

Comparison of the Transarterial and Transthoracic Approaches in Nontransfemoral Transcatheter Aortic Valve Implantation



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Transfemoral approach stands as the reference access-route for transcatheter aortic valve implantation (TAVI). Nonetheless, alternatives approaches are still needed in a significant proportion of patients. This study aimed at comparing outcomes between transthoracic-approach (transapical or transaortic) and transarterial-approach (transcarotid or subclavian) TAVI. Data from 191 consecutive patients who underwent surgical-approach TAVI from May 2009 to September 2017 were analyzed. Patients were allocated in 2 groups according to the approach. The primary end point was the 30-day composite of death of any cause, need for open surgery, tamponade, stroke, major or life-threatening bleeding, stage 2 or 3 acute kidney injury, coronary obstruction, or major vascular complications. During the study period, 104 patients underwent transthoracic TAVI (transapical: 60.6%, transaortic: 39.4%) whereas 87 patients underwent transarterial TAVI (subclavian: 83.9%, transcarotid: 16.1%). Logistic EuroSCORE I tended to be higher in transthoracic-TAVI recipients. In-hospital and 30-day composite end point rates were 25.0% and 11.5% ($p = 0.025$), and 26.0% and 14.9% ($p = 0.075$) for the transthoracic and transarterial cohorts, respectively. Propensity score-adjusted logistic regression demonstrated no significant detrimental association between the 30-day composite end point and transthoracic access (odds ratio 2.12 95% confidence interval 0.70 to 6.42; $p = 0.18$). Transarterial TAVI was associated with a shorter length of stay (median: 6 vs 7 days, $p < 0.001$). TAVI approach was not an independent predictor of midterm mortality. In conclusion, non-transfemoral transarterial-approach TAVI is safe, feasible, and associated with comparable rates of major perioperative complications, and midterm mortality compared with transthoracic-approach TAVI. © 2019 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;123:1501–1509)

Since the publication of the randomized Placement of Aortic Transcatheter Valves trials,^{1–3} transcatheter aortic valve implantation (TAVI) is recognized as an efficient therapy for treatment of severe aortic stenosis in inoperable, high, and intermediate-risk patients. Transfemoral approach, as the less invasive and safest access, stands as the reference access route for TAVI. Although nontransfemoral approaches are decreasing with the

miniaturization of delivery systems, in a recent national registry 17.2% of patients were still treated by nontransfemoral accesses.⁴ Alternative approaches requiring a surgical contribution include transaortic, transapical, subclavian, and, lately, transcarotid access. Transapical access is well-described⁵ and provides acceptable results. The transaortic approach requires to expose the ascending aorta using a mini-sternotomy or a right thoracotomy, and is associated with similar outcomes as transapical access.^{6,7} Considering their invasiveness, the use of these transthoracic approaches is decreasing. Subclavian access is a safe method, showing comparable results to transfemoral approach,⁸ however with the same limitations regarding vessel anatomy, and being unsuited for patients with thoracic artery grafts. Transcarotid access tends to represent a growing proportion of alternative accesses, despite ongoing questions regarding the risk of stroke.^{9,10} Given the paucity of direct comparisons of alternative accesses in the current literature, the aim of this study was to compare short and midterm outcomes between patients who underwent transthoracic (transapical or transaortic) TAVI and transarterial (transcarotid or subclavian) TAVI.

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Methods

All patients who underwent a nontransfemoral approach TAVI at our institution (Rennes University Hospital, Rennes, France) from May 2009 to September 2017 were included. Details regarding the preprocedural evaluation and follow-up methods were previously published.¹¹ Details regarding the access selection process by the Heart Team are provided in the Supplementary Appendix. All patients gave written informed consent for the procedures and anonymous collection of their data, which were prospectively gathered in an electronic database. The institutional review board waived specific consent for this study due to its retrospective and observational nature.

Chronic lung disease was defined as a restrictive lung disease or a chronic obstructive pulmonary disease. Cerebrovascular disease was defined as a previous carotid surgery or a stenosis $\geq 50\%$ of carotid or vertebral arteries. Peripheral artery disease included artery stenosis $\geq 50\%$, claudication and previous vascular surgery. Surgical risk was estimated with the logistic EuroScore I, the logistic EuroScore II, and the Society of Thoracic Surgeons Predicted Risk of Mortality score. Valve Academic Research Consortium 2 standards were used to define hostile chest, severe liver disease, and all study end points.¹²

The primary end point was the 30-day rate of major perioperative complications defined as the composite of death of any cause, need for open surgery, tamponade, stroke, major or life-threatening bleeding, stage 2 or 3 acute kidney injury, coronary obstruction, or major vascular complications. Secondary end points were in-hospital and 30-day rates of the components of the primary end point and survival at follow-up.

Patients were included, according to the access site used, in the transthoracic (transapical or transaortic access) or transarterial (subclavian or transcarotid access) groups. Continuous variables are presented as mean \pm standard deviation or median (interquartile range) depending on their distribution, which was assessed using the Kolmogorov-Smirnov test, and were compared using *t* tests or the Mann-Whitney *U* test as appropriate. Categorical variables are summarized as numbers (percentages), and were compared using chi-square tests or the Fisher exact test. Survival rates were summarized using Kaplan-Meier estimates, and log-rank tests were used to compare groups. To evaluate the impact of access-site on the rate of the primary end point while adjusting for baseline differences between groups, propensity score-adjusted multivariable logistic regression was performed. Results are expressed as adjusted odds ratio with its 95% confidence interval (CI). The propensity score was calculated as the probability of who underwent transthoracic access using a nonparsimonious logistic regression model. Details regarding variables included in the propensity score can be found in the Supplementary Appendix. The propensity score model had adequate calibration (Hosmer-Lemeshow goodness-of-fit $p = 0.46$) and discrimination (c -statistic = 0.93, 95% CI 0.89 to 0.97). Predictors of all-cause mortality were analyzed using univariable and multivariable proportional hazard models (cumulative outcomes). The proportional hazard assumption was tested by plotting log-minus-log survival. Variables with *p* values

< 0.1 in univariable analysis and the access-route were included in the multivariable analysis. Statistical analysis was performed with the use of Statistical Package for Social Sciences version 22 (SPSS, Chicago, Illinois). All tests were 2-sided at the 0.05 significance level.

Results

During the study period, 191 patients (female gender: 39%) had a nontransfemoral approach TAVI, in which 87 patients (mean-age: 79.3 ± 6.7 years) underwent a transarterial approach and 104 patients (mean-age: 78.0 ± 9.9 years) a transthoracic approach. Subclavian access was performed in 73 patients (38.2%), transcarotid in 14 patients (7.3%), transaortic in 41 patients (21.5%), and transapical in 63 patients (33.0%). Supplemental Figures 1 and 2 show the annual number of each alternative access, and the annual proportion of all TAVI represented by each of these accesses. Baseline characteristics of the study population according to the approach are summarized in Table 1. Coronary artery disease was significantly more frequent in the transthoracic group than in the transarterial group (68.3% vs 48.4%; $p = 0.008$). Patients of the transthoracic group harbored a higher burden of cerebrovascular disease (18.4% vs 3.4%; $p = 0.001$) and hostile chest (5.8% vs 0.0%; $p = 0.03$). Prevalence of peripheral artery disease was similar in both groups. Mean Logistic EuroScore I tended to be higher in patients treated with the transthoracic approach (14.9% vs 12.0%; $p = 0.053$). Echocardiographic parameters were similar between groups.

Procedural characteristics are described in Table 2. General anaesthesia was used in all transthoracic procedures, and in 90.8% of the transarterial ones ($p = 0.002$). Balloon-expandable valves were much more frequently implanted in the transthoracic group (96.2% vs 26.4%; $p < 0.001$). Device success was achieved in 95.2% of transthoracic TAVI recipients compared with 85.1% of their transarterial counterparts ($p = 0.024$). Major intraprocedural complications were comparable between groups (Table 2).

In-hospital and 30-day outcomes of the 2 groups are depicted in Table 3. Supplemental Tables 1 and 2 present a comparison of subclavian versus transcarotid approaches, and transaortic versus transapical approaches, respectively. In univariate analysis, the in-hospital composite end point rate was significantly higher in the transthoracic access cohort (25.0% vs 11.5%; $p = 0.025$), yet this difference did not persist at 30-day (26.0 vs 14.9%, $p = 0.075$). Propensity score-adjusted logistic regression confirmed the absence of a significant association between the 30-day composite end point and transthoracic access (odds ratio 2.12, 95% CI 0.70 to 6.42; $p = 0.18$). Albeit numerically higher in the transthoracic cohort, there was no significant difference between groups for in-hospital (4.6% vs 7.7%; $p = 0.55$) and 30-days (4.6% vs 8.7%; $p = 0.39$) mortality. Also numerically higher in the transthoracic group, incidences of most major periprocedural complications were statistically comparable between groups. One contralateral transient ischemic attack occurred 24 hours postprocedure in a patient who underwent left transcarotid TAVI under general anesthesia without balloon predilation. New-onset atrial fibrillation and acute kidney injury

Table 1
Baseline characteristics of the study population according to TAVI approach

| | Transarterial TAVI group (n = 87) | Transthoracic TAVI group (n = 104) | p value |
|--|--------------------------------------|---------------------------------------|---------|
| Age (years) | 79.3 ± 6.7 | 78.0 ± 9.9 | 0.60 |
| Female sex | 35 (40%) | 40 (39%) | 0.88 |
| Body-mass index (kg/m ²) | 29.1 ± 6.7 | 26.4 ± 4.8 | 0.024 |
| Body-surface area (m ²) | 1.83 ± 0.21 | 1.75 ± 0.20 | 0.025 |
| NYHA class III or IV | 40 (46%) | 51 (49%) | 0.77 |
| Previous acute heart failure | 31 (36%) | 33 (32%) | 0.65 |
| <i>Medical history</i> | | | |
| Hypertension | 62 (71%) | 77 (74%) | 0.75 |
| Diabetes mellitus | 24 (28%) | 18 (17%) | 0.11 |
| Coronary artery disease* | 42 (48%) | 71 (68%) | 0.008 |
| Previous myocardial infarction | 12 (14%) | 17 (16%) | 0.69 |
| Previous coronary artery bypass grafting | 15 (17%) | 28 (27%) | 0.12 |
| Previous percutaneous coronary intervention | 22 (25%) | 31 (30%) | 0.52 |
| Previous balloon aortic valvuloplasty | 8 (9%) | 12 (12%) | 0.64 |
| Previous surgical aortic valve replacement | 7 (8%) | 5 (5%) | 0.39 |
| Other cardiac surgery | 2 (2%) | 3 (3%) | 1.00 |
| Atrial fibrillation | 39 (45%) | 34 (33%) | 0.10 |
| Previous permanent pacemaker | 8 (9%) | 13 (13%) | 0.50 |
| Cerebrovascular disease | 3 (3%) | 19 (18%) | 0.001 |
| Previous Stroke/TIA | 8 (9%) | 11 (11%) | 0.81 |
| Peripheral artery disease | 33 (38%) | 46 (44%) | 0.46 |
| Active cancer | 3 (3%) | 7 (7%) | 0.35 |
| Previous chest radiotherapy | 5 (6%) | 8 (8%) | 0.78 |
| Hostile chest | — | 6 (6%) | 0.03 |
| Respiratory failure | 23 (26%) | 27 (26%) | 1.00 |
| Renal failure | | | 0.64 |
| Moderate | 39 (45%) | 45 (43%) | |
| Severe | 3 (3%) | 7 (7%) | |
| Dialysis | 2 (2%) | 1 (1%) | 0.59 |
| Severe liver disease | — | 1 (1%) | 1.00 |
| Logistic EuroScore I | 12.0 (7.0-21.0) | 14.9 (9.7-23.0) | 0.053 |
| Logistic EuroScore II | 3.4 (1.9-5.8) | 3.4 (2.4-6.9) | 0.22 |
| STS-PROM Score | 3.1 (2.2-4.8) | 3.5 (2.4-4.9) | 0.18 |
| <i>Echocardiography</i> | | | |
| LVEF (%) | 54.2 ± 12.5 | 54.0 ± 13.3 | 0.54 |
| LVEF <50% | 25 (29%) | 27 (26%) | 0.75 |
| Aortic valve area (cm ²) | 0.74 ± 0.16 | 0.75 ± 0.32 | 0.56 |
| Mean aortic gradient (mm Hg) | 49.0 ± 15.7 | 47.1 ± 14.8 | 0.60 |
| Mean aortic gradient <40 mm Hg | 20 (23%) | 26 (25%) | 0.87 |
| Aortic regurgitation ≥mild | 21 (24%) | 34 (33%) | 0.20 |
| Mitral regurgitation ≥mild | 23 (26%) | 37 (36%) | 0.21 |
| Moderate or severe mitral stenosis | 3 (3%) | 3 (3%) | 1.00 |
| Systolic pulmonary artery pressure > 60 mm Hg [†] | 10/64 (16%) | 17/79 (22%) | 0.40 |

* Coronary artery disease defined as previous myocardial infarction, or previous percutaneous coronary intervention, or previous coronary artery bypass grafting, or presence of at least one lesion ≥50% on the preoperative coronary angiogram.

[†] Systolic pulmonary artery pressure was measurable by echocardiography in 145 patients.

stage 2 or 3 were more prevalent in the transthoracic cohort. In the transthoracic access group, consistently with the lower use of self-expendable valves, TAVI resulted in a lower rate of permanent pacemaker implantation than in the transarterial cohort. Length of hospitalization was higher (7.0 days vs 6.0 days; $p < 0.001$) and patients were less often discharged at home (42.0% vs 68.7%; $p = 0.002$) in the transthoracic cohort. Echocardiographic findings at discharge are presented in Table 3.

Median follow-up was 395 days (interquartile range [IQR]: 320 to 974) and was significantly longer in the transthoracic cohort (676 days, IQR: 367 to 1182, vs 367 days,

IQR: 204 to 427; $p < 0.001$). The 1-year Kaplan-Meier survival curves are shown in Figure 1. At 1 year, overall survival was similar in both groups (89.6%; 95% CI 80.1 to 94.7 and 84.5%; 95% CI 75.9 to 90.2 with the transarterial and transthoracic approach, respectively; $p = 0.30$). Figure 2 summarizes the multivariable predictors of all-cause mortality at follow-up. Atrial fibrillation (hazard ratio [HR] 2.52; 95% CI 1.33 to 4.78; $p = 0.005$), STS-PROM score (HR 1.18; 95% CI 1.01 to 1.39; $p = 0.04$) and periprocedural stroke (HR 5.85; 95% CI 1.51 to 22.63; $p = 0.011$) were found as independent predictors of overall mortality. Transthoracic access-route was not independently

Table 2
Procedural characteristics of the study population according to TAVI approach

| | Transarterial TAVI group (n = 87) | Transthoracic TAVI group (n = 104) | p value |
|--|--------------------------------------|---------------------------------------|---------|
| Urgent procedure | 3 (3%) | 4 (4%) | 1.00 |
| General anesthesia | 79 (91%) | 104 (100%) | 0.002 |
| Approach | | | |
| Subclavian | 73 (84%) | — | |
| Carotid | 14 (16%) | — | |
| Transaortic | — | 41 (39%) | |
| Transapical | — | 63 (61%) | |
| Balloon-expandable valve | 23 (26%) | 100 (96%) | <0.001 |
| Newer-generation valve* | 70 (81%) | 44 (42%) | <0.001 |
| Valve type | | | <0.001 |
| Edwards SAPIEN | 1 (1%) | 27 (26%) | |
| Edwards SAPIEN XT | — | 30 (29%) | |
| Edwards SAPIEN 3 | 22 (25%) | 43 (41%) | |
| Medtronic CoreValve | 13 (15%) | 3 (3%) | |
| Medtronic Evolut R | 48 (55%) | 1 (1%) | |
| Valve size (mm) | | | <0.001 |
| 23 | 15 (17%) | 34 (33%) | |
| 26 | 27 (31%) | 50 (48%) | |
| 29 | 39 (45%) | 18 (17%) | |
| 31 | 3 (3%) | 2 (2%) | |
| Number of implanted valve | | | 0.09 |
| 0 | 3 (3%) | — | |
| 1 | 84 (97%) | 103 (99%) | |
| 2 | — | 1 (1%) | |
| Fluoroscopy time (min) | 20.4 ± 7.9 | 13.0 ± 6.3 | <0.001 |
| Dosimetry (Gy.cm ²) | 82 (55-132) | 82 (55-128) | 0.99 |
| Contrast volume (ml) | 140 (110-199) | 140 (108-177) | 0.66 |
| Device success | 74 (85%) | 99 (95%) | 0.024 |
| <i>Perprocedural complications</i> | | | |
| Perprocedural death | 3 (3%) | 1 (1%) | 0.33 |
| Valve embolization or ectopic deployment | 1 (1%) | 2 (2%) | 1.00 |
| Conversion to open surgery | 2 (2%) | 4 (4%) | 0.69 |
| Coronary obstruction | 1 (1%) | — | 0.46 |
| Tamponade | 2 (2%) | — | 0.21 |
| Annulus rupture | — | 1 (1%) | 1.00 |
| Left ventricular perforation | 1 (1%) | 1 (1%) | 1.00 |

* Edwards SAPIEN 3 or Medtronic Evolut R.

associated with mortality at follow-up (HR 1.16; 95% CI 0.55 to 2.45; p = 0.70).

Discussion

The main findings of this study are the following: despite a numerically lower incidence in transarterial TAVI patients, transthoracic approaches were not significantly associated with an increased rate of 30-day major perioperative adverse events or decreased midterm survival (Figure 3). However, a shorter length of stay and a higher likelihood of being discharge at home were observed among transarterial TAVI recipients.

At the inception of the TAVI era, when a transfemoral approach was not feasible, a “transapical-first” policy was usually applied. Currently, strategies tend to evolve, with a priority for less invasive approaches. In a recent analysis of temporal trends in French registries,⁴ transapical TAVI drastically decreased over time (from 27.9% in 2010 to 4.7% in 2015 in patients receiving a balloon-expandable

valve). This evolution can be explained by an increase of transfemoral TAVI (73.4% vs 82.8%) and the expansion of alternative access-sites of more recent emergence such as the direct aortic, and, particularly, transcarotid routes (5.5% and 3.4% of 12,804 patients included in the FRANCE TAVI registry, respectively). Comparable findings were previously reported in the UK registry.¹³ However, the transcarotid approach being the latest implemented in routine practice, the above-mentioned trend will likely accentuate regarding this specific access.

Transapical and transaortic TAVI are associated with similar rates of complications and comparable outcomes.^{6,7} Our results regarding the in-hospital and 30-day morbidity and mortality of transthoracic TAVI are consistent with these recent studies. On the contrary to transthoracic TAVI, some groups reported favourable outcomes, sometimes comparable with the transfemoral approach, with the use of transcarotid and subclavian TAVI.^{8,14,15} Therefore, these alternative transarterial accesses could conceivably be superior to transthoracic ones, and should represent the first

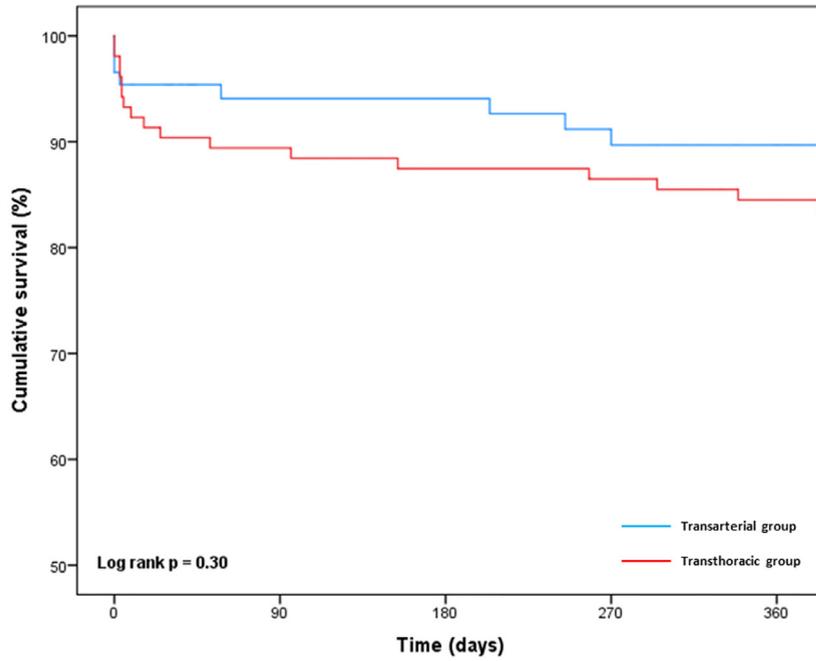
Table 3
Outcomes of the study population according to TAVI approach

| | Transarterial TAVI group (n = 87) | Transthoracic TAVI group (n = 104) | p value |
|--|-----------------------------------|------------------------------------|---------|
| <i>Cumulative in-hospital outcomes</i> | | | |
| In-hospital composite end point | 10 (12%) | 26 (25%) | 0.025 |
| In-hospital death | 4 (5%) | 8 (8%) | 0.55 |
| Coronary obstruction | 1 (1%) | — | 0.46 |
| Tamponade | 2 (2%) | 4 (4%) | 0.69 |
| Myocardial infarction | — | 1 (1%) | 1.00 |
| Acute heart failure | 3 (3%) | 10 (10%) | 0.15 |
| Stroke/Transient ischemic attack | 1 (1%) | 4 (4%) | 0.38 |
| Stroke | — | 4 (4%) | |
| Transient ischemic attack | 1 (1%) | — | |
| Major or life-threatening bleeding | | | |
| BARC 5 | — | — | — |
| BARC 3—total | 5 (6%) | 10 (10%) | 0.42 |
| BARC 3a | 2 (2%) | 5 (5%) | 0.46 |
| BARC 3b | 3 (3%) | 5 (5%) | 0.73 |
| BARC 3c | — | — | — |
| Minor bleeding—BARC definition | 1 (1%) | 5 (5%) | 0.22 |
| Vascular complications | | | |
| Major | — | — | — |
| Minor | 2 (2%) | 1 (1%) | 0.59 |
| Acute kidney injury stage 2 or 3 | — | 8 (8%) | 0.008 |
| Septic shock | 1 (1%) | 2 (2%) | 1.00 |
| Pneumopathy | 2 (2%) | 8 (8%) | 0.11 |
| Need for reintubation | 1 (1%) | 5 (5%) | 0.22 |
| Delirium | 3 (3%) | 10 (10%) | 0.15 |
| New-onset atrial fibrillation | 4 (5%) | 19 (19%) | 0.003 |
| Permanent pacemaker implantation* | 13/79 (17%) | 4/91 (4%) | 0.011 |
| Discharged at home | 58/83 (69%) | 43/93 (42%) | 0.002 |
| Length of hospitalization, days [†] | 6.0 (4.0-7.0) | 7.0 (6.0-9.0) | <0.001 |
| <i>Echocardiographic findings at discharge</i> | | | |
| Left ventricular ejection fraction (%) | 55.8 ± 13.2 | 54.9 ± 12.0 | 0.39 |
| Aortic valve area (cm ²) | 1.95 ± 0.54 | 1.78 ± 0.46 | 0.016 |
| Patient-prosthesis mismatch | n = 82 | n = 95 | 0.67 |
| Moderate | 9 (11%) | 15 (16%) | |
| Severe | 5 (6%) | 5 (5%) | |
| Mean aortic gradient (mm Hg) | 11.4 ± 7.1 | 11.4 ± 5.3 | 0.55 |
| Paravalvular leak | n = 83 | n = 98 | 0.39 |
| None/trace | 58 (70%) | 74 (76%) | |
| Mild | 21 (25%) | 23 (24%) | |
| Moderate | 3 (4%) | 1 (1%) | |
| Severe | 1 (1%) | — | |
| <i>Cumulative 30-day outcomes</i> | | | |
| 30-day composite end point | 13 (15%) | 27 (26%) | 0.075 |
| 30-day death | 4 (5%) | 9 (9%) | 0.39 |
| Stroke | 1 (1%) | 4 (4%) | 0.38 |
| Myocardial infarction | 1 (1%) | 1 (1%) | 1.00 |
| Rehospitalization for heart failure | 7 (11%) | 7 (9%) | 0.78 |
| Major or life-threatening bleeding | | | |
| BARC 5 | — | — | — |
| BARC 3—total | 8 (9%) | 11 (11%) | 0.81 |
| BARC 3a | 3 (3%) | 5 (5%) | 0.73 |
| BARC 3b | 5 (6%) | 6 (6%) | 1.00 |
| BARC 3c | — | — | — |
| Major vascular complications | 1 (1%) | — | 0.46 |
| Permanent pacemaker implantation* | 13/79 (17%) | 4/91 (4%) | 0.011 |

* In patients without previous permanent pacemaker.

[†] In patients discharged alive from the hospital.

Composite end point: in-hospital occurrence of any of the following: death, need for open surgery, tamponade, stroke, major/life-threatening bleeding, stage 2 or 3 acute kidney injury, coronary obstruction, major vascular complications.



| Patients at risk | 0 | 90 | 180 | 270 | 360 |
|---------------------|-----|----|-----|-----|-----|
| Transarterial group | 87 | 71 | 68 | 61 | 52 |
| Transthoracic group | 104 | 93 | 90 | 89 | 84 |

Figure 1. Rates of all-cause mortality. Kaplan-Meier curves at 1-year follow-up for overall mortality according to the access site.

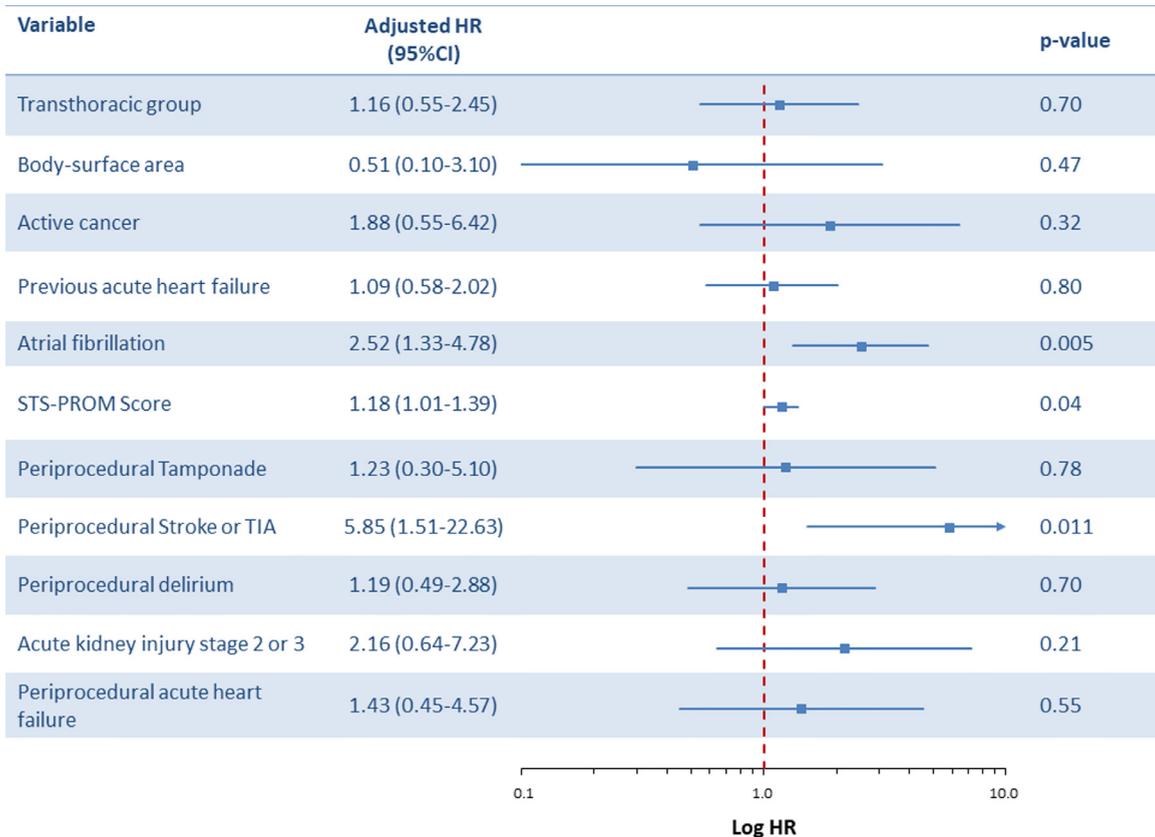


Figure 2. Predictors of all-cause mortality at follow-up. Forest-plot showing the multivariable model for all-cause mortality, including all variables with a p value <0.1 in univariate analysis. CI = confidence interval; HR = hazard ratio; STS-PROM = Society of thoracic surgeons predicted risk of mortality; TIA = transient ischemic attack.

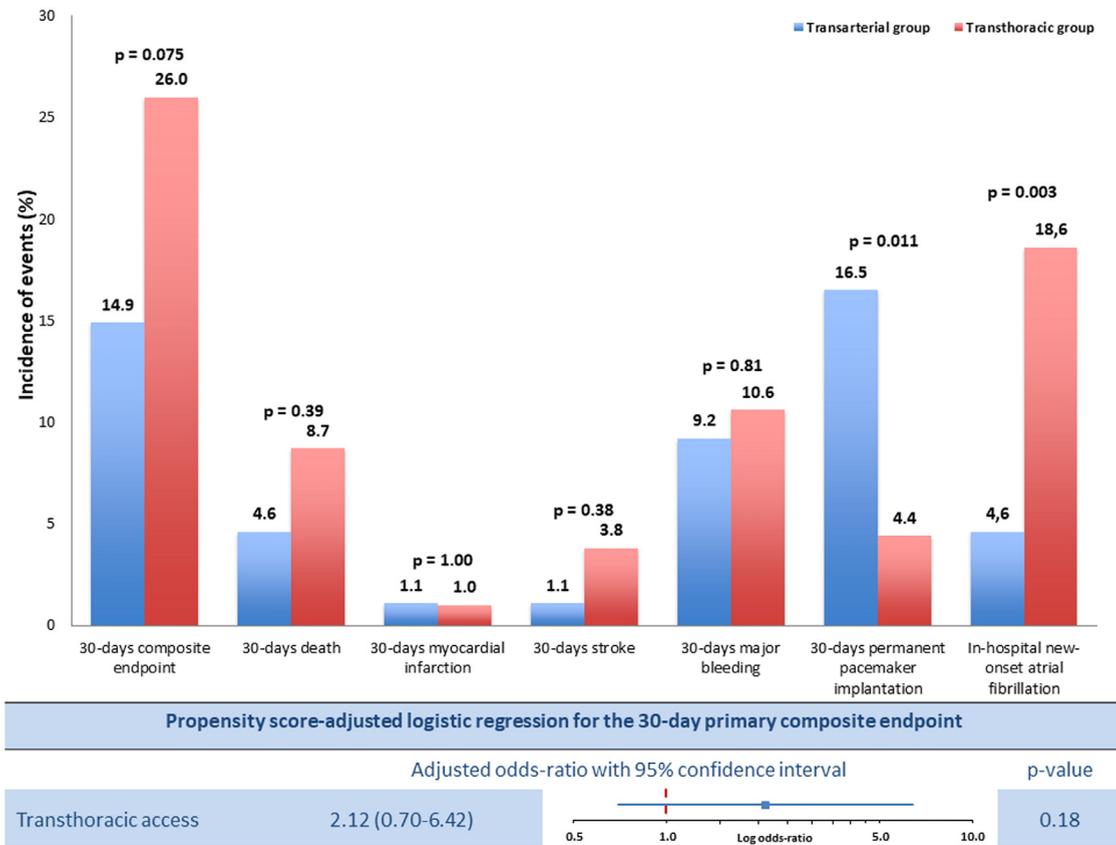


Figure 3. In-hospital and 30-day outcomes according to TAVI approach.

option when transfemoral TAVI cannot be performed. However, the paucity of direct comparisons between non-transfemoral approaches supporting this assumption is highlighted by the observation that transthoracic access still represents the majority of alternative access TAVI in some regions, such as the United States.¹⁶ The present study adds to a small number of publications, which investigated the potential benefits of practicing a transarterial instead of a transthoracic approach.^{9,17–19} As in the present study, a 3 Italian centers retrospective study also reported a nonsignificant trend to increased periprocedural events, which did not impact midterm survival, with the use of transapical versus subclavian TAVI.¹⁸ Within the larger UK registry, Fröhlich et al demonstrated a significantly higher 2-year mortality after transapical or transaortic access than after transfemoral or subclavian TAVI.¹⁷ Recently, using propensity score-matching, Chamandi et al published the largest comparative analysis specifically involving alternative access.¹⁹ Ninety-four transcarotid TAVI recipients were matched with 163 transthoracic TAVI patients. Transcarotid access was associated with reduced 30-day rates of new-onset atrial fibrillation, major or life-threatening bleeding, stage 2 or 3 acute kidney injury, and a shorter length of stay. Mortality, stroke, and device success were comparable between groups while early safety favored transcarotid access. The present study reports largely consistent findings.

Stroke was numerically higher in the transthoracic cohort, without significant difference between groups (3.8% vs 1.1%; $p = 0.38$), which may be related to the small

sample size. Beyond their heavier atherosclerotic burden, new-onset atrial fibrillation, a condition considerably more prevalent after transthoracic TAVR and associated with a higher risk of 30-day cerebrovascular events,²⁰ may significantly contribute to an increased risk in recipients of this approach. This finding may be of paramount importance, as consistently with our results, periprocedural stroke was an independent predictor of mortality in previous studies.²¹ Moreover, although local anesthesia was not consistently associated with better outcomes,²² a higher rate of periprocedural stroke has been suggested with general anesthesia after transcarotid TAVI.²³ Only 50% of transcarotid approach patients were treated under local anesthesia with sedation in the present study. Whether a broader use of local anesthesia and sedation with growing experience with this approach improves neurological outcomes should be the focus of future studies.

On the contrary, permanent pacemaker implantation was more frequent in the transarterial-access cohort. As reported in previous studies,²⁴ this finding is related to the higher implantation rate of self-expandable valves in the transarterial group. With the expansion of TAVI to lower-surgical risk and younger patients, this result raises the major issue of potentially negative effects of long-term pacing, even if the impact of permanent pacemaker implantation after TAVI remains debated.^{24,25} However, during the early experience of TAVI, subclavian approach was almost exclusively performed with self-expandable valve. Yet, with growing experience, balloon-expandable valves are

increasingly implanted through this access, which should mitigate its detrimental association with postprocedural pacemaker implantation.

Several limitations need to be acknowledged. First, there were significant differences in baseline characteristics between the 2 groups, which we attempted to adjust for by propensity score-adjustment. Nonetheless, no statistical method can provide the degree of bias reduction obtained with randomization. Therefore, residual confounding, related to the higher burden of co-morbidities observed in the transthoracic group, cannot be ruled out. Second, this is a retrospective analysis, based on a single center population with a limited number of patients in both cohorts, which implies a significant risk of type II error. Furthermore, because of the relatively recent development of this strategy in our center, the transcarotid approach was less represented than the subclavian access-route in the transarterial cohort. Considering the well-known learning-curve effect with other approaches,^{26,27} we can hypothesized that our lower experience regarding transcarotid procedures in comparison with others approaches potentially influenced our results. Conversely, transcarotid TAVI was likely performed using more advanced valve technologies in patients with a lower surgical risk, which may have balanced our limited experience.

Conclusion

Nontransfemoral transarterial-approach TAVI is safe, feasible, and associated with comparable rates of major perioperative complications, and midterm mortality compared with transthoracic-approach TAVI. Nonetheless, transarterial access may be associated with lower rates of new-onset atrial fibrillation, acute kidney injury, and shorter hospitalization.

Disclosures

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Supplementary materials

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.amjcard.2019.01.040>.

- Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S. PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363:1597–1607.
- Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ. PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;364:2187–2198.
- Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, Thourani VH, Tuzcu EM, Miller DC, Herrmann HC, Doshi D, Cohen DJ, Pichard AD, Kapadia S, Dewey T, Babaliaros V, Szezo

- WY, Williams MR, Kereiakes D, Zajarias A, Greason KL, Whisenant BK, Hodson RW, Moses JW, Trento A, Brown DL, Fearon WF, Pibarot P, Hahn RT, Jaber WA, Anderson WN, Alu MC, Webb JG. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2016;374:1609–1620.
- Auffret V, Lefevre T, Van Belle E, Eltchaninoff H, Jung B, Koning R, Motreff P, Leprince P, Verhoye JP, Manigold T, Souteyrand G, Boulmier D, Joly P, Pinaud F, Himbert D, Collet JP, Rioufol G, Ghostine S, Bar O, Dibie A, Champagnac D, Leroux L, Collet F, Teiger E, Darremont O, Folliguet T, Leclercq F, Lhermusier T, Olhmann P, Huret B, Lorgis L, Drogoul L, Bertrand B, Spaulding C, Quilliet L, Cuisset T, Delomez M, Beygui F, Claudel J-P, Hepp A, Jegou A, Gommeaux A, Mirode A, Christiaens L, Christophe C, Cassat C, Metz D, Mangin L, Isaaz K, Jacquemin L, Guyon P, Pouillot C, Makowski S, Bataille V, Rodés-Cabau J, Gilard M, Le Breton H. Temporal trends in transcatheter aortic valve replacement in France: FRANCE 2 to FRANCE TAVI. *J Am Coll Cardiol* 2017;70:42–55.
- D'Onofrio A, Salizzoni S, Agrifoglio M, Cota L, Luzi G, Tartara PM, Cresce GD, Aiello M, Savini C, Cassese M, Cerillo A, Punta G, Cioni M, Gabbieri D, Zanchettin C, Agostinelli A, Mazzaro E, Di Gregorio O, Gatti G, Faggian G, Filippini C, Rinaldi M, Gerosa G. Medium term outcomes of transapical aortic valve implantation: results from the Italian registry of trans-apical aortic valve implantation. *Ann Thorac Surg* 2013;96:830–835.
- Arai T, Romano M, Lefèvre T, Hovasse T, Farge A, Le Houerou D, Hayashida K, Watanabe Y, Garot P, Benamer H, Untersee T, Bouvier E, Morice M-C, Chevalier B. Direct comparison of feasibility and safety of transfemoral versus transaortic versus transapical transcatheter aortic valve replacement. *JACC Cardiovasc Interv* 2016;9:2320–2325.
- Thourani VH, Jensen HA, Babaliaros V, Suri R, Vemulapalli S, Dai D, Brennan JM, Rumsfeld J, Edwards F, Tuzcu EM, Svensson L, Szeto WY, Herrmann H, Kirtane AJ, Kodali S, Cohen DJ, Lerakis S, Devir-eddy C, Sarin E, Carroll J, Holmes D, Grover FL, Williams M, Maniar H, Shahian D, Mack M. Transapical and transaortic transcatheter aortic valve replacement in the United States. *Ann Thorac Surg* 2015;100:1718–1726.
- Gleason TG, Schindler JT, Hagberg RC, Deeb GM, Adams DH, Conte JV, Zorn GL, Hughes GC, Guo J, Popma JJ, Reardon MJ. Subclavian/axillary access for self-expanding transcatheter aortic valve replacement renders equivalent outcomes as transfemoral. *Ann Thorac Surg* 2018;105:477–483.
- Kirker EB, Hodson RW, Spinelli KJ, Korngold EC. The carotid artery as a preferred alternative access route for transcatheter aortic valve replacement. *Ann Thorac Surg* 2017;104:621–629.
- Folliguet T, Laurent N, Bertram M, Zannis K, Elfarra M, Vanhuysse F, Maureira P, Modine T. Transcarotid transcatheter aortic valve implantation: multicentre experience in France. *Eur J Cardio-Thorac Surg* 2018;53:157–161.
- Auffret V, Boulmier D, Oger E, Bedossa M, Donal E, Laurent M, Sost G, Beneux X, Harmouche M, Verhoye J-P, Le Breton H. Predictors of 6-month poor clinical outcomes after transcatheter aortic valve implantation. *Arch Cardiovasc Dis* 2014;107:10–20.
- Kappetein AP, Head SJ, Généreux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, Es G-A van, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodés-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the valve academic research consortium-2 consensus document. *Eur Heart J* 2012;33:2403–2418.
- Ludman PF, Moat N, Belder MA de, Blackman DJ, Duncan A, Banya W, MacCarthy PA, Cunningham D, Wendler O, Marlee D, Hildick-Smith D, Young CP, Kovac J, Uren NG, Spyt T, Trivedi U, Howell J, Gray H. UK TAVI Steering Committee and the National Institute for Cardiovascular Outcomes Research. Transcatheter aortic valve implantation in the United Kingdom: temporal trends, predictors of outcome, and 6-year follow-up: a report from the UK Transcatheter Aortic Valve Implantation (TAVI) Registry, 2007 to 2012. *Circulation* 2015;131:1181–1190.
- Paone G, Eng M, Kabbani LS, Borgi J, Peterson E, Novitsky B, Burroughs B, Wang DD, O'Neill WW, Greenbaum AS. Transcatheter aortic valve replacement: comparing transfemoral, transcarotid and transcaraval access. *Ann Thorac Surg* 2018;106:1105–1112.
- Petronio AS, De Carlo M, Bedogni F, Maisano F, Ettori F, Klugmann S, Poli A, Marzocchi A, Santoro G, Napodano M, Ussia GP, Giannini

- C, Brambilla N, Colombo A. 2-year results of CoreValve implantation through the subclavian access: a propensity-matched comparison with the femoral access. *J Am Coll Cardiol* 2012;60:502–507.
16. Damluji AA, Murman M, Byun S, Moscucci M, Resar JR, Hasan RK, Alfonso CE, Carrillo RG, Williams DB, Kwon CC, Cho PW, Dijos M, Peltan J, Heldman AW, Cohen MG, Leroux L. Alternative access for transcatheter aortic valve replacement in older adults: a collaborative study from France and United States. *Catheter Cardiovasc Interv* 2018;92:1182–1193.
 17. Fröhlich GM, Baxter PD, Malkin CJ, Scott DJA, Moat NE, Hildick-Smith D, Cunningham D, MacCarthy PA, Trivedi U, Belder MA de, Ludman PF, Blackman DJ. National Institute for Cardiovascular Outcomes Research. Comparative survival after transapical, direct aortic, and subclavian transcatheter aortic valve implantation (data from the UK TAVI registry). *Am J Cardiol* 2015;116:1555–1559.
 18. Ciuca C, Tarantini G, Latib A, Gasparetto V, Savini C, Di Eusanio M, Napodano M, Maisano F, Gerosa G, Sticchi A, Marzocchi A, Alfieri O, Colombo A, Saia F. Trans-subclavian versus transapical access for transcatheter aortic valve implantation: a multicenter study. *Catheter Cardiovasc Interv* 2016;87:332–338.
 19. Chamandi C, Abi-Akar R, Rodés-Cabau J, Blanchard D, Dumont E, Spaulding C, Doyle D, Pagny JY, DeLarochelière R, Lafont A, Paradis JM, Puri R, Karam N, Maes F, Rodriguez-Gabella T, Chassaing S, Le Page O, Kalavrouziotis D, Mohammadi S. Transcatheter compared with other alternative access routes for transcatheter aortic valve replacement. *Circ Cardiovasc Interv* 2018;11:e006388.
 20. Auffret V, Regueiro A, Del Trigo M, Abdul-Jawad Altisent O, Campelo-Parada F, Chiche O, Puri R, Rodés-Cabau J. Predictors of early cerebrovascular events in patients with aortic stenosis undergoing transcatheter aortic valve replacement. *J Am Coll Cardiol* 2016;68:673–684.
 21. Nombela-Franco L, Webb JG, Jaegers PP de, Toggweiler S, Nuis R-J, Dager AE, Amat-Santos IJ, Cheung A, Ye J, Binder RK, Boon RM van der, Van Mieghem N, Benitez LM, Pérez S, Lopez J, San Roman JA, Doyle D, Delarochelière R, Urena M, Leipsic J, Dumont E, Rodés-Cabau J. Timing, predictive factors, and prognostic value of cerebrovascular events in a large cohort of patients undergoing transcatheter aortic valve implantation. *Circulation* 2012;126:3041–3053.
 22. Maas EHA, Pieters BMA, Van de Velde M, Rex S. General or local anesthesia for TAVI? A systematic review of the literature and meta-analysis. *Curr Pharm Des* 2016;22:1868–1878.
 23. Debry N, Delhay C, Azmoun A, Ramadan R, Fradi S, Brenot P, Sudre A, Moussa MD, Tchetché D, Ghostine S, Mylotte D, Modine T. Transcatheter aortic valve replacement: general or local anesthesia. *JACC Cardiovasc Interv* 2016;9:2113–2120.
 24. Auffret V, Puri R, Urena M, Chamandi C, Rodriguez-Gabella T, Philippon F, Rodés-Cabau J. Conduction disturbances after transcatheter aortic valve replacement: current status and future perspectives. *Circulation* 2017;136:1049–1069.
 25. Chamandi C, Barbanti M, Munoz-Garcia A, Latib A, Nombela-Franco L, Gutiérrez-Ibanez E, Veiga-Fernandez G, Cheema AN, Cruz-Gonzalez I, Serra V, Tamburino C, Mangieri A, Colombo A, Jiménez-Quevedo P, Elizaga J, Laughlin G, Lee D-H, Garcia Del Blanco B, Rodriguez-Gabella T, Marsal J-R, Côté M, Philippon F, Rodés-Cabau J. Long-term outcomes in patients with new permanent pacemaker implantation following transcatheter aortic valve replacement. *JACC Cardiovasc Interv* 2018;11:301–310.
 26. Minha S, Waksman R, Satler LP, Torguson R, Alli O, Rihal CS, Mack M, Svensson LG, Rajeswaran J, Blackstone EH, Tuzcu EM, Thourani VH, Makkar R, Ehrlinger J, Lowry AM, Suri RM, Greason KL, Leon MB, Holmes DR, Pichard AD. Learning curves for transfemoral transcatheter aortic valve replacement in the PARTNER-I trial: success and safety. *Catheter Cardiovasc Interv* 2016;87:165–175.
 27. Suri RM, Minha S, Alli O, Waksman R, Rihal CS, Satler LP, Greason KL, Torguson R, Pichard AD, Mack M, Svensson LG, Rajeswaran J, Lowry AM, Ehrlinger J, Mick SL, Tuzcu EM, Thourani VH, Makkar R, Holmes D, Leon MB, Blackstone EH. Learning curves for transapical transcatheter aortic valve replacement in the PARTNER-I trial: technical performance, success, and safety. *J Thorac Cardiovasc Surg* 2016;152:773–780. e14.