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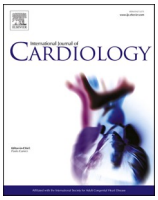

Percutaneous axillary vs femoral access for transcatheter aortic valve replacement: Insights from a 2164-patient study

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ABSTRACT

Background: Transaxillary (TAx) access is increasingly adopted for transcatheter aortic valve implantation (TAVR) in patients with challenging iliofemoral anatomy. We aimed at evaluating the early clinical outcomes of TAx vs transfemoral (TF) access for TAVR.

Methods: We conducted a retrospective observational study stemming from the prospective RISPEVA registry, including all consecutive patients undergoing TAVR since 2013 at our Institution, where TAx is the only alternative access site whenever TF is contraindicated.

Results: A total of 2164 patients were included: 60 (2.8 %) in the TAx group, and 2104 (97.2 %) in the TF group. Notably, no patient required alternative accesses or was referred for surgical aortic valve replacement. Baseline characteristics, including surgical risk scores such as EuroScore II (TAx = 5.3 ± 5.7, TF = 3.6 ± 3.7, $p < 0.001$) and comorbidities such as prior myocardial infarction (TAx = 10 [17.2 %], TF = 157 [8.1 %], $p = 0.025$), were clearly disfavoring the TAx group. Despite higher procedural times in the TAx group (69 ± 24 vs 59 ± 13 min, $p < 0.001$), procedural success rates were high in both groups (TAx = 58 [96.7 %], TF = 2077 [98.7 %], $p = 0.191$). Similarly, at 1-month follow-up there were no significant differences in all-cause mortality (TAx = 1 [1.7 %], TF = 26 [1.2 %], $p = 0.534$), stroke (TAx = 1 [1.7 %], TF = 11 [0.5 %], $p = 0.287$), myocardial infarction (TAx = 1 [1.7 %], TF = 8 [0.4 %], $p = 0.224$), major vascular complication (TAx = 4 [6.7 %], TF = 90 [4.3 %], $p = 0.329$), or major bleeding (TAx = 1 [1.7 %], TF = 36 [1.7 %], $p = 1$), as well as their composite (TAx = 7 [11.7 %], TF = 155 [7.4 %], risk difference = 4.3 % [95 % confidence interval − 3.9 % to 12.5 %], $p = 0.210$). Similar findings were obtained at multivariable adjusted analyses and those based on inverse probability of treatment weighting, despite their limited reliability given low event-per-variable ratios and instability.

Conclusions: In this single-center retrospective study, TAx TAVR was feasible whenever TF was not envisionable, and yielded quite favorable short-term clinical outcomes. While promising, these findings remain descriptive and hypothesis-generating, thus requiring additional prospective and randomized validation.

1. Introduction

Transcatheter aortic valve implantation (TAVR) has become the preferred therapy for patients with severe symptomatic aortic stenosis in patients at high surgical risk, with transfemoral (TF) access being the vascular route [1–4] However, many patients present with iliofemoral anatomy that is unsuitable for TF access, requiring alternative access strategies. [5,6] Among non-femoral options, transaxillary (TAx) access has emerged as a reliable and anatomically favorable route that enables retrograde aortic valve delivery while avoiding more invasive routes such as transapical or transaortic approaches. [7–10]

Nonetheless, percutaneous TAx TAVR poses technical challenges,

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particularly related to hemostasis and vascular closure, and may be associated with unique complications, including brachial plexus injury and upper extremity ischemia. [5,6] Moreover, some series have reported an increased incidence of cerebrovascular events with TAx access compared to TF, possibly due to proximity to the aortic arch and catheter manipulation in supra-aortic vessels. [11,12]

Despite the growing use of TAx access, contemporary data directly comparing percutaneous TAx and TF TAVR are limited by design, sample or operator expertise. [8–11] As such, there remains uncertainty regarding the optimal access strategy in patients with borderline or ambiguous iliofemoral anatomy.

We thus aimed at conducting a retrospective observational study comparing outcomes between percutaneous TAx and TF access in patients undergoing TAVR.

2. Methods

This study stems from the Pineta Grande Hospital cohort of the RISPEVA trial. Briefly, RISPEVA is an Italian prospective, multicenter, observational cohort study using a dedicated electronic case report form, enforcing common definitions and processes, and including thousands of patients every year. [13] Its design has been registered at clinicaltrials.gov (NCT02713932), all participating centers, including Pineta Grande Hospital, obtained institutional review board approval, and all patients provided written informed consent. [14] Consecutive patients undergoing TAVR were enrolled after providing written informed consent. The study was conducted in accordance with the Declaration of Helsinki and approved by the competent institutional ethics committee. Inclusion criteria consisted of adult patients with severe, symptomatic aortic stenosis deemed suitable for TAVR by the local heart team. Exclusion criteria included emergency procedures, non-percutaneous axillary access, or concomitant enrollment in interventional randomized trials. For the present analysis, we retrospectively compared all consecutive patients undergoing TAVR at Pineta Grande Hospital, focusing on TF vs TAx access, which is the only alternative access site when TF is not feasible.

The access strategy for TAVR was determined by a multidisciplinary heart team based on pre-procedural imaging, primarily computed tomography angiography (CTA), and clinical evaluation. [15] TF access was the default strategy when iliofemoral anatomy was suitable, whereas TAx access was used in the presence of hostile iliofemoral features, including severe calcification, small vessel diameter, or excessive tortuosity. TAx procedures were performed percutaneously using ultrasound-guided puncture and closure with dedicated devices. Notably, in all cases in which TF access was deemed unfeasible or unsafe, TAx was attempted, without any patient being approached with a different (percutaneous or surgical) access strategy, nor any individual being referred to surgical aortic valve replacement (SAVR). All TAVR procedures were conducted according to best practices and device manufacturer guidelines, with selection of valve type and sizing left to the discretion of the treating team, and performed by a team of highly experienced TAVR operators (AG and NC, with most procedures performed as first operator by AG).

Data were recorded in a standardized electronic case report form. Collected variables included baseline demographics, comorbidities, echocardiographic parameters, procedural characteristics, and clinical outcomes. All endpoints were defined according to the Valve Academic Research Consortium-3 (VARC-3) criteria. [16] Neurological events were classified per neurological adjudication or treating physician documentation. Vascular complications, bleeding, and other adverse events were captured during the index hospitalization, with procedural success defined also in keeping with VARC-3 criteria, as follows: freedom from mortality, successful access, delivery of the device, and retrieval of the delivery system, correct positioning of a single prosthetic heart valve into the proper anatomical location, and freedom from surgery or intervention related to the device or to a major vascular or access-related, or cardiac structural complication.

The primary endpoint was the composite of in-hospital all-cause mortality, major vascular complications, and stroke. Secondary endpoints included procedural success, access-site failure, device success, need for unplanned surgical repair, and length of hospitalization.

Continuous variables are reported as mean ± standard deviation and compared using the Student's *t*-test. Categorical variables are expressed as counts (percentages) and compared using the Fisher exact test. Risk differences and accompanying 95 % confidence intervals (CI) were also provided for key outcomes. Multivariable logistic regression was employed to account for potential confounders in access site selection, and was reported using odds ratios (OR), 95 % C) and *p* values. In addition, an exploratory analysis based on inverse probability of treatment weighting (IPTW) was conducted to further adjust for potential confounders. [17] A two-sided *p*-value <0.05 was considered statistically significant, without multiplicity adjustment. All analyses were conducted using Stata version 17.0 (StataCorp, College Station, TX, USA).

3. Results

A total of 2164 patients undergoing TAVR were included, with 60 (2.8 %) receiving TAx access and 2104 (97.2 %) undergoing TF access (Table 1, Table 2), without any individual requiring alternative accesses

Table 1
Baseline features.

Feature	TF access	TAx access	P value
Patients	2104	60	–
Age (years)	80.8 ± 5.7	79.4 ± 6.4	0.053
Female gender	1295 (61.6 %)	22 (36.7 %)	<0.001
Body mass index	27.3 ± 4.2	26.2 ± 3.8	0.033
Pacemaker dependent	273 (13.0 %)	11 (18.3 %)	0.242
Family history of coronary artery disease	59 (5.1 %)	5 (14.3 %)	0.036
Dyslipidemia	1617 (82.9 %)	55 (91.7 %)	0.080
Hypertension	1887 (96.2 %)	58 (100 %)	0.274
Current or former smoking	113 (9.1 %)	7 (17.1 %)	0.097
Diabetes mellitus			0.019
No	1573 (74.8 %)	37 (61.7 %)	
Non-insulin-dependent	377 (17.9 %)	13 (21.7 %)	
Insulin-dependent	154 (7.3 %)	10 (16.7 %)	
Coronary artery disease	290 (27.6 %)	20 (48.8 %)	0.005
Prior myocardial infarction	157 (8.1 %)	10 (17.2 %)	0.025
Prior percutaneous coronary intervention	524 (30.2 %)	20 (40.0 %)	0.160
Prior cardiac surgery	162 (7.7 %)	12 (20.0 %)	0.002
Prior aortic valve surgery	59 (62.1 %)	8 (80.0 %)	0.322
Prior valvuloplasty	37 (2.1 %)	3 (6.1 %)	0.086
Peripheral artery disease	367 (27.9 %)	60 (100 %)	<0.001
Prior endovascular therapy	75 (3.6 %)	11 (18.3 %)	<0.001
Chronic obstructive pulmonary disease	470 (22.3 %)	20 (33.3 %)	0.059
New York heart association			0.688
I	40 (1.9 %)	2 (3.3 %)	
II	1442 (68.5 %)	40 (66.7 %)	
III	586 (27.9 %)	17 (28.3 %)	
IV	36 (1.7 %)	1 (1.7 %)	
Euroscore II	3.6 ± 3.7	5.3 ± 5.7	<0.001
Risk			<0.001
Intermediate	765 (36.4 %)	12 (20.0 %)	
High	1270 (60.4 %)	42 (70.0 %)	
Inoperable	69 (3.3 %)	6 (10.0 %)	
Hemoglobin (g/dL)	12.3 ± 1.6	11.9 ± 1.6	0.071
Estimated glomerular filtration rate	64.4 ± 22.9	64.1 ± 23.1	0.926

TAx = transaxillary; TF = transfemoral.

Table 2
Imaging features.

Feature	TF access	TAx access	P value
Patients	2104	60	–
Significant coronary artery disease at coronary angiography	429 (20.4 %)	22 (36.7 %)	0.005
Porcelain aorta	38 (1.8 %)	3 (5.0 %)	0.103
Bicuspid aortic valve disease	47 (2.2 %)	1 (1.7 %)	1
Aortic valve area (cm2)	0.64 ± 0.14	0.64 ± 0.15	0.975
Mean aortic valve gradient (mm hg)	49.0 ± 15.9	45.3 ± 14.7	0.074
Aortic regurgitation			0.895
None or minimal	761 (36.2 %)	23 (38.3 %)	
Mild	762 (36.2 %)	21 (35.0 %)	
Moderate	465 (22.1 %)	12 (20.0 %)	
Moderate-severe	100 (4.8 %)	4 (6.7 %)	
Severe	16 (0.8 %)	0	
Aortic valve calcification			0.012
None or minimal	534 (25.4 %)	19 (31.7 %)	
Mild	195 (9.3 %)	1 (1.7 %)	
Moderate	914 (43.4 %)	23 (38.3 %)	
Severe	461 (22.0 %)	17 (28.4 %)	
Left ventricular ejection fraction (%)	52.7 ± 8.1	52.1 ± 9.5	0.529
Mitral regurgitation			0.008
None or minimal	37 (1.8 %)	0	
Mild	1004 (47.7 %)	18 (30.0 %)	
Moderate	901 (42.8 %)	32 (53.3 %)	
Moderate-severe	139 (6.6 %)	10 (16.7 %)	
Severe	1 (1.1 %)	0	

TAx = transaxillary; TF = transfemoral.

or being referred for SAVR. Baseline characteristics showed several imbalances disfavoring the TAx group, including higher rates of peripheral artery disease (100 % vs 27.9 %, $p < 0.001$), prior cardiac surgery (20.0 % vs 7.7 %, $p = 0.002$), and coronary artery disease (48.8 % vs 27.6 %, $p = 0.005$). The TAx cohort also had higher EuroSCORE II values (5.3 ± 5.7 vs 3.6 ± 3.7, $p < 0.001$) and a greater proportion of patients deemed inoperable (10.0 % vs 3.3 %, $p < 0.001$). Despite these differences, echocardiographic markers of aortic stenosis severity and left ventricular function were not significantly different between groups (all $p > 0.05$). Anatomical features such as aortic valve area and ejection fraction did not differ significantly (both $p > 0.05$), though moderate or greater mitral regurgitation was more common in TAx patients (53.3 % vs 42.8 %, $p = 0.008$).

Procedural characteristics and short-term outcomes are summarized in Table 3 and Table 4. TAx procedures were significantly longer in duration (69.1 ± 24.1 vs 58.9 ± 13.7 min, $p < 0.001$) and more frequently required general anesthesia (5.0 % vs 0.3 %, $p = 0.004$), while the use of self-expanding valves was more prevalent in the TAx group (98.3 % vs 89.4 %, $p = 0.017$). Nonetheless, device success (100 % vs 99.6 %, $p = 1.0$) and procedural success (96.7 % vs 98.7 %, $p = 0.191$) were not significantly different. Similarly, in-hospital clinical outcomes did not differ significantly, including death (1.7 % vs 1.2 %, $p = 0.534$), stroke (1.7 % vs 0.5 %, $p = 0.287$), myocardial infarction (1.7 % vs 0.4 %, $p = 0.224$), major vascular complications (6.7 % vs 4.3 %, $p = 0.329$), major bleeding (1.7 % in both groups, $p = 1$), permanent pacemaker implantation (8.3 % vs 16.8 %, $p = 0.110$), and major adverse events (11.7 % vs 7.4 %; risk difference = 4.3 % [−3.9 % to 12.5 %], $p = 0.210$; Table 3S, Fig. 1).

Table 3
Procedural features.

Feature	TF access	TAx access	P value
Patients	2104	60	–
Access site			–
Right femoral	1802 (85.7 %)	–	
Left femoral	302 (14.4 %)	–	
Right axillary	–	19 (31.7 %)	
Left axillary	–	41 (68.3 %)	
Anesthesia			
Local	2094 (99.5 %)	57 (95.0 %)	0.004
Spinal	3 (0.1 %)	0	
General	7 (0.3 %)	3 (5.0 %)	
Self-expandable device	1881 (89.4 %)	59 (98.3 %)	0.017
Post-dilation	863 (41.0 %)	24 (40.0 %)	0.895
Valve migration	12 (0.6 %)	0	1
Bailout valve-in-valve	25 (1.2 %)	0	1
Residual aortic regurgitation			0.195
None or minimal	1834 (87.2 %)	58 (96.7 %)	
Mild	252 (12.0 %)	2 (3.3 %)	
Moderate	12 (0.6 %)	0	
Moderate-severe	1 (0.1 %)	0	
Severe	5 (0.2 %)	0	
Fluoroscopy time (minutes)	18.5 ± 8.2	20.3 ± 7.5	0.095
Contrast volume (mL)	86.9 ± 26.4	84.2 ± 18.3	0.443
Procedural time (minutes)	58.9 ± 13.7	69.1 ± 24.1	<0.001
Device success	2096 (99.6 %)	60 (100 %)	1
Procedural success	2077 (98.7 %)	58 (96.7 %)	0.191

TAx = transaxillary; TF = transfemoral.

Table 4
Clinical and imaging outcomes up to 1 month of follow-up.

Feature	TF access	TAx access	P value
Patients	2104	60	–
Total hospital stay (days)	6.3 ± 3.3	6.9 ± 4.0	0.339
Major adverse events*	155 (7.4 %)	7 (11.7 %)	0.210
Death	26 (1.2 %)	1 (1.7 %)†	0.534
Stroke	11 (0.5 %)	1 (1.7 %)	0.287
Myocardial infarction	8 (0.4 %)	1 (1.7 %)	0.224
Major vascular complication	90 (4.3 %)	4 (6.7 %)	0.329
Major bleeding	36 (1.7 %)	1 (1.7 %)	1
Surgical conversion	1 (0.1 %)	0	1
Percutaneous coronary intervention	7 (0.3 %)	0	1
Permanent pacemaker implantation	353 (16.8 %)	5 (8.3 %)	0.110
Peak aortic valve gradient (mm hg)	6.3 ± 3.3	6.7 ± 4.0	0.339
Mean aortic valve gradient (mm hg)	14.4 ± 6.0	14.8 ± 8.0	0.664
Aortic regurgitation			0.349
None or minimal	922 (43.8 %)	24 (40.0 %)	
Mild	1108 (52.7 %)	32 (53.3 %)	
Moderate	60 (2.9 %)	4 (6.7 %)	
Moderate-severe	14 (0.1 %)	0	
Severe	0	0	

*composite of death, stroke, myocardial infarction, major vascular complication, or major bleeding; †both outcomes occurred in the same patient; TAx = transaxillary; TF = transfemoral.

Multivariable adjusted analyses (Table 5), albeit evidently limited by low event-per-variable ratios, did not show significant differences in the primary composite endpoint or in individual outcomes. Adjusted OR for major adverse events was 0.78 (CI = 0.25–2.43, $p = 0.666$), with similar findings for death (OR = 1.12, $p = 0.919$), stroke (OR = 2.32, $p = 0.469$), and myocardial infarction (OR = 3.72, $p = 0.228$). Similarly non-significant differences were found for vascular complications, major bleeding and permanent pacemaker implantation. Even IPTW analysis showed non-significant differences when comparing TAx vs TF accesses for the risk of major adverse events, stroke, vascular complications, major bleeding and permanent pacemaker implantation (all $p > 0.05$; Table 2S, Table 3S, Fig. 2). Notably, IPTW suggested a nominally statistically significant reduction in the risk of death (OR = 0.11 [0.01–0.88], $p = 0.037$), but this finding should be viewed with caution given the risk of multiplicity and type I error inflation, as well as the

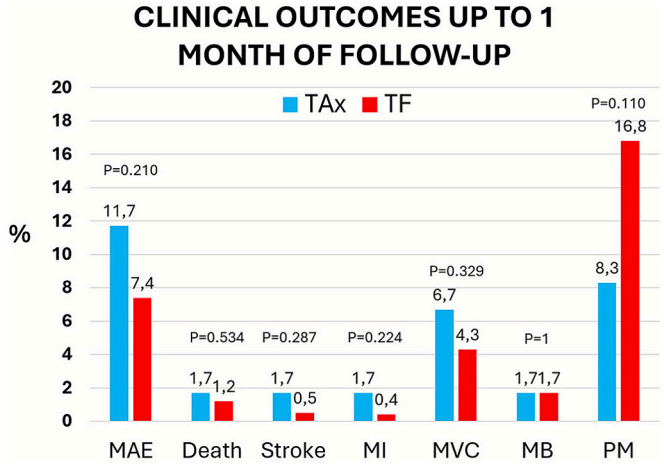

Fig. 1. Clinical and imaging outcomes up to 1 month of follow-up. TAx = transaxillary; TF = transfemoral.

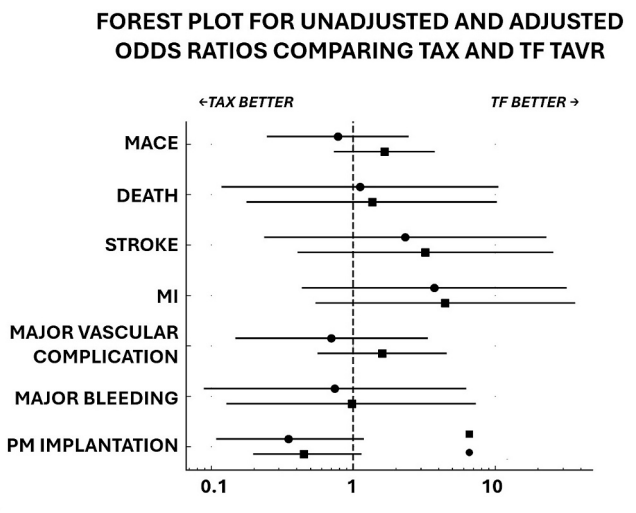

Fig. 2. Forest plot for unadjusted and adjusted odds ratios (OR) comparing transaxillary (TAx) and transfemoral (TF) accesses for transcatheter aortic valve replacement (TAVR).

Table 5
Unadjusted and multivariable adjusted analysis for key outcomes.

Feature	Unadjusted analysis	Adjusted analysis[†]
	Reported as odds ratios (95 % confidence intervals) and corresponding p values (OR < 1 indicates lower risk in the transaxillary group vs transfemoral group)	
Major adverse events*	1.66 (0.74–3.71), *p* = 0.217	0.78 (0.25–2.43), p = 0.666
Death	1.36 (0.18–10.15), *p* = 0.768	1.12 (0.12–10.37), p = 0.919
Stroke	3.22 (0.41–25.39), *p* = 0.266	2.32 (0.24–22.59), p = 0.469
Myocardial infarction	4.44 (0.55–36.08), *p* = 0.163	3.72 (0.44–31.51), p = 0.228
Major vascular complication	1.60 (0.57–4.51), *p* = 0.357	0.70 (0.15–3.31), *p* = 0.649
Major bleeding	0.98 (0.13–7.22), *p* = 0.979	0.74 (0.09–6.19), *p* = 0.779
Permanent pacemaker implantation	0.45 (0.20–1.13), *p* = 0.091	0.35 (0.11–1.17), *p* = 0.087

*composite of death, stroke, myocardial infarction, major vascular complication, or major bleeding; [†]adjusting for age, gender, diabetes mellitus, history of coronary artery disease, risk category, and EuroSCORE II, with event per variable ratios ranging between 51 for permanent pacemaker implantation and 1 for stroke.

likelihood of model instability due to unstable or extreme weights.

4. Discussion

Since its introduction more than 20 years ago, TAVR has undergone a transformative evolution since its clinical introduction, becoming the standard treatment for symptomatic aortic stenosis across all surgical risk categories. [18–20] Although TF access remains the default route due to its simplicity and favorable outcomes, anatomic and clinical constraints often preclude its use. [5,6] In these cases, alternative access strategies such as TAx have become increasingly adopted, with the TAx route offering an appealing retrograde pathway without requiring thoracotomy or sternotomy (Fig. 1S). [8,21], Despite its growing clinical use, comparative evidence evaluating the safety and efficacy of TAx versus TF access remains limited, especially from prospectively designed studies. [5,11] The present retrospective analysis stemming from the prospective RISPEVA registry aimed to address this gap by describing outcomes between percutaneous TAx and TF TAVR within a well-characterized, single center cohort.

As expected, patients undergoing TAx TAVR in our study presented with higher procedural risk and more complex clinical profiles, including a greater prevalence of peripheral artery disease, prior cardiac surgery, and elevated surgical risk scores. These imbalances reflect the real-world rationale behind access route selection, wherein TAx is typically reserved for patients with iliofemoral anatomical contraindications. Procedural characteristics such as increased duration and higher rates of general anesthesia in the TAx group mirror the technical complexity of the approach. Nonetheless, device selection remained largely consistent across both access types, and procedural success rates were high irrespective of route—highlighting that even in anatomically complex cases, percutaneous TAx can be executed safely in experienced hands.

Clinical outcomes were favorable in both groups, with low rates of in-hospital mortality, stroke, myocardial infarction, and major bleeding. Although stroke and vascular complications were numerically higher in the TAx group, these differences did not reach statistical significance, and no excess in all-cause mortality was observed. Importantly, the rate of permanent pacemaker implantation appeared lower in TAx patients, suggesting potential procedural or anatomical advantages that merit further investigation. Yet, most likely other features such as age, gender, extent of calcification. Conduction system proximity, valve type, and implant depth may have contributed, at least in part, to such differences.

These findings provide reassurance that percutaneous TAx access can serve as a safe alternative to TF, even in patients with elevated baseline risk.

Our data complement previous observational series, such as the TAXI registry, and expand the evidence base recently reviewed by Sherwood et al., which suggested that TAx access may be associated with an increased risk of adverse events compared to other non-femoral routes. [5,8,9] While their conclusions raise legitimate concerns, they stem from the pooling of heterogenous datasets, and key caveats in how TAx was implemented and carried out. In contrast, the prospective design of the RISPEVA registry, from which the present retrospective analysis stems, strict endpoint definitions, and execution in high-volume centers offer a distinct clinical perspective. The low stroke rate in our TAx cohort, despite higher baseline risk, underscores the critical role of operator expertise and structured procedural protocols. Unlike prior multicenter analyses, [9,12] our study offers a unique single-center perspective wherein all TAVR procedures, across both TF and TAx accesses, were performed by a highly experienced team of just two operators. This uniform procedural expertise minimizes inter-operator variability and provides a controlled insight into the feasibility and

safety of TAx access in a real-world setting. As such, our findings not only corroborate earlier multicenter results but also represent a contemporary benchmark for the technical execution and short-term outcomes of percutaneous TAx TAVR in expert hands. Another key strength of our work is that it included all patients undergoing TAVR at our institution, without anyone being turned down or referred elsewhere, with TAx proving an effective alternative access in all those unfit for TF TAVR. These considerations support a more balanced interpretation of TAx access risk, emphasizing individualization and technical excellence.

This study is not without limitations. As an observational, non-randomized and retrospective registry, residual confounding cannot be excluded despite multivariable adjustments and additional IPTW analyses. [17] The relatively small size of the TAx group limits statistical power for rare events, and long-term follow-up data are still pending. Most importantly, the low event-per-variable ratios of multivariable models imply that they are quite statistically unstable and thus should be viewed as exploratory only. Notably, IPTW models cannot be considered confirmatory given their likely instability (eg because of extreme statistical weights). Furthermore, the interaction between play of chance and small sample could explain the low rate of permanent pacemaker implantation in the TAx group, even if slightly lower age and higher prevalence of male gender could also be contributing factors. As previously stated, other important patient or procedural features may have however impacted on pacemaker implantation rates, ranging from anatomical ones (eg left ventricular outflow tract calcium) to procedural ones (eg device type and implant depth). In addition, the lack of long-term follow-up limit the informativeness of our work on the long-term outlook of these patients. Nevertheless, these results provide valuable prospective insights into a clinically important population often underrepresented in randomized trials. Future work should also focus on refining patient selection, standardizing percutaneous TAx techniques, and validating our findings in broader multicenter cohorts, as these aspects are crucial to maximize the safe adoption of demanding techniques in the TAVR setting. [22,23]

In conclusion, percutaneous TAx access appears to be an appealing alternative to TF access for TAVR in patients with unsuitable iliofemoral anatomy. Indeed, despite differences in baseline risk and procedural complexity largely disfavoring the TAx group, clinical outcomes were not significantly different across access strategies. Yet, while promising, these findings remain evidently descriptive and hypothesis-generating, thus requiring additional prospective and randomized validation.

Disclosure

Giuseppe Biondi-Zoccai has consulted, lectured and/or served as advisory board member for Abiomed, Advanced Nanotherapies, Aleph, Amarin, AstraZeneca, Balmed, Cardionovum, Cepton, Crannmedical, Endocore Lab, Eukon, Guidotti, Innovheart, Meditrial, Menarini, Microport, Opsens Medical, Synthesa, Terumo, and Translumina, outside the present work. All other authors report no conflict of interest.

CRediT authorship contribution statement

Nicola Corcione: Writing – original draft, Resources, Methodology, Conceptualization. **Salvatore Giordano:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Paolo Ferraro:** Writing – review & editing, Methodology, Investigation, Data curation. **Alberto Morello:** Writing – review & editing, Validation, Methodology, Investigation, Data curation. **Michele Cimmino:** Writing – review & editing, Supervision, Software, Investigation, Data curation. **Michele Albanese:** Writing – review & editing, Visualization, Formal analysis, Data curation. **Raffaella Avellino:** Writing – review & editing, Validation, Methodology, Data curation. **Giuseppe Biondi-Zoccai:** Writing – review & editing, Supervision, Methodology, Investigation, Data curation, Conceptualization. **Martino Pepe:** Writing – review & editing, Validation, Methodology, Investigation, Data curation. **Arturo Giordano:** Writing – original draft, Resources, Methodology, Funding acquisition, Data curation, Conceptualization.

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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.2025.134093.

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