5.9) | 294 (5.9) | 49 (5.9) | 0.909 |
| Major vascular complication | 69 (1.2) | 56 (1.1) | 13 (1.6) | 0.259 |
| Pacemaker or ICD* | 237 (4.1) | 217 (4.4) | 20 (2.5) | 0.011 |
| Pacemaker or ICD† | 229 (4.9) | 209 (5.3) | 20 (3.0) | 0.010 |
| Aortic valve re-intervention | 29 (0.5) | 28 (0.6) | 1 (0.1) | 0.101 |
| Valve related readmission | 23 (0.4) | 21 (0.4) | 2 (0.2) | 0.467 |
| Non-valve-related readmission | 351 (6.2) | 318 (6.6) | 33 (4.2) | 0.012 |
| 1-Y | | | | |
| All-cause mortality | 412 (9.7) | 361 (9.8) | 51 (9.2) | 0.974 |
| Any stroke | 154 (2.9) | 134 (2.9) | 20 (3.1) | 0.819 |
| Myocardial infarction | 40 (0.9) | 30 (0.8) | 10 (1.8) | 0.020 |
| Endocarditis | 17 (0.5) | 14 (0.4) | 3 (0.7) | 0.455 |
| Major or life-threatening bleeding event | 389 (7.1) | 336 (7.2) | 53 (6.8) | 0.922 |
| Major vascular complication | 70 (1.2) | 57 (1.1) | 13 (1.6) | 0.281 |
| Pacemaker or ICD* | 301 (5.9) | 276 (6.2) | 25 (3.8) | 0.007 |
| Pacemaker or ICD† | 287 (7.0) | 262 (7.4) | 25 (4.5) | 0.007 |
| Aortic valve re-intervention | 51 (1.1) | 48 (1.2) | 3 (0.6) | 0.133 |
| Valve-related readmission | 87 (2.2) | 79 (2.3) | 8 (1.8) | 0.404 |
| Non-valve-related readmission | 994 (24.2) | 893 (24.7) | 101 (20.8) | 0.026 |

In-hospital data presented as no. of patients with event (proportion of subjects with events as percentage). Thirty-day and 1-year data presented as no. of patients with an event (Kaplan–Meier estimates as percentage). ICD indicates implantable cardioverter defibrillator.

*Subjects with pacemaker or ICD at baseline are included.

†Subjects with pacemaker or ICD at baseline are not included.

understanding of current practice. The key findings of this study were as follows: (1) Low mortality and stroke rates after TAV-in-SAV for both valve types through 1 year; (2) Low pacemaker rates with significantly lower rates in Evolut PRO compared with Evolut R group; (3) Favorable hemodynamics after TAV-in-SAV for both valve types, with Evolut PRO valves delivering statistically lower gradients compared with the Evolut R valves through 1 year; and (4) Low rates of moderate or severe PVR were observed for both valves with an advantage of Evolut PRO in the initial 30 days. Despite favorable performance of both Evolut PRO and R groups in terms of clinical and echocardiographic parameters, >50% of patients in both groups exhibited some degree of PPM postprocedure.

We observed high rates of device implantation success (98.4%) and low mortality at 30 days and 1 year that were comparable to rates reported in prior

**Table 4. Echocardiographic Measures for All Patients and by Valve Type Over Time**

| Measurement | All Patients (N=5897) | Evolut R (N=5061) | Evolut PRO (N=836) | *P* value (EVR vs PRO) |
|---|---|---|---|---|
| Postprocedure | | | | |
| Mean gradient, mm Hg | 15.4±9.0 (5269) | 15.5±9.1 (4487) | 14.9±8.4 (782) | 0.058 |
| Effective orifice area, $cm^2$ | 1.5±0.6 (4292) | 1.5±0.6 (3626) | 1.6±0.6 (666) | 0.022 |
| Total aortic regurgitation | | | | 0.002 |
| None/trace | 4327/5287 (81.8) | 3670/4510 (81.4) | 657/777 (84.6) | |
| Mild | 838/5287 (15.9) | 725/4510 (16.1) | 113/777 (14.5) | |
| Moderate | 115/5287 (2.2) | 108/4510 (2.4) | 7/777 (0.9) | |
| Severe | 7/5287 (0.1) | 7/4510 (0.2) | 0/777 (0.0) | |
| Moderate/severe | 122/5287 (2.3) | 115/4510 (2.5) | 7/777 (0.9) | 0.005 |
| Paravalvular regurgitation | | | | 0.003 |
| None | 3905/4848 (80.5) | 3298/4130 (79.9) | 607/718 (84.5) | |
| Mild | 844/4848 (17.4) | 740/4130 (17.9) | 104/718 (14.5) | |
| Moderate | 90/4848 (1.9) | 84/4130 (2.0) | 6/718 (0.8) | |
| Severe | 9/4848 (0.2) | 8/4130 (0.2) | 1/718 (0.1) | |
| Moderate/severe | 99/4848 (2.0) | 92/4130 (2.2) | 7/718 (1.0) | 0.029 |
| 30-D | | | | |
| Mean gradient, mm Hg | 14.4±8.0 (4245) | 14.5±8.1 (3605) | 13.8±7.5 (640) | 0.037 |
| Total aortic regurgitation | | | | 0.005 |
| None/trace | 3392/4256 (79.7) | 2869/3620 (79.3) | 523/636 (82.2) | |
| Mild | 757/4256 (17.8) | 653/3620 (18.0) | 104/636 (16.4) | |
| Moderate | 98/4256 (2.3) | 90/3620 (2.5) | 8/636 (1.3) | |
| Severe | 9/4256 (0.2) | 8/3620 (0.2) | 1/636 (0.2) | |
| Moderate/severe | 107/4256 (2.5) | 98/3620 (2.7) | 9/636 (1.4) | 0.055 |
| Paravalvular regurgitation | | | | 0.024 |
| None | 3115/3909 (79.7) | 2625/3319 (79.1) | 490/590 (83.1) | |
| Mild | 714/3909 (18.3) | 621/3319 (18.7) | 93/590 (15.8) | |
| Moderate | 72/3909 (1.8) | 67/3319 (2.0) | 5/590 (0.8) | |
| Severe | 8/3909 (0.2) | 6/3319 (0.2) | 2/590 (0.3) | |
| Moderate/severe | 80/3909 (2.0) | 73/3319 (2.2) | 7/590 (1.2) | 0.109 |
| 1-Y | | | | |
| Mean gradient, mm Hg | 14.2±8.5 (2321) | 14.3±8.6 (2044) | 13.2±7.7 (277) | 0.023 |
| Total aortic regurgitation | | | | 0.511 |
| None/trace | 1933/2342 (82.5) | 1698/2059 (82.5) | 235/283 (83.0) | |
| Mild | 355/2342 (15.2) | 311/2059 (15.1) | 44/283 (15.5) | |
| Moderate | 49/2342 (2.1) | 46/2059 (2.2) | 3/283 (1.1) | |
| Severe | 5/2342 (0.2) | 4/2059 (0.2) | 1/283 (0.4) | |
| Moderate/severe | 54/2342 (2.3) | 50/2059 (2.4) | 4/283 (1.4) | 0.397 |
| Paravalvular regurgitation | | | | 0.598 |
| None | 1831/2164 (84.6) | 1610/1906 (84.5) | 221/258 (85.7) | |
| Mild | 295/2164 (13.6) | 261/1906 (13.7) | 34/258 (13.2) | |
| Moderate | 35/2164 (1.6) | 33/1906 (1.7) | 2/258 (0.8) | |
| Severe | 3/2164 (0.1) | 2/1906 (0.1) | 1/258 (0.4) | |
| Moderate/severe | 38/2164 (1.8) | 35/1906 (1.8) | 3/258 (1.2) | 0.615 |

Values are mean±SD (n) and no./total no. (percentage). *P* values are comparing Evolut R and Evolut PRO

low- and intermediate-risk patient TAVR studies in native valves,[11,15–18] and comparable with the results reported in previous TAV-in-SAV studies.[6,9,19–21] Furthermore, low stroke and major vascular complication rates in our study demonstrate the overall favorable safety profile of TAV-in-SAV with either Evolut PRO or Evolut R valves.

The risk for coronary occlusion poses a potential concern for TAV-in-SAV[22]; however, coronary

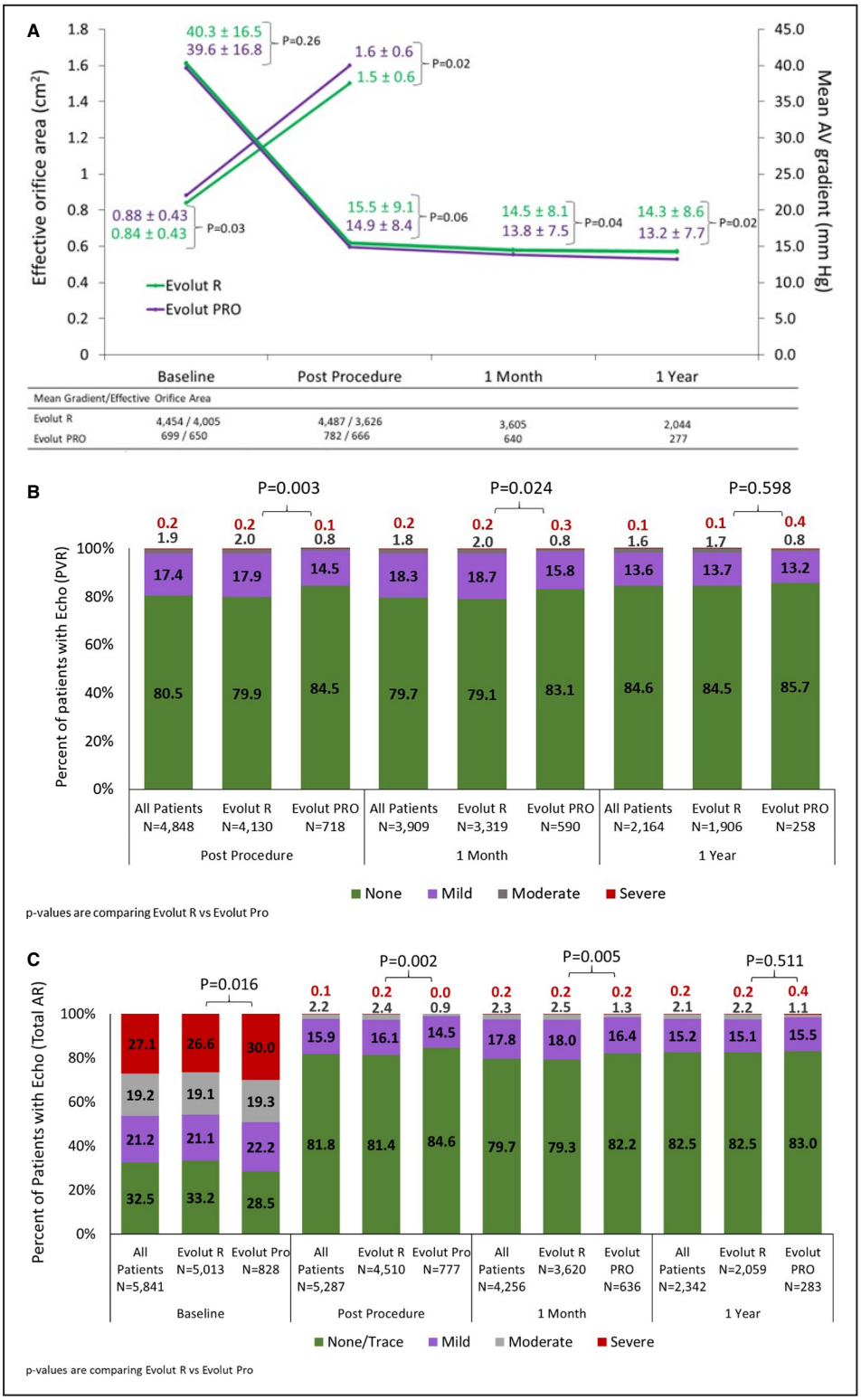


**Figure. Hemodynamic measures at baseline, postprocedure, 30-d, and 1-y follow-up by valve type.**

**A**, Mean aortic gradient and effective orifice area over time. Effective orifice area is not collected beyond postprocedure in the TVT Registry. Paravalvular regurgitation is not collected at baseline in the TVT Registry. Values represent no. of patients with nonmissing values. *P* values are comparing Evolut R vs Evolut Pro. **B**, PVR over time. **C**, Total aortic regurgitation measurements. AV indicates aortic valve; PVR, paravalvular regurgitation; and TVT, Transcatheter Valve Therapy.

occlusion was low (0.5%) in our study. Because of inherent limitations of the TVT Registry data, we have no available information on the percentage of coronary artery protection and stents deployed during the procedure or on the utilization of intentional bioprosthetic leaflet laceration to prevent iatrogenic coronary artery obstruction[23] before TAV-in-SAV. However, the low rates of procedural-related myocardial infarction (0.3%) are reassuring about the safety profile in this setting. In addition, the ability to recapture the valve during the procedure may deliver additional safety in this scenario and further aids in preventing coronary obstruction.[24,25] The low rates of myocardial infarction and coronary occlusion may have been because of operator experience and carefully detailed preprocedural planning based on the combination of findings from the computed tomography angiogram and cinecoronariography.[26,27] In addition, we do not have information on how many patients were considered for TAV-in-SAV but were declined by the local team because of prohibitive anatomy that would increase potential for coronary obstruction.

The median length of stay after the procedure was 2 days, and most patients were discharged home. Most of the TAV-in-SAV cases in this analysis were performed with patients under general anesthesia, but the number of procedures done with patients under conscious sedation is increasing worldwide, which ultimately may lead to reduction in length of stay, streamlined efficiencies, and reduction in resource utilization.[27,28] While our analysis did not compare resource utilization and quality-of-life metrics between TAV-in-SAV and re-do SAVR, reducing hospital stay and enabling patients to go back to routine life earlier postprocedure is an advantage of TAV-in-SAV.[7,29] Further studies are warranted to completely elucidate these hypotheses.

The need for PPI after TAVR has been linked to increased procedural costs and longer length of stay, and possibly poor long-term prognosis[30–32] The observation of very low 30-day rates (4.9%) of permanent pacemaker or implantable cardioverter defibrillator implantation, consistent with previous TAV-in-SAV studies,[33,34] and markedly lower than balloon- and self-expandable TAVR in native valves[16,18] was, therefore, reassuring in our study. While patients treated with the Evolut PRO exhibited lower rates of PPI compared with the Evolut R group, the within-group difference was small and its clinical significance is unclear. Potential explanations for this finding might include the learning curve of operators with the most recent iteration (Evolut PRO), and performance of shallower implants, which could potentially reduce PPI risk.[35,36]

Supra-annular self-expandable valves have demonstrated favorable hemodynamics compared with balloon-expandable valves in native aortic valve TAVR.[10,12,17,37] The mean gradients in this analysis were low (mean gradient of 14.4±8.0 mm Hg at 30 days) and sustained through 1 year. Although postprocedural gradients were expectedly higher than TAVR in native aortic valves,[16] they were similar to those reported for TAV-in-SAV using balloon-expandable valves.[38] While we did not aim at performing a direct comparison between the transvalvular gradients observed in our study and prior studies with different valves, these are important observations that might carry a long-term clinical impact. Furthermore, the favorable hemodynamic results seen in this analysis were observed without data on rates of contemporary postprocedure techniques that may be performed to optimize valve hemodynamics, such as bioprosthetic valve fracturing. These data were not collected in the TVT Registry at the time of this analysis, but several smaller studies have shown success when the technique was used before or after TAV-in-SAV.[39,40] However, these procedures can also pose major risks to both the patient and TAV being used.[41]

Almost half of the patients in our study received the smallest available self-expandable valve (23 mm, 49.2%), which is consistent with prior TAV-in-SAV trials.[33] While factors such as surgical valve size, implantation depth, and valve fracture might have significantly impacted the hemodynamic results of TAV-in-SAV,[41,42] we were not able to capture them because of the limitations of the information provided by the TVT Registry. Although gradients were similar between the groups, there was a statistically significant advantage of Evolut PRO compared with Evolut R devices through 30 days, but which was not sustained through 1 year. These differences could potentially be explained by shallower implants performed over time with the learning curve of operators, more common utilization of bigger valves in the Evolut PRO group (Table 2), and potentially higher rates of surgical valve fracture performed with Evolut PRO valves because it is the latest iteration of the device. Importantly, it is yet to be determined whether these subtle differences in gradients would be clinically meaningful.

There were no differences in the distribution of the severity of PPM between groups but, as expected, the rates of moderate and severe PPM were higher than observed in TAVR for native valves in the TVT Registry (37%).[43] Recently, Bleiziffer et al[38] demonstrated that the size of the original degenerated surgical valve may impact rates of re-intervention while influencing long-term mortality. The limited follow-up (ie, 1 year) of our analysis, however, might not have been enough to show these differences. In addition, the exclusive utilization of self-expandable valves in our analysis, which deliver better hemodynamics and reduces the likelihood of re-intervention post TAV-in-SAV compared with balloon-expandable valves, might also have played a role in our findings.[38,44] While severe PPM post–native valve TAVR have been recently associated with increased mortality and hospitalizations in a large (≈62 000 patients) national registry,[43] we did not observe similar differences.

One could speculate that a larger sample size would be needed to be able to show those differences. Longer-term follow-up and larger samples would be required to completely elucidate these findings.

We observed low rates of moderate and severe PVR with numerically better performance of Evolut PRO compared with Evolut R through 30 days. At 1-year follow-up, however, these differences were no longer observed. These differences could be explained by the design of the Evolut PRO valve with the additional outer pericardial wrap that might reduce postprocedure and 30-day PVR. Importantly, based on our overall results and considering that the current generation of Evolut PRO valve (ie, Evolut PRO+, Medtronic, Minneapolis, MN) is a 14F compatible device for valve sizes 23–29 mm (versus 16F like its prior generation), it should be considered the valve of choice for TAV-in-SAV compared with Evolut R.[24,45]

## Limitations

Our results should be interpreted considering several limitations. First, this was a post hoc retrospective data analysis from TVT with its inherent limitations, such as a potential for underreporting clinical outcomes and a selection bias typical of administrative data sets. Second, although we discussed our results in perspective with prior studies of balloon-expandable valves, it is important to highlight that a randomized study would be required to completely elucidate the comparison between balloon-expandable and self-expandable valves in this scenario. Third, our follow-up data were limited to 1 year. Long-term follow-up is therefore required to enable more comprehensive understanding of TAV-in-SAV with self-expandable valves. In addition, echocardiographic measures were site reported. Fourth, in the comparison between Evolut PRO and R valves, we did not perform statistical adjustments to account for the differences in baseline characteristics between groups or valve sizes. However, the relative differences between these variables were low, so it is unlikely they would change the results significantly. Fifth, we did not have access to data regarding the pre-implanted surgical valve sizes or types or how long since they were implanted. Although those data would be relevant for us to understand the mechanisms of surgical valve degeneration, they did not impair the peri- and postprocedural analyses. We did not have access to information on balloon valve fracturing or information on how many patients were considered ineligible for TAV-in-SAV because of challenging anatomy (leading to potential coronary obstruction) and were declined for the procedure. Lastly, only the Evolut PRO and Evolut R valves were used in these analyses; thus, the results may not be generalizable to other self-expandable bioprostheses.

# CONCLUSIONS

In the largest current practice study of TAV-in-SAV, the use of the Evolut PRO and Evolut R self-expandable valves has very favorable results with regard to clinical and hemodynamic outcomes, with potential small advantages of Evolut PRO compared with Evolut R valves. Therefore, the utilization of these devices should be considered a safe and effective treatment option in patients with a degenerated bioprosthetic valve.

# ARTICLE INFORMATION

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## Disclosures

Dr Forrest is a consultant for Edwards Lifesciences and Medtronic and receives grant support from Edwards Lifesciences, and Medtronic; Dr Reardon is a consultant for Medtronic, W.L. Gore and Associates, and Boston Scientific; Dr Szeto is a consultant for VDyne, MitreMedical, CardioMech, WL Gore, and Atricure; Dr George is on the advisory board and an investigator for Medtronic, Edwards Lifesciences, and Terumo Aortic, and is a consultant for Microinterventional Device; Dr Kleiman is a consultant for Medtronic, Abbott, and Boston Scientific and receives grant support from Medtronic; Dr Yakubov is a consultant for Medtronic, Boston Scientific, and Foldax; Dr Grubb is a proctor, PI, and on the advisory board for Medtronic and Ancora Heart; is a proctor, and is on the advisory board for Boston Scientific; is a PI and on the advisory board for BioVentrix; and is a PI for Edwards Lifesciences; Dr Liu is an employee and shareholder of Medtronic; Dr Attizzani is a consultant and serves as a proctor and is on the advisory board of Medtronic and is a consultant for Abbott Vascular. The remaining authors have no disclosures to report.

## Supplementary Material

Table S1–S4

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# Supplemental Material

**Table S1. Clinical outcomes at 30 days and 1 year by post procedure patient prosthesis mismatch (PPM).**

| | No PPM (N=1896) | Moderate PPM (N=1064) | Severe PPM (N=1327) | p-value (Moderate vs. No PPM) | p-value (Severe vs. No PPM) |
|---|---|---|---|---|---|
| 30 days | | | | | |
| All-Cause Mortality | 36 (1.9) | 17 (1.7) | 27 (2.1) | 0.5889 | 0.7783 |
| Re-Hospitalization | 126 (6.9) | 58 (5.7) | 92 (7.2) | 0.2387 | 0.7237 |
| Valve Related Readmission | 10 (0.5) | 3 (0.3) | 7 (0.6) | 0.3423 | 0.9991 |
| Non-Valve Related Readmission | 117 (6.4) | 55 (5.4) | 85 (6.7) | 0.3191 | 0.7446 |
| 1-year | | | | | |
| All-Cause Mortality | 126 (9.9) | 57 (7.7) | 93 (10.0) | 0.1110 | 0.8328 |
| Re-Hospitalization | 339 (26.0) | 175 (23.7) | 229 (24.2) | 0.2151 | 0.5123 |
| Valve Related Readmission | 35 (2.9) | 14 (2.0) | 16 (1.7) | 0.2217 | 0.1287 |
| Non-Valve Related Readmission | 315 (24.3) | 165 (22.4) | 222 (23.7) | 0.3234 | 0.9330 |

Total number of patients from Evolut R and Evolut PRO Valves are represented. Data is represented as no. patients with event (Kaplan-Meier event rate as percentage). PPM is based of post-procedure and is calculated based on the following definition. If BMI < 30 kg/$m^2$ : No PPM >0.85 $cm^2/m^2$; Moderate PPM 0.85 - 0.65 $cm^2/m^2$; Severe PPM <0.65 $cm^2/m^2$
If BMI ≥ 30 kg/$m^2$ : No PPM >0.70 $cm^2/m^2$; Moderate PPM 0.60 - 0.70 $cm^2/m^2$; Severe PPM <0.60 $cm^2/m^2$

**Table S2. Patient prosthesis mismatch (PPM) by valve size for Evolut R and PRO valves.**

| | Valve Size 23mm | | | Valve Size 26mm | | | Valve Size 29mm | | | Valve Size 34mm |
|---|---|---|---|---|---|---|---|---|---|---|
| **Measurement** | **EVR (N=1823)** | **PRO (N=270)** | **p-value** | **EVR (N=1215)** | **PRO (N=256)** | **p-value** | **EVR (N=453)** | **PRO (N=139)** | **p-value** | **EVR (N=131)** |
| PPM | | | 0.6862 | | | 0.2061 | | | 0.9645 | |
| None PPM | 36.6% (667/1823) | 36.3% (98/270) | | 45.7% (555/1215) | 50.8% (130/256) | | 59.6% (270/453) | 58.3% (81/139) | | 72.5% (95/131) |
| Moderate PPM | 26.1% (475/1823) | 28.9% (78/270) | | 26.3% (320/1215) | 23.0% (59/256) | | 17.9% (81/453) | 22.3% (31/139) | | 15.3% (20/131) |
| Severe PPM | 37.4% (681/1823) | 34.8% (94/270) | | 28.0% (340/1215) | 26.2% (67/256) | | 22.5% (102/453) | 19.4% (27/139) | | 12.2% (16/131) |

If BMI < 30 kg/$m^2$ : No PPM - >0.85 $cm^2/m^2$; Moderate PPM - 0.85 - 0.65 $cm^2/m^2$; Severe PPM - <0.65 $cm^2/m^2$
If BMI >= 30 kg/$m^2$ : No PPM - >0.70 $cm^2/m^2$; Moderate PPM - 0.60 - 0.70 $cm^2/m^2$; Severe PPM - <0.60 $cm^2/m^2$

**Table S3. Clinical outcomes overtime for Evolut R and Evolut PRO by valve size.**

| | Valve Sizes | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **23 mm** | | **p-value** | **26 mm** | | **p-value** | **29 mm** | | **p-value** | **34 mm** |
| **In-hospital** | **EVR N=2567** | **PRO N=341** | | **EVR N=1685** | **PRO N=316** | | **EVR N=637** | **PRO N=179** | | **EVR N=172** |
| All-cause mortality | 45 (1.8) | 9 (2.6) | 0.255 | 29 (1.7) | 7 (2.2) | 0.544 | 10 (1.6) | 3 (1.7) | >0.999 | 3 (1.7) |
| Any stroke | 38 (1.5) | 7 (2.1) | 0.421 | 41 (2.4) | 5 (1.6) | 0.354 | 15 (2.4) | 2 (1.1) | 0.390 | 1 (0.6) |
| Myocardial infarction | 8 (0.3) | 3 (0.9) | 0.129 | 4 (0.2) | 1 (0.3) | 0.577 | 0 (0.0) | 0 (0.0) | NA | 0 (0.0) |
| Major or life-threatening bleeding event | 163 (6.3) | 24 (7.0) | 0.626 | 72 (4.3) | 18 (5.7) | 0.263 | 27 (4.2) | 6 (3.4) | 0.595 | 7 (4.1) |
| Major vascular complication | 34 (1.3) | 6 (1.8) | 0.517 | 8 (0.5) | 5 (1.6) | 0.025 | 9 (1.4) | 1 (0.6) | 0.700 | 0 (0.0) |
| Pacemaker or ICD* | 88 (3.4) | 9 (2.6) | 0.446 | 64 (3.8) | 4 (1.3) | 0.018 | 30 (4.7) | 4 (2.2) | 0.202 | 7 (4.1) |
| Pacemaker or ICD† | 87 (4.2) | 9 (3.1) | 0.386 | 61 (4.6) | 4 (1.6) | 0.024 | 28 (5.7) | 4 (2.7) | 0.196 | 7 (5.0) |
| Aortic valve re-intervention | 13 (0.5) | 0 (0.0) | 0.386 | 4 (0.2) | 0 (0.0) | > 0.9999 | 1 (0.2) | 1 (0.6) | 0.391 | 2 (1.2) |
| **30 days** | | | | | | | | | | |
| All-cause mortality | 66 (2.6) | 10 (3.0) | 0.661 | 37 (2.2) | 9 (2.9) | 0.457 | 15 (2.4) | 4 (2.3) | 0.926 | 4 (2.4) |
| Any stroke | 45 (1.8) | 7 (2.1) | 0.681 | 45 (2.7) | 5 (1.6) | 0.273 | 20 (3.2) | 3 (1.7) | 0.292 | 1 (0.6) |
| Myocardial infarction | 9 (0.4) | 4 (1.2) | 0.031 | 5 (0.3) | 1 (0.3) | 0.949 | 0 (0.0) | 0 (0.0) | NA | 0 (0.0) |
| Major or life-threatening bleeding event | 179 (7.0) | 23 (6.8) | 0.907 | 78 (4.7) | 19 (6.1) | 0.261 | 29 (4.6) | 7 (3.9) | 0.701 | 8 (4.7) |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Major vascular complication | 38 (1.5) | 6 (1.8) | 0.685 | 9 (0.5) | 6 (1.9) | 0.009 | 9 (1.4) | 1 (0.6) | 0.359 | 0 (0.0) |
| Pacemaker or ICD* | 101 (4.0) | 10 (3.0) | 0.378 | 74 (4.5) | 4 (1.3) | 0.010 | 34 (5.4) | 6 (3.4) | 0.267 | 8 (4.7) |
| Pacemaker or ICD† | 99 (4.8) | 10 (3.5) | 0.330 | 71 (5.5) | 4 (1.6) | 0.010 | 32 (6.6) | 6 (4.16) | 0.258 | 7 (5.0) |
| Aortic valve re-intervention | 20 (0.8) | 0 (0.0) | 0.105 | 4 (0.2) | 0 (0.0) | 0.391 | 1 (0.2) | 1 0.6) | 0.339 | 3 (1.8) |
| Valve related readmission | 12 (0.5) | 0 (0.0) | 0.212 | 7 (0.4) | 2 (0.7) | 0.574 | 1 (0.2) | 0 (0.0) | 0.596 | 1 (0.6) |
| Non-valve related readmission | 174 (7.1) | 16 (5.0) | 0.178 | 93 (5.8) | 9 (3.0) | 0.055 | 43 (7.1) | 8 (4.6) | 0.280 | 8 (4.9) |
| **1 year** | | | | | | | | | | |
| All-cause mortality | 214(11.2) | 21 (9.2) | 0.648 | 100 (8.4) | 19 (9.4) | 0.567 | 35 (7.3) | 11 (9.1) | 0.549 | 12 (9.3) |
| Any stroke | 56 (2.4) | 10 (3.9) | 0.290 | 56 (3.8) | 7 (3.0) | 0.368 | 20 (3.2) | 3 (1.7) | 0.292 | 2 (1.5) |
| Myocardial infarction | 23 (1.2) | 7 (3.0) | 0.018 | 6 (0.4) | 3 (1.6) | 0.120 | 0 (0.0) | 0 (0.0) | NA | 1 (1.0) |
| Major or life-threatening bleeding event | 211 (8.9) | 25 (7.8) | 0.724 | 86 (5.4) | 20 (6.7) | 0.305 | 29 (4.6) | 8 (4.9) | 0.954 | 10 (6.4) |
| Major vascular complication | 39 (1.5) | 6 (1.8) | 0.724 | 9 (0.5) | 6 (1.9) | 0.009 | 9 (1.4) | 1 (0.6) | 0.359 | 0 (0.0) |
| Pacemaker or ICD* | 126 (5.5) | 13 (4.8) | 0.494 | 94 (6.4) | 4 (1.3) | 0.002 | 44 (8.1) | 8 (6.1) | 0.271 | 12 (8.8) |
| Pacemaker or ICD† | 123 (6.7) | 13 (5.6) | 0.439 | 89 (7.7) | 1.6% (4) | 0.002 | 39 (9.0) | 8 (7.3) | 0.327 | 11 (10.0) |
| Aortic valve re-intervention | 31 (1.5) | 2 (1.3) | 0.394 | 8 (0.7) | 0 (0.0) | 0.246 | 3 (0.7) | 1 (0.6) | 0.816 | 6 (4.5) |
| Valve related readmission | 47 (2.6) | 4 (2.6) | 0.654 | 21 (1.8) | 4 (1.9) | 0.775 | 7 (1.9) | 0 (0.0) | 0.197 | 4 (3.2) |
| Non-valve related readmission | 493(26.3) | 47 (23.2) | 0.286 | 273(23.5) | 30 (17.3) | 0.028 | 103(22.8) | 24 (22.3) | 0.781 | 24 (19.8) |

In-hospital data presented as no. of patients with event (proportion of subjects with events as percentage)
30-day and 1-year data presented as no. of patients with an event (Kaplan-Meier estimates as percentage).
*Subjects with pacemaker or ICD at baseline are included;
† Subjects with pacemaker or ICD at baseline are not included.

**Table S4. Echocardiographic overtime for Evolut R and Evolut PRO by valve size.**

| | Valve Sizes | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | **23 mm** | | **p-value** | **26 mm** | | **p-value** | **29 mm** | | **p-value** | **34 mm** |
| **Baseline** | **EVR N=2567** | **PRO N=341** | | **EVR N=1685** | **PRO N=316** | | **EVR N=637** | **PRO N=179** | | **EVR N=172** |
| Mean gradient (mm Hg) | 42.3 ± 16.1 (2413) | 42.0 ± 15.9 (315) | 0.759 | 39.5 ± 16.2 (1479) | 39.3 ± 16.7 (264) | 0.879 | 34.9 ± 16.6 (483) | 33.7 ± 17.9 (120) | 0.514 | 29.2 ± 19.6 (79) |
| Aortic valve area ($cm^2$) | 0.76 ± 0.37 (2184) | 0.76 ± 0.34 (289) | 0.854 | 0.87 ± 0.41 (1328) | 0.92 ± 0.44 (250) | 0.099 | 1.01 ± 0.53 (425) | 1.10 ± 0.49 (111) | 0.100 | 1.56 ± 0.81 (68) |
| Total aortic regurgitation | | | 0.761 | | | 0.704 | | | 0.006 | |
| None | 635/2545 (25.0) | 87/336 (25.9) | | 323/1668 (19.4) | 62/315 (19.7) | | 83/628 (13.2) | 11/177 (6.2) | | 10/172 (5.8) |
| Trace/trivial | 384/2545 (15.1) | 32/336 (9.5) | | 172/1668 (10.3) | 34/315 (10.8) | | 53/628 (8.4) | 10/177 (5.6) | | 4/172 (2.3) |
| Mild | 577/2545 (22.7) | 94/336 (28.0) | | 349/1668 (20.9) | 62/315 (19.7) | | 114/628 (18.2) | 28/177 (15.8) | | 17/172 (9.9) |
| Moderate | 450/2545 (17.7) | 58/336 (17.3) | | 360/1668 (21.6) | 60/315 (19.0) | | 118/628 (18.8) | 42/177 (23.7) | | 31/172 (18.0) |
| Severe | 499/2545 (19.6) | 65/336 (19.3) | | 464/1668 (27.8) | 97/315 (30.8) | | 260/628 (41.4) | 86/177 (48.6) | | 110/172 (64.0) |
| Moderate/severe | 949/2545 (37.3) | 123/336 (36.6) | 0.808 | 824/1668 (49.4) | 157/315 (49.8) | 0.886 | 378/628 (60.2) | 128/177 (72.3) | 0.003 | 141/172 (82.0) |
| **Post Procedure** | | | | | | | | | | |
| Mean gradient (mm Hg) | 18.0 ± 10.1 (2265) | 17.4 ± 9.7 (320) | 0.380 | 13.9 ± 7.2 (1511) | 14.1 ± 7.4 (296) | 0.624 | 11.6 ± 6.0 (559) | 11.3 ± 5.3 (166) | 0.500 | 9.0 ± 5.6 (152) |
| Aortic valve area ($cm^2$) | 1.3 ± 0.5 (1825) | 1.4 ± 0.5 (271) | 0.539 | 1.6 ± 0.6 (1217) | 1.7 ± 0.6 (256) | 0.266 | 1.9 ± 0.7 (453) | 1.9 ± 0.7 (139) | 0.633 | 2.2 ± 0.9 (131) |
| Total aortic regurgitation | | | 0.040 | | | 0.025 | | | 0.241 | |
| None | 1338/2277 (58.8) | 203/317 (64.0) | | 850/1516 (56.1) | 187/296 (63.2) | | 281/563 (49.9) | 90/164 (54.9) | | 66/154 (42.9) |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Trace/trivial | 552/2277 (24.2) | 74/317 (23.3) | | 391/1516 (25.8) | 64/296 (21.6) | | 149/563 (26.5) | 39/164 (23.8) | | 43/154 (27.9) |
| Mild | 334/2277 (14.7) | 36/317 (11.4) | | 242/1516 (16.0) | 43/296 (14.5) | | 114/563 (20.2) | 34/164 (20.7) | | 35/154 (22.7) |
| Moderate | 50/2277 (2.2) | 4/317 (1.3) | | 32/1516 (2.1) | 2/296 (0.7) | | 16/563 (2.8) | 1/164 (0.6) | | 10/154 (6.5) |
| Severe | 3/2277 (0.1) | 0/317 (0.0) | | 1/1516 (0.1) | 0/296 (0.0) | | 3/563 (0.5) | 0/164 (0.0) | | 0/154 (0.0) |
| Moderate/severe | 53/2277 (2.3) | 4/317 (1.3) | 0.306 | 33/1516 (2.2) | 2/296 (0.7) | 0.105 | 19/563 (3.4) | 1/164 (0.6) | 0.059 | 10/154 (6.5) |
| Paravalvular regurgitation | | | 0.017 | | | 0.118 | | | 0.129 | |
| None | 1712/2095 (81.7) | 255/292 (87.3) | | 1116/1391 (80.2) | 230/273 (84.2) | | 375/505 (74.3) | 122/153 (79.7) | | 95/139 (68.3) |
| Mild | 343/2095 (16.4) | 34/292 (11.6) | | 251/1391 (18.0) | 40/273 (14.7) | | 111/505 (22.0) | 30/153 (19.6) | | 35/139 (25.2) |
| Moderate | 37/2095 (1.8) | 3/292 (1.0) | | 22/1391 (1.6) | 3/273 (1.1) | | 16/505 (3.2) | 0/153 (0.0) | | 9/139 (6.5) |
| Severe | 3/2095 (0.1) | 0/292 (0.0) | | 2/1391 (0.1) | 0/273 (0.0) | | 3/505 (0.6) | 1/153 (0.7) | | 0/139 (0.0) |
| Moderate/severe | 40/2095 (1.9) | 3/292 (1.0) | 0.477 | 24/1391 (1.7) | 3/273 (1.1) | 0.605 | 19/505 (3.8) | 1/153 (0.7) | 0.058 | 9/139 (6.5) |
| **30 days** | | | | | | | | | | |
| Mean gradient (mm Hg) | 16.9 ± 8.7 (1809) | 17.0 ± 8.1 (253) | 0.887 | 12.7 ± 6.8 (1208) | 12.5 ± 6.7 (241) | 0.640 | 11.4 ± 6.2 (465) | 10.5 ± 5.4 (146) | 0.091 | 8.5 ± 5.2 (123) |
| Total aortic regurgitation | | | 0.108 | | | 0.068 | | | 0.020 | |
| None | 1101/1813 (60.7) | 165/249 (66.3) | | 672/1213 (55.4) | 148/240 (61.7) | | 214/469 (45.6) | 83/147 (56.5) | | 50/125 (40.0) |
| Trace/trivial | 385/1813 (21.2) | 45/249 (18.1) | | 289/1213 (23.8) | 50/240 (20.8) | | 124/469 (26.4) | 32/147 (21.8) | | 34/125 (27.2) |
| Mild | 287/1813 (15.8) | 34/249 (13.7) | | 217/1213 (17.9) | 39/240 (16.3) | | 114/469 (24.3) | 31/147 (21.1) | | 35/125 (28.0) |
| Moderate | 36/1813 (2.0) | 4/249 (1.6) | | 31/1213 (2.6) | 3/240 (1.3) | | 17/469 (3.6) | 1/147 (0.7) | | 6/125 (4.8) |
| Severe | 4/1813 (0.2) | 1/249 (0.4) | | 4/1213 (0.3) | 0/240 (0.0) | | 0/469 (0.0) | 0/147 (0.0) | | 0/125 (0.0) |
| Moderate/severe | 40/1813 (2.2) | 5/249 (2.0) | 0.841 | 35/1213 (2.9) | 3/240 (1.3) | 0.185 | 17/469 (3.6) | 1/147 (0.7) | 0.089 | 6/125 (4.8) |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Paravalvular regurgitation | | | 0.137 | | | 0.095 | | | 0.150 | |
| None | 1361/1676 (81.2) | 203/238 (85.3) | | 7882/1112 (9.3) | 180/214 (84.1) | | 305/424 (71.9) | 107/138 (77.5) | | 77/107 (72.0) |
| Mild | 290/1676 (17.3) | 31/238 (13.0) | | 203/1112 (18.3) | 32/214 (15.0) | | 102/424 (24.1) | 30/138 (21.7) | | 26/107 (24.3) |
| Moderate | 24/1676 (1.4) | 3/238 (1.3) | | 23/1112 (2.1) | 2/214 (0.9) | | 16/424 (3.8) | 0/138 (0.0) | | 4/107 (3.7) |
| Severe | 1/1676 (0.1) | 1/238 (0.4) | | 4/1112 (0.4) | 0/214 (0.0) | | 1/424 (0.2) | 1/138 (0.7) | | 0/107 (0.0) |
| Moderate/severe | 25/1676 (1.5) | 4/238 (1.7) | 0.776 | 27/1112 (2.4) | 2/214 (0.9) | 0.210 | 17/424 (4.0) | 1/138 (0.7) | 0.090 | 4/107 (3.7) |
| **1 year** | | | | | | | | | | |
| Mean gradient (mm Hg) | 16.9 ± 9.2 (1065) | 16.1 ± 7.9 (112) | 0.280 | 12.0 ± 6.2 (659) | 12.0 ± 7.0 (108) | 0.952 | 10.7 ± 6.2 (248) | 9.8 ± 6.4 (57) | 0.291 | 8.9 ± 12.1 (72) |
| Total aortic regurgitation | | | 0.596 | | | 0.492 | | | 0.730 | |
| None | 693/1080 (64.2) | 74/111 (66.7) | | 403/665 (60.6) | 71/111 (64.0) | | 136/244 (55.7) | 35/61 (57.4) | | 35/70 (50.0) |
| Trace/trivial | 219/1080 (20.3) | 22/111 (19.8) | | 147/665 (22.1) | 122/111 (9.8) | | 45/244 (18.4) | 11/61 (18.0) | | 20/70 (28.6) |
| Mild | 142/1080 (13.1) | 11/111 (9.9) | | 101/665 (15.2) | 18/111 (16.2) | | 55/244 (22.5) | 15/61 (24.6) | | 13/70 (18.6) |
| Moderate | 23/1080 (2.1) | 3/111 (2.7) | | 13/665 (2.0) | 0/111 (0.0) | | 8/244 (3.3) | 0/61 (0.0) | | 2/70 (2.9) |
| Severe | 3/1080 (0.3) | 1/111 (0.9) | | 1/665 (0.2) | 0/111 (0.0) | | 0/244 (0.0) | 0/61 (0.0) | | 0/70 (0.0) |
| Moderate/severe | 26/1080 (2.4) | 4/111 (3.6) | 0.517 | 14/665 (2.1) | 0/111 (0.0) | 0.240 | 8/244 (3.3) | 0/61 (0.0) | 0.365 | 2/70 (2.9) |
| Paravalvular regurgitation | | | 0.979 | | | 0.663 | | | 0.241 | |
| None | 870/1003 (86.7) | 87/100 (87.0) | | 518/612 (84.6) | 87/101 (86.1) | | 174/230 (75.7) | 47/57 (82.5) | | 48/61 (78.7) |
| Mild | 114/1003 (11.4) | 10/100 (10.0) | | 86/612 (14.1) | 14/101 (13.9) | | 49/230 (21.3) | 10/57 (17.5) | | 12/61 (19.7) |
| Moderate | 17/1003 (1.7) | 2/100 (2.0) | | 8/612 (1.3) | 0/101 (0.0) | | 7/230 (3.0) | 0/57 (0.0) | | 1/61 (1.6) |
| Severe | 2/1003 (0.2) | 1/100 (1.0) | | 0/612 (0.0) | 0/101 (0.0) | | 0/230 (0.0) | 0/57 (0.0) | | 0/61 (0.0) |
| Moderate/severe | 19/1003 (1.9) | 3/100 (3.0) | 0.442 | 8/612 (1.3) | 0/101 (0.0) | 0.609 | 7/230 (3.0) | 0/57 (0.0) | 0.352 | 1/61 (1.6) |

Values are mean ± SD (n) for continuous variables and no. patients/total no. patients (percentage). for categorical variables. p values are comparing Evolut R and Evolut PRO within each valve size