Transcatheter Aortic Valve Implantation in Patients Who Cannot Undergo Transfemoral Access

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Abstract

Introduction Though transfemoral (TF) access has emerged as a gold standard access for patients with aortic stenosis who undergo transcatheter aortic valve implantation (TAVI), there has been no study that has characterized patients who cannot undergo TF access in detail. We aim to evaluate the contraindications for TF access, their incidence, classify them, and provide the outcomes of patients who failed to be TF candidates.

Methods From 925 patients who underwent TAVI between February 2014 and May 2020 at our heart center, 130 patients failed to be TF candidates and underwent transapical-transcatheter aortic valve implantation (TA-TAVI). In this study, we included all those patients who failed to be TF candidates and underwent TA-TAVI using the third-generation balloon expandable valve (Edwards SAPIEN 3 valve [S3]) (116 patients; STS score 6.07 ± 4.4; age 79.4 ± 7).

Results The incidence of patients unsuitable for TF access at our heart center was 14%. We classified this TAVI population into absolute contraindication for TF access $n = 84$ (72.5%) and increased interventional risk for TF access $n = 32$ (27.5%). After TA-TAVI of this specific population using S3, the in-hospital mortality and stroke were 1.7 and 1.7%, respectively. The vascular injury rate was 1.7%. We registered no paravalvular leakage ≥ 2. The pacemaker rate was 7.4%. The mean transvalvular pressure gradient was 8.7 mm Hg.

Conclusion The incidence of patients who cannot undergo TF access or who are at high interventional risk is considerably high. TA-TAVI, supported with sufficient interventional experience and appropriate valve system, represents an excellent alternative for patients with distinct vasculopathy.

Keywords
- heart center
- transapical
- TF-TAVI
- COPD
- peripheral vascular disease
- aorta

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Introduction

The excellent outcomes of patients with aortic stenosis who undergo transfemoral-transcatheter aortic valve implantation (TF-TAVI) in recent years, supported by mature interventional skills in compatibility with technological advances and design factors, have revolutionized the ideology of the treatment of aortic stenosis. Accordingly, TF-TAVI has emerged as a gold standard approach for patients who undergo transcatheter therapies. In recent years, this development has helped concentrate the focus of research mainly on the TF route. Despite these advances in the TF-TAVI, there are TAVI candidates with clinical characteristics who cannot undergo TF-TAVI or who are at high interventional risk for TF-TAVI. Recent studies reported rates of this specific population as ranging from 10 to 15%.[1–3] However, no study has been conducted that has characterized patients who cannot undergo TF-TAVI in detail. We aimed to evaluate the contraindications for TF-TAVI, their incidence, classify them, and provide outcomes of patients who failed to be TF candidates. Additionally, we aimed to evaluate the clinical and procedural strengths and weaknesses between the TF and TA approaches using contemporary valve systems after continuous use of both approaches.

Methods

This single-center retrospective study was conducted to evaluate the incidence, the patient and procedural characteristics as well as in-hospital outcomes of patients who failed to be TF candidates and underwent transapical (TA)-TAVI using the third generation of balloon-expandable SAPIEN 3 valve; Edwards Lifesciences, Irvine, California (S3) at our institution. Furthermore, we aimed to characterize this specific population classifying into patients with absolute contraindication for TF-TAVI and patients with increased interventional risk for TF-TAVI. Between February 2014 and May 2020, 925 patients underwent TAVI at our heart center of whom 130 patients failed in the heart team to be TF candidates, as the first preferred approach at our center and underwent TA-TAVI. We included in this study all patients who failed to be TF candidates and underwent TA-TAVI using S3 valve (116 patients). For comparison, we included in this study all consecutive patients who underwent TF-TAVI using the S3 valve during the same period (between February 2014 and May 2020). In addition, we adjusted for New York Heart Association class (NYHA), left ventricular ejection fraction (LVEF) and chronic obstructive pulmonary disease (COPD). In our institution we maintained a stringent TA protocol in the S3 era aimed at identifying patients who may still benefit from an aggressive strategy aimed at reducing vascular complication. The study population comprised of all 265 consecutive elderly patients with symptomatic severe aortic stenosis. The specific vascular diagnosis of this specific cohort was determined based on clinical and computed tomographic findings. Additionally, a subanalysis of the TA-TAVI cohort was performed comparing patients exhibiting COPD and/ or poor LVEF (LVEF $<30\%$) (34 patients) with those who did not exhibit COPD or had poor LVEF (non-LVEF $<30\%$, non-COPD) (82 patients).

We employed the Valve Academic Research Consortium-2 criteria to define all clinical end points.[4] All patients gave informed consent for data collection. The Ethics Committee approval has been obtained (Reg. No. 18–6339).

Distributions of quantitative variables are described as means $\pm$ standard deviation). Qualitative variables are summarized by count and percentage. Comparisons of the data were assessed using Fisher's exact test for categorical variables, and the Mann–Whitney U test was used for continuous variables. All statistical tests were two-sided, and p-values of 0.05 or less were considered statistically significant. Data were managed with the SPSS statistical package, version SPSS 23.0.0.2.

Operative Technique in Patients Who Cannot Undergo TF Access

Patients were carefully screened with regard not only to the native aortic valve but also regarding the individual femoral, iliac, and aortic pathologies such as calcification patterns, calcification burden, morphologic changes of the vessels, focusing on the pathologic changed femoral and iliac segments as well as aortic segments, considering the presence and position of the previous surgical or endovascular implanted grafts or stents. All cases underwent TA-TAVI under general anesthesia. We performed the procedure as described before.[5] However, we modified the procedure if necessary, to ensure "aorta and femoral/iliac no touch technique" as appropriate, depending on vessel pathology and affected segments of the vessels. In cases with pathologies of the descending aorta or distinct pathologies of the femoral or iliac arteries we disclaimed insertion of a femoral artery wire and 6-French sheath. We provided the "Safety Net" and the line (pigtail) for angiographic visualization and for "landmarking" of the aortic valve through the axillar artery. In some cases, with critical alteration of the aortic arch/ascending aorta or subclavian artery we inserted the pigtail into the left ventricle through the ventricle wall and introduced into the ascending aorta. Before completing the valve expansion, we put it back into the left ventricle. We positioned a stiff guidewire across the aortic arch and into the descending aorta with the help of a right Judkins catheter. We did not use the balloon predilatation as a mandatory step.

Results

Patient Characteristics

►**Table 1** shows the preoperative data of the patient population. Among all 265 patients, 116 underwent TA-TAVI and 149 underwent TF-TAVI. Among the groups, the TA-TAVI group exhibited a significantly higher level of surgical risk (Society of Thoracic Surgery-Predicted Risk of Mortality score [STS score] and EuroScore II), whereas the TF-TAVI group had a significantly older patient population. Notably, the TA-TAVI group exhibited a significantly higher rate of severe peripheral artery disease (PAD) than did the TF-TAVI group (85.3 vs. 7.4%, respectively; $p < 0.001$). The COPD rate

Table 1 Baseline characteristics

	TA-TAVI $N=116$; $n=(\%)$	TF-TAVI $N=149$; $n=(\%)$	*p*-Value
Age (years)	79.4 ± 7	82.5 ± 4.8	$p=0.001$
Male sex	77 (66.3)	67 (45)	$p=0.001$
Body mass index (kg/m^2)	27 ± 4.9	28.5 ± 5	$p=0.031$
STS score (%)	6.07 ± 4.4	3.8 ± 2.1	$p<0.001$
EuroScore II (%)	11.03 ± 9.4	6.1 ± 4.7	$p=0.001$
New York Heart Association III/IV	108 (93.1)	139 (93.3)	$p=0.891$
Arterial hypertension	96 (82.7)	116 (77.9)	$p=0.630$
Severe pulmonary hypertension	26 (22.4)	23 (15.4)	$p=0.126$
Diabetes mellitus	42 (36.2)	47 (31.5)	$p=0.578$
Coronary artery disease	88 (75.8)	81 (54.4)	$p=0.002$
PTCA/PCI	47 (40.5)	56 (37.8)	$p=0.688$
Left ventricular ejection fraction (%)	50 ± 11.5	54.6 ± 9.7	$p<0.001$
Severe peripheral artery disease	99 (85.3)	11 (7.4)	$p<0.001$
Carotid artery stenosis ≥75%	15 (12.9)	7 (4.7)	$p=0.027$
Previous stroke	22 (18.9)	19 (12.8)	$p=0.147$
Chronic kidney failure	53 (45.6)	57 (38.3)	$p=0.285$
Preoperative creatinine (mg/dL)	1.2 ± 0.4	1.1 ± 0.4	$p=0.009$
eGFR (mL/min)	59.2 ± 20	58 ± 19.4	$p=0.967$
Chronic obstructive pulmonary disease	30 (25.8)	17 (11.4)	$p=0.005$
Atrial fibrillation	51 (43.9)	64 (43)	$p=0.690$
Previous cardiac operation	37 (31.8)	19 (12.8)	$p<0.001$
Mitral regurgitation ≥2	27 (23.2)	30 (20.4)	$p=0.747$
Permanent pacemaker	8 (6.9)	21 (14.2)	$p=0.092$

Abbreviations: eGFR, estimated glomerular filtration rate; PTCA/PCI, percutaneous transluminal coronary angioplasty/intervention; STS, Society of Thoracic Surgery-Predicted Risk of Mortality score; TA-TAVI, transapical-transcatheter aortic valve implantation; TF-TAVI, transfemoral-transcatheter aortic valve implantation.

was significantly higher in the TA-TAVI group than in the TF-TAVI group ($p=0.005$). The LVEF was significantly lower in the TA-TAVI group than in the TF-TAVI group ($p<0.001$).

Procedural Characteristics

In the TA-TAVI group, all valves were implanted successfully without embolization, aortic dissection, annulus rupture, aortic perforation, or aortic injury. There was no intraprocedural death. Only two patients experienced major vascular injury (1.7%). Both patients were high surgical risk patients with severe PAD and concomitant porcelain aorta. Vascular injury occurred during the attempt to provide the venous "Safety Net" through the femoral vein. In both cases vascular surgery was necessary due to relevant bleeding with retroperitoneal hematoma and relevant spurious aneurysm of the femoral artery. No conversion to open heart surgery or valve-in-valve procedure was necessary. A balloon predilatation (balloon aortic valvuloplasty or BAV) was performed in 20.6% of the patients and a post dilation in 11.2% of the patients. In the TF-TAVI group, we registered one patient with valve embolization into the descending aorta (the patient survived after subsequently Re-TAVI) and one patient with annulus rupture (patient deceased despite rescue surgical aortic valve replacement attempt). Eleven patients experienced major vascular injury (7.6%) with subsequent vascular surgery or endovascular intervention. The common complications were: artery perforation with retroperitoneal bleeding, local artery dissection, and significant artery narrowing. A BAV was performed in 62.6% of the patients and a post dilation in 10.6% of the patients. ►**Table 2** shows detailed procedural data.

In-hospital Clinical Outcomes

The in-hospital all-cause mortality and all-stroke in the both groups was low: 1.7% in TA-TAVI and 2.7% in TF-TAVI; $p=0.699$, respectively. The acute kidney injury network 2/3 (AKIN 2/3) was considerably higher after TA-TAVI than after TF-TAVI (7.7% vs. 2.7%; $p=0.074$). The new permanent pacemaker implantation (PPI) rate was 7.4% in TA-TAVI and 15.6% in TF-TAVI, $p=0.072$ (►**Table 3**).

Table 2 Procedural characteristics

	TA-TAVI $N = 116$; $n = (\%)$	TF-TAVI $N = 149$; $n = (\%)$	*p*-Value
Baseline ΔP max (mm Hg)	65 ± 18.7	71.8 ± 26.2	$p = 0.136$
Baseline ΔP mean (mm Hg)	38.9 ± 12	44.9 ± 16.8	$p = 0.061$
Baseline AOA (cm^2)	0.7 ± 0.1	0.7 ± 0.1	$p = 0.713$
Procedural time (min)	99 ± 23.4	77.6 ± 27.5	$p < 0.001$
Fluoroscopy time (min)	7.2 ± 2.8	16.3 ± 6.8	$p < 0.001$
Radiation ($cGycm^2$)	$2{,}109 \pm 1{,}699$	$5{,}202 \pm 4{,}589$	$p < 0.001$
Contrast agent (mL)	57.7 ± 27.8	163.4 ± 51.2	$p < 0.001$
Edwards SAPIEN 3 valve	116 (100)	149 (100)	$p = 1$
Prosthesis diameter (mm)	25.4 ± 2	25.3 ± 2	$p = 0.553$
20 mm	1 (0.8)	0 (0)	/
23 mm	36 (31)	55 (36.9)	$p = 0.412$
26 mm	60 (51.7)	72 (48.3)	$p = 0.600$
29 mm	19 (16.3)	22 (14.8)	$p = 0.856$
Predilatation	24 (20.6)	77 (62.6)	$p < 0.001$
Postdilation	13 (11.2)	13 (10.6)	$p = 0.828$
Conversion/CPB	1 (0.8)	3 (2)	$p = 1$
General anesthesia	116 (100)	0 (0)	/
Procedural death	0 (0)	1 (0.6)	/

Abbreviations: AOA, aortic orifice area; CPB, cardiopulmonary bypass; TA-TAVI, transapical-transcatheter aortic valve implantation; TF-TAVI, transfemoral-transcatheter aortic valve implantation.

Table 3 In-hospital outcomes

	TA-TAVI $N = 116$; $n = (\%)$	TF-TAVI $N = 149$; $n = (\%)$	*p*-Value
In-hospital			
Hospital stay (days)	10.2 ± 5.7	7.8 ± 2.2	$p < 0.001$
All-cause mortality	2 (1.7)	4 (2.7)	$p = 0.699$
All stroke	2 (1.7)	4 (2.7)	$p = 0.699$
Myocardial infarction	1 (0.8)	1 (0.6)	$p = 1$
Acute kidney injury network 2/3	9 (7.7)	4 (2.7)	$p = 0.074$
Re-thoracotomy for bleeding	3 (2.5)	2 (1.3)	$p = 0.402$
Major vascular complications	2 (1.7)	11 (7.6)	$p = 0.043$
Re BAV/TAVI/SAVR	0 (0)	3 (2)	$p = 0.259$
Paravalvular leakage ≥ 2	0 (0)	1 (0.6)	/
$P_{mean} > 20$ mm Hg	0 (0)	1 (0.6)	/
New permanent pacemaker	8 (7.4)	21 (15.6)	$p = 0.072$
Endocarditis	0 (0)	0 (0)	/
Valve thrombosis	0 (0)	0 (0)	/
Tracheotomy	1 (0.8)	0 (0)	/
Wound infection	2 (1.7)	0 (0)	/
Re-intubation	6 (5.1)	1 (0.6)	$p = 0.04$
Delirium	21 (18.1)	12 (8.1)	$p = 0.002$
Left bundle branch block	32 (31.6)	36 (28.3)	$p = 0.662$

Abbreviations: BAV, balloon aortic valvuloplasty; SAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation; TA-TAVI, transapical-transcatheter aortic valve implantation; TF-TAVI, transfemoral-transcatheter aortic valve implantation.

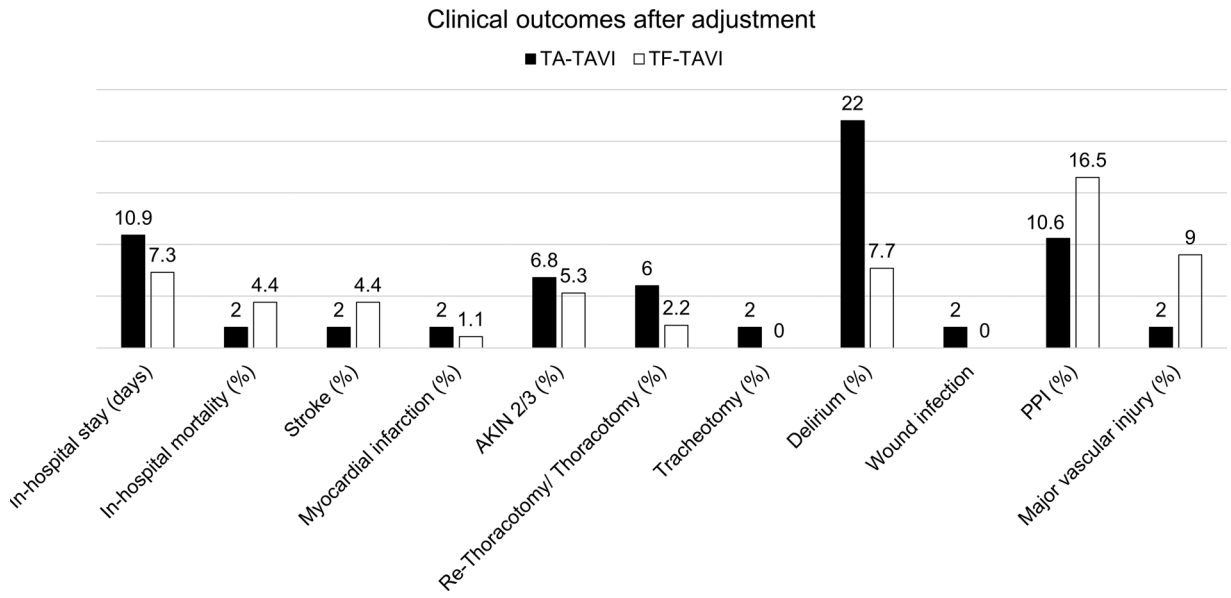

Fig. 1 Clinical outcomes after adjustment. AKIN, acute kidney injury network; PPI, permanent pacemaker implantation; TA-TAVI, transapical-transcatheter aortic valve implantation; TF-TAVI, transfemoral-transcatheter aortic valve implantation.

Hemodynamics

The baseline echocardiographic data in this study population confirmed severe aortic stenosis (►**Table 2**). The mean gradients at discharge were 8.7 ± 4.3 mm Hg in TA-TAVI and 10.8 ± 4 mm Hg in TF-TAVI; $p = 0.002$. At discharge, we registered no severe paravalvular leakage (PVL) in both the groups. One patient exhibited moderate PVL. Trace to mild PVL was at 27.8% in TA-TAVI group and 38.3% in TF-TAVI group; $p = 0.169$.

Strengths and Weaknesses of TF and TA Approaches after Adjustment

After adjustment for NYHA, LVEF, and COPD, 91 patients who underwent TF-TAVI and 50 patients who underwent TA-TAVI were compared. Even after adjustment, in TA-TAVI cohort the STS score remained significantly higher compared with TF-TAVI (5.3 ± 3.2 vs. 3.6 ± 1.8, $p = 0.002$). Similarly, the PAD rate remained significantly higher in TA-TAVI cohort (98 vs. 5.5%, $p < 0.001$). Clinical and procedural outcomes after adjustment are presented in ►**Figs. 1** and **2**, respectively. The differences of in-hospital stay, delirium, procedural time, fluoroscopy time, radiation, contrast agent, and mean pressure gradient were statistically significant.

Outcomes of Patients with COPD and/or LVEF <30% in the TA-TAVI Cohort

Patients with COPD and/or LVEF <30% exhibited significant higher STS score than non-LVEF <30%, non-COPD-group; ($p = 0.009$). Major vascular injury and PPI were higher in patients with COPD and/ or LVEF <30%. However, these differences did not reach the statistical significance; $p = 0.160$ and $p = 0.603$, respectively. All other outcomes were similar in both groups. Details are presented in ►**Fig. 3**.

Transfemoral Access-Related Characteristics of Patients

Based on the TAVI expertise of our heart team, we classified this non-TF cohort in patients with absolute contraindications for TF access (84 patients [72.5%]) and patients with increased risk for TF access (32 patients [27.5%]). The most often clinical/pathoanatomical occurrence was the patient group with severe calcification of both femoral and iliac arteries on both sides with or without previous intervention and with or without clinical manifestation (50 patients [43.1%]). In ►**Table 4**, we provide detailed TF access-related characteristics of the cohort. Thirty-two patients (27.5%) were registered with combined TF access-related characteristics (two or more from the diagnosis mentioned in ►**Table 4**. In ►**Table 4**, we provide further details of the cohort, as well.

Incidence of Patients Who Are Absolutely Contraindicated for TF-TAVI

Out of 925 patients on which TAVI was performed at our heart center (February 2014–May 2020), 130 failed to be TF candidates. In this study, we included only patients who received S3 valve (116 patients). Out of 14 excluded patients, no one had absolute contraindication for TF-TAVI. Out of 116 patients included in the study, 84 patients were classified as having absolute contraindication for TF-TAVI. The overall incidence of this patient collective at our center was 9.1%.

Discussion

Meanwhile, the TF first strategy for patients with aortic stenosis who undergo transcatheter therapy has been established for a long time, and the most recent efforts are to apply this minimally invasive method in as many patients with aortic stenosis as possible. While in the PARTNER 2A trial, in 23.7% of the patients, TA-TAVI was necessary,[6] or, in a national registry, a non-TF approach was required in 17.2% of patients,[7] in the present time—because of numerous technological advances and design factors in compatibility with matured interventional skills and experience gained in

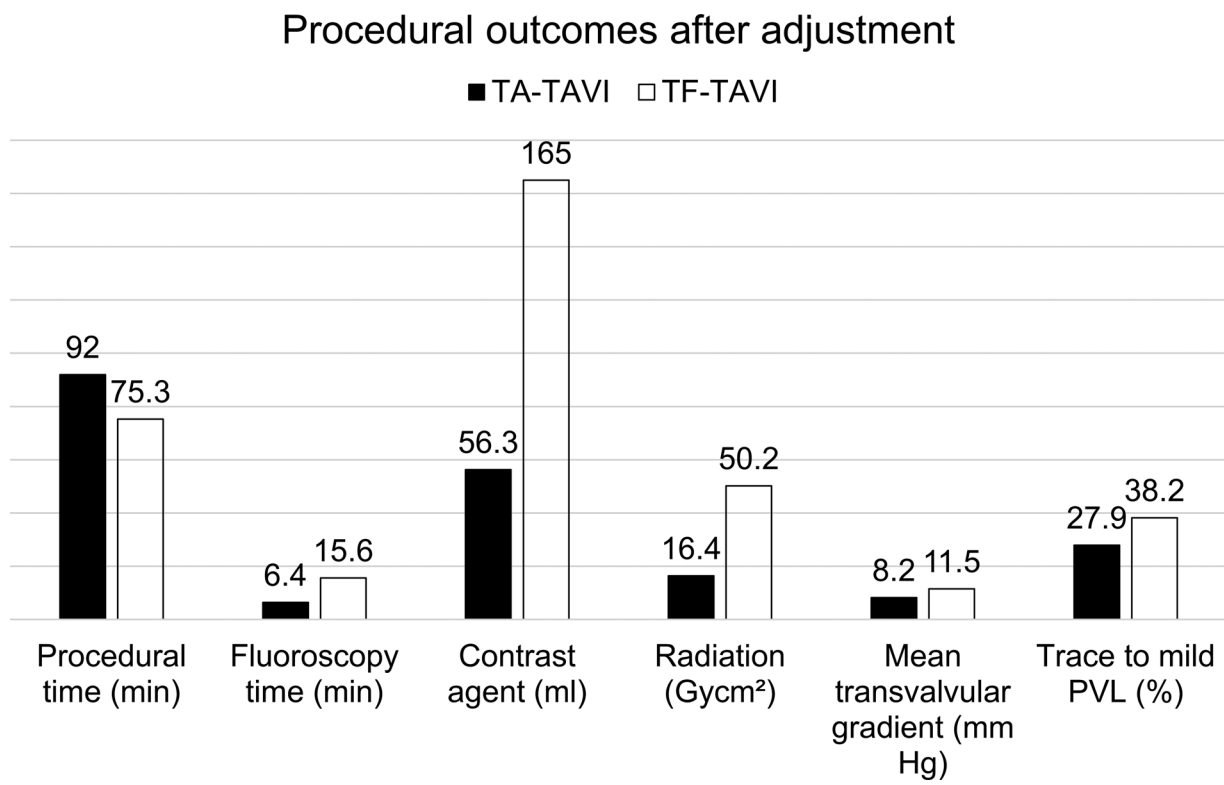

Fig. 2 Procedural outcomes after adjustment. PVL, paravalvular leakage; TA-TAVI, transapical-transcatheter aortic valve implantation; TF-TAVI, transfemoral-transcatheter aortic valve implantation.

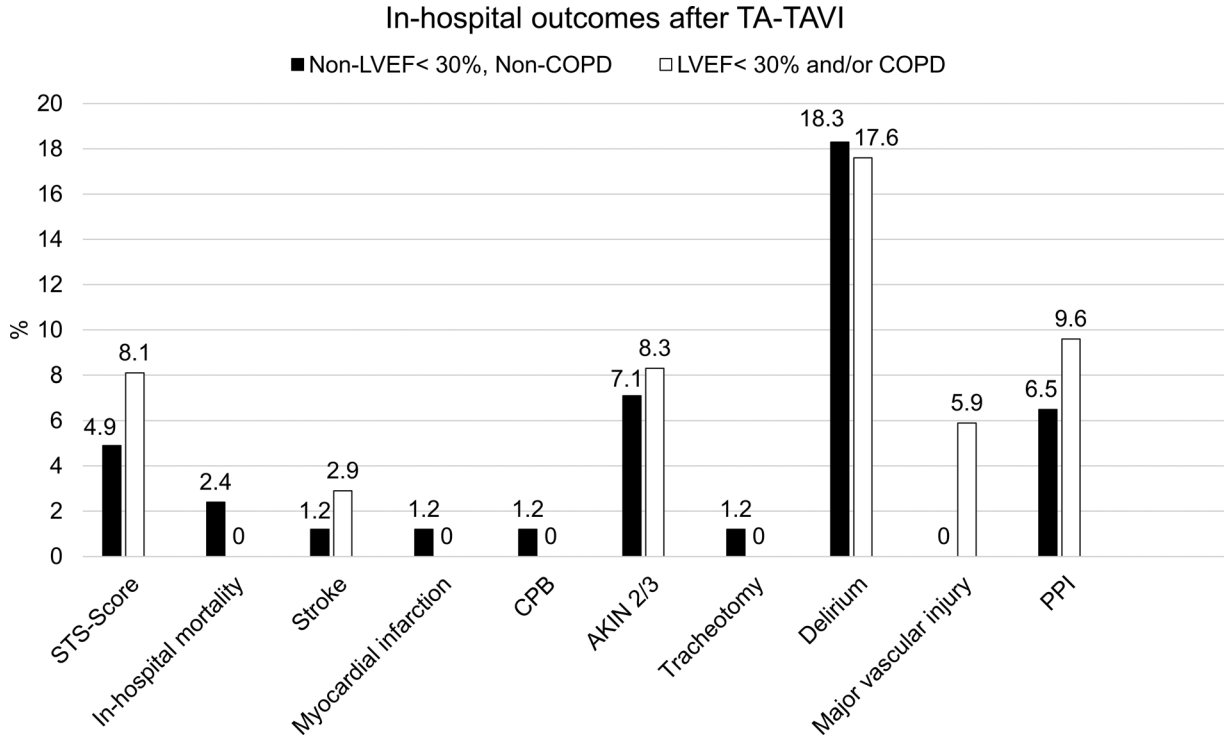

Fig. 3 In-hospital outcomes after TA-TAVI in patients with COPD and LVEF <30%. AKIN, acute kidney injury network; COPD, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; LVEF, left ventricular ejection fraction; PPI, permanent pacemaker implantation; STS, Society of Thoracic Surgery-Predicted Risk of Mortality score; TA-TAVI, transapical-transcatheter aortic valve implantation.

Table 4 Detailed vascular characteristics of patients who cannot undergo TF-TAVI

	All *n* (%) *n* = 116 (100%)	Patients with absolute contraindications for TF-TAVI *n* (%) *n* = 84 (100%)	Patients with increased interventional risk for TF-TAVI *n* (%) *n* = 32 (100%)
Lerische syndrome	3 (2.5)	3 (3.6)	/
Severe calcified of both femoral and iliac arteries on both sides, ± previous intervention with or without clinical manifestation	50 (43.1)	50 (59.5)	/
Small femoral arteries (<5 mm)	9 (7.7)	9 (10.7)	/
Aortic or iliac thrombus	4 (3.4)	4 (4.7)	/
Unsuccessful TF-TAVI attempt	5 (4.3)	5 (5.9)	/
Iliac diameter reduction on both sides <5 mm	5 (4.3)	5 (5.9)	/
Descending aortic aneurysm >55 mm	5 (4.3)	5 (5.9)	/
Multiple aortic ulcers	1 (0.8)	1 (1.2)	/
Type B aortic dissection	2 (1.7)	2 (2.4)	/
Previous aortic intervention	4 (3.4)	/	4 (12.5)
Severe calcified femoral and/or iliac arteries on one side, ± previous intervention with or without clinical manifestation	14 (12)	/	14 (43.7)
Aortic, iliac, or femoral kinking	3 (2.5)	/	3 (9.4)
Descending aortic aneurysm ≤55 mm	1 (0.8)	/	1 (3.1)
Porcelain aorta	3 (2.5)	/	3 (9.4)
One side femoral or iliac aneurysm, local dissection or inguinal hematoma after heart catheterization	4 (3.4)	/	4 (12.5)
Severe bilateral lower limb PAD	2 (1.7)	/	2 (6.2)
Distinct limb lymphedema	1 (0.8)	/	1 (3.1)
Further vascular characteristics of the entire cohort			
PAD stadium IV Fontaine	12 (10.3)		
Femoropopliteal or Iliofemoral bypass	14 (12)		
Aortofemoral bypass	10 (8.6)		
PTA or stenting of iliac or femoral arteries	36 (31)		
Iliac or femoral endarterectomy and patch plasty	14 (12)		
Patients with two different femoral or iliac interventions	11 (9.5)		
Patients with ≥3 different femoral or iliac interventions	12 (10.3)		

Abbreviations: PAD, peripheral artery disease; PTA, percutaneous transluminal angioplasty; TF-TAVI, transfemoral-transcatheter aortic valve implantation.

the "TF field"—speculation is increasingly arising to forecast that up to 95% or higher portion of patients will be eligible for the TF approach. But is there any limit? Furthermore, what is the role of alternative TAVI approaches that are utilized marginally at the present time, such as the TA approach? The key findings of our study are:

- The incidence of patients who are absolutely contraindicated for TF-TAVI is considerably high.
- TA-TAVI, supported with sufficient interventional experience and appropriate valve system, represents an excellent alternative for patients with distinct vasculopathy.
- Utilizing TA-TAVI using S3 in patients with distinct vasculopathy, low PPI, and PVL rates can be achieved.
- After continuous performance of TA-TAVI using contemporary valve systems in patients who cannot undergo TF-TAVI, comparable satisfactory outcomes to TF-TAVI can be achieved.

The actual incidence of patients who are contraindicated for TF-TAVI is unknown. Among others, this is because of continuous improvement of delivery devices and valve systems as well as the experience gained, which have led interventionalists to be engaged with TAVI cases who are

at high interventional risk. So, for instance, while in the PARTNER trial, different aortic pathologies were exclusion criteria,[8] very recently Patsalis et al proved the feasibility of TF-TAVI in patients with previous endovascular aortic repair or descending aortic aneurysms.[9] Furthermore, iliofemoral kinking pathologies without calcification are increasingly the domain of TF-TAVI, using different stiff wire strategies. All these patient characteristics, including—among others—severe PAD, were used in the literature with general jargon, using terms such as: unfavorable, not suitable for TF-TAVI, or hostile iliofemoral arteries.[2,10,11] On the basis of our TAVI expertise, with our experience of more than 900 TAVI implants, we divided patients who are unfavorable for TF-TAVI into two groups: patients with absolute contraindications for TF access and patients with increased interventional risk for TF access.

Interestingly, as not every PAD is contraindicated for TF approach, the severity of PAD—being the leading reason for TF contraindication—has been not specified, graduated, or described in the studies concerning TAVI with alternative approaches.[10–13] The patients in our cohort represent mainly high-to end-stadium PAD (►**Table 4**) with extended vessel pathologies, comprising not only the iliac and femoral segments but also coronary arteries (75% of the patients), carotid arteries (13% of the patients), and the aorta itself (in the form of porcelain aorta, previous aortic interventions, and descending aneurysms), resulting in high surgical risk patients, thus also making the performance of other transvascular, non-TF approaches not so easy.

The S3 valve has been developed to potentially improve implantation and reduce typical TAVI complications.[14] After releasing S3 valve, the trend of TA utility was dramatically arrested. However, the role of TA-TAVI, particularly in patients with PAD, also continued in the S3 era, improving the outcomes and reducing vascular injuries.[15] In general, we have used the TA-approach liberally for more than a decade, and, in the last 2 years (2019–2020), only if the TF-TAVI is contraindicated. Thanks to our long experience, we are more versed in and familiar with the TA approach, so we continue to use this approach in the current time as well. The learning curve for TA-TAVI has been well highlighted.[16] The early outcomes of our study are best reported for TA-TAVI. We achieved 100% device success with very low in-hospital adverse events and low PPI and PVL rates as well.

Transapical versus Nontransfemoral Transvascular Options

As it is well known, the TA option has traditionally significant higher proportion of PAD when compared with TF option.

Even as the research on alternative transvascular TAVI approaches (transsubclavian [Tsc], transcarotid [Tc], transaortic, transcaval) is going on, there has been no study that necessarily reflected patients and patient characteristics that are absolutely contraindicated for the TF approach. First, the incidence of PAD in most of these published studies is relatively low: 56.6,[10] 67,[11] 50.1,[12] 23.3, 36.4,[17] and 38%.[18] Second, the severity of PAD is not specified.

On the first line, alternative approaches should be feasible in patients with distinct vasculopathy, and, at the same time, should protect for vascular injuries. All the transvascular approaches require some predefined vascular preconditions, such as predefined minimal vascular diameter for Tsc and Tc approaches[2,10] as well as stenotic free of the approach-related vessels.[19] As we can see from our study, patients with severe PAD are very likely to have attendant vasculopathies beyond femoral and iliac arteries. It is obvious that not all candidates from this group of patients may undergo alternative transvascular approaches.

Vascular injuries are one of the hot topics in the TAVI-World. Indeed, it has been proved that vascular injury appears as an independent predictor of mortality among TAVI patients.[20] Vascular injuries among patients with alternative transvascular approaches have not been deeply discussed. Recent studies have reported considerably high rates of vascular injuries (between 4.8 and 6.9%).[21] We report a very low vascular injury rate of 1.7% after TA-TAVI.

Studies that directly compare TA with alternative transvascular approaches are very scarce. A study published very recently compared the transthoracic approaches with the alternative nonfemoral transvascular approaches, and concluded similar early and midterm mortality and major perioperative complications.[18] Further studies reported considerably high early mortality (4.3 and 5.2%) after utilizing Tsc-TAVI and Tc-TAVI, even though the latest generations of valve systems such as SAPIEN 3 and SAPIEN 3 *Ultra* were used.[13] In 2019, France Registry reported 4% procedural mortality after nonfemoral, transvascular TAVI.[12] Folliguet et al reported 6.25% 30-day mortality after Tc-TAVI.[10] The Society of Thoracic Surgeons/American College of Cardiology TVT (transcatheter valve therapy) Registry registered a 30-day mortality rate of 5.3% in patients undergoing transaxillary TAVI with the SAPIEN 3 prosthesis.[11] After the worse outcomes of TA-TAVI in the initial transcatheter era, performed mainly in high- to extremely high-risk populations, the utility and the research on TA approach were almost completely locked down. We could show that with longer experience and appropriate valve device, excellent early outcomes with an in-hospital mortality of 1.7% can be reached. Another major issue concerning transvascular non-TF approaches is the perioperative stroke.

The Society of Thoracic Surgeons/American College of Cardiology TVT (transcatheter valve therapy) Registry registered a 30-day stroke rate of 6.3% in patients undergoing transaxillary TAVI with the SAPIEN 3 prosthesis.[11] France Registry reported a stroke rate of 3.35% after nonfemoral, transvascular TAVI.[12] Very recently, Kirker et al reported a very high stroke rate of 7.4% after utilizing Tsc-TAVI, using the last generations of valve systems such as SAPIEN 3 and SAPIEN 3 *Ultra*.[13] Moreover, Folliguet et al reported 5.5% 30-day stroke after Tc-TAVI.[10] TA-TAVI has been shown as a most protective method regarding the stroke in distinct vasculopathies compared with the vascular approach.[22] In

our study, we registered an in-hospital all-stroke rate of 1.7%.

PVL and PPI outcomes after TAVI are substantially relevant outcomes. It has already been proved that these attributes significantly influence the outcomes at mid-term. PVL and PPI have been shown to be independent mortality predictors after TAVI.[23,24] It is remarkable that in the very recent published studies of the Society of Thoracic Surgeons/American College of Cardiology TVT (transcatheter valve therapy) Registry[11] and FRANCE Registry[12] regarding nonfemoral, transvascular approaches with mainly the last generations of valve systems, nothing about the PVL outcomes has been reported. Amazingly, Kirker et al reported no PVL data after utilizing Tsc- and Tc-TAVI using the last generations of valve systems, such as SAPIEN 3 and SAPIEN 3 *Ultra*.[13] On the other hand, Folliguet et al reported 18.6% moderate to severe PVL after Tc-TAVI.[10] Furthermore, Beve and Auffret could show 5% moderate to severe PVL after nonfemoral, transarterial TAVI and 1% moderate to severe PVL after transthoracic TAVI, and also significantly higher device success in the transthoracic group.[18] The advantage of TA-TAVI in easier positioning of the valve over other transvascular TAVI methods is well known.[2,19] We registered no, moderate to severe PVL, and quite low mild PVL in our study. The valve positioning-related advantage in the TA-TAVI may also explain the differences in the PPI rates between TA-TAVI and transvascular TAVI. Hence, Beve and Auffret concluded significantly higher PPI rates after nonfemoral, transarterial TAVI (17%) compared with transthoracic group (4%).[18] In the recent relevant studies that reported PPI after nonfemoral, transarterial TAVI using SAPIEN 3 and SAPIEN 3 *Ultra*,[11,13] we see rates that are considerably higher (12, 11, 9%) than contemporary PPI rates, using SAPIEN 3, such as in PARTNER 3 trial (6.6% after TF-TAVI)[25] and in our study (7.4%) as well.

The abovementioned studies regarding outcomes of patients undergoing diverse non-TF TAVI procedures, inclusive our study, mainly report short-term outcomes. The PPI and PVL outcomes in these circumstances are of great relevance because they are not only a surrogate short-term marker but also a window to the eventual prediction of long-term outcomes. Therefore, these outcomes should be taken into consideration. As TA-TAVI shows very good PPI and PVL outcomes, this procedure should be liberally performed in present times in patients who cannot undergo TF-TAVI. However, to determine the first preferred TAVI alternative, long-term studies are necessary.

Contemporary Strengths and Weaknesses of TF and TA Approaches

The superiority of TF approach compared with TA approach in terms of clinical outcomes is well proved.[26] Accordingly the TF-TAVI has been emerged as a gold standard therapy and represents a "first-line" approach for patients who undergo transcatheter therapies, whereas the utility of TA-TAVI strongly decreased. In addition, new and sophisticated generation valve systems have been developed. This development has helped in recent years to concentrate the research focus mainly on TF route. In light of this evolvement, studies comparing TF with TA approach using contemporary valve systems are missing. The aim of the comparison of both approaches in our study was to evaluate clinical and procedural strengths and weaknesses between TF and TA approaches using contemporary valve systems after continuous use of both approaches.

We saw that by using TA-TAVI, comparable to TF-TAVI clinical and procedural outcomes can be achieved. These findings suggest that TA-TAVI represents an excellent alternative when TF-TAVI is contraindicated.

Conclusion

Although TA-TAVI does not represent the first preferred TAVI alternative at present because of its invasiveness, this method showed excellent early clinical and hemodynamic outcomes in high-risk patients with an end stadium vasculopathy who cannot undergo TF-TAVI. The incidence of such patients is considerably high, and TA-TAVI can be performed in all those candidates who are contraindicated for TF-TAVI and express not only femoral and iliac distinct vasculopathy, but also vascular disorders beyond these arterial segments.

Limitation

This study is a retrospective and nonrandomized single-center study with limited number of patients.

Authors' Contributions

D.U. contributed to the conception, design, data collection, acquisition, analysis, interpretation of data, drafting, and revising of the work. B.B. contributed to the conception, design, and revising of the work. H.C. contributed to the statistics, analysis, and interpretation of data and revision. M.S., P.P., and P.H. contributed to data collection and revision. J.S. contributed substantially to the design and intellectual revision of the work. All authors approve this final version for publication and agree to be accountable for all aspects of this work.

Conflict of Interest

P.P. is proctor for Edwards Lifesciences. All other authors declare no potential conflict of interest.

References

1 Buzzatti N, Sala A, Alfieri O. Comparing traditional aortic valve surgery and transapical approach to transcatheter aortic valve implant. Eur Heart J Suppl 2020;22(suppl E):E7–E12
2 Patel JS, Krishnaswamy A, Svensson LG, Tuzcu EM, Mick S, Kapadia SR. Access options for transcatheter aortic valve replacement in patients with unfavorable aortoiliofemoral anatomy. Curr Cardiol Rep 2016;18(11):110
3 Vemulapalli S, Carroll JD, Mack MJ, et al. Procedural volume and outcomes for transcatheter aortic-valve replacement. N Engl J Med 2019;380(26):2541–2550
4 Kappetein AP, Head SJ, Généreux P, et al; Valve Academic Research Consortium-2. Updated standardized endpoint definitions for

transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. J Thorac Cardiovasc Surg 2013;145(01):6–23
5 Walther T, Dewey T, Borger MA, et al. Transapical aortic valve implantation: step by step. Ann Thorac Surg 2009;87(01): 276–283
6 Leon MB, Smith CR, Mack MJ, et al; PARTNER 2 Investigators. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med 2016;374(17):1609–1620
7 Auffret V, Lefevre T, Van Belle E, et al; FRANCE TAVI Investigators. Temporal trends in transcatheter aortic valve replacement in France: FRANCE 2 to FRANCE TAVI. J Am Coll Cardiol 2017;70(01): 42–55
8 Leon MB, Smith CR, Mack M, et al; PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010;363 (17):1597–1607
9 Patsalis PC, Alotaibi S, Wolf A, et al. Feasibility of transfemoral aortic valve implantation in patients with aortic disease and simultaneous or sequential endovascular aortic repair. J Invasive Cardiol 2019;31(10):289–295
10 Folliguet T, Laurent N, Bertram M, et al. Transcarotid transcatheter aortic valve implantation: multicentre experience in France. Eur J Cardiothorac Surg 2018;53(01):157–161
11 Dahle TG, Kaneko T, McCabe JM. Outcomes following subclavian and axillary artery access for transcatheter aortic valve replacement: Society of the Thoracic Surgeons/American College of Cardiology TVT Registry Report. JACC Cardiovasc Interv 2019; 12(07):662–669
12 Beurtheret S, Karam N, Resseguier N, et al. Femoral versus non-femoral peripheral access for transcatheter aortic valve replacement. J Am Coll Cardiol 2019;74(22):2728–2739
13 Kirker E, Korngold E, Hodson RW, et al. Transcarotid versus subclavian/axillary access for transcatheter aortic valve replacement with SAPIEN 3. Ann Thorac Surg 2020;110(06):1892–1897
14 Binder RK, Rodés-Cabau J, Wood DA, et al. Transcatheter aortic valve replacement with the SAPIEN 3: a new balloon-expandable transcatheter heart valve. JACC Cardiovasc Interv 2013;6(03): 293–300
15 Toppen W, Suh W, Aksoy O, et al. Vascular complications in the Sapien 3 Era: continued role of transapical approach to transcatheter aortic valve replacement. Semin Thorac Cardiovasc Surg 2018;30(02):144–149
16 Suri RM, Minha S, Alli O, et al. Learning curves for transapical transcatheter aortic valve replacement in the PARTNER-I trial: technical performance, success, and safety. J Thorac Cardiovasc Surg 2016;152(03):773–780.e14
17 Long A, Mahoney P. Comparative intermediate-term outcomes of subclavian and transcaval access for transcatheter aortic valve replacement. J Invasive Cardiol 2020;32(12):463–469
18 Beve M, Auffret V, Belhaj Soulami R, et al. Comparison of the transarterial and transthoracic approaches in nontransfemoral transcatheter aortic valve implantation. Am J Cardiol 2019;123 (09):1501–1509
19 Madigan M, Atoui R. Non-transfemoral access sites for transcatheter aortic valve replacement. J Thorac Dis 2018;10(07): 4505–4515
20 Généreux P, Webb JG, Svensson LG, et al; PARTNER Trial Investigators. 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
21 Zhan Y, Lofftus S, Kawabori M, Soin A, Chen FY. A meta-analysis comparing transaxillary and transaortic transcatheter aortic valve replacement. Gen Thorac Cardiovasc Surg 2021;69(01):19–26
22 Useini D, Haldenwang P, Schlömicher M, et al. Mid-term outcomes after transapical and transfemoral transcatheter aortic valve implantation for aortic stenosis and porcelain aorta with a systematic review of transfemoral versus transapical approach. Thorac Cardiovasc Surg 2020;68(07):623–632
23 Vasa-Nicotera M, Sinning JM, Chin D, et al. Impact of paravalvular leakage on outcome in patients after transcatheter aortic valve implantation. JACC Cardiovasc Interv 2012;5(08):858–865
24 Nazif TM, Dizon JM, Hahn RT, et al; PARTNER Publications Office. Predictors and clinical outcomes of permanent pacemaker implantation after transcatheter aortic valve replacement: the PARTNER (Placement of AoRtic TraNscathetER Valves) trial and registry. JACC Cardiovasc Interv 2015;8(1 Pt A):60–69
25 Mack MJ, Leon MB, Thourani VH, et al; PARTNER 3 Investigators. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med 2019;380(18):1695–1705
26 Ghatak A, Bavishi C, Cardoso RN, et al. Complications and mortality in patients undergoing transcatheter aortic valve replacement with Edwards SAPIEN & SAPIEN XT valves: a meta-analysis of world-wide studies and registries comparing the transapical and transfemoral accesses. J Interv Cardiol 2015;28(03):266–278