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# Clinical Impact of Moderate-to-Severe Paravalvular Leak in Modern Transcatheter Aortic Valve Implantation

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## Abstract

Paravalvular leak (PVL) was first noted as a frequent adverse event after transcatheter aortic valve implantation (TAVI) and has often been connected to poorer patient prognosis, such as higher death rates. This investigation aimed to examine the extended clinical consequences of PVL in individuals receiving the most recent models of transcatheter aortic valves, drawing on the national, prospective, multicenter OBSERVANT II registry. The OBSERVANT II registry prospectively collected data on every successive patient with severe aortic stenosis treated by TAVI at 28 Italian institutions between December 2016 and September 2018. In total, 2125 patients formed the basis of this evaluation. They were categorized by the presence of moderate-to-severe PVL (significant PVL, n = 155) versus absent or trace-to-mild PVL (no significant PVL, n = 1970). The main outcome measure was 5-year major adverse cardiac and cerebrovascular events (MACCE), which combined all-cause mortality, stroke, myocardial infarction, and coronary revascularization procedures. Additional endpoints consisted of 5-year overall mortality and readmission due to heart failure (HF). Within the studied population, moderate-to-severe PVL occurred in 7% of cases. Key factors associated with PVL development included advancing age, greater aortic annulus perimeter, and the use of self-expandable valves. After five years, the likelihood of experiencing MACCE, overall death, or heart failure readmission showed no meaningful variation across the two groups [HR = 1.07 (95% CI: 0.85–1.34) P = 0.571; HR = 1.10 (95% CI: 0.87–1.39) P = 0.435; HR = 1.20 (95% CI: 0.88–1.62) P = 0.245, respectively]. According to this OBSERVANT II registry evaluation, the presence of moderate or severe PVL did not correlate with elevated rates of MACCE or heart failure re-hospitalization over the 5-year observation period.

**Keywords:** TAVI, TAVR, Paravalvular leak, Aortic stenosis

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## Introduction

At present, transcatheter aortic valve implantation (TAVI) stands as a standard therapeutic approach for managing symptomatic severe aortic stenosis (AS), above all in older adults and those facing elevated operative risk [1]. In advanced economies, TAVI procedures have now exceeded surgical aortic valve replacement in frequency and are increasingly applied to lower-risk and younger candidates [2]. For this reason, thorough monitoring of the procedure's durability and long-term results remains vital. Paravalvular leak (PVL) emerged early on as one of the leading issues following TAVI and has frequently been associated with unfavorable outcomes, notably increased mortality [3, 4]. To counteract this, contemporary TAVI systems feature an additional outer sealing skirt around the valve frame, intended to markedly reduce PVL [5, 6]. Earlier research exploring the importance of this imperfect procedural outcome has delivered mixed conclusions [3, 4, 7-9]. Hence, by utilizing information from the Italian nationwide prospective multicenter registry — the Observational Study of the Effectiveness of Transcatheter Aortic Valve Implantation with New-Generation Devices for Severe Aortic Stenosis Treatment (OBSERVANT II) — the current work seeks to establish the rate of this complication with modern valves, pinpoint related predisposing elements, and determine its effect on extended patient prognosis.

## Materials and Methods

### *Research cohort*

OBSERVANT II consisted of a countrywide, forward-looking, multicenter observational investigation that recruited every consecutive case of severe aortic stenosis undergoing TAVI across 30 specialized cardiology centers in Italy, spanning December 2016 to September 2018. The present analysis drew on information from 28 centers that met the protocol's specified thresholds for acceptable data reliability [10]. Another three centers could not be included due to missing or inadequate computed tomography (CT) records. Each center obtained approval from its local ethics committee to participate in OBSERVANT II, and participants provided informed consent, with data handled under pseudonymization. This particular sub-analysis was confined to patients implanted with contemporary transcatheter valve models (Evolut R and PRO, Medtronic, Minneapolis, MN, USA; Sapien 3 Ultra, Edwards Lifesciences Corp., Irvine, CA, USA; Accurate, Boston Scientific, Marlborough, MA, USA; Lotus, Boston Scientific, Marlborough, MA, USA) exclusively through the transfemoral access route. Cases involving prior-generation valves, active endocarditis, urgent interventions, valve-in-valve procedures, or TAVI performed within bicuspid aortic valves were deliberately excluded. All relevant patient details at baseline, procedural aspects, and complications arising during the initial hospital stay were systematically documented using a standardized electronic case report form for each participant [10].

### *Paravalvular leak assessment*

After the procedure, transthoracic echocardiography (TTE) was routinely performed before hospital discharge. Aortic regurgitation was graded using color-flow Doppler according to the Valve Academic Research Consortium (VARC)-2 classification [11]. This choice was made because patient inclusion had begun before the VARC-3 update became available [12] (although the two sets of criteria are largely aligned). Post-TAVI aortic regurgitation was therefore classified into five distinct grades: none, trivial, mild, moderate, or severe. Assessment of both the native valve and the post-implantation regurgitation adhered to the European Association of Echocardiography guidelines [13] and the American Society of Echocardiography recommendations [14]. A multiparametric, integrative approach was employed rather than relying on a single echocardiographic measure. In post-TAVI cases, where leaks are predominantly paravalvular, particular weight was assigned to the circumferential extension of the jets, evaluated in the short-axis view just inferior to the bioprosthesis. This parameter describes the percentage of the prosthetic valve's circumference involved by the regurgitant jet. In practice, the arc length of the jet along the valve's curved edge is measured and expressed as a proportion of the complete valve ring perimeter, yielding a percentage value. As a guide, circumferential extension below 10% is usually considered mild PVR, 10–30% corresponds to moderate PVL, and values above 30% indicate severe PVL [15]. Quantification of circumferential jet extension in the short-axis plane is regarded as one of the most important elements when determining the severity of aortic regurgitation following TAVI.

### *Clinical follow-up and outcomes*

Events arising after discharge were identified through linkage of the study database to the Italian Ministry of Health's National Hospital Discharge Records and additional administrative datasets, facilitated by cooperation with the Italian National Program for Outcome Evaluation (PNE-AGENAS). This approach allowed complete capture of 5-year follow-up information for all patients who could be matched to the administrative records. The primary study endpoint was major adverse cardiac and cerebrovascular events (MACCE). This composite outcome included all-cause death, readmission for non-fatal myocardial infarction (MI), non-fatal stroke, and any coronary revascularization (CABG or PCI) occurring up to 5 years. All-cause mortality was evaluated separately as a secondary endpoint to isolate the contribution of fatal events. Readmission for heart failure was analyzed as a secondary endpoint to assess the potential hemodynamic effects of PVL.

### *Statistical analysis*

Categorical data were expressed as absolute numbers and percentages, whereas continuous variables were presented as means with their standard deviations. Comparisons of baseline and procedural characteristics between the two groups were performed using the Mann–Whitney U test, the Kruskal–Wallis test, or the chi-square test, as appropriate. Fisher's exact test was used whenever any expected cell frequency was less than 5. Owing to noticeable imbalances in baseline and operative variables between groups, logistic regression with backward selection was applied to identify independent predictors of significant PVL. Unadjusted 5-year differences in MACCE and all-cause mortality were examined using Kaplan–Meier curves and the log-rank test. For 5-year heart failure re-hospitalization, a competing-risk analysis was conducted (considering death as the competing event) with Gray's test. Adjusted comparisons for MACCE and mortality were obtained from multivariate Cox proportional hazards regression models that accounted for key baseline and procedural risk factors. Time to heart failure re-hospitalization was modeled using the Fine and Gray competing-risk regression, again treating death as the competing risk. A stepwise selection procedure automatically chose relevant variables from the following candidate covariates: female sex, age, previous MI, diabetes, peripheral artery disease, chronic obstructive pulmonary disease, oxygen therapy, dialysis, pulmonary hypertension, active cancer, neurological dysfunction, liver diseases, previous cardiac surgery, previous percutaneous coronary intervention, coronary artery disease, frailty class, EuroSCORE II, NYHA class, BMI class, eGFR class, moderate/severe mitral regurgitation, left ventricular ejection fraction, aortic mean gradient, self-expandable transcatheter valve, valve post-dilation, and annulus perimeter. All statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

## Results and Discussion

The OBSERVANT II registry recruited 2989 individuals with severe aortic stenosis who underwent TAVI between December 2016 and September 2018 at 28 Italian centers. After applying the exclusion criteria, the analysis included 2125 patients. According to the post-procedural evaluation of PVL, these patients were split into two distinct categories: 1970 cases showing no, trivial, or mild PVL (classified as no significant PVL) and 155 cases (7%) exhibiting moderate or severe PVL (classified as significant PVL) **(Figure 1)**. The rate of severe PVL alone stood at 0.3%.

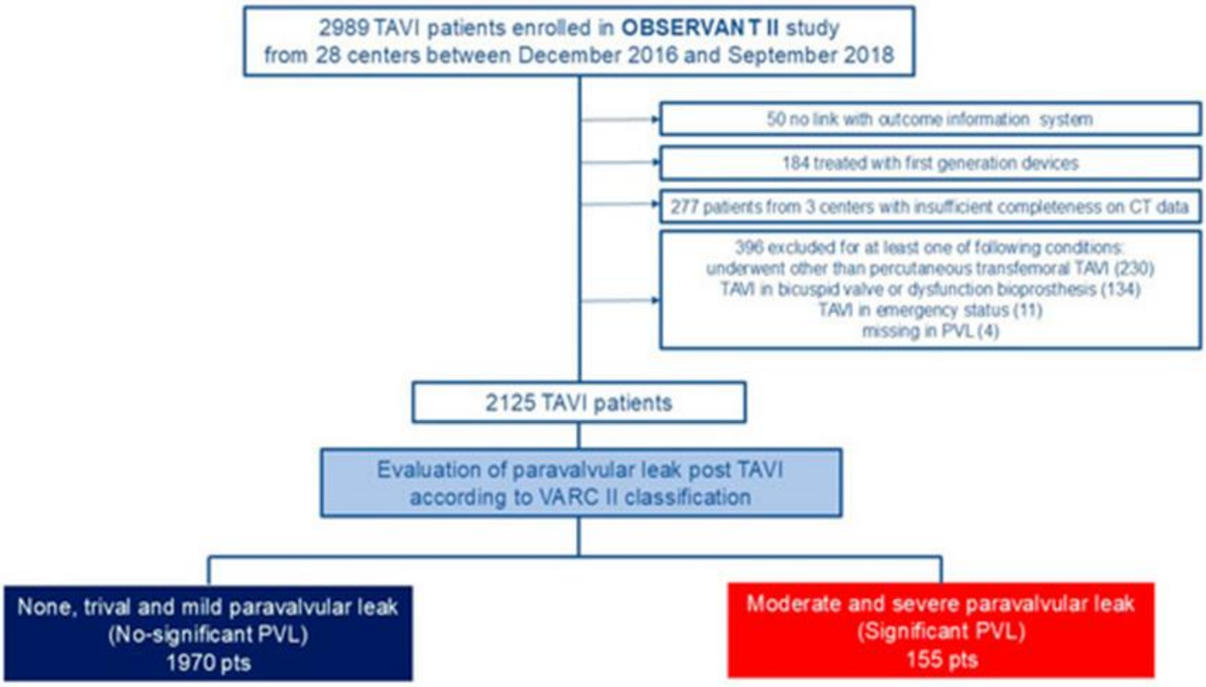



**Figure 1.** Study flow chart.

Patient characteristics at baseline appear in **Table 1** and indicate several notable contrasts between the groups. Those without significant PVL were generally younger than those with significant PVL (82.1 ± 6.2 vs. 83.4 ± 6, P = 0.012). The presence of diabetes was higher among patients without significant PVL (28.9% vs. 21.3%, P = 0.044). On the other hand, peripheral artery disease and a history of percutaneous coronary intervention occurred more often in the significant PVL group (23.4% vs. 14.3%, P = 0.002, and 18.7% vs. 12.4%, P = 0.024, respectively). EuroSCORE II values remained comparable between the two groups. **Table 2** outlines the primary echocardiographic, anatomical, and procedural details. No differences were found regarding associated mitral regurgitation or left ventricular ejection fraction between the groups. However, the average aortic gradient proved higher in the significant PVL group (49.8 ± 15.3 mmHg vs. 47.3 ± 14.7 mmHg, P = 0.048). The aortic annulus perimeter measured larger in patients with significant PVL (76.2 ± 0.9 mm vs. 74.4 ± 0.9 mm, P = 0.019). Implantation of self-expandable valves happened far more commonly in the significant PVL group (28.5% vs. 8.4%, P < 0.001). Post-dilation procedures were also carried out more frequently when significant PVL was detected (41.9% vs. 22.1%, P < 0.001). Valve migration likewise arose more often in this group (2.6% vs. 0.01%, P = 0.001). Independent factors predicting significant PVL turned out to be advancing age, increased aortic annulus perimeter, and implantation of a self-expandable valve (OR 1.04, 95% CI 1.01–1.08, P = 0.018; OR 1.41, 95% CI 1.09–1.83, P = 0.010; OR 3.44, 95% CI 1.75–6.67, P < 0.001, respectively) **(Table 3)**.

**Table 1.** Baseline characteristics of the study population.

| Variable | P-value | Significant PVL (n = 155) | No significant PVL (n = 1970) |
|---|---|---|---|
| **Female gender, n (%)** | 0.653 | 85 (54.8) | 1117 (56.7) |
| **Age (years)** | 0.012 | 83.4 ± 6.1 | 82.1 ± 6.2 |
| **History of myocardial infarction, n (%)** | 0.320 | 6 (3.9) | 41 (2.1) |
| **Diabetes mellitus, n (%)** | 0.044 | 33 (21.3) | 566 (28.9) |
| **Peripheral artery disease, n (%)** | 0.002 | 36 (23.4) | 279 (14.3) |
| **Chronic obstructive pulmonary disease, n (%)** | 0.936 | 24 (15.5) | 300 (15.2) |
| **Use of oxygen therapy, n (%)** | 0.336 | 3 (1.9) | 66 (3.4) |
| **Dialysis dependence, n (%)** | 0.406 | 5 (3.2) | 43 (2.2) |
| **Pulmonary hypertension, n (%)** | 0.801 | 9 (5.8) | 105 (5.3) |
| **Active malignancy, n (%)** | 0.666 | 5 (3.2) | 76 (3.9) |
| **Neurological dysfunction, n (%)** | 0.214 | 6 (3.87) | 45 (2.3) |
| **Liver pathology, n (%)** | 0.696 | 3 (1.9) | 30 (1.5) |
| **Prior cardiac surgery, n (%)** | 0.432 | 15 (9.7) | 232 (11.8) |
| **Coronary artery disease, n (%)** | 0.014 | | |
| **└─ Single-vessel disease** | | 24 (15.7) | 280 (14.3) |
| **└─ Multi-vessel disease (≥ 2)** | | 24 (15.7) | 173 (8.9) |
| **Previous CABG, n (%)** | 0.392 | 11 (7.1) | 180 (9.1) |
| **Previous PCI, n (%)** | 0.024 | 29 (18.7) | 244 (12.4) |
| **GSS frailty score 3–4, n (%)** | 0.871 | 32 (20.6) | 396 (20.1) |
| **EuroSCORE II** | 0.082 | 7.4 ± 7.0 | 6.5 ± 6.4 |
| **NYHA class III/IV, n (%)** | 0.362 | 117 (75.5) | 1407 (72.1) |
| **Body mass index category, n (%)** | <0.001 | | |
| **└─ ≤ 25** | | 87 (56.1) | 821 (41.8) |
| **└─ 25–30** | | 52 (33.5) | 708 (36.1) |
| **└─ > 30** | | 16 (10.3) | 433 (22.1) |
| **eGFR category, n (%)** | 0.261 | | |
| **└─ < 30** | | 22 (14.2) | 198 (10.1) |
| **└─ 30–60** | | 64 (41.3) | 870 (44.2) |
| **└─ > 60** | | 69 (44.5) | 899 (45.7) |

Abbreviations: PAD = peripheral artery disease; COPD = chronic obstructive pulmonary disease; CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention; GSS = geriatric status scale; NYHA = New York Heart Association; BMI = body mass index; eGFR = estimated glomerular filtration rate.

**Table 2.** Echocardiography, anatomical, and procedural characteristics of the study population.

| Parameter | P-value | PVL Moderate/Severe (n = 155) | PVL None/Mild (n = 1970) |
|---|---|---|---|
| **Echocardiographic characteristics** | | | |
| **Moderate-to-severe mitral regurgitation, n (%)** | 0.416 | 55 (35.71) | 639 (32.5) |
| **Left ventricular ejection fraction (LVEF)** | 0.370 | 53.4 ± 11.3 | 53.9 ± 11.1 |
| **Mean aortic valve gradient** | 0.048 | 49.8 ± 15.3 | 47.3 ± 14.7 |
| **Anatomical characteristics** | | | |
| **Aortic valve area** | 0.220 | 4.5 ± 1.1 | 4.39 ± 1.0 |

| | | | |
|---|---|---|---|
| **Aortic valve perimeter** | 0.019 | 76.2 ± 9 | 74.4 ± 8.6 |
| **Diameter of the aortic annulus** | 0.039 | 23.1 ± 2.8 | 22.4 ± 2.3 |
| **Procedural characteristics** | | | |
| **Use of self-expanding TAVI valve, n (%)** | <0.001 | 13 (91.6) | 1410 (71.5) |
| **Valve re-sheathing performed, n (%)** | 0.641 | 28 (18.1) | 366 (18.6) |
| **Occurrence of valve migration, n (%)** | 0.001 | 4 (2.6) | 8 (0.4) |
| **Post-dilatation of valve, n (%)** | <0.001 | 65 (41.9) | 435 (22.1) |
| **Pre-dilatation of valve, n (%)** | 0.871 | 72 (46.5) | 900 (45.8) |

Abbreviation: LVEF = left ventricular ejection fraction.

**Table 3.** Determinants of moderate-to-severe paravalvular leak after TAVI.

| Variable | P-value | 95% confidence interval (CI) | Odds ratio (OR) |
|---|---|---|---|
| **Age (per year increase)** | 0.018 | 1.01–1.08 | 1.04 |
| **Female gender** | 0.532 | 0.74–1.77 | 1.15 |
| **Annular perimeter** | 0.010 | 1.09–1.83 | 1.41 |
| **Use of a self-expanding transcatheter valve** | < 0.001 | 1.75–6.67 | 3.44 |
| **Mean transvalvular gradient** | 0.138 | 1.00–1.02 | 1.01 |
| **Valve post-dilatation performed** | < 0.001 | 1.38–2.96 | 2.02 |

The overall mean follow-up time was 3.7 years (4.8 years for those still living at the end of the observation period). Adjusted curves illustrating freedom from MACCE are displayed in **Figure 2** and reveal no meaningful distinction between the significant PVL and no significant PVL groups (HR = 1.07, 95% CI: 0.85–1.34, P = 0.571). In the same way, heart failure re-hospitalization rates and 5-year all-cause mortality showed no significant variation between the two groups (HR = 1.20, 95% CI: 0.88–1.62, P = 0.245; HR = 1.10, 95% CI: 0.87–1.39, P = 0.435, respectively, **Figure 3**). Detailed multivariate Cox regression models for each endpoint are presented in **Table 4**. Within the studied population, the existence of moderate or severe PVL (in comparison with none or mild) did not independently predict MACCE (HR = 1.07, 95% CI: 0.85–1.34, P = 0.517), all-cause mortality (HR = 1.10, 95% CI: 0.87–1.39, P = 0.435), or heart failure re-hospitalization (HR = 1.20, 95% CI: 0.88–1.62, P = 0.245) over the 5 years. By contrast, factors such as increasing age, comorbidities, and certain hemodynamic measurements played a substantial role in shaping long-term outcomes following TAVI. In particular, each additional year of age was associated with a higher risk of MACCE (HR = 1.02, 95% CI: 1.01–1.03, P = 0.002) and all-cause mortality (HR = 1.02, 95% CI: 1.01–1.04, P < 0.001). Furthermore, conditions like pulmonary hypertension (HR for MACCE = 1.50, 95% CI: 1.16–1.93, P = 0.002; HR for death = 1.65, 95% CI: 1.28–2.14, P < 0.001; HR for HF re-hospitalization = 1.63, 95% CI: 1.19–2.23, P = 0.003) and markedly reduced kidney function (eGFR < 30 vs. > 60: HR for MACCE = 1.76, 95% CI: 1.43–2.17, P < 0.001; HR for death = 1.87, 95% CI: 1.51–2.32, P < 0.001; HR for HF re-hospitalization = 1.83, 95% CI: 1.39–2.39, P < 0.001) ranked among the strongest predictors for all examined endpoints.

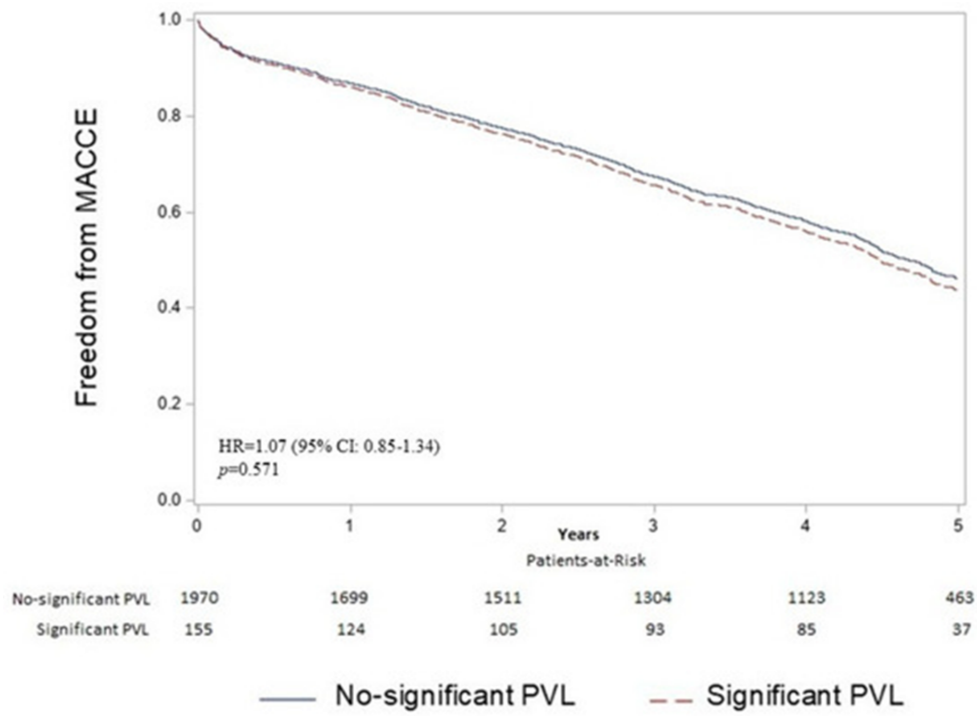
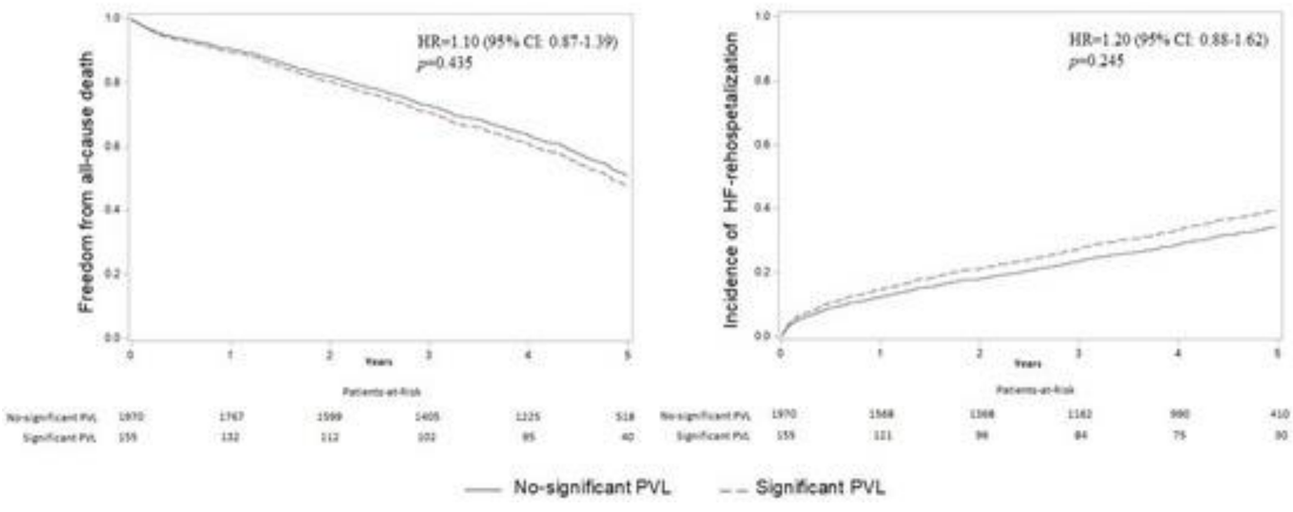



**Figure 2.** Adjusted survival curves for freedom from MACCE. This illustration presents adjusted survival curves for freedom from MACCE (all-cause death, non-fatal myocardial infarction, non-fatal stroke, CABG, and PCI) among study participants grouped by paravalvular leak (PVL) status. The no-significant PVL category encompassed cases with no, trivial, or mild paravalvular leak. The significant PVL category included cases with moderate or severe paravalvular leak. **Table 4** specifies the variables incorporated into the multivariate adjustment.




a) b)

**Figure 3.** Death and incidence of heart failure re-hospitalization according to the severity of paravalvular leak. This illustration presents the adjusted survival curves for all-cause death (panel a) and the adjusted cumulative incidence curves for heart failure re-hospitalization (panel b), categorized by paravalvular leak (PVL) severity. No significant PVL was defined as the combination of no, trivial, or mild paravalvular leak. Significant PVL was defined as moderate or severe paravalvular leak. **Table 4** specifies the variables incorporated into the multivariate adjustment.

**Table 4.** Results of multivariable analysis for 5-year MACCE, all-cause death, and re-hospitalization for HF.

| Variable | HF Re-hospitalization HR (95% CI) | P-value | All-cause mortality HR (95% CI) | P-value | MACCE HR (95% CI) | P-value |
|---|---|---|---|---|---|---|
| **Age** | 1.00 (0.99–1.02) | 0.789 | 1.02 (1.01–1.04) | < 0.001 | 1.02 (1.01–1.03) | 0.002 |
| **Female gender** | 0.96 (0.81–1.14) | 0.627 | 0.71 (0.62–0.81) | < 0.001 | 0.72 (0.63–0.81) | <0.001 |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Presence of significant PVL** | 1.20 (0.88–1.62) | 0.245 | 1.10 (0.87–1.39) | 0.435 | 1.07 (0.85–1.34) | 0.571 |
| **Mean aortic valve gradient** | 0.98 (0.97–0.98) | < 0.001 | 0.99 (0.99–1.00) | < 0.001 | 0.99 (0.99–1.00) | 0.001 |
| **Prior myocardial infarction** | – | – | 1.30 (0.88–1.92) | 0.185 | 1.39 (0.96–2.01) | 0.084 |
| **Requirement for oxygen therapy** | 1.62 (1.07–2.45) | 0.023 | 1.38 (0.99–1.91) | 0.056 | 1.38 (1.00–1.89) | 0.049 |
| **Active malignancy** | 0.61 (0.34–1.09) | 0.096 | – | – | – | – |
| **Pulmonary hypertension** | 1.63 (1.19–2.23) | 0.003 | 1.65 (1.28–2.14) | < 0.001 | 1.50 (1.16–1.93) | 0.002 |
| **Peripheral artery disease** | – | – | 1.22 (1.03–1.44) | 0.025 | 1.19 (1.01–1.40) | 0.042 |
| **Chronic obstructive pulmonary disease** | 1.58 (1.26–1.97) | < 0.001 | 1.42 (1.19–1.69) | < 0.001 | 1.29 (1.09–1.53) | 0.004 |
| **Diabetes mellitus** | 1.47 (1.24–1.75) | < 0.001 | 1.38 (1.20–1.58) | < 0.001 | 1.36 (1.19–1.56) | <0.001 |
| **Dialysis dependence** | – | – | 1.66 (1.16–2.39) | 0.006 | 1.63 (1.14–2.33) | 0.007 |
| **Neurological impairment** | – | – | – | – | 1.36 (0.95–1.96) | 0.097 |
| **Liver disease** | – | – | 1.88 (1.15–3.09) | 0.012 | 1.48 (0.90–2.42) | 0.120 |
| **NYHA class II/III** | 1.26 (1.04–1.53) | 0.019 | 1.19 (1.02–1.38) | 0.025 | 1.18 (1.02–1.36) | 0.025 |
| **GSS frailty score 3–4 vs. 1–2** | – | – | 1.23 (1.05–1.44) | 0.009 | 1.19 (1.02–1.38) | 0.024 |
| **Coronary artery disease** | | | | | | |
| **└─ 1 vs. 0 vessels** | 0.82 (0.64–1.06) | 0.126 | – | – | – | – |
| **└─ ≥ 2 vs. 0 vessels** | 1.07 (0.82–1.41) | 0.603 | – | – | – | – |
| **eGFR category** | | | | | | |
| **└─ 30–60 vs. ≥ 60** | 1.04 (0.86–1.25) | 0.689 | 1.10 (0.96–1.27) | 0.184 | 1.09 (0.95–1.25) | 0.225 |
| **└─ < 30 vs. ≥ 60** | 1.83 (1.39–2.39) | < 0.001 | 1.87 (1.51–2.32) | < 0.001 | 1.76 (1.43–2.17) | <0.001 |
| **Body mass index** | | | | | | |
| **└─ < 25 vs. 25–30** | – | – | 1.34 (1.16–1.55) | < 0.001 | 1.22 (1.06–1.40) | 0.006 |
| **└─ ≥ 30 vs. 25–30** | – | – | 1.07 (0.89–1.29) | 0.490 | 1.00 (0.84–1.20) | 0.999 |
| **Moderate-to-severe mitral regurgitation** | 1.27 (1.07–1.51) | 0.007 | 1.13 (0.99–1.30) | 0.081 | 1.10 (0.97–1.26) | 0.151 |
| **EuroSCORE II** | 1.01 (1.00–1.02) | 0.189 | – | – | – | – |

Abbreviation: PAD = peripheral artery disease; COPD = chronic obstructive pulmonary disease; NYHA = New York Heart Association; GSS = geriatric status scale; CAD = coronary artery disease; BMI = body mass index; eGFR = estimated glomerular filtration rate.

Transcatheter aortic valve implantation (TAVI) first emerged as a less invasive option for managing severe symptomatic aortic stenosis in individuals considered at high or unacceptable risk for open-heart surgery. At present, its application is steadily extending toward younger patients and those with lower surgical risk profiles [5, 6]. Consequently, careful and repeated examination of the durability and distant results of this catheter-based therapy for aortic stenosis is vitally important. The current sub-analysis drawn from the OBSERVANT II registry yielded the following key observations:

- Moderate or severe PVL developed in 7% of patients after TAVI, with severe PVL accounting for 0.3% of the entire cohort.
- The strongest factors associated with the development of moderate or severe PVL were older age, greater aortic annulus perimeter, and deployment of self-expandable valve systems.
- The presence of moderate or severe PVL had no detectable effect on clinical endpoints during the 5-year observation window.

In the early years of TAVI, moderate-to-severe paravalvular leaks were a frequent issue, affecting up to 22% of treated patients [7]. Despite substantial progress in valve design and accumulated procedural expertise, moderate-to-severe PVL still arises more often after TAVI than following conventional surgical aortic valve replacement [15, 16]. In this sub-analysis, the frequency of moderate or severe PVL was 7% among TAVI cases performed in 28 Italian centers from December 2016 to September 2018. This figure is considerably lower than the 19.4% rate documented in the France-TAVI registry for procedures performed between 2010 and 2019 [7].

Consistent with earlier research, the present data confirmed that self-expandable valves and larger annulus dimensions were significant predictors of PVL [17-19]. Older patient age also surfaced as an independent predictor. This relationship likely stems from the greater extent of valve calcification commonly observed in advanced age. Regrettably, detailed information regarding the severity of aortic annulus and leaflet calcification — recognized as major contributors to PVL in previous reports — was unavailable in this registry. An additional explanation may involve clinicians' tendency to tolerate slightly imperfect results (such as performing post-dilatation less aggressively) in frail elderly patients to reduce the chance of serious procedural complications.

The increased frequency of post-dilation among patients exhibiting significant PVL highlights the critical role of procedural refinement during implantation. The use of sophisticated pre-procedural imaging, particularly computed tomography, combined with accurate valve placement and controlled deployment techniques, is vital for reducing PVL. Such methods facilitate more accurate annular measurements, enhanced prosthesis expansion, and effective sealing, thereby reducing the need for additional corrective measures, such as post-dilation.

The clinical significance of moderate or severe paravalvular leaks remains a topic of debate in the literature. Earlier studies have noted that mild PVL commonly occurs after TAVI and typically has a benign prognosis [20]. In contrast, several other reports have linked PVL to elevated long-term mortality [21, 22]. One meta-analysis pooling 38 observational studies and more than 25,000 patients concluded that any level of PVL following TAVI adversely affects both survival and functional capacity [23]. More contemporary evidence from the France-TAVI registry, involving 20,878 patients treated between 2010 and 2019 with a 6.5-year follow-up, similarly demonstrated the detrimental effect of moderate or severe PVL on patient prognosis [7]. Conversely, results from the Polish national POL-TAVI registry indicated that although PVL remains a recurring issue after TAVI, no difference in six-month mortality was observed between patients with no or mild PVL and those with moderate PVL [9]. In keeping with this, the present sub-analysis detected no variation in MACCE rates or heart failure re-hospitalization between the no-significant-PVL and significant-PVL groups during extended follow-up.

The relatively low prevalence of significant PVL in the current cohort may have reduced the statistical power to detect meaningful differences in MACCE, particularly over an extended observation interval. Improvements in candidate selection, implantation methods, and valve engineering likely contributed to diminishing the overall clinical relevance of PVL. Moreover, patient-related factors such as advanced age, comorbidities, and hemodynamic status emerged as stronger drivers of MACCE, exerting a greater effect on long-term prognosis than PVL alone. These observations underscore the multifaceted nature of PVL's influence and the need for additional studies exploring its interactions with comorbidities and long-term outcomes.

As an observational investigation, this study is subject to the typical constraints of such designs, including the possibility of residual confounding arising from both recorded and unrecorded variables. Nevertheless, its strengths include a large nationwide sample covering all commercial TAVI cases performed in Italy during a contemporary timeframe, along with linkage to national administrative registries that provided thorough long-term tracking for every participant. Some degree of underreporting or incomplete data cannot be ruled out entirely. Finally, the relationship between aortic root measurements, calcification burden, and PVL could not be fully clarified. Although aortic annulus and leaflet calcifications are well-established predictors of PVL after TAVI, this registry did not collect information on calcification severity or pattern, thereby limiting evaluation of their contribution in the present analysis.

## Conclusion

In summary, data from the OBSERVANT II registry indicated that significant PVL (moderate or severe) occurred in 7% of patients undergoing TAVI. Several predisposing factors, chiefly related to patient anatomy and choice of TAVI device, were recognized for this complication. A thorough pre-procedural assessment focusing on annulus dimensions, valve anatomy, and the degree of calcification involving the aortic annulus and leaflets is advised to lower the likelihood of significant PVL. Modern imaging tools, especially computed tomography angiography (CTA), are indispensable for optimal prosthesis selection and sizing. Intra-procedural techniques, including precise valve positioning and selective post-dilatation when indicated, play a key part in decreasing significant PVL rates. Adopting these measures in routine practice has the potential to improve overall TAVI outcomes. Significant PVL did not correlate with an increased risk of MACCE, all-cause mortality, or heart failure re-hospitalization during the 5-year follow-up period.

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