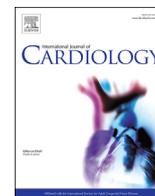




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Outcomes of transcatheter aortic valve replacement without predilation of the aortic valve: Insights from 1544 patients included in the SOURCE 3 registry



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ABSTRACT

Aims: To investigate the impact of transcatheter aortic valve replacement (TAVR) without preliminary balloon aortic valvuloplasty (pre-BAV) on periprocedural outcomes in a large, real-world registry.

Methods and results: The SOURCE 3 registry was an observational, multi-center, single-arm study of patients with severe, symptomatic aortic stenosis at high surgical risk treated with the SAPIEN 3 transcatheter heart valve (THV). Procedural and 30-day outcomes were compared between two groups of 772 patients each (retrospectively matched) with or without pre-BAV. All baseline clinical, echocardiographic, and anatomical valve characteristics were comparable between groups except for Society of Thoracic Surgeons (STS) score, which was lower in the direct TAVR group (6.0 ± 5.9 vs 7.8 ± 8.3 ; $p = 0.003$). In the direct TAVR group, there were less post-dilatations (8.1% vs. 13.1%, $p = 0.002$), shorter procedural time (70.9 ± 39.8 min vs 73.0 ± 32.2 min, $p = 0.033$) and fluoroscopy time (13.4 ± 7.0 min vs 14.9 ± 7.4 min, $p < 0.001$). Other procedural outcomes and echocardiographic variables at 30 days did not differ significantly between the two groups: safety endpoint (10.4% with pre-BAV vs 13.5% with direct TAVR, $p = 0.059$), mortality (2.1% vs 2.3%, $p = 0.730$), disabling strokes (0.4% vs 0.5%, $p = 0.704$), and moderate to severe paravalvular leak (PVL) (3.2% vs 2.2%, $p = 0.40$). Unexpectedly, new permanent pacemaker implantation and life-threatening bleeds were less frequently observed with pre-BAV group than with direct TAVR (10.4% vs 13.9%, $p = 0.032$ and 3.5% vs 6.5%, $p = 0.007$, respectively).

Conclusion: In this large TAVR dataset, direct implantation of the SAPIEN 3 THV without pre-BAV was feasible and safe and resulted in shorter procedures, without impact on 30-day prosthesis function and PVL.

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Abbreviations: AS, Aortic stenosis; BAV, Balloon aortic valvuloplasty; LVOT, Left ventricular outflow tract; PPMI, Permanent pacemaker implantation; PVL, Paravalvular leak; SOURCE, SAPIEN 3 Aortic bioprosthesis Multi-Region Outcome Registry; TAVR, Transcatheter Aortic Valve Replacement.

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1. Introduction

In clinical trials, balloon aortic valvuloplasty (BAV) prior to transcatheter aortic valve replacement (TAVR) with the SAPIEN 3 valve (Edwards Lifesciences; Irvine, CA) has been required per protocol [1,2]. The historical rationale for this requirement was that BAV would facilitate the passage of the prosthesis into the calcified

aortic valve and facilitate its deployment and apposition. Direct implantation of the transcatheter aortic valve without preliminary BAV (i.e., direct TAVR) has emerged as an option, due to technological improvements in the device design and a trend toward procedural simplification. Several studies have shown direct TAVR to be feasible, either with the self-expandable [3] or balloon-expandable prostheses [4]. Considering the specific risk of mechanical complications related to BAV [5], some investigators have speculated about potential safety benefits (e.g., reduction of acute stroke, reduced need for new permanent pacemaker implantation [PPMI]) if this step is eliminated from the procedure. Single-center studies used in meta-analyses and multicenter registries [6–10] tried to address these issues, as well. However, unadjusted results and aggregation of different prosthesis outcomes led to uncertainties about the impact of BAV avoidance on TAVR procedural outcomes according to prosthesis type.

We investigated the potential safety and efficacy of TAVR without pre-BAV (i.e., direct TAVR) using the SAPIEN 3 prosthesis in the post-approval SOURCE 3 (SAPIEN 3 Aortic Bioprosthesis European Outcome) registry.

2. Methods

2.1. SOURCE 3 registry design

SOURCE 3 is a European post-approval, multicenter, observational study designed to assess the safety and performance of the SAPIEN 3 transcatheter heart valve (THV) in real-world clinical practice for patients with severe aortic stenosis (AS) who were at high risk for surgery. The study rationale and detailed design information, as well as 30-day and 1-year outcomes have been previously published [11,12].

Patient selection, valve size, and access route choices were performed according to the manufacturer's recommendations and the European Society of Cardiology guidelines [13].

The research protocol complies with the Declaration of Helsinki. Written informed consent was obtained from all participants and the protocol was approved by the local ethics committee.

Edwards Lifesciences sponsored this study. The propensity matching was done by an independent party. The concept and manuscript were proposed by the first and last author and developed under the supervision of the study steering committee members. The biostatistician for this study is an author and employee of Edwards Lifesciences. All authors followed GPP3 guidelines for ethical publication practices.

2.2. Data collection and follow-up

All data were entered into an electronic data capture system by the participating centers and were monitored by Edwards Lifesciences. Follow-up was active; patients were assessed at discharge, 30 days post-discharge, one year, and annually up to five years post-implantation. The analyses reported herein include data up to the 30-day visit.

2.3. Study objectives and endpoints definitions

The purpose of this study was to assess whether performing BAV before a SAPIEN 3 prosthesis implantation was associated with differences in outcomes for safety and device performance to 30 days post implantation. The choice to perform pre-BAV was left to the discretion of the operator.

A pre-operative CT scan for procedural planning and valve size selection was also used to evaluate annular and subannular calcification. Operators made a qualitative assessment of the degree of annular and sub-annular calcification, graded as none to mild, moderate, or severe.

Procedural success was defined as 1) patients alive at the end of the procedure, 2) the SAPIEN 3 THV implanted in the intended position on the first attempt, and 3) the valve was performing as intended at the time of discharge.

Key clinical events included the following: early safety endpoint, all-cause death, cardiac death, disabling stroke, major vascular complications, life-threatening bleeding, acute kidney injury, PPMI, and procedural complications. These events were adjudicated by an independent clinical events committee that followed VARC-2 definitions [14].

Functional status was assessed using the New York Heart Association (NYHA) functional class. Valve performance endpoints (mean gradient, effective orifice area [EOA], and paravalvular leak) were assessed by echocardiography.

2.4. Statistical analysis

This was a non-randomized, post-hoc analysis of prospectively collected data. Continuous variables were calculated as mean \pm standard deviation, and were compared between groups using a 2-sample *t*-test or Wilcoxon rank-sum test. Categorical variables were calculated as percentages and compared by Fisher exact test.

The comparison of 30-day outcomes from the SOURCE 3 registry for patients who received pre-BAV versus those who received direct TAVR was assessed using a propensity score matching methodology. This analysis was performed on the as-treated analysis population, which was defined as all patients who were enrolled in the study and for whom the study valve implant procedure was begun, defined as the time in which the SAPIEN 3 delivery catheter was placed in the patient.

The primary endpoints for the propensity score analysis were 30-day all-cause mortality, all strokes, life-threatening bleeds, and major vascular complications. The secondary 30-day endpoints included cardiac mortality, stroke, myocardial infarction (MI), new onset of atrial fibrillation, and new permanent pacemaker implantation. In addition, device success and early safety composite endpoints were included along with the individual components for each composite.

Propensity score methodology was used to reduce confounding in the statistical comparison of outcomes for the two treatment groups (i.e., pre-BAV vs. direct TAVR) by accounting for differences in baseline patient characteristics. First, a logistic regression model was performed on the pre-specified baseline characteristic variables to calculate the propensity score for each patient. The variables used for matching were demographics and baseline conditions (gender, age, body mass index, NYHA class, Canadian Cardiovascular Society grading for angina pectoris, prior stroke, porcelain aorta, chronic obstructive pulmonary disease, diabetes, renal insufficiency, peripheral vascular disease, prior percutaneous coronary intervention, hypertension, MI, previous pacemaker implantation, prior aortic valvuloplasty, prior coronary artery bypass graft, carotid disease, coronary artery disease, dyslipidemia/hyperlipidemia, previous or current smoker, and atrial fibrillation), baseline hemodynamics (effective aortic area [EOA], mean gradient, aortic annular diameter, left ventricle [LV] ejection fraction measured intraprocedurally), CT data (annulus dimensions degree of annulus calcification, presence of subannular calcification classification), and the implant approach (transfemoral [TF] or non-TF). We had an unequal distribution of patients across the 80 study centers. Because the sample size per center for some sites would not have been large enough to draw any conclusion about the BAV use by hospital, we did not add this variable to the matching process.

The propensity score represents the conditional probability (based on baseline characteristics) that the patient received the BAV procedure. For one-to-one matching, a pre-defined caliper threshold was used to determine the similarity of two patients in terms of propensity scores. The caliper threshold was found by grid searching a range of thresholds that achieved the best variable balance. The variable balance was assessed to confirm the adequacy of the propensity model. Within each arm, patients in both groups had similar degrees of residual bias from randomness. An independent biostatistician, blinded to the treatment groups and clinical outcome data, carried out the propensity score analyses. To address missing baseline covariates, multiple imputation techniques were used before the propensity score model was finalized, and propensity score and quintiles were derived for the outcome analyses adjustments.

The two groups were compared using the Fisher test for the early safety composite at discharge and the log rank test for 30-day clinical outcomes. We used the threshold of $p < 0.05$ to indicate statistically significant associations, with no adjustments for multiple comparisons.

All statistical analysis was performed using SAS software version 9.4 (SAS Institute Inc.; Cary, NC, USA).

3. Results

3.1. Baseline clinical and anatomical characteristics

A total of 772 direct TAVR and pre-BAV patients each were matched and analyzed for a total patient population of 1544. Most patients were about 82 years old and more than half were male (Table 1). Patients had similar overall medical histories. All patients had severe AS, with an EOA of 0.7 cm². The logistic EuroSCORE was similar between groups, at about 18%. The STS score was significantly higher for pre-BAV-treated patients than for direct TAVR-treated patients (7.8% vs 6.0%, respectively; $p = 0.003$). The rate of patients with an atrio-ventricular or intra-ventricular conduction disturbance was similar at baseline, as was the number of patients with a previous pacemaker.

The pre-operative CT scan detected no significant differences in annulus dimensions between treatment groups, regardless of the measurement (Table 2). The calcium burden was similar in both groups at the level of the aortic annulus and the left ventricular outflow tract (LVOT).

3.2. Procedural characteristics and outcomes

The majority of procedures were performed via TF approach (90%), and less than half of patients underwent general anesthesia (Table 3). No differences were found for prosthesis size, valve to annulus ratio, or correct valve placement between the two groups, post-matching. Compared with the pre-BAV-treated patients, patients who underwent direct TAVR had a significantly shorter mean procedural duration (2.1 min shorter; $p = 0.033$) and X-ray exposure (1.5 min shorter; $p < 0.001$), and 4.8 ml less contrast dye was used ($p = 0.005$). Patients in the pre-BAV group required significantly more post-dilatation compared with the direct TAVR group (13.0% vs 8.1%; $p = 0.002$).

All other procedural outcomes and complications were similar between treatment groups. There was a trend toward less bailout valve-in-valve implantation in the direct TAVR group vs pre-BAV group ($p = 0.057$).

The device success rate was over 90% for both treatment groups (Table 4).

3.3. Main 30-day outcomes

All-cause mortality was about 2% for both treatment groups (Table 5). Also similar was the frequency of stroke (<2%), major vascular complications, acute kidney injury (AKI) stage II or III, and MI. However, life-threatening bleeds occurred with twice as many in the direct TAVR group than the pre-BAV group ($p = 0.007$). Several variables were looked at to understand the reasons that could have explained these results. The prevalence of frailty was higher in the direct group vs. the pre-BAV group (17.7% vs. 11.8%, $p = 0.001$); nevertheless no other variables differed between groups (including baseline hemoglobin, peripheral vascular

disease, access site closure success rate, and vascular complications). New PPMIs were also implanted with a significant greater frequency in the direct TAVR group vs. the pre-BAV group ($p = 0.032$). Similarly, after a thorough review of the variables that could have explained these results (including proportion of baseline PPM, right bundle branch block or other atrio-ventricular or intra-ventricular conduction disturbances, and valve size/annulus diameter) no differences was found between groups.

The early safety composite endpoint at 30 days was not significantly different between groups (Table 5). Life-threatening bleeds was the only individual safety composite components that was significantly different between the treatment groups.

3.4. Functional status and prosthesis performance

At the 30-day follow-up, functional status was good in both matched groups; the rate of worsening NYHA class compared with baseline was low (3.1% in pre-BAV patients vs 1.6% in the direct TAVR patients). Compared with baseline, groups had no significant differences in prosthesis function, improvement of aortic valve area, and mean gradient decrease (Fig. 1). The amount of moderate and/or severe paravalvular leak at 30 days was 3.2% for the pre-BAV cohort and 2.2% for the direct TAVR patients (Fig. 2). A crude comparison showed a significant benefit of the direct TAVR strategy compared with the pre-BAV strategy in the residual amount of moderate to severe paravalvular leak (PVL) that was not evident after the matched comparison (Fig. 2). Patients who had a direct TAVR procedure initially had less calcification at both the annular and sub-annular level than pre-BAV patients; however, this significant difference was not evident after the matched comparison, as calcification level was among the variables used for propensity score analysis (Fig. 2).

4. Discussion

The rationale for direct TAVR versus TAVR with pre-BAV is to simplify the standard TAVR procedure. A trend for direct TAVR has been widely observed [9]. While previously reported post-direct TAVR outcomes have been published, our current analysis assessed the largest population size to date of a single, current generation, balloon-expandable valve (SAPIEN 3 THV), implanted mainly via TF access, with a matched comparison of the two strategies. Results of this study demonstrated that direct TAVR with the SAPIEN 3 THV allowed for shorter procedure times with less exposure to radiation and lower contrast volume. The matched analysis demonstrated that direct TAVR with the SAPIEN 3 valve in a real-world setting is feasible and comparable to pre-BAV TAVR with regards to early safety endpoints, mortality, stroke, and main 30-day outcomes, as well as prosthesis function. Importantly, as previous studies with unadjusted comparisons suggested, a direct TAVR strategy could result in a lower rate of 30-day PVL [9]. Our study found no difference in PVL at 30 days between direct TAVR and pre-BAV groups when the amount of aortic valve calcifications was included in the group matching. Two outcomes of interest occurred more frequently in the direct TAVR group than the pre-BAV TAVR: new PPMI and life-threatening or major bleeds.

4.1. Impact of direct TAVR vs. pre-BAV TAVR on procedure and 30-day safety outcomes

The feasibility of TAVR without pre-BAV has been reported for balloon-expandable valves. However, these studies have been mostly limited to the previous generation of SAPIEN XT prosthesis [4]; although, some have been conducted for the currently commercially available SAPIEN 3 prosthesis [9,15]. Larger studies,

Table 1
Baseline characteristics.

Patient characteristics	Direct TAVR (N = 772)	Pre-BAV (N = 772)	p-Value
Age, years, mean (SD)	81.6 (6.7)	81.7 (6.6)	0.965
Female, n/N (%)	377 (48.8)	376 (48.7)	0.959
LVEF <30%, n/N (%)	42/671 (6.3)	39/635 (6.1)	0.930
NYHA class IV, n/N (%)	53/757 (7.0)	54/736 (7.3)	0.868
Logistic EuroScore, mean (SD)	17.5 (12.7) (n = 715)	18.6 (13.2) (n = 707)	0.051
STS score, mean (SD)	6.0 (5.9) (n = 467)	7.8 (8.3) (n = 404)	0.003
Hypertension, n (%)	632 (81.9)	634 (82.1)	0.895
Diabetes, n (%)	232 (30.1)	219 (28.4)	0.467
Coronary artery disease, n (%)	383 (49.6)	377 (48.8)	0.760
Peripheral vascular disease, n (%)	117 (15.2)	112 (14.5)	0.720
Stroke, n/N (%)	62 (8.0)	65 (8.4)	0.781
COPD, n (%)	124 (16.1)	118 (15.3)	0.675
RBBB, n/N (%)	77/418 (18.4)	70/380 (18.4)	>0.999
LBBB, n/N (%)	82/430 (19.1)	81/387 (20.9)	0.506
1st degree AV block, n/N (%)	90/738 (12.2)	88/745 (11.8)	0.821
Atrial flutter, n/N (%)	4/738 (0.5)	13/745 (1.7)	0.023
Atrial fibrillation, n/N (%)	175/738 (23.7)	166/745 (22.3)	0.513
Pacemaker, n/N (%)	88/771 (11.4)	89/772 (11.5)	0.944
Renal insufficiency, n (%)	201 (26.0)	203 (26.3)	0.908
Cirrhosis, n (%)	17 (2.2)	15 (1.9)	0.721
Hostile chest, n (%)	29 (3.8)	30 (3.9)	0.894
Porcelain aorta, n (%)	31 (4.0)	35 (4.5)	0.615
EOA, cm ² , mean (SD)	0.71 (0.21) (n = 640)	0.70 (0.19) (n = 584)	0.576
Mean gradient, mmHg, mean (SD)	43.3 (15.1) (n = 702)	44.4 (14.9) (n = 677)	0.131

BAV = balloon aortic valvuloplasty; COPD = chronic obstructive pulmonary disease, EOA = effective orifice area; LBBB = left bundle branch block; LVEF = left ventricle ejection fraction; NYHA = New York Heart Association, RBBB = right bundle branch block; TAVR = transcatheter aortic valve replacement.

Table 2
Computerized tomography characteristics, pre-implantation.

Characteristics	Direct TAVR (N = 772)	Pre-BAV (N = 772)	p-Value
Annulus diameter, mm, mean (SD)	24.4 (2.9) (n = 365)	24.6 (2.5) (n = 393)	0.340
Annulus area, mm ² , mean (SD)	429 (172) (n = 296)	467 (251) (n = 308)	0.168
Annulus circumference, mm, mean (SD)	83 (54) (n = 185)	80 (46) (n = 182)	0.344
Presence of calcification at level of iliac bifurcation, n/N (%)	177/561 (31.6)	190/570 (33.3)	0.526
Degree of annulus calcification, n/N (%)			0.430
None/mild	69/335 (20.6)	60/332 (18.1)	
Moderate	117/335 (34.9)	108/332 (32.5)	
Severe	149/335 (44.5)	164/332 (49.4)	
Presence of subannular calcification classification, n/N (%)			0.812
None/mild	159/188 (84.5)	164/186 (88.2)	
Moderate	20/188 (10.6)	15/186 (8.1)	
Severe	9/188 (4.8)	7/186 (3.8)	

including for self-expanding valves, are also available. For instance, the meta-analysis by Auffret et al. [8] detected a reduction in procedure time, radiation exposure, and contrast volume with direct TAVR with the SAPIEN valve and Corevalve (Medtronic; Minneapolis, MN, USA), which is consistent with our findings for the SAPIEN 3. Our results also compare well with two other meta-analyses and a large, nationwide, multicenter registry (N = 1395, N = 10,752, and N = 5784 patients, respectively), that all found no statistically significant differences in mortality, cardiovascular mortality, stroke, or safety composite endpoint across multiple valve platforms, including the SAPIEN, SAPIEN XT, and SAPIEN 3 balloon-expandable valves and the self-expandable Corevalve [6,7,9]. We should, however, acknowledge that there was a trend toward a worse composite safety endpoint in the direct TAVR group, although it was not statistically significant. No clinical benefit for stroke reduction was related to direct TAVR, although avoidance of additional aortic arch and valve crossing was a theoretical argument for supporting this strategy [3,16]. There was a trend toward less THV in THV implantations (0.3% in direct TAVR group vs 1.0% in pre-BAV group, $p=0.057$), with a theoretical rationale of a greater

prosthesis stability in the case of direct implantation, linked to preserved mechanical interaction with the native valve and less aortic regurgitation caused by pre-BAV. But this is speculative and was not found in other studies.

4.2. Permanent pacemaker implantation

One of the two unexpected findings of our analysis was the statistically significant lower rate of PPMI with pre-BAV compared to the rate with direct TAVR. The reason this result was unanticipated is because BAV, per se, carries a potential risk of high-degree atrio-ventricular conduction disturbances requiring PPMI [5]. No significant difference was noticed between the two strategies in the proportion of patients having a baseline right bundle branch block, first degree atrio-ventricular block, or previously implanted pacemaker, or degree of oversizing of the valve implanted relative to the native anatomy. The degree of oversizing noticed in this study should, however, be interpreted cautiously as CT data were available in only about 50% of subjects, and there was no information regarding the annular measurement method, i.e., whether systolic

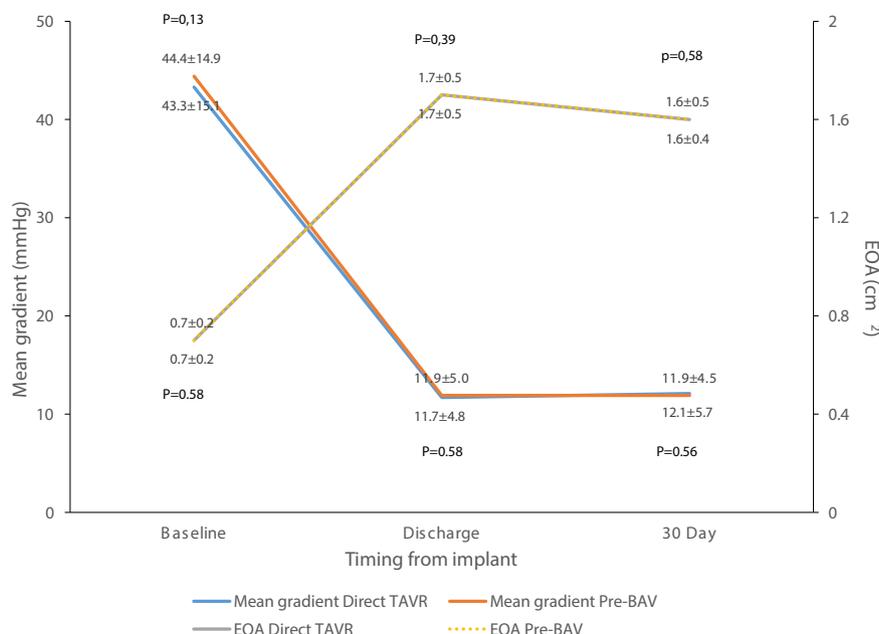


Fig. 1. Mean gradient and effective orifice area to 30 days post-implantation.

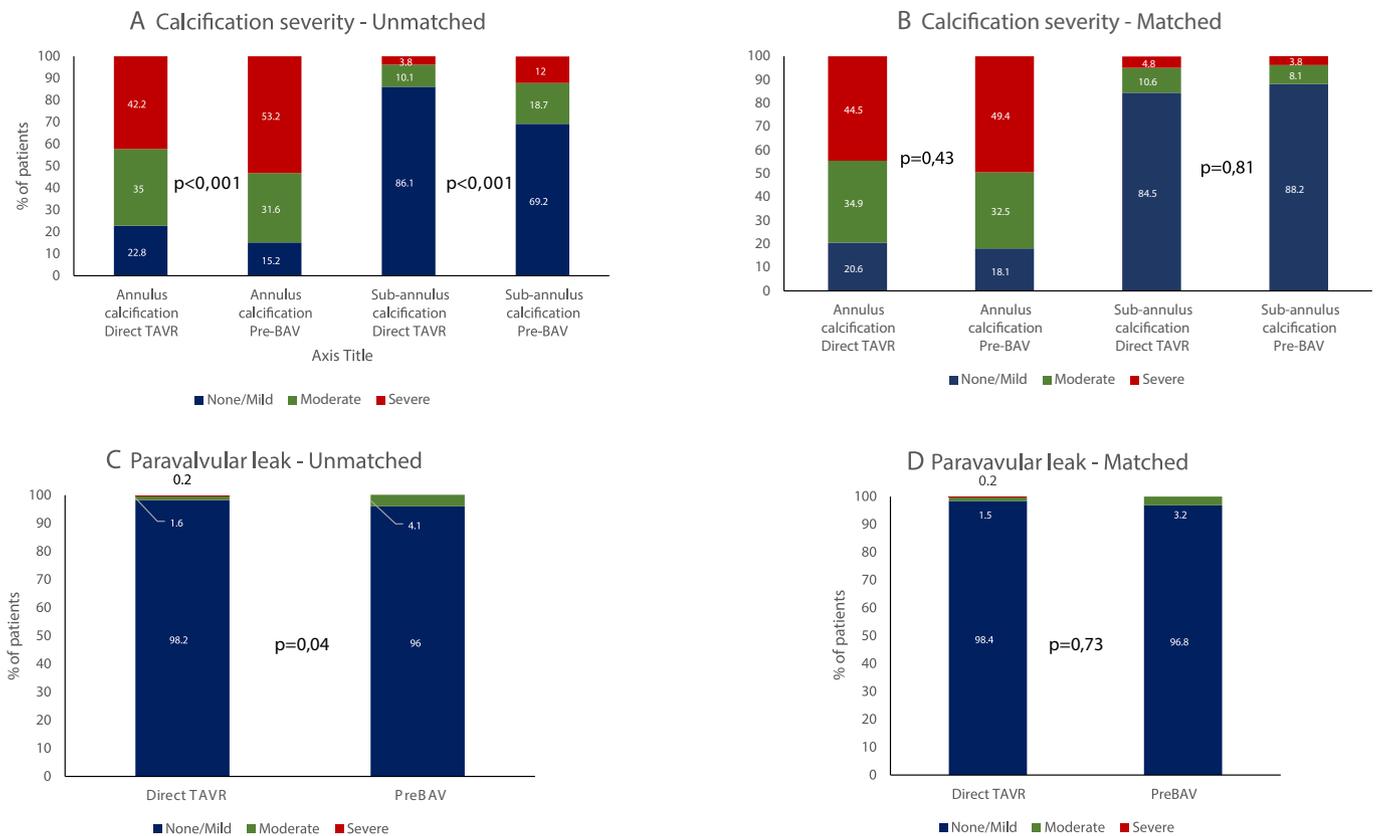


Fig. 2. Unmatched annular and sub-annular calcium severity (2A), matched annular and sub-annular calcium severity (2B), at baseline and paravalvular leak at 30-days post-implantation unmatched (2C) and matched (2D) analysis.

or diastolic reconstructions were used. The matching process harmonized the degree of sub-annular calcification. We also explored the hypothesis that there was possibly a learning curve effect influencing the rate of PPMI, but did not find a strong relationship between new permanent pacemaker implantation and procedure date. But, there were some potential factors that could have interfered with this observation that we were unable to capture in this study, such as implantation depth of the prosthesis. We did not find any clear explanation for this observation, apart from this factor and possible other confounders not captured in the database. While the meta-analysis by Bagur et al. [6] did not find differences for PPMI between the two strategies, other meta-analyses published found a trend for a lower risk of PPMI with direct TAVR [8] and a lower PPMI rate with direct TAVR [7].

4.3. Vascular complications and life-threatening/major bleeding

For patients receiving direct TAVR, there were no differences in vascular complications between the two groups. However, there were statistically more life-threatening bleeds and also more composite life-threatening and major bleeds for patients with direct TAVR, which was unexpected. The baseline hemoglobin levels patients in both treatment groups who experienced these hemorrhagic complications were not significantly different. A non-TF procedure was performed in about 10% of patients in both groups; the rate of successful access site percutaneous closure was also the same. Despite a one-by-one review of the cases of life-threatening bleedings, we could not discern the reason for the significant difference between the two study groups. Similar to the finding of more PPMI in the direct TAVR cohort, we did not find any clear explanation for this observation, apart from potential

confounders not captured in the database. Finally, Auffret et al. [8] and Banerjee et al. [7] meta-analyses did not report any difference in bleeding related to a direct TAVR strategy, further suggesting that this finding may not be directly related to pre-BAV and requires further investigation.

4.4. Prosthesis valve function, at 30 days

Prosthesis valve function did not appear to be influenced by the lack of pre-BAV at the 30-day follow-up; similar effective orifice area improvement and mean gradient decrease were found, irrespective of prosthesis sizes. This is contrary to what was previously reported by Kim et al. [15].

We investigated the annular calcification severity and sub-annular calcification severity at baseline, before and after the matching of the groups. Before matching, the pre-BAV cohort displayed a higher percentage of both annular and subannular calcium than the direct TAVR cohort, possibly explaining the use of pre-dilatation of the native aortic valve in this group. After matching, this difference was no longer seen, as calcium burden was one of the variables used in the model. Similarly, the 30-day moderate to severe PVL was statistically different before matching with an incidence of moderate to severe PVL that was half as much in the direct TAVR group as it was in the pre-BAV group, but was not different after matching. These findings confirm that a high calcium burden is an anatomical predictor of a higher rate of PVL. This also may suggest that the choice to perform pre-BAV was driven by the calcium burden, but this would, of course require further investigation to be conclusive. In the most recent meta-analyses on BAV pre-TAVR and the FRANCE and UK TAVI registries, [7–10] results suggest a significantly decreased risk of moderate to severe PVL

rates with direct TAVR. Those studies reported non-adjusted data; however, specifically regarding the calcium burden of the aortic valve, which may account for this difference in findings.

4.5. Study limitations

This non-randomized, post-hoc analysis of prospectively collected data was inevitably biased by confounders beyond our control. We chose to exclude some variables in the matching process that were poorly described, e.g., STS score was assessed for only about half of the population, and the incidence of atrial flutter was extremely low, numerically. Another variable not completely described was baseline ECG conduction disturbances, where only 50% of both study groups had data available. These exclusions kept the sample size at a reasonable level, because each variable included in the analysis effectively reduces the sample size. Also, statistically significant differences between those variables could have introduced a bias in our observations. Prosthesis implantation depth, which is an important predictor of permanent pacemaker implantation, was unfortunately not captured in the database. The participating centers submitted consecutive series of data for patients treated with the SAPIEN 3, but because this was not a controlled trial, there was no echocardiographic core lab for valve function and PVL assessment, and no routine neurological assessment for strokes, or systematic diffusion-weighted magnetic resonance imaging [17]. The decision to predilate the aortic valve before SAPIEN 3 valve implantation was left to the discretion of the operators. The reasons for this choice, as well as failures of direct TAVR attempts, were not documented. We did not use a random effect model to exclude clustering of direct TAVI and to assess different thresholds for permanent pacemaker implantations across centers. Finally, as a result of all these limitations, some unexpected differences appeared in the comparison of the 2 groups regarding bleedings and pacemaker implantation that cannot be explained with existing evidence in the literature, nor is it possible to explain it with the available data.

5. Conclusion

The study demonstrated the feasibility of direct TAVR (i.e., without pre-BAV) with the SAPIEN 3 valve, when performed by experienced operators. The direct TAVR approach reduced procedure time and the patient's exposure to radiation and contrast. Compared to the pre-BAV approach, it was not associated with any difference in mortality, stroke, or 30-day valve function, including PVL. Uncertainties remain about other potential clinical impact. We hope these will be clarified by the randomized comparison trial of the ongoing DIRECTAVI [18].

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Declaration of Competing Interest

N. Dumonteil is proctor for Abbott Vascular, Boston Scientific, Edwards Lifesciences, and Medtronic.

T. Lefèvre is proctor for Abbott Vascular, Boston Scientific and Edwards Lifescience.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcard.2019.06.013>.

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