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ORIGINAL RESEARCH

STRUCTURAL

Femoral or Radial Secondary Access in TAVR

A Subanalysis From the Multicenter PULSE Registry

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ABSTRACT

BACKGROUND Transradial secondary access (TR-SA) may serve as an alternative to the traditional femoral secondary access (TF-SA) for pigtail placement in transcatheter aortic valve replacement (TAVR).

OBJECTIVES The aim of this study was to assess the incidence of secondary access–related vascular complications after TR-SA or TF-SA in TAVR.

METHODS The PULSE (Plug or sUture based vascuLar cloSurE after TAVR) registry retrospectively evaluated data of 10,120 patients who underwent transfemoral TAVR at 10 heart centers from 2016 to 2021. We compared TR-SA and TF-SA groups of 8,851 patients with available data regarding the secondary access location and validated observed data in 1:1 propensity score matching. Outcomes were evaluated according to Valve Academic Research Consortium 3 definitions.

RESULTS The median age was 82.0 $\pm$ 6.9 years, and 49.1% (4,346/8,851) of patients were female. TR-SA was selected in 1,686 patients (19.0%) and TF-SA in 7,165 (81.0%) overall. Vascular complications at the secondary access occurred in 0.3% (5/1,686 [TR-SA]) vs 3.2% (232/7,165 [TF-SA]; $P < 0.001$) and were considered major in 0.2% (3/1,686 [TR-SA]) vs 1.5% (109/7,165 [TF-SA]) and minor in 0.1% (2/1,686 [TR-SA]) vs 1.7% (123/7,165 [TF-SA]; $P < 0.001$ for both). Surgical repair was required in 0 TR-SA patients and in 0.9% (66/7,165) of TF-SA patients. Primary access vascular complications were similar (11.6% (196/1,686 [TR-SA]) vs 11.5% (825/7,165 [TF-SA]); $P = 0.93$); bleeding type III/IV occurred less with TR-SA (2.5% [42/1,686] vs 4.7% [334/7,165] with TF-SA; $P < 0.001$). After propensity score matching, secondary access–related vascular complication rates remained lower for TR-SA (0.2% [1/512] vs 2.9% [15/512] for TF-SA; $P < 0.001$).

CONCLUSIONS During transfemoral TAVR, TR-SA was associated with lower rates of access site complications and severe bleeding compared to TF-SA. In fact, secondary access–related complications were 10× higher for TF-SA and frequently required invasive treatments. These findings challenge the fact that most TAVR procedures are still performed with TF-SA. (JACC Cardiovasc Interv. 2024;17:2923–2932) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

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ABBREVIATIONS AND ACRONYMS

BMI = body mass index

PAD = peripheral artery disease

PS = propensity score

STS-PROM = Surgeons of Thoracic Surgeons Predicted Risk of Mortality

TAVR = transcatheter aortic valve replacement

TF-SA = transfemoral secondary access

THV = transcatheter heart valve

TR-SA = transradial secondary access

VARC-3 = Valve Academic Research Consortium-3

Transcatheter aortic valve replacement (TAVR) has become the preferred treatment for most patients with severe symptomatic aortic stenosis.[1] The transfemoral route is most commonly used in the procedure because of low complication rates compared with alternative accesses.[2] In addition to the primary large-bore access for the delivery of transcatheter heart valves (THVs), a secondary access is used for pigtail placement and aortic root angiography to guide implantation. This secondary access is most frequently acquired via a second transfemoral puncture.[3] Available data suggest that the secondary access can be linked to access-related vascular complications during TAVR.[4] Also, it is well established that vascular complications are associated with impaired outcome after the procedure.[5-8] Radial access has become the primary choice for percutaneous coronary intervention because of low complication rates; therefore, a radial approach may serve as a potentially safer alternative to the traditional femoral strategy for the secondary access in TAVR.[9] Because of the paucity of large-scale data on the impact of secondary access strategies on clinical outcomes, we compared both approaches during TAVR in a large multicenter registry and evaluated outcomes according to the latest Valve Academic Research Consortium-3 (VARC-3) criteria.[10]

METHODS

PATIENT POPULATION. The PULSE registry (Plug or sUture based vascuLar cloSurE after TAVR) retrospectively analyzed data of 10,120 consecutive patients who received transfemoral TAVR at 10 German high-volume heart centers from 2016 to 2021 (**Figure 1**). All patients with transfemoral TAVR and either left or right transradial secondary access (TR-SA) (n = 1,686; left TR-SA: n = 18, right TR-SA: n = 1,668) or transfemoral secondary access (n = 7,165) were included in this study. The exclusion criteria were alternative secondary access strategies and hostile access requiring intervention to gain access. All patients provided informed consent to the procedure and data acquisition. Ethics committee approval was obtained according to local requirements. The study was performed in accordance with the 1964 Declaration of Helsinki and its later amendments.

COMPUTED TOMOGRAPHY ASSESSMENT. Vascular anatomy data were collected from contrast-enhanced multidetector computed tomography performed during TAVR evaluation. For the left or right primary access calcification severity, divided into none/mild (spotty), moderate (coalescing), and severe (bulky, protruding, horseshoe, or circumferential) categories, and tortuosity severity from puncture site to aortic bifurcation, divided into none/mild (30°-60°), moderate (60°-90°), and severe (≥90°) categories, were

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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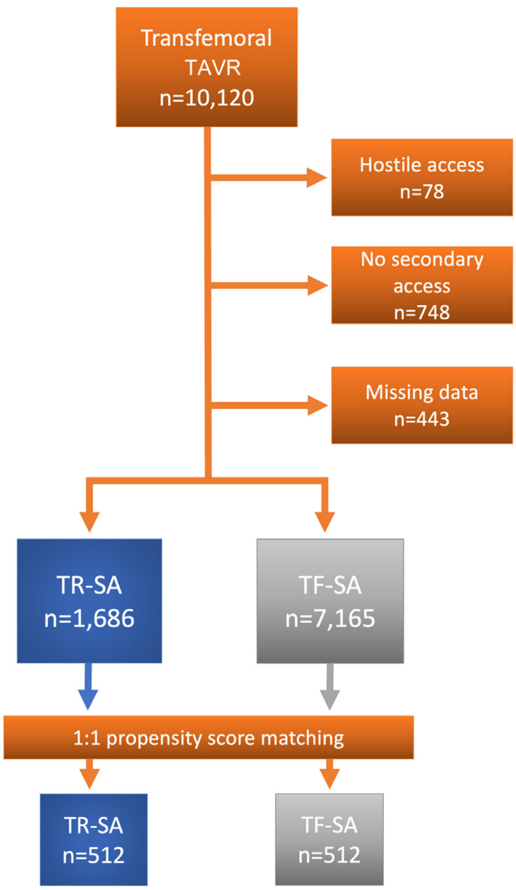
FIGURE 1 Study Flowchart



Overall, 10,120 patients with transfemoral transcatheter aortic valve replacement (TAVR) were evaluated in the PULSE (Plug or sUture based vascuLar cloSurE after TAVR) registry. After the exclusion of patients with hostile access (peripheral transluminal angioplasty or stent implantation to gain transfemoral access), no secondary access, or missing data, a 1:1 propensity score matching was performed. TF-SA = transfemoral secondary access; TR-SA = transradial secondary access.

assessed as described previously.[11,12] The minimal lumen diameter was measured of the common femoral artery at the primary access site.

TRANSCATHETER AORTIC VALVE REPLACEMENT. Each patient was reviewed individually by the local heart team. TAVR was performed according to local practice and expertise. The choice of secondary access was at the operator's discretion. Secondary access was used for angiographic guidance of the procedure, and if gained via the transfemoral route, vascular closure was performed with Angio-Seal (St Jude Medical). Documentation of procedural variables occurred in a standardized manner. Heparin reversal was achieved by using protamine at the operator's discretion.

CLINICAL OUTCOMES AND ENDPOINT DEFINITIONS. Outcomes were evaluated at 30 days after the index procedure according to VARC-3 definitions and were compared between groups.[10] Primary outcomes were major and minor access-related vascular complications at the secondary access. These were subclassified as bleeding, stenosis/occlusion, femoral dissection, pseudoaneurysm, or other for each access site. Treatment was characterized as surgical repair, endovascular stenting, endovascular balloon inflation, manual compression/conservative treatment, or other. Major and minor access-related vascular complications at the primary access as well as bleeding, stroke, acute kidney injury, myocardial infarction, pacemaker implantation, length of hospitalization, and mortality according to VARC-3 were classified as secondary outcomes.

STATISTICAL ANALYSIS. Binary variables were shown as absolute numbers or percentages and were compared using the chi-square test. The Fisher hypergeometric test was applied for variables with an event rate <5. Continuous variables were shown as median (IQR) and were compared using the Mann-Whitney test. All *P* values had a significance threshold of <0.05. Statistical analyses were performed using R version 4.1.2 (R Foundation for Statistical Computing). Because confounding variables were present at baseline, we applied a propensity score (PS) matching method for adjustment between TR-SA and TF-SA patients. This model was calculated using the nearest neighbor method with a caliper of 0.05, the Mahalanobis distance measure, and a ratio of 1:1 without replacement; the matching takes place in ascending order of distance measures (m.order = "smallest"). The target estimand was the average treatment effect in the treated patients, and the covariates used for matching were age, sex, body mass index (BMI), diabetes, glomerular filtration rate, anemia, peripheral artery disease (PAD), atrial fibrillation, NYHA functional class IV, Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM), chronic obstructive pulmonary disease, left ventricular ejection fraction <30%, antithrombotic therapy during TAVR (dual antiplatelet medication, triple antiplatelet medication [anticoagulation as well as dual antiplatelet medication], anticoagulation monotherapy, or dual therapy [anticoagulation as well as single antiplatelet medication]), and center. The original number of observations after removing missing values in covariates was 3,688 (Supplemental Table 1). After matching, 1,024 observations

TABLE 1 Baseline Characteristics Before Propensity Score Matching

	All (N = 8,851)	TR-SA (n = 1,686)	TF-SA (n = 7,165)	*P* Value
Baseline				
Age, y	82.0 (78.3-85.2)	81.5 (77.5-85.1)	82.0 (78.5-85.2)	0.003
Female	4,346 (49.1)	751 (44.6)	3,595 (50.2)	<0.001
BMI, kg/m^2	26.4 (23.8-29.7)	26.1 (23.7-29.3)	26.5 (23.8-29.8)	0.009
CAD	5,268 (60.0)	963 (58.6)	4,305 (60.3)	0.21
Prior CABG	750 (10.3)	126 (8.0)	624 (10.9)	0.001
Prior myocardial infarction	978 (11.1)	204 (12.4)	774 (10.8)	0.078
Prior PCI	3,077 (39.6)	621 (39.1)	2,456 (39.7)	0.68
COPD	1,262 (14.4)	172 (10.4)	1,090 (15.3)	<0.001
PAD	1,228 (14.0)	185 (11.3)	1,043 (14.6)	<0.001
Atrial fibrillation	3,659 (43.1)	671 (41.0)	2,988 (43.6)	0.066
Prior stroke	990 (12.1)	195 (12.3)	795 (12.0)	0.82
Diabetes	2,387 (27.2)	461 (28.0)	1,926 (27.0)	0.44
eGFR, mL/min/1.73 m^2	56.0 (41.0-73.0)	54.0 (40.0-70.0)	56.7 (41.0-73.0)	<0.001
Anemia (hemoglobin <11 g/dL)	1,854 (21.0)	360 (21.4)	1,494 (20.9)	0.65
NYHA functional class IV	717 (8.3)	98 (6.2)	619 (8.8)	<0.001
STS-PROM	3.4 (2.3-5.2)	2.9 (2.0-4.4)	3.5 (2.4-5.4)	<0.001
Antithrombotic medication				
Dual antiplatelet medication	2,762 (40.4)	640 (40.3)	2,122 (40.5)	0.90
Anticoagulation monotherapy	1,010 (14.8)	321 (20.2)	689 (13.1)	<0.001
Dual therapy (anticoagulation and single antiplatelet medication)	1,958 (28.7)	374 (23.5)	1,584 (30.2)	<0.001
Triple therapy	191 (2.8)	61 (3.8)	130 (2.5)	0.005
Computed tomography				
MLD of the common femoral artery at primary access site, mm	7.4 (6.3-8.5)	7.6 (6.4-8.7)	7.3 (6.2-8.4)	<0.001
Vascular calcification (moderate or severe)	2,312 (27.1)	708 (42.9)	1,604 (23.3)	<0.001
Vessel tortuosity (moderate or severe)	2,401 (32.9)	602 (38.1)	1,799 (31.4)	<0.001
Echocardiography				
LVEF <30%	391 (5.0)	73 (4.6)	318 (5.1)	0.46
Mean transvalvular gradient, mm Hg	40.0 (30.0-50.0)	36.0 (27.0-45.0)	41.0 (31.0-50.0)	<0.001
Effective orifice area, cm^2	0.7 (0.6-0.9)	0.8 (0.6-0.9)	0.7 (0.6-0.8)	<0.001
Severe aortic regurgitation	150 (1.8)	37 (2.3)	113 (1.7)	0.099

Values are median (Q1-Q3) or n (%). Binary variables were compared using the chi-square or Fisher test. Continuous variables were compared using the Mann-Whitney test.

BMI = body mass index; CABG = coronary artery bypass grafting; CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; MLD = minimal lumen diameter; PAD = peripheral artery disease; PCI = percutaneous coronary intervention; STS-PROM = Society of Thoracic Surgeons Preicted Risk of Mortality; TF-SA = transfemoral secondary access; TR-SA = transradial secondary access.

remained. Balance was assessed by the average absolute standardized difference and amounts 0.239 before matching and 0.064 after matching.[13] The Cochran-Armitage test was conducted to examine a potential trend in major, minor, or no vascular access complications over the time intervals. The null hypothesis of no trend in data was tested for every group against the others. *P* values were corrected with the Bonferroni method and indicated a trend if <0.05.

RESULTS

BASELINE CHARACTERISTICS. The median age was 82.0 years (Q1-Q3: 78.3-85.2 years), and the median STS-PROM was 3.4% (Q1-Q3: 2.3%-5.2%) overall. Before PS matching, significant differences between the TR-SA and TF-SA groups regarding several baseline risk factors were observed, including sex, BMI, prior coronary artery bypass grafting, chronic obstructive pulmonary disease, PAD, estimated glomerular filtration rate, NYHA functional class IV, antithrombotic medication, STS-PROM, moderate/severe vascular calcification, and mean transvalvular gradients, among others (**Table 1**). After 1:1 PS matching, comorbidities and clinical variables at baseline were well-balanced between both groups (Supplemental Table 2). Significant differences persisted for atrial fibrillation (47.9% [245/512] vs 41.4% [212/512]; $P = 0.044$), prevalence of moderate/severe vascular calcification at TAVR access (56.7% [284/501] vs 39.2% [199/508]; $P < 0.001$), and dual antiplatelet medication (34.0% [174/512] vs 49.6% [254/512]; $P < 0.001$) in TR-SA compared to TF-SA groups.

TABLE 2 Procedural Characteristics Before Propensity Score Matching

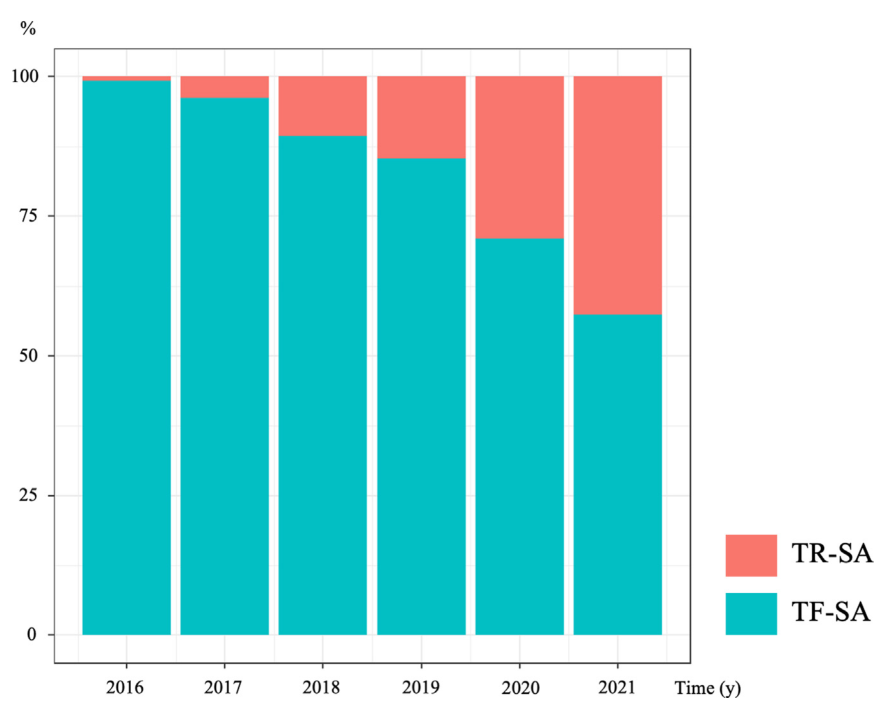
	All (N = 8,851)	TR-SA (n = 1,686)	TF-SA (n = 7,165)	*P* Value
Secondary access sheath size (F)	6.0 (6.0-6.0)	6.0 (5.0-6.0)	6.0 (6.0-6.0)	<0.001
Primary access sheath size (F)	14.0 (14.0-16.0)	14.0 (14.0-14.0)	14.0 (14.0-16.0)	<0.001
Vascular closure strategy primary access				
S-VCD	7,074 (80.0)	1,156 (68.6)	5,918 (82.7)	<0.001
P-VCD	1,254 (14.2)	514 (30.5)	740 (10.3)	<0.001
Other	515 (5.8)	16 (0.9)	499 (7.0)	<0.001
Balloon-expandable THV	3,068 (41.5)	984 (61.2)	2,084 (36.0)	<0.001
Heparin reversal with protamine	6,647 (79.2)	614 (37.3)	6,033 (89.4)	<0.001
Procedure duration, min	52.0 (38.0-68.0)	51.0 (38.0-65.0)	52.0 (38.0-68.0)	0.035
Contrast agent, mL	100.0 (76.0-145.0)	120.0 (80.0-170.0)	100.0 (75.0-140.0)	<0.001
Fluoroscopy time, min	11.1 (8.0-16.0)	12.3 (9.4-17.2)	11.0 (7.8-15.6)	<0.001

Values are median (IQR) or n (%). Binary variables were compared using the chi-square or Fisher test. Continuous variables were compared using the Mann-Whitney test. P-VCD = plug-based vascular closure; S-VCD = suture-based vascular closure; THV = transcatheter heart valve; other abbreviations as in Table 1.

PROCEDURAL CHARACTERISTICS. Procedural characteristics are outlined in Table 2. TR-SA was selected in 1,686 (19.0%) and TF-SA in 7,165 patients (81.0%) overall. For the secondary access, the mean sheath size was smaller in TR-SA compared to TF-SA patients (6.0 [Q1-Q3: 5.0-6.0] vs 6.0 [Q1-Q3: 6.0-6.0], respectively; $P < 0.001$).

At the primary large-bore access, differences regarding sheath size (14.0 [Q1-Q3: 14.0-14.0] vs 14.0 [Q1-Q3: 14.0-16.0]; $P < 0.001$) and choice of vascular

FIGURE 2 Temporal Trend of Secondary Access Approach in the PULSE Registry



A significant increase of the radial compared to the femoral secondary access was observed in the unmatched PULSE registry from 2016 to 2021, but the majority of secondary accesses remained femoral in the investigated time frame ($P < 0.001$ according to the Cochrane-Armitage test with the Bonferroni-corrected P value). Abbreviations as in Figure 1.

TABLE 3 30-Day Outcomes (Before Propensity Score Matching)

	All (N = 8,851)	TR-SA (n = 1,686)	TF-SA (n = 7,165)	*P* Value
Access-related vascular complications (secondary access)				
All	237 (2.7)	5 (0.3)	232 (3.2)	<0.001
Major	112 (1.3)	3 (0.2)	109 (1.5)	<0.001
Minor	125 (1.4)	2 (0.1)	123 (1.7)	<0.001
Type				
Bleeding	109 (1.2)	4 (0.2)	105 (1.5)	<0.001
Dissection	4 (0.0)	0 (0)	4 (0.1)	1.00
Pseudoaneurysm	108 (1.2)	1 (0.1)	107 (1.5)	<0.001
Stenosis/occlusion	13 (0.1)	0 (0)	13 (0.2)	0.15
Other (%)	2 (0.0)	0 (0)	2 (0.0)	1.00
Treatment				
Conservative/manual compression	134 (1.5)	4 (0.2)	130 (1.8)	<0.001
Prolonged endovascular balloon inflation	1 (0.0)	0 (0)	1 (0.0)	1.00
Stent implantation	8 (0.1)	0 (0)	8 (0.1)	0.37
Surgical repair	66 (0.7)	0 (0)	66 (0.9)	<0.001
Other	26 (0.3)	1 (0.1)	25 (0.3)	0.046
Access-related vascular complications (primary access)				
All (%)	1,021 (11.5)	196 (11.6)	825 (11.5)	0.93
Major (%)	393 (4.4)	64 (3.8)	329 (4.6)	0.17
Minor (%)	628 (7.1)	132 (7.8)	496 (6.9)	0.21
Access-related nonvascular complication	48 (0.6)	9 (0.6)	39 (0.6)	0.87
Bleeding (type III/IV)	376 (4.2)	42 (2.5)	334 (4.7)	<0.001
Stroke (disabling and nondisabling)	206 (2.3)	40 (2.4)	166 (2.3)	0.96
Severe acute kidney injury (AKIN III and AKIN IV)	212 (2.4)	20 (1.2)	192 (2.7)	<0.001
Myocardial infarction	25 (0.3)	5 (0.3)	20 (0.3)	1.00
Permanent pacemaker implantation	1,039 (11.7)	225 (13.3)	814 (11.4)	0.025
Length of stay in-hospital, d	7.0 (5.7-9.0)	6.0 (5.0-8.0)	7.0 (6.0-10.0)	<0.001
All-cause death	503 (5.8)	41 (2.6)	462 (6.6)	<0.001

Values are n (%) or median (IQR). Binary variables were compared using the chi-square or Fisher test. Other indicates unspecified treatment of access-related vascular complications, mainly reflecting thrombin injection for the treatment of pseudoaneurysm in both groups.

AKIN = Acute Kidney Injury Network; other abbreviations as in Table 1.

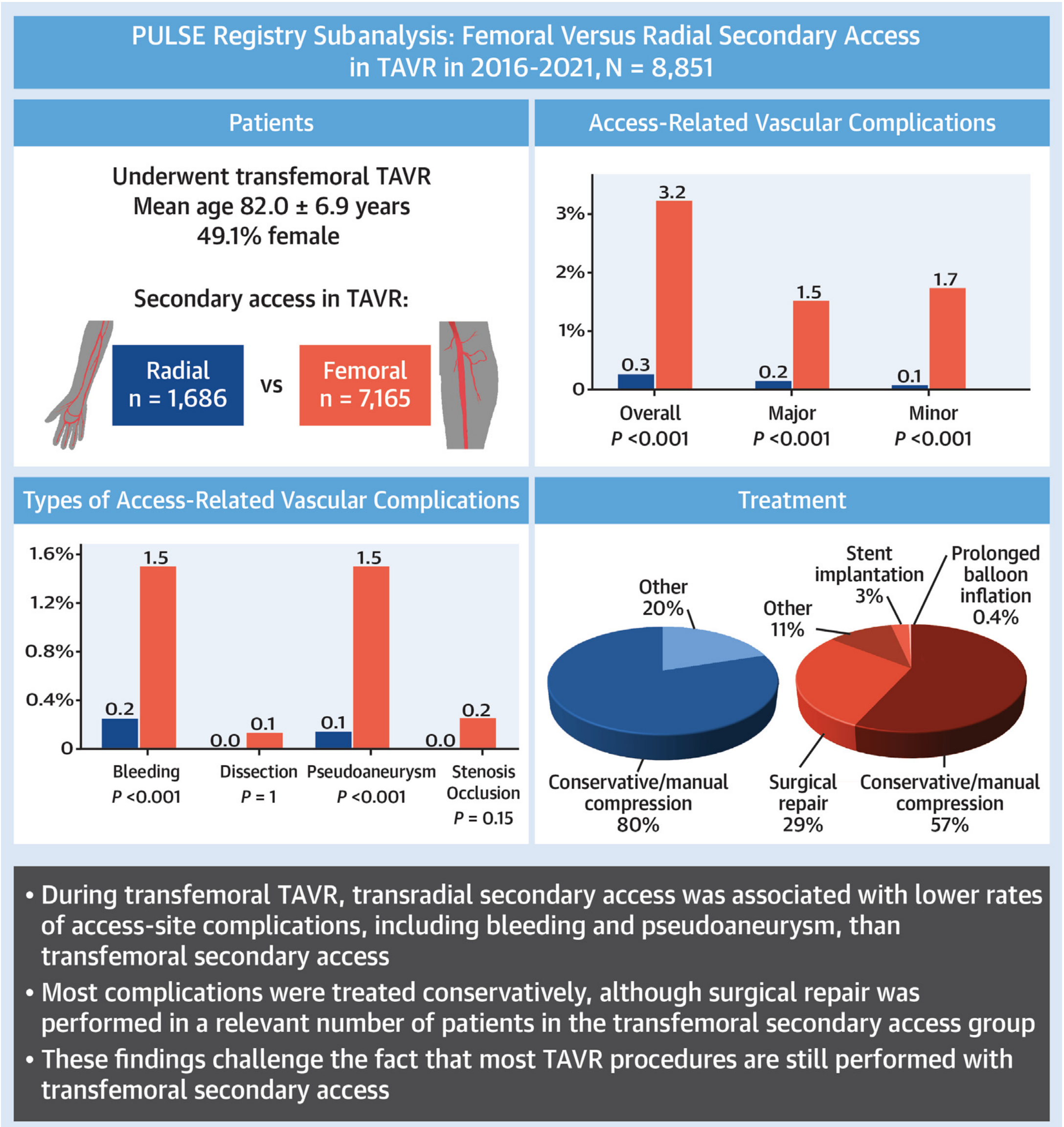
closure device were observed. Balloon-expandable THVs were more often used in TR-SA (61.2% [984/1,609] vs 36.0% [2,084/5,787] in TF-SA; $P < 0.001$). Heparin reversal with protamine was performed in 37.3% (614/1,648) of TR-SA patients and 89.4% (6,033/6,746) of TF-SA patients accordingly ($P < 0.001$). The amount of contrast agent and fluoroscopy time were higher in the TR-SA group, whereas the procedure time was shorter in the TR-SA group. Procedural characteristics after PS matching remained similar (Supplemental Table 3). Overall, an increase of TR-SA compared to TF-SA was observed in the unmatched cohort during the study period (Figure 2).

CLINICAL OUTCOMES. Vascular complications at the secondary access site occurred in 0.3% (5/1,686) of TR-SA patients and 3.2% (232/7,165) of TF-SA patients ($P < 0.001$). These were major in 0.2% (3/1,686) in the TR-SA group vs 1.5% (109/7,165; $P < 0.001$) in the TF-SA group and minor in 0.1% (2/1,686) in the TR-SA group vs 1.7% (123/7,165; $P < 0.001$) in the TF-SA group (Table 3, Central Illustration). In both groups, most of these complications were related to bleeding (0.2% [4/1,686] vs 1.5% [105/7,165]; $P < 0.001$) or pseudoaneurysms (0.1% [1/1,686] vs 1.5% [107/7,165]; $P < 0.001$). The majority in both groups were treated conservatively; however, surgical repair was performed in none of the secondary access vascular complications in the TR-SA group and in 0.09% (66/7,165) in the TF-SA group. Treatment of secondary access vascular complications classified as "other," which comprised thrombin injections for the treatment of pseudoaneurysms, was observed more frequently in the TF-SA group compared to the TR-SA group (0.1% [1/1,686] vs 0.3% [25/7,165], respectively; $P = 0.046$).

In contrast, vascular complication rates related to the primary large-bore TAVR access were similar (11.6% [196/1,686] vs 11.5% [825/7,165]; $P = 0.93$) in both groups. (For types and treatment of primary access vascular complications before and after PS matching, see Supplemental Tables 4 and 5). Type III or IV bleeding (2.5% [42/1,686] in TR-SA vs 4.7% [334/7,165] in TF-SA; $P < 0.001$) and severe acute kidney injury (1.2% (20/1686) in TR-SA vs 2.7% [192/7,165] in TF-SA; $P < 0.001$) were more frequent in TF-SA patients, possibly resulting in a longer length of stay in-hospital (6.0 days [Q1-Q3: 5.0-8.0 days] in TR-SA vs 7.0 days [Q1-Q3: 6.0-10.0 days] in TF-SA; $P < 0.001$) and higher all-cause mortality (2.6% [41/1,598] in TR-SA vs 6.6% [462/7,040] in TF-SA; $P < 0.001$). Although the permanent pacemaker implantation rate was higher in TR-SA (13.3% [225/1,686] vs 11.4% [814/7,165]; $P = 0.025$), access-related nonvascular complications, stroke, and myocardial infarction rates were similar in both groups.

After 1:1 PS matching, a significantly higher rate of secondary access-related vascular complications in TF-SA compared to TR-SA patients persisted (0.2% [1/512] vs 2.9% [15/512], respectively; $P = 0.001$; Table 4). This difference was driven by more minor vascular complications (0.2% [1/512] vs 2.0% [10/512]; $P = 0.011$) and a trend toward major vascular complications (0% [0/512] vs 1% [5/512] $P = 0.062$). Vascular complication rates related to the primary large-bore TAVR access, bleeding type III/IV, acute kidney injury, myocardial infarction, stroke, and permanent pacemaker implantation were similar between both groups; however, all-cause death remained lower in TR-SA vs TF-SA patients (1.2%

CENTRAL ILLUSTRATION Secondary Arterial Access During Transcatheter Aortic Valve Replacement



Grundmann D, et al. JACC Cardiovasc Interv. 2024;17(24):2923-2932.

Bar charts depict the relative frequency of absolute values of binary variable severity of vascular complications or the type of vascular complication. PULSE = Plug or sUture based vascuLar cloSurE after TAVR. Adapted from https://smart.servier.com/wp-content/uploads/2016/10/Systeme_arteriel_3.png.

[6/512] vs 3.6% (18/512), respectively; $P = 0.021$). Patients excluded from PS matching differed from the included patients regarding BMI, PAD, and estimated glomerular filtration rate, among other things (Supplemental Table 6).

DISCUSSION

In this study, VARC-3-adjudicated outcomes of different secondary access strategies during transfemoral TAVR were compared as part of the large real-

TABLE 4 30-Day Outcomes (After Propensity Score Matching)

	All (N = 1,024)	TR-SA (n = 512)	TF-SA (n = 512)	*P* Value
Access-related vascular complications (secondary access)				
All	16 (1.6)	1 (0.2)	15 (2.9)	0.001
Major	5 (0.5)	0 (0)	5 (1.0)	0.062
Minor	11 (1.1)	1 (0.2)	10 (2.0)	0.011
Access-related vascular complications (primary access)				
All	145 (14.2)	77 (15.0)	68 (13.3)	0.47
Major	56 (5.5)	29 (5.7)	27 (5.3)	0.89
Minor	89 (8.7)	48 (9.4)	41 (8.0)	0.51
Access-related nonvascular complication	2 (0.2)	0 (0)	2 (0.4)	0.50
Bleeding (type III/IV)	28 (3.1)	15 (3.4)	13 (2.8)	0.79
Stroke (disabling and nondisabling)	24 (2.3)	13 (2.5)	11 (2.1)	0.84
Severe acute kidney injury (AKIN III and AKIN IV)	8 (0.9)	5 (1.1)	3 (0.6)	0.50
Myocardial infarction	5 (0.5)	2 (0.4)	3 (0.6)	1.00
Permanent pacemaker implantation	142 (13.9)	75 (14.6)	67 (13.1)	0.53
All-cause death	24 (2.4)	6 (1.2)	18 (3.6)	0.021

Values are n (%). Binary variables were compared using the chi-square test or the Fisher test. Abbreviations as in Tables 1 and 3.

world multicenter PULSE registry. Our main findings were as follows: 1) TR-SA was associated with lower rates of vascular access site complications and severe bleeding compared to TF-SA; 2) vascular complications related to the secondary access alone were 10× higher in patients with TF-SA and required invasive treatment in a relevant number of patients; and 3) vascular complications at the primary large-bore access were similar in both groups.

Since the implementation of TAVR into clinical routine, numerous advancements have been introduced including improved procedure planning using contrast enhanced multidetector computed tomography, better patient selection as part of the heart team process, and routine use of local instead of general anesthesia. In this context, the transfemoral route has become the primary access for TAVR because of lower complication rates compared to alternative access routes.[14] In addition to the primary large-bore access for THV delivery, the secondary access has traditionally been facilitated by a femoral puncture, although alternative approaches (eg, radial) may be beneficial.[9] Our data showed that TR-SA was associated with significantly lower major, minor, and overall access-related complications compared to TF-SA in this large multicenter registry, which is in line with previous smaller studies.[3,4,15,16] Of note, almost one-third of these secondary access complications in the femoral group led to a surgical repair, emphasizing the clinical significance of these results that were exclusively linked to complications at the small 6-F femoral access. These outcomes were largely consistent with those achieved in the present matched population. Importantly, secondary access complications were responsible for more than one-fifth of all vascular complications, comprising a potentially large negative impact on postprocedural outcomes, especially in patients with advanced age, frailty, and comorbidities.

In case of access-related vascular complications at the primary large-bore access, crossover techniques from the contralateral TF-SA are often used for bailout endovascular treatment. Importantly, despite the absence of this straightforward crossover option in TR-SA patients, we did not observe more complications at the primary access in the TR-SA group. Furthermore, endovascular treatment from the radial access may also facilitate bailout maneuvers in case of vascular complications but may require additional devices and endovascular balloons or stents with extra-long shafts.[16] Furthermore, a bailout contra- or ipsilateral femoral access for complication management may be gained after achieving temporary hemostasis via the TR-SA. Also, despite the fact that no standard guidewire insertion was performed either from the radial or contralateral femoral access in this study, there were no more complications at the primary access. TF-SA was also associated with higher rates of severe bleeding because of increased vascular complications. Moreover, radial access was associated with shorter total length of in-hospital stay compared to femoral access in our study and other studies, likely because of increased patient mobility.[3,17]

Rates of TR-SA increased during the study period. Nevertheless, TF-SA was chosen over TR-SA in more than 80% of procedures and was predominantly used even in recent years. Based on our results, the radial approach should be established as the first choice for secondary access to minimize the risk for vascular or bleeding complications in these patients at risk.

STUDY LIMITATIONS. Despite the strengths of this large multicenter registry, several limitations should be considered. This was a retrospective analysis including different site-specific TAVR protocols to mirror clinical reality in a large sample. Despite well-balanced PS matching, several parameters remained different and may have influenced the results. The difference in mortality may be based on different risk profiles and possibly preference of TF-SA over TR-SA in cases with increased complexity rather than a direct link to vascular complications. However, results regarding vascular and bleeding complications that were related to the secondary access remain clear and consistent throughout the analysis. Because of the low event rate of the primary endpoint, valid regression analyses in subpopulations were not feasible. Furthermore, we focused on access-related complications and 30-day outcomes with a short-term follow-up to analyze the immediate periprocedural phase.

CONCLUSIONS

In patients treated with transfemoral TAVR, TR-SA was associated with lower rates of access site and bleeding complications compared to a (bi-)femoral strategy. In fact, vascular complications related to the secondary access alone were 10× higher in patients with TF-SA and were followed by invasive treatments in a relevant number of patients. These findings suggest TR-SA may be considered preferable compared to TF-SA and challenge the fact that most TAVR procedures are still performed with TF-SA.

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PERSPECTIVES

WHAT IS KNOWN? Access-related complications in TAVR, of which a relevant share can be linked to the secondary access, remain a concern. As radial access has become the primary choice for percutaneous coronary intervention because of low access-related complication rates, a radial approach may serve as a safer alternative to the traditional femoral strategy for the secondary access in TAVR. There is a paucity of large-scale data on the impact of secondary access strategies on clinical outcomes after TAVR.

WHAT IS NEW? In this large real-world multicenter registry, the transradial secondary access strategy was associated with 10× lower rates of access site as well as lower bleeding complications compared to a (bi-)femoral strategy. Vascular complications related to the transfemoral secondary access were followed by invasive treatments in a relevant number of patients.

WHAT IS NEXT? These results suggest transradial secondary access may be considered preferable compared to a transfemoral approach and challenge the fact that most TAVR procedures are still performed with a femoral secondary access. Additional strategies to reduce access-related vascular and bleeding complications in TAVR are needed. A randomized trial comparing both secondary access approaches could provide further conclusive data.

REFERENCES

1. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J*. 2022;43(7):561–632. https://doi.org/10.1093/eurheartj/ehab395

2. Carroll JD, Mack MJ, Vemulapalli S, et al. STS-ACC TVT registry of transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2020;21:2492–2516. https://doi.org/10.1016/j.jacc.2020.09.595

3. Junquera L, Urena M, Latib A, et al. Comparison of transfemoral versus transradial secondary access in transcatheter aortic valve replacement. *Circ Cardiovasc Interv*. 2020;13(3):e008609. https://doi.org/10.1161/CIRCINTERVENTIONS.119.008609

4. Allende R, Urena M, Cordoba JG, et al. Impact of the use of transradial versus transfemoral approach as secondary access in transcatheter aortic valve implantation procedures. *Am J Cardiol*. 2014;114(11):1729–1734. https://doi.org/10.1016/j.amjcard.2014.09.009

5. Généreux P, Webb JG, Svensson LG, et al. Vascular complications after transcatheter aortic valve replacement: insights from the PARTNER (placement of AoRTic TraNscathetER valve) trial. *J Am Coll Cardiol*. 2012;60(12):1043–1052. https://doi.org/10.1016/j.jacc.2012.07.003

6. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med*. 2019;380(18):1706–1715. https://doi.org/10.1056/nejmoa1816885

7. Reardon MJ, Van Mieghem NM, Popma JJ, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients - SURTAVI. *N Engl J Med*. 2017;376(14):1321–1331. https://doi.org/10.1056/NEJMoa1700456

8. Okuyama K, Jilaihawi H, Abramowitz Y, et al. The clinical impact of vascular complications as defined by VARC-1 vs. VARC-2 in patients following transcatheter aortic valve implantation. *EuroIntervention*. 2016;12(5):e636–e642. https://doi.org/10.4244/EIJV12I5A104

9. Jolly SS, Yusuf S, Cairns J, et al. Radial versus femoral access for coronary angiography and intervention in patients with acute coronary syndromes (RIVAL): a randomised, parallel group, multicentre trial. *Lancet*. 2011;377(9775):1409–1420. https://doi.org/10.1016/S0140-6736(11)60404-2

10. Généreux P, Piazza N, Alu MC, et al. Valve Academic Research Consortium 3: updated endpoint definitions for aortic valve clinical research. *Eur Heart J*. 2021;42(19):1825–1857. https://doi.org/10.1093/eurheartj/ehaa799

11. Blanke P, Weir-McCall JR, Achenbach S, et al. Computed tomography imaging in the context of transcatheter aortic valve implantation (TAVI)/transcatheter aortic valve replacement (TAVR): an expert consensus document of the Society of Cardiovascular Computed Tomography. *JACC Cardiovasc Imaging*. 2019;12(1):1–24. https://doi.org/10.1016/j.jcmg.2018.12.003

12. Eltchaninoff H, Kerkeni M, Zajarias A, et al. Aorto-iliac angiography as a screening tool in selecting patients for transfemoral aortic valve implantation with the Edwards SAPIEN bioprosthesis. *EuroIntervention*. 2009;5(4):438–442. https://doi.org/10.4244/EIJV5I4A69

13. Ho D, Imai K, King G, Stuart EA. MatchIt: nonparametric preprocessing for parametric causal inference. *J Stat Softw*. 2011;42:1–28. https://doi.org/10.18637/jss.v042.i08

14. Wendler O, Schymik G, Treede H, et al. SOURCE 3: 1-year outcomes post-transcatheter aortic valve implantation using the latest generation of the balloon-expandable transcatheter heart valve. *Eur Heart J*. 2017;38(36):2717–2726. https://doi.org/10.1093/eurheartj/ehx422

15. Ferrante G, Rao SV, Jüni P, et al. Radial versus femoral access for coronary interventions across the entire spectrum of patients with coronary artery disease: a meta-analysis of randomized trials. *JACC Cardiovasc Interv*. 2016;9(14):1419–1434. https://doi.org/10.1016/j.jcin.2016.04.014

16. Fernandez-Lopez L, Chevalier B, Lefèvre T, et al. Implementation of the transradial approach as an alternative vascular access for transcatheter aortic valve replacement guidance: experience from a high-volume center. *Catheter Cardiovasc Interv*. 2019;93(7):1367–1373. https://doi.org/10.1002/ccd.28024

17. Agostoni PL, Biondi-Zoccai GG, Luisa De Benedictis M, et al. Radial versus femoral approach for percutaneous coronary diagnostic and interventional procedures systematic overview and meta-analysis of randomized trials. *J Am Coll Cardiol*. 2004;44(2):349–356. https://doi.org/10.1016/j.jacc.2004.04.034

KEY WORDS access, femoral, radial, secondary, TAVR

APPENDIX For a video of the interactive central illustration and supplemental tables, please see the online version of this paper.