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# Three Generations of Self-Expanding Transcatheter Aortic Valves

## A Report From the STS/ACC TVT Registry

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**ABSTRACT**

**OBJECTIVES** The aim of this study was to assess the evolution of early outcomes for 3 iterative self-expanding transcatheter aortic valves.

**BACKGROUND** Over the past decade there have been rapid advancements in transcatheter aortic valve replacement (TAVR) technologies, including 3 generations of supra-annular self-expanding transcatheter systems.

**METHODS** Data from the Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapy) Registry for patients undergoing TAVR with CoreValve, Evolut R, or Evolut PRO valves to treat tricuspid aortic stenosis between January 2014 and September 2017 were obtained. Patient risk and echocardiographic data are site reported. Valves analyzed included 23-, 26-, and 29-mm sizes to fit 18- to 26-mm annular diameters. Propensity score matching was performed using the Evolut PRO group as the common reference.

**RESULTS** Of 18,874 patients undergoing TAVR at 381 centers, 5,514 patients were implanted with CoreValve, 11,295 with Evolut R, and 2,065 with Evolut PRO valves. At 30 days, there were significantly fewer patients with more than mild aortic regurgitation for the unmatched (7.8% CoreValve, 5.2% Evolut R, and 2.8% Evolut PRO; $p < 0.001$) and matched populations (8.3% CoreValve, 5.4% Evolut R, and 3.4% Evolut PRO; $p = 0.032$). The mean aortic valve gradients at 30 days in the matched populations were <8 mm Hg for all 3 valves (7.3 mm Hg CoreValve, 7.5 mm Hg Evolut R, 7.2 mm Hg Evolut PRO).

**CONCLUSIONS** Advancements in transcatheter valve technologies and expanding indications for TAVR have resulted in improved outcomes for patients undergoing TAVR in the United States with self-expanding, supra-annular valves. In particular, the addition of an outer pericardial tissue wrap designed to enhance sealing at the level of the aortic annulus has resulted in very low rates of significant aortic regurgitation while maintaining excellent hemodynamic status. (J Am Coll Cardiol Intv 2020;13:170–9) © 2020 Published by Elsevier on behalf of the American College of Cardiology Foundation.

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Over the past 10 years, there have been rapid advancements in transcatheter aortic valve replacement (TAVR) technologies for the treatment of severe symptomatic aortic stenosis. The CoreValve transcatheter bioprosthesis (Medtronic, Minneapolis, Minnesota) was the first self-expanding valve studied in the United States (1,2) and became commercially available in January 2014. This was the first transcatheter aortic valve designed with the leaflets of the bioprosthetic valve positioned above the aortic annulus (**Central Illustration**). The second-generation self-expanding Evolut R valve (Medtronic) was the first U.S. Food and Drug Administration-approved transcatheter valve to enable complete recapture and repositioning, thereby allowing optimized implantation depth upon deployment (3). Additional modifications present in the Evolut R valve included changes to the Nitinol frame designed to optimal radial force. Sorajja et al. (4) previously compared data on these 2 valves from the Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapy) Registry and showed improvements in procedural success, a decreased incidence of new permanent pacemaker implantation (PPI), and lower early mortality with the Evolut R versus CoreValve.

SEE PAGE 180

The Evolut PRO (Medtronic; approved by the Food and Drug Administration in March 2017) is the third-generation self-expanding transcatheter valve. The Evolut PRO valve is built on the Evolut R valve platform, differing only by the addition of an external pericardial tissue wrap around the valve inflow, designed to minimize paravalvular leak (PVL). In the initial study of the Evolut PRO valve, performed in 60 patients in the United States, the Evolut PRO eliminated more than mild PVL at 30 days, and 72.4% of patients had no or trace PVL (5). Additionally, the Evolut PRO valve maintained excellent hemodynamic status (mean gradient 6.4 ± 2.1 mm Hg, mean valve area 2.0 ± 0.5 $cm^2$) with a low 30-day incidence of PPI of 11.8% (5).

The purpose of this study was to investigate the real-world effects these progressive iterative improvements of self-expanding valve technology have had on procedural outcomes in the United States, by comparing both unmatched and propensity score-matched cohort data from the TVT Registry, with a primary focus on PVL given the addition of the pericardial wrap on the Evolut PRO valve.

## METHODS

**VALVE DESIGN.** Patients treated with 3 generations of self-expanding transcatheter aortic valves were evaluated: CoreValve, Evolut R, and Evolut PRO. Valve design details have been previously reported (2,3,6). The Evolut PRO valve can be implanted through a 16-F in-line sheath, the Evolut R valve through a 14-F in-line sheath, and the CoreValve through a separate 18-F introducer sheath.

**STUDY POPULATION.** Site-reported data were extracted from the TVT Registry database for patients with native tricuspid aortic valve stenosis treated with Medtronic self-expanding transcatheter aortic valves from January 2014 to September 2017 with follow-up through December 2017 (Online Figure S1). Studied valves include the 23-, 26-, and 29-mm sizes for each valve generation, designed to treat aortic annuli from 18 to 26 mm in diameter. Data for the 31-mm CoreValve and the 34-mm Evolut R valve were excluded because there is presently no equivalent Evolut PRO valve for comparison. Patients with primary aortic insufficiency, with pre-existing surgical or transcatheter valves, and with bicuspid or other nontrileaflet native aortic anatomy were excluded from analysis.

Data from patients treated with the CoreValve bioprosthesis were first added to the TVT Registry in January 2014, data from patients with the Evolut R valve were added in July 2015, and data from patients with the Evolut PRO valve in March 2017 (**Figure 1**). Therefore, this report includes the first 2 quarters of the use with the Evolut PRO valve in commercial clinical practice. The temporal trends show a rapid adoption of the Evolut R platform, which within the first 2 quarters of its commercial release accounted for >95% of the self-expanding valves being used. The adoption of the Evolut PRO valve has also been rapid (>70% in the first 2 quarters), although not as rapid as from CoreValve to Evolut R.

**PROCEDURAL DETAILS.** The TVT Registry serves as the national database for medical device tracking of transcatheter aortic valves implanted following commercialization. Entry of patient data into the TVT Registry is a condition of coverage by the Centers for Medicare and Medicaid Services. A random audit of 10% of data elements is performed either on site or remotely. The TVT Registry publication committee has reviewed the final paper. The requirement to obtain patient consent is waived for this registry.

**ABBREVIATIONS AND ACRONYMS**

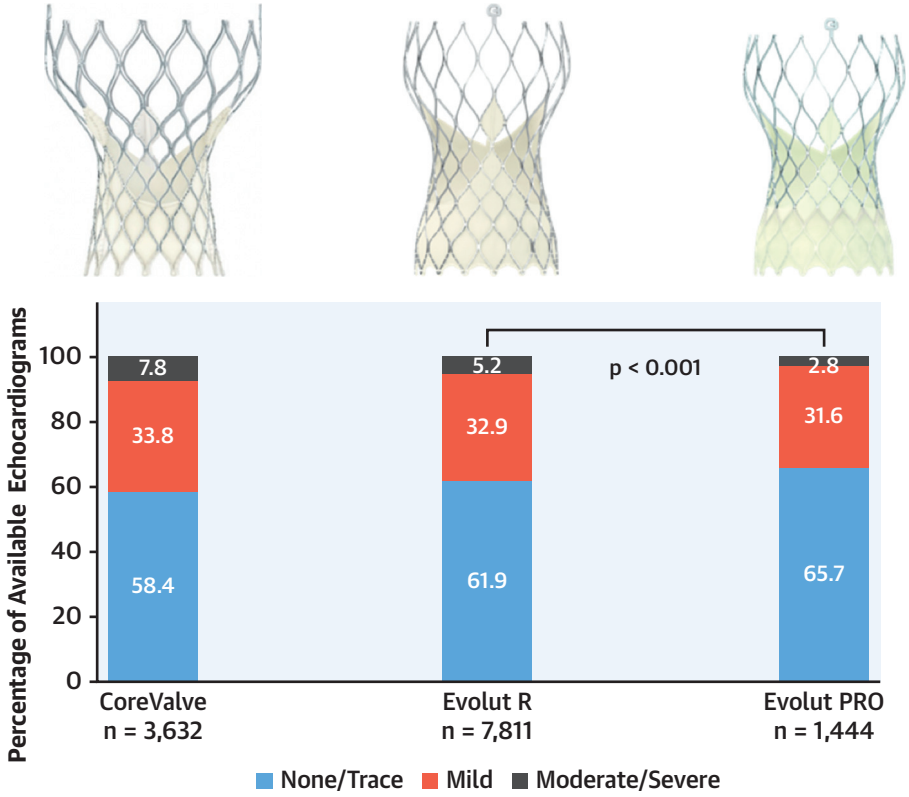
**AR** = aortic regurgitation

**PVL** = paravalvular leak

**PPI** = permanent pacemaker implantation

**TAVR** = transcatheter aortic valve replacement

**CENTRAL ILLUSTRATION Total Aortic Regurgitation at 30 Days With 3 Generations of Self-Expanding, Supra-Annular Transcatheter Valves**




**Forrest, J.K. et al. J Am Coll Cardiol Intv. 2020;13(2):170–9.**

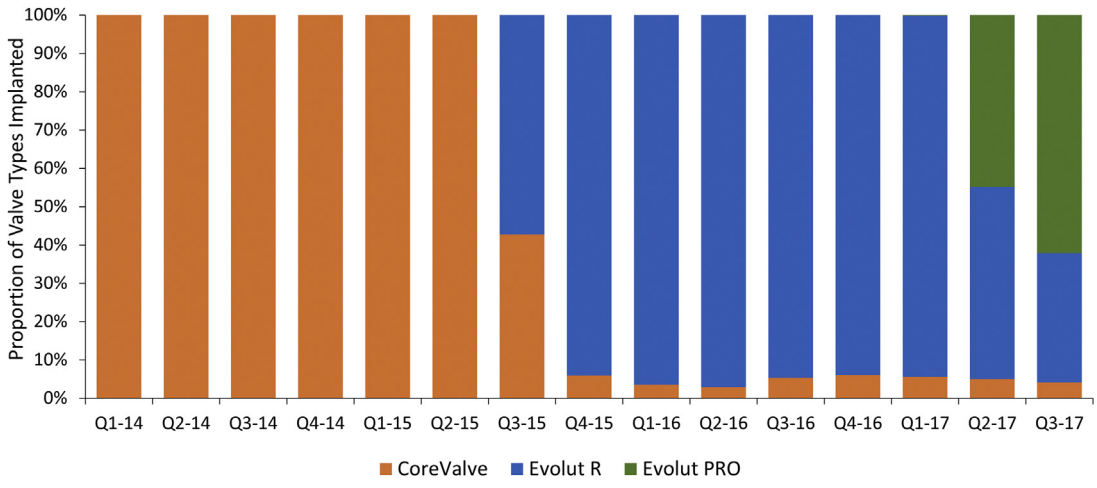
From **left to right** are the CoreValve, the Evolut R, and the Evolut PRO valves. The p value represents the differences in moderate or severe aortic regurgitation between the Evolut PRO and Evolut R valve unmatched groups. Reproduced with permission from Medtronic 2019.

**ECHOCARDIOGRAPHIC ANALYSIS.** All echocardiographic assessments are performed on the basis of standard practices and are site reported. Baseline, post-procedural, and 30-day echocardiographic measurements are analyzed.

**ENDPOINTS.** Data included in this report are based on version 2.0 of the TVT Registry data collection form. Risk status, baseline characteristics, demographics, medical history, procedural characteristics, and in-hospital and 30-day outcomes are reported. Device success reported in the TVT Registry is defined on the basis of the original Valve Academic Research Consortium definitions (7). We included data for patients treated with all 3 generations of valves but restricted statistical comparisons in outcomes to the Evolut R and Evolut PRO valves. The Evolut R and Evolut PRO valves are the only 2 self-expanding valves presently available for commercial use in the United States, and prior direct comparisons have been previously performed between the CoreValve and Evolut R valves (4).

**STATISTICAL METHODS.** Patients were compared before and after propensity score matching. Propensity score matching was performed to account for potential imbalances, including a changing patient population eligible for TAVR. Matching was performed using the Evolut PRO patients as the common reference group. Matching variables were selected on the basis of clinical judgment of potential confounders and include baseline characteristics, medical history, and procedural characteristics (anesthesia and iliofemoral access) known to have changed in use over time (Online Table S1). Multivariate logistic regression models (one for Evolut PRO vs. CoreValve and a second for Evolut PRO vs. Evolut R) were built to calculate the propensity scores. A greedy matching

**FIGURE 1 The Number of Procedures per Valve Type**




The number of procedures over time for the 3 self-expanding valves in this report starting with the first quarter reporting the self-expanding valves in the TVT Registry and ending with implantations performed through September 2017. Q = calendar quarter.

algorithm was used to find matched pairs between Evolut PRO and Evolut R and between Evolut PRO and CoreValve. Evolut PRO patients who were in common from both propensity matches and their matched Evolut R or CoreValve patients were considered as matched cohorts across 3 valve types. To confirm matching success, absolute standardized differences were determined for 3 comparisons: CoreValve versus Evolut PRO, Evolut R versus Evolut PRO, and CoreValve versus Evolut R. Balance between comparator groups was defined as an absolute standardized difference <10% (Online Table S2).

Continuous variables are reported as mean ± SD or as median (interquartile range) as appropriate and were compared using Student's *t*-test or the Wilcoxon rank sum test as appropriate. Categorical variables are reported as counts and percentages and were compared using the chi-square test. In-hospital outcomes are reported as frequencies and were compared between the Evolut R and Evolut PRO patient groups using the chi-square test. Adverse event rates at 30 days are reported as Kaplan-Meier estimates, and comparisons between the Evolut R and Evolut PRO patient groups were made using the log-rank test. A p value of <0.05 was considered to indicate statistical significance. Given previous analysis from the TVT Registry comparing CoreValve and Evolut R (4), and because the CoreValve is no longer commercially available in the United States, we did not report direct comparisons for CoreValve (vs. Evolut or Evolut PRO) but included the data for completeness and historical reference. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina).

## RESULTS

**BASELINE CHARACTERISTICS.** A total of 18,874 patient procedures at 381 centers were analyzed, which included 5,514 patients undergoing attempted implantation with CoreValve, 11,295 with Evolut R, and 2,065 with Evolut PRO valves from January 2014 to September 2017. Propensity score matching resulted in 1,500 matched sets. For consistency, all data are reported as (CoreValve, Evolut R, and Evolut PRO), and all p values and absolute standardized differences reported are for the comparisons between the Evolut R and Evolut PRO valves.

Baseline characteristics for the unmatched and matched patients are shown in **Table 1**. Within the unmatched groups, there were significant differences in baseline characteristics. Patients in the Evolut PRO group had significantly lower Society of Thoracic Surgeons risk scores (8.7%, 7.7%, and 6.7%; $p < 0.001$) and were more often considered at intermediate risk (4.7%, 8.1%, and 22.6%; $p < 0.001$). Fewer Evolut PRO patients had peripheral vascular disease (30.1%, 30.7%, and 23.7%; $p < 0.001$), moderate to severe mitral regurgitation (27.8%, 27.2%,

**TABLE 1 Baseline Characteristics**

| | Unmatched | | | | | Matched | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | CoreValve (n = 5,514) | Evolut R (n = 11,295) | Evolut PRO (n = 2,065) | p Value* | Absolute Standardized Difference* | CoreValve (n = 1,500) | Evolut R (n = 1,500) | Evolut PRO (n = 1,500) | p Value* | Absolute Standardized Difference* |
| Age, yrs | 82.1 ± 7.3 | 81.4 ± 7.7 | 81.3 ± 7.7 | 0.69 | 0.9 | 81.5 ± 7.3 | 81.3 ± 7.5 | 81.6 ± 7.7 | 0.27 | 4.1 |
| Female | 3,585 (65.0) | 7,187 (63.6) | 1,365 (66.1) | 0.03 | 5.1 | 975 (65.0) | 978 (65.2) | 989 (65.9) | 0.67 | 1.5 |
| STS-PROM, % | 8.7 ± 5.3 | 7.7 ± 5.3 | 6.7 ± 4.4 | <0.001 | 21.0 | 7.4 ± 4.2 | 7.2 ± 4.5 | 7.2 ± 4.8 | 0.84 | 0.7 |
| Risk status | | | | | | | | | | |
| Extreme risk | 1,724 (31.3) | 1,861 (16.5) | 187 (9.1) | <0.001 | 22.4 | 193 (12.9) | 186 (12.4) | 175 (11.7) | 0.54 | 2.3 |
| High risk | 3,479 (63.1) | 8,397 (74.3) | 1,395 (67.6) | | | 1,164 (77.6) | 1,170 (78.0) | 1,017 (67.8) | | |
| Intermediate risk | 258 (4.7) | 910 (8.1) | 466 (22.6) | | | 120 (8.0) | 129 (8.6) | 296 (19.7) | | |
| Low risk | 36 (0.7) | 104 (0.9) | 16 (0.8) | | | 21 (1.4) | 15 (1.0) | 12 (0.8) | | |
| NYHA functional class III or IV | 4,557 (83.2) | 8,981 (80.1) | 1,483 (72.2) | <0.001 | 18.0 | 1,126 (75.1) | 1,171 (78.1) | 1,132 (75.5) | 0.09 | 6.2 |
| Diabetes mellitus | 2,005 (36.4) | 4,228 (37.5) | 767 (37.2) | 0.81 | 0.6 | 568 (37.5) | 537 (35.8) | 564 (37.6) | 0.31 | 3.7 |
| Chronic renal replacement therapy | 193 (3.5) | 495 (4.4) | 72 (3.5) | 0.06 | 4.6 | 59 (3.9) | 57 (3.8) | 58 (3.9) | 0.92 | 0.4 |
| History of hypertension | 5,004 (90.8) | 10,250 (90.8) | 1,904 (92.2) | 0.04 | 5.0 | 1,370 (91.3) | 1,384 (92.3) | 1,384 (92.3) | >0.99 | 0.0 |
| Peripheral vascular disease | 1,661 (30.1) | 3,462 (30.7) | 489 (23.7) | <0.001 | 15.7 | 403 (26.9) | 402 (26.8) | 393 (26.2) | 0.71 | 1.4 |
| Prior stroke | 666 (12.1) | 1,343 (11.9) | 250 (12.1) | 0.77 | 0.7 | 187 (12.5) | 192 (12.8) | 189 (12.6) | 0.87 | 0.6 |
| Chronic lung disease/COPD | 2,571 (46.9) | 4,796 (42.7) | 791 (38.5) | <0.001 | 8.6 | 641 (42.7) | 626 (41.7) | 624 (41.6) | 0.94 | 0.3 |
| Home oxygen | 703 (12.8) | 1,162 (10.3) | 174 (8.4) | 0.009 | 6.4 | 146 (9.7) | 138 (9.2) | 147 (9.8) | 0.58 | 2.1 |
| Cardiac history | | | | | | | | | | |
| Previous PCI | 1,974 (35.8) | 3,884 (34.4) | 631 (30.6) | <0.001 | 8.2 | 477 (31.8) | 511 (34.1) | 481 (32.1) | 0.24 | 4.3 |
| Prior CABG | 1,292 (23.4) | 2,396 (21.2) | 346 (16.8) | <0.001 | 11.4 | 248 (16.5) | 293 (19.5) | 274 (18.3) | 0.38 | 3.2 |
| Atrial fibrillation/ atrial flutter | 2,145 (39.0) | 4,135 (36.7) | 701 (34.0) | 0.02 | 5.7 | 558 (37.2) | 533 (35.5) | 532 (35.5) | 0.97 | 0.1 |
| Pre-existing IPG/ICD | 1,046 (19.0) | 1,964 (17.4) | 315 (15.3) | 0.02 | 5.7 | 239 (15.9) | 228 (15.2) | 249 (16.6) | 0.29 | 3.8 |
| CHF (recent 2 weeks) | 4,445 (80.7) | 9,205 (81.6) | 1,617 (78.3) | <0.001 | 8.2 | 1,187 (79.1) | 1,218 (81.2) | 1,185 (79.0) | 0.13 | 5.5 |
| Baseline echocardiographic characteristics | | | | | | | | | | |
| AV area, $cm^2$ | 0.67 ± 0.23 | 0.69 ± 0.24 | 0.70 ± 0.21 | 0.02 | 5.2 | 0.68 ± 0.18 | 0.69 ± 0.21 | 0.70 ± 0.22 | 0.49 | 2.5 |
| Maximum AV velocity, m/s | 4.2 ± 0.7 | 4.1 ± 0.7 | 4.1 ± 0.7 | 0.49 | 1.7 | 4.2 ± 0.8 | 4.1 ± 0.7 | 4.1 ± 0.7 | 0.14 | 5.5 |
| Mean AV gradient, mm Hg | 44.1 ± 14.7 | 42.7 ± 15.0 | 42.9 ± 14.8 | 0.75 | 0.8 | 44.5 ± 15.3 | 43.3 ± 15.2 | 42.4 ± 14.4 | 0.09 | 6.2 |
| LVEF, % | 55.1 ± 14.0 | 56.0 ± 13.5 | 57.5 ± 12.4 | <0.001 | 11.2 | 56.4 ± 13.6 | 56.6 ± 13.4 | 56.7 ± 12.9 | 0.85 | 0.7 |
| Moderate to severe AR | 1,067 (19.4) | 1,968 (17.6) | 290 (14.2) | <0.001 | 9.3 | 300 (20.1) | 255 (17.2) | 207 (13.9) | 0.02 | 9.0 |
| Moderate to severe MR | 1,524 (27.8) | 3,057 (27.2) | 454 (22.1) | <0.001 | 12.0 | 387 (26.0) | 392 (26.2) | 353 (23.6) | 0.10 | 6.1 |
| Moderate to severe TR | 1,368 (25.0) | 2,656 (23.7) | 412 (20.1) | <0.001 | 8.8 | 366 (24.6) | 328 (22.1) | 314 (21.1) | 0.48 | 2.6 |
| Frailty | | | | | | | | | | |
| BMI <21 $kg/m^2$ | 636 (11.5) | 1,221 (10.8) | 180 (8.7) | 0.004 | 7.1 | 143 (9.5) | 158 (10.5) | 138 (9.2) | 0.22 | 4.5 |
| Albumin <3.3 g/dl | 888 (18.0) | 1,806 (18.0) | 281 (15.0) | 0.002 | 8.1 | 228 (17.3) | 226 (17.0) | 216 (15.7) | 0.34 | 3.6 |
| 5-m gait speed >6 s | 2,738 (74.8) | 5,914 (72.3) | 1,118 (68.5) | 0.002 | 8.4 | 796 (76.0) | 806 (71.6) | 831 (69.9) | 0.39 | 3.6 |
| Prohibitive anatomic factors | | | | | | | | | | |
| Annular calcification | 4,478 (82.4) | 9,087 (81.4) | 1,660 (81.1) | 0.74 | 0.8 | 1,231 (82.1) | 1,192 (79.5) | 1,234 (82.3) | 0.05 | 7.1 |
| Porcelain aorta | 314 (5.7) | 452 (4.0) | 70 (3.4) | 0.19 | 3.2 | 76 (5.1) | 52 (3.5) | 53 (3.5) | 0.92 | 0.4 |
| Hostile mediastinum/chest | 371 (6.7) | 728 (6.4) | 114 (5.5) | 0.11 | 3.9 | 91 (6.1) | 95 (6.3) | 84 (5.6) | 0.39 | 3.1 |

Values are mean ± SD or n (%), reflecting missing values. *p value comparing Evolut R and Evolut PRO groups and absolute standardized differences as percentage (>10% represents imbalance).

AR = aortic regurgitation; AV = aortic valve; BMI = body mass index; CABG = coronary artery bypass grafting; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; ICD = implantable cardioverter defibrillator; IPG = implantable pulse generator; LVEF = left ventricular ejection fraction; MR = mitral valve regurgitation; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TR = tricuspid valve regurgitation.

**TABLE 2 Procedural Characteristics**

| | Unmatched | | | | Matched | | | |
|---|---|---|---|---|---|---|---|---|
| | CoreValve (n = 5,514) | Evolut R (n = 11,295) | Evolut PRO (n = 2,065) | p Value* | CoreValve (n = 1,500) | Evolut R (n = 1,500) | Evolut PRO (n = 1,500) | p Value* |
| Elective procedure | 5,045 (91.6) | 10,311 (91.3) | 1,903 (92.2) | 0.17 | 1,387 (92.6) | 1,381 (92.1) | 1,374 (91.7) | 0.68 |
| General anesthesia† | 4,659 (84.7) | 7,407 (65.7) | 998 (48.5) | <0.001 | 873 (58.2) | 839 (55.9) | 896 (59.7) | 0.04 |
| Vascular access† | | | | | | | | |
| Iliofemoral | 4,946 (89.8) | 10,321 (91.5) | 1,954 (94.7) | <0.001 | 1,404 (93.6) | 1,403 (93.5) | 1,412 (94.1) | 0.49 |
| Subclavian | 262 (4.8) | 610 (5.4) | 62 (3.0) | <0.001 | 49 (3.3) | 63 (4.2) | 44 (2.9) | 0.06 |
| Direct aortic | 231 (4.2) | 167 (1.5) | 32 (1.6) | 0.81 | 27 (1.8) | 12 (0.8) | 30 (2.0) | 0.005 |
| Valve size implanted | | | | | | | | |
| 23 mm | 271 (5.0) | 444 (4.0) | 79 (3.9) | 0.82 | 62 (4.2) | 69 (4.6) | 47 (3.2) | 0.04 |
| 26 mm | 1,874 (34.5) | 3,869 (34.5) | 695 (33.9) | 0.61 | 487 (32.9) | 528 (35.4) | 500 (33.6) | 0.31 |
| 29 mm | 3,294 (60.6) | 6,913 (61.6) | 1,277 (62.3) | 0.56 | 932 (62.9) | 896 (60.0) | 942 (63.3) | 0.07 |
| Intraprocedural death§ | 32 (0.6) | 31 (0.3) | 5 (0.2) | 0.79 | 5 (0.3) | 3 (0.2) | 4 (0.3) | >0.99 |
| More than 1 valve used | 239 (4.3) | 228 (2.0) | 26 (1.3) | 0.02 | 62 (4.1) | 32 (2.1) | 19 (1.3) | 0.76 |
| Coronary obstruction§ | 26 (0.5) | 23 (0.2) | 2 (0.1) | 0.41 | 8 (0.5) | 1 (0.1) | 1 (0.1) | >0.99 |
| Conversion to open heart surgery | 58 (1.1) | 40 (0.4) | 7 (0.3) | 0.91 | 20 (1.3) | 4 (0.3) | 4 (0.3) | >0.99 |
| Bleeding at access site§ | 97 (1.8) | 186 (1.6) | 25 (1.2) | 0.14 | 26 (1.7) | 28 (1.9) | 17 (1.1) | 0.10 |
| Device success‡ | 5,187 (94.8) | 10,811 (96.7) | 1,985 (96.8) | 0.82 | 1,413 (95.1) | 1,443 (97.2) | 1,447 (96.9) | 0.68 |
| Procedure time, min | 128.6 ± 65.4 | 112.6 ± 58.2 | 100.1 ± 53.4 | <0.001 | 124.6 ± 62.3 | 109.4 ± 53.5 | 100.9 ± 53.9 | <0.001 |
| Median length of stay, days | 5.0 (3.0–8.0) | 4.0 (2.0–7.0) | 3.0 (2.0–5.0) | <0.001 | 4.0 (3.0–7.0) | 3.0 (2.0–6.0) | 3.0 (2.0–5.0) | <0.001 |
| Discharged home | 3,745 (70.4) | 8,673 (78.5) | 1,699 (83.4) | <0.001 | 1,096 (75.2) | 1,187 (80.7) | 1,211 (81.9) | 0.39 |

Values are n (%), mean ± SD, or median (1st and 3rd quartiles), reflecting missing values. *p values comparing Evolut R and Evolut PRO valve groups. †Used in propensity score matching. ‡Per Valve Academic Research Consortium-1 (8). §In-hospital events. Hospitalizations reported as median (interquartile range).

and 22.1%; $p < 0.001$), and prior coronary artery bypass grafting (23.4%, 21.2%, and 16.8%; $p < 0.001$). After propensity score matching, the CoreValve, Evolut R, and Evolut PRO groups were well matched and balanced, with absolute standardized differences of <10% across all measured baseline characteristics (Table 1).

**PROCEDURAL CHARACTERISTICS.** Procedural characteristics for the unmatched and matched datasets are shown in Table 2. The unmatched data demonstrate a decline in the use of general anesthesia (84.7%, 65.7%, and 48.5%; $p < 0.001$) and increased use of the iliofemoral approach (89.8%, 91.5%, and 94.7%; $p < 0.001$). These 2 procedural characteristics were used in propensity score analysis and were well balanced after matching.

In the matched groups, the rates of coronary obstruction (0.5%, 0.1%, and 0.1%; $p > 0.99$) and conversion to open heart surgery (1.3%, 0.3%, and 0.3%; $p > 0.99$) remained low in all 3 valve groups (Table 2). With the recapturable Evolut system, the need for more than 1 valve remained very low (4.1%, 2.1%, and 1.3%; $p = 0.07$), and there was no significant difference in access site bleeding (1.7%, 1.9%, and 1.1%; $p = 0.10$) (Table 2).

**CLINICAL OUTCOMES.** The 30-day outcomes for the valve groups before and after matching are shown in Table 3. Vital status at 30 days was available for 83.2% of CoreValve, 84.0% of Evolut R, and 84.9% of Evolut PRO patients. Within the matched groups, there was no significant difference in all-cause mortality at 30 days (4.1%, 3.0%, and 2.7%; $p = 0.51$), stroke (2.8%, 3.9%, and 3.3%; $p = 0.35$), or need for PPI (22.4%, 18.7%, and 16.9%; $p = 0.51$). There was less major bleeding in the Evolut PRO group (0.6%, 0.9%, and 0.2%; $p = 0.01$).

**AORTIC REGURGITATION.** The percentages of patients with greater than mild aortic regurgitation (AR) at 30 days for the unmatched and matched cohorts are shown in Table 3 and Figure 2. In both the unmatched and matched groups, patients treated with the Evolut PRO had a lower incidence of more than mild AR compared with patients treated with the Evolut R (unmatched: CoreValve 7.8%, Evolut R 5.2%, and Evolut PRO 2.8% [$p < 0.001$]; matched: 8.3%, 5.4%, and 3.4% [$p = 0.03$]).

**HEMODYNAMIC STATUS.** Valve hemodynamic parameters for the matched patient cohorts are shown in Figure 3. The hemodynamic performance of the 3

**TABLE 3 30-Day Outcomes**

| | Unmatched | | | | Matched | | | |
|---|---|---|---|---|---|---|---|---|
| | CoreValve (n = 5,514) | Evolut R (n = 11,295) | Evolut PRO (n = 2,065) | p Value* | CoreValve (n = 1,500) | Evolut R (n = 1,500) | Evolut PRO (n = 1,500) | p Value* |
| All-cause mortality | 287 (5.3) | 353 (3.2) | 47 (2.5) | 0.06 | 61 (4.1) | 44 (3.0) | 37 (2.7) | 0.51 |
| Stroke | 175 (3.2) | 388 (3.5) | 64 (3.2) | 0.48 | 41 (2.8) | 58 (3.9) | 48 (3.3) | 0.35 |
| Ischemic | 152 (2.8) | 327 (2.9) | 58 (2.9) | 0.88 | 36 (2.4) | 48 (3.2) | 44 (3.0) | 0.71 |
| Hemorrhagic | 5 (0.1) | 19 (0.2) | 2 (0.1) | 0.47 | 1 (0.1) | 1 (0.1) | 1 (0.1) | 0.99 |
| Myocardial infarction | 27 (0.5) | 40 (0.4) | 7 (0.3) | 0.95 | 5 (0.3) | 2 (0.1) | 6 (0.4) | 0.15 |
| Life-threatening bleeding† | 2 (0.0) | 7 (0.1) | 1 (0.1) | 0.84 | 2 (0.1) | 0 (0.0) | 0 (0.0) | NA |
| Major bleeding† | 39 (0.8) | 66 (0.6) | 4 (0.2) | 0.03 | 8 (0.6) | 13 (0.9) | 3 (0.2) | 0.01 |
| Vascular complications | 317 (5.8) | 633 (5.6) | 99 (4.8) | 0.15 | 71 (4.8) | 85 (5.7) | 70 (4.7) | 0.23 |
| Major vascular complication | 100 (1.8) | 176 (1.6) | 25 (1.2) | 0.24 | 20 (1.3) | 26 (1.7) | 16 (1.1) | 0.12 |
| Permanent pacemaker or ICD‡ | 1,037 (19.1) | 1,822 (16.4) | 294 (14.6) | 0.05 | 279 (18.8) | 227 (15.3) | 209 (14.2) | 0.45 |
| New permanent pacemaker or ICD§ | 1,034 (23.5) | 1,808 (19.6) | 292 (17.1) | 0.01 | 279 (22.4) | 226 (18.0) | 207 (16.9) | 0.51 |
| Aortic valve reintervention | 26 (0.5) | 21 (0.2) | 4 (0.2) | 0.91 | 10 (0.7) | 2 (0.1) | 2 (0.1) | 0.99 |
| Valve thrombosis | 0 (0.0) | 2 (0.0) | 0 (0.0) | 0.57 | 0 (0.0) | 0 (0.0) | 0 (0.0) | NA |
| Percutaneous coronary intervention | 32 (0.6) | 28 (0.3) | 4 (0.2) | 0.66 | 5 (0.3) | 6 (0.4) | 3 (0.2) | 0.33 |
| Valve-related readmission | 50 (1.0) | 116 (1.1) | 17 (0.9) | 0.47 | 12 (0.9) | 19 (1.3) | 10 (0.7) | 0.11 |
| Moderate or severe aortic regurgitation | 284/3,632 (7.8) | 408/7,811 (5.2) | 40/1,444 (2.8) | <0.001 | 85/1,026 (8.3) | 55/1,025 (5.4) | 36/1,048 (3.4) | 0.03 |

Values are number of patients with events (Kaplan-Meier rates as percentages) or proportions of patients for moderate or severe aortic regurgitation. *The p values comparing Evolut R and Evolut PRO patient groups. †Bleeding events after the index hospitalization. ‡Includes patients with pacemakers or ICDs at baseline. §Includes patients without pacemakers or ICD at baseline.

ICD = implantable cardioverter-defibrillator; NA = not analyzable.

types of self-expanding valves was very similar, with effective orifice area post-procedure >1.9 $cm^2$ and mean gradients at 30 days that were <8 mm Hg for all 3 generations of self-expanding valves.

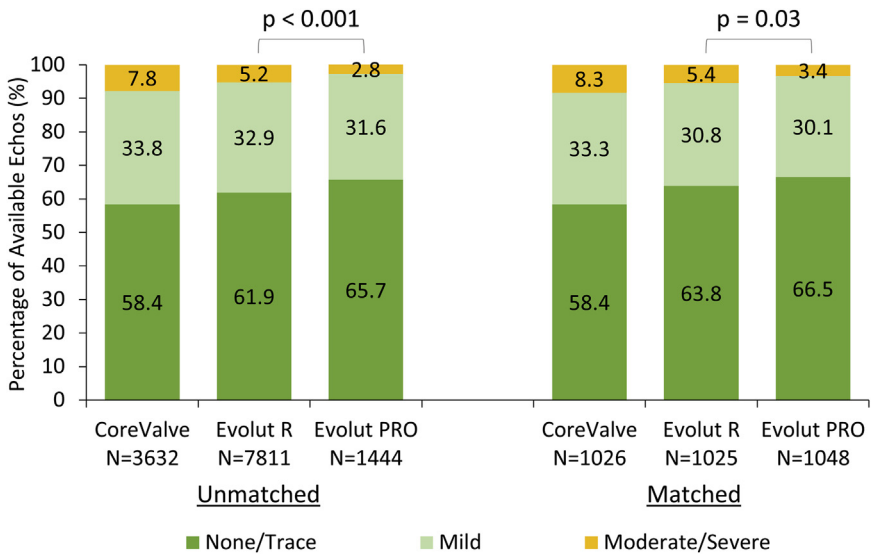
## DISCUSSION

The Evolut PRO valve was designed to maintain the advantages of the Evolut R valve while decreasing PVL through the addition of an outer pericardial tissue wrap. We found in this real-world analysis from the TVT Registry that use of the Evolut PRO valve, compared with the Evolut R valve, is associated with a decreased incidence of greater than mild AR. The distribution of AR from early commercial use of the Evolut PRO in the TVT Registry analysis (65.7% none or trace, 31.6% mild, 2.8% moderate, and 0% severe) (**Figure 2**) is very similar to that reported in the Evolut PRO US Study (72.4% none or trace, 27.6% mild, 0% moderate, and 0% severe) (5). These confirmatory findings in a real-world setting demonstrate that TAVR continues to edge closer to the gold standard of near complete elimination of significant PVL set by surgical aortic valve replacement.

**HEMODYNAMIC STATUS.** From its origin, the CoreValve bioprosthesis was designed as a supra-annular self-expanding valve. Although there have been modifications to the frame structure, leaflet anticalcification, and the delivery system in subsequent iterations, the supra-annular and self-expanding features of the valve have remained a hallmark of this platform. This design has resulted in post-TAVR hemodynamic parameters consistently superior to both surgical aortic valve replacement and balloon-expanding valve systems (1,6,8,9). Importantly, this analysis confirms findings from the initial Evolut PRO US Study that the addition of the outer pericardial wrap did not affect the hemodynamic profile, with mean gradients in the single digits and effective orifice areas of >1.9 $cm^2$.

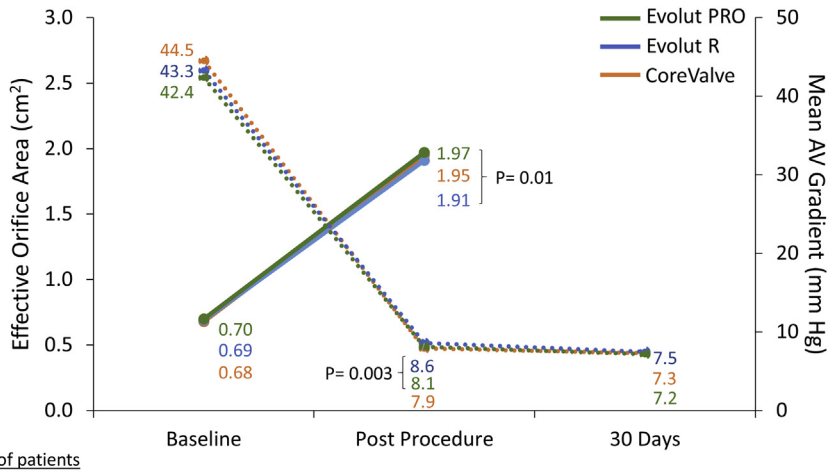
**PACEMAKERS.** Certain features of TAVR valve design intended to decrease PVL, such as increased radial force and sealing at and below the level of the annulus, may increase the incidence of conduction system disturbances. The inverse relationship between PVL and the need for PPI has been shown in both balloon and self-expanding valves (10–12). The Evolut R system was designed, in part, to optimize the interaction of the valve at the level of the annulus and left ventricular outflow tract, leading to lower rates of new PPI compared with the CoreValve bioprostheses (1,4,13). Importantly, our

**FIGURE 2 Total Aortic Regurgitation at 30 Days**




Site-reported aortic valve regurgitation at 30 days for patients in the unmatched **(left)** and matched **(right)** cohorts. The p values report the differences in moderate or severe aortic regurgitation for comparison between the Evolut PRO and Evolut R groups.

**FIGURE 3 Valve Hemodynamic Status to 30 Days for Matched Patients**




| No. of patients | | | |
|---|---|---|---|
| CoreValve EOA | 1481 | 1007 | |
| Evolut R EOA | 1474 | 1115 | |
| Evolut PRO EOA | 1481 | 1152 | |
| CoreValve MVG | 1480 | 1245 | 1011 |
| Evolut R MVG | 1481 | 1336 | 1011 |
| Evolut PRO MVG | 1481 | 1343 | 1038 |

Site reported mean aortic valve (AV) gradient and effective orifice area (EOA) at baseline, post-procedure, and 30 days (gradient only). Dashed lines represent mean gradients. The p values for comparison between the Evolut PRO and Evolut R groups. Baseline values were calculated for patients who underwent attempted TAVR procedure. Post-procedure and 30-day values were calculated in patients who were successfully implanted.

study demonstrates that the addition of the outer pericardial wrap on the Evolut PRO valve decreased AR without increasing the need for a new pacemaker.

**STUDY LIMITATIONS.** Our study was limited by its retrospective and observational design, using the TVT Registry, in which data are site reported and echocardiographic outcomes are not adjudicated by a core laboratory. Additionally, excluding the larger valve sizes led to a study cohort with an increased proportion of women than the general TAVR population, and differences in early outcomes and complications by sex have been reported (14,15). To account for a changing patient population and approved indications, we performed this analysis using both unmatched and matched data. Although we matched for many baseline patient characteristics and procedural characteristics (including mode of sedation and femoral approach), this matching could not take into account operator experience with TAVR. Although correlations between procedural volume and outcomes in TAVR has been previously shown (16,17), given that within the matched groups there were not significant differences in mortality, stroke, or PPI between the Evolut R and Evolut PRO valve groups, the finding of a significant difference in greater than mild AR between these 2 valves is unlikely to be due to operator volume. In addition, certain factors that may contribute to outcome differences, including the presence of a right bundle branch block, pre- and post-dilation, and implantation depth, are not captured in the TVT Registry (18).

## CONCLUSIONS

Advancements in valve technologies and expanded indications for TAVR have resulted in improved outcomes for patients undergoing TAVR in the United States with self-expanding, supra-annular valves. In particular, the addition of an outer pericardial tissue wrap designed to enhance sealing at the level of the aortic annulus has resulted in very low rates of significant AR while maintaining excellent hemodynamic status.

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## PERSPECTIVES

**WHAT IS KNOWN?** Recent advances in transcatheter therapies have focused on improved sealing at the annulus while decreasing the incidence of new pacemakers and maintaining excellent hemodynamic status. These advances have occurred in conjunction with an expanding patient population who are candidates for TAVR.

**WHAT IS NEW?** In real-world clinical use, the Evolut PRO valve demonstrated exceptionally low rates of significant PVL while maintaining excellent hemodynamic status and low complication rates compared with prior generations of self-expanding, supra-annular transcatheter valves.

**WHAT IS NEXT?** As TAVR becomes a viable option for younger and lower risk patients, continued technological advances as well as tailoring of both the approach and prosthesis type for each patient and their unique anatomy may continue to drive improved patient outcomes.

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**KEY WORDS** aortic stenosis, paravalvular leak, self-expanding, transcatheter aortic valve replacement

**APPENDIX** For supplemental tables and a figure, please see the online version of this paper.