Review Article

# Non-transfemoral access sites for transcatheter aortic valve replacement

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**Abstract:** Transfemoral access is currently the standard and preferred access site for transcatheter aortic valve replacement (TAVR), though novel approaches are emerging to expand treatment options for the increasing numbers of patients with a contraindication for the traditional route. Previous publications have provided comparisons between two TAVR access sites, primarily transfemoral versus one of the novel approaches, while others have compared three or four novel approaches. The aim of this report is to provide a comprehensive summary of publications that analyse and compare the six non-transfemoral access sites currently described in the literature. These include the transapical, transaortic, axillary/subclavian, brachiocephalic, transcarotid, and transcaval approaches. Though there remains little consensus as to the superiority or non-inferiority of TAVR approaches, and there has yet to be randomized clinical trials to support published findings, with careful patient and procedural selection, outcomes for novel approaches have been reported to be comparable to standard transfemoral access when performed by skilled physicians. As such, choice of procedure is primarily based on registry data and the judgement of surgical teams as to which approach is best in each individual case. As TAVR continues to be an increasingly widespread treatment, search for the optimal access site will grow, and focus should be placed on the importance of educating surgeons as to all possible approaches so they may review and chose the most appropriate technique for a given patient.

**Keywords:** Transcatheter aortic valve replacement (TAVR); transcatheter aortic valve implantation (TAVI); non-transfemoral

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## Introduction

Aortic stenosis (AS) is the most common acquired valvular disease in adults, with a life expectancy of approximately 2–5 years after symptom onset (1,2). Surgical aortic valve replacement (SAVR) using cardiopulmonary bypass is the current standard therapy for treatment of severe AS. In response to the expanding elderly population with multiple medical comorbidities and thus the growing number of patients not suitable for SAVR, transcatheter aortic valve replacement (TAVR) was developed as an alternative and is now the standard therapy for high risk patients with severe AS (3). Further details outlining indications, contraindications, pre-operative assessment measures, and operative techniques for TAVR have been published elsewhere (2).

Retrograde transfemoral (TF) access remains the standard and preferred procedure due to its lower invasiveness, ability to be performed without general anaesthesia, ease of patient recovery, and shorter hospital

stays (2). Although most inoperable patients can be treated with TF-TAVR, especially in high volume centers (4) and with the development of smaller delivery sheaths and newer generation valves, it is reported that up to 1/3 of eligible patients may not be candidates for this approach (2,5-7). Primary contraindications to TF access include unsuitable iliofemoral vessel size and anatomy, and significant vessel tortuosity (2,8). Thus, alternate routes have emerged in order to expand treatment options for patients. Data ranging from single center case-series to multicentre registries has demonstrated the use of alternative routes, yet results vary and there remain many unknowns. A number of studies have reported worse outcomes, including reduced survival after non-TF TAVR, yet others have reported differently. Furthermore, studies have frequently been retrospective and include self-reported clinical events and case examples rather than impartial, prospective standardized results.

Previous publications have provided comparisons between two TAVR access sites, primarily TF versus one of the novel approaches, while others have compared three or four novel approaches. The aim of this report is to provide a comprehensive summary of publications that analyse and compare the six non-TF access sites currently described in the literature. These include the transapical (TA), transaortic (TAo), axillary/subclavian (SC), brachiocephalic, transcarotid (TC), and transcaval approaches. A summary of publications will attempt to give a comprehensive overview of what has previously been done in order to guide future research.

## Methods

A PubMed search was done using key words such as "non-transfemoral TAVR", "non-transfemoral TAVI", "transapical TAVR", "transapical TAVI", "transaortic TAVI", "subclavian TAVI", "carotid TAVI". Secondary search strategy included cross-referencing articles from primary resources.

## Results

*Table 1* provides a summary outline of the main advantages and disadvantages of the six non-transfemoral TAVR routes that are described in the literature and that will be discussed below in this report.

### *Registry data*

In 2013, Agarwal and colleagues published a review of 11 TAVR registries along with the two PARTNER trial cohorts. Data came from 282 centers across over 10 countries, including 8,795 patients with study periods ranging from 1–4 years. Various pooled comparative measures between data sets were reported and can be seen in the original article (9).

In looking at access site, TF was favoured in the majority of reports, used in 44.6–100% of cases. Of the alternative sites used, TA was performed most frequently, used in 3.7–55.4% of cases, with the SOURCE (10) and Canadian (6) registries being the only ones to use TA more frequently than TF. Other routes were used in 3% of cases overall and consisted of TAo and SC access.

In the registry cohorts, pooled 30-day and 1-year mortality rates were 6.8% and 20.8% in the TF group respectively, compared to 3.9% and 26.2% in the PARTNER-TF cohort. In the TA groups, registry cohorts showed 30-day and 1-year mortality rates of 12.2% and 32.2% *vs.* 3.8% and 29.0% in the PARTNER TA group (9). The pooled 30-day mortality rate from the registries was significantly higher than in the PARTNER trial (9.2% *vs.* 3.8%), though medium-term and 1-year all-cause mortality rates were similar (22.9% and 26.9% respectively). Factors that may have contributed to lower 30-day mortality rates in the PARTNER trial include rigorous patient screening and assessment, extensive procedural planning, as well as high volume valve centers used as trial sites. Though many of the registries showed that approach had no prognostic value, reporting similar 1 and 2-year mortality rates in TF versus TA cohorts, others have reported significantly higher all-cause mortality among patients undergoing TA-TAVR (11-13). The difference is likely a result of higher risk profiles of these patients.

Procedural success in the registries ranged from 88.5–98.4%, compared to 95.4% and 96.6% in cohorts A and B of the PARTNER trial respectively (9). However, success rates are difficult to evaluate and compare, mainly owing to the lack of consistent operational definitions of what constitutes "procedural success". It is additionally challenging to derive conclusions from registry data as most reports recount pooled outcomes from all aspects of the learning phase including patient selection, imaging, procedural expertise, and improvements in TAVR technology. Furthermore, outcomes are difficult to compare since use of valve devices is not consistent, varying from center to center.

In another large registry study, Fröhlich and colleagues compared survival amongst non-TF procedures from the UK-TAVR registry over a 5-year period (14). Results from 3,962 patients were presented, of which 2,828 underwent TAVR

 

**Table 1** Advantages and disadvantages for alternative TAVR routes

| TAVR route | Advantages | Disadvantages |
|---|---|---|
| TA | ❖ Fewer vascular complications than percutaneous routes, less use of contrast and fluoroscopy, short distance from sheath to annulus, improved valve alignment before deployment (fewer PVLs)<br>❖ Allows accommodation of larger sheaths, relatively no access limitation | ❖ Invasive, risk of myocardial injury and complications related to puncture site (bleeding, ventricular apex pseudo-aneurysm, accidental coronary artery damage, resulting arrhythmias or wall motion abnormalities) |
| TAo | ❖ Fewer vascular complications than percutaneous routes, direct visualization of the aorta facilitates positioning and deployment<br>❖ Avoids major risks/contraindications of TA approach (no cannulation of LV apex, avoiding tissue injury in patients with friable myocardium)<br>❖ Surgeon familiarity of accessing and cannulating aorta | ❖ Invasive, requires sternotomy or a right mini-thoracotomy for access<br>❖ Caution in patients with prior sternotomy or bypass grafts that overlie aorta |
| SC/axillary | ❖ Percutaneous option, less invasive than transthoracic access, shorter procedure time, decreased need for general anaesthesia, decrease length of hospital stay<br>❖ Procedure similar to femoral approach and SC access is familiar to most cardiac surgeons<br>❖ Only non-TF approach with equivalent mortality rates to standard TF | ❖ Increased risk of vessel injury (thinner and more frail than femoral artery)<br>❖ Restricted by similar limitations in vessel caliber and presence of calcification as TF-care must be taken in patients with prior CABG with LIMA graft due to risk of occlusive sheath if crossing LIMA origin<br>❖ Adequate closure of axillary artery can be challenging with percutaneous rather than cut-down approach<br>❖ Risk of brachial plexus injury |
| Brachiocephalic | ❖ Percutaneous option, less invasive than transthoracic access<br>❖ Offers another alternative for patients with contraindications to other TAVR approaches | ❖ Recent development, only 2 case series exist, thus more studies are required to establish safety/efficacy and indications/contraindications |
| TC | ❖ Percutaneous option, less invasive than transthoracic access<br>❖ Straightforward procedure with similarities to carotid endarterectomy<br>❖ Offers another alternative for patients with contraindications to other TAVR approaches | ❖ Potential risk of stroke (comprehensive neurovascular workup is necessary to rule out significant atherosclerotic disease and assess patency of the Circle of Willis) |
| Transcaval | ❖ Offers another femoral route similar to standard femoral artery access<br>❖ Femoral vein not subject to same limitations as artery (i.e., presence of calcification) | ❖ Risk of bleeding at caval-aortic puncture site<br>❖ Recent development, more studies required to establish safety/efficacy and indications/contraindications |

TF, trans-femoral; TA, trans-apical; TAo, trans-aortic; SC, subclavian; TC, trans-carotid; PVL, paravalvular leak; CABG, coronary artery bypass graft; LIMA, left internal mammary artery; TAVR, transcatheter aortic valve replacement.

through TF access, 761 via TA access, 185 via TAo access, and 188 via SC access. Results showed TA and TAo approaches to have nearly identical survival rates, both significantly lower than TF cases. Subclavian access was demonstrated to be the only non-femoral approach for which survival was not significantly different from TF and may currently represent

 

the safest alternate access route for TAVR.

Grover and colleagues published the latest update to United States (US) data from the STS/ACC TVT (Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy) Registry in 2017. They reported results on 54,782 procedures from 418 sites that performed TAVR throughout the US between December 2011 and December 2015 (4). TF access was used in 86.6% of TAVR procedures, showing an increase from 75.9% in 2012, TA access was used in 6.1% of cases, down from 14.5% in 2012, and other access sites were used in 6.8% of patients in 2015. The pooled 30-day and 1-year mortality for all TAVR procedures performed in the 4-year period was 5.7% and 22.6% respectively. Specific access site mortality rates were not reported in the publication, thus direct comparisons to data from other registries are difficult to make. However, the pooled (TF, TA, other) 30-day mortality rates from the TVT registry are lower than the TF rates reported in other registries mentioned above (5.7% *vs.* 6.8%) (9). This difference, as well as the difference in access site use (US registry favoring TF) can be attributed to the high volumes of TAVR patients in those centers.

### *Transapical TAVR*

The first TA-TAVR was performed in 2005 using the Edwards Sapien valve (15), and has been reported as the primary alternative procedure at many institutions when TF is contraindicated (2,16,17). Advantages include fewer vascular complications, less use of contrast and fluoroscopy, short distance from sheath to annulus, and improved alignment of the stent valve before deployment leading to fewer paravalvular leaks than in TF-TAVR (2,16,18). Additionally, access is not restricted by peripheral vascular anatomy and size, thus allowing accommodation of larger sheaths and posing essentially no access limitation since the apex can be exposed in virtually all patients (16).

Invasiveness is the main disadvantage to this route, making it a higher-risk procedure associated with increased morbidity and mortality, especially in frail elderly patients. Relative contraindications include low ejection fraction (EF <15–20%), and significant parenchymal lung disease [forced expiratory volume in 1 second (FEV1) <35–40% of predicted values] (2,19). Haemostatic control of the apex is considered the most critical step during this procedure, with several surgical techniques as well as new sutureless apical closure devices being described to minimize incision and blood loss (20,21). European SOURCE registry data reports greater incidence of major bleeding among patients undergoing TA (3.9%) compared to TF (2.3%) procedures (10). Yet, the incidence of major (11.3% *vs.* 2.0%) and minor (10.4% *vs.* 1.0%) vascular access-related complications was significantly higher in TF patients than in TA patients.

Potential complications that contribute to the higher risk of TA-TAVR include bleeding from the puncture site, ventricular apex pseudo-aneurysm, or accidental coronary artery damage (21,22). Risk of myocardial injury is also of concern, potentially resulting in long-term effects of arrhythmias as well as new apical hypokinesia or akinesia (23,24). It is also worth noting that despite being performed with less contrast, TA-TAVR has shown to be associated with a significantly increased risk of acute kidney injury and renal failure, possibly explained by the known association between surgical trauma, systemic inflammatory response, and renal damage (25). Additionally, analysis of OBSERVANT registry data (26) showed that despite its direct antegrade approach, TA access does not decrease the risk of stroke which had been proposed by some studies (27-29).

However, the context of reported outcomes must be considered since more favorable results have been demonstrated by centers performing higher volumes of TA procedures, suggesting the possibility of a significant volume-outcome relationship with the novel technique compared to the well-established TF approach (30). In 2016 Papadopoulos and colleagues published a review of their 10-year experience with TA-TAVR (22). Mean survival was 73% at 3 years and 56% at 5 years. Perioperative and 30-day mortality was 1.3% and 8.2% respectively, with 30-day mortality decreasing to 4.2% in later years, suggesting that time and practice contribute to successful outcomes. Authors suggest that TA-TAVR is an established alternative with the possibility of being as safe and effective as TF-TAVR, and that though results on long-term haemodynamic and structural valve behavior are lacking, 11 patients from their study who were followed for 8 years showed no signs of structural valve dysfunction.

Overall, though centers performing high volumes of TA-TAVR suggest it to be an established alternative when performed by experienced surgeons, it is suggested that not enough arguments or consistent data in favor of TA access exist, and that it should only be considered in patients with contraindications to any endovascular approach (26).

### *Transaortic TAVR*

The first use of TAo-TAVR was in 2009 as an option for

 

patients without feasible TF, SC or TA access (31). It is suggested that given the invasive nature and uncertain outcomes of the TA route, direct access to the ascending aorta has emerged as an alternative non-TF option (32). As a consequence, its use has expanded rapidly with both the Edwards Sapien and Medtronic CoreValve systems (33,34). Previously, the TA approach had been considered the primary option for non-TF TAVR, however, the TAo approach has become increasingly preferred among non-TF patients (32,35), avoiding the major risks/contraindications of the TA approach (2), such as not involving cannulation of the left ventricular apex, avoiding tissue injury in patients with friable myocardium.

Publications comparing TA and TAo approaches have demonstrated no significant differences in procedural complications, equivalent or higher 30-day mortality rates, as well as lower 1-year mortality rates and significantly lower cardiovascular related mortality in TAo groups (36-38). O'Sullivan 2015 provides a meta-analysis of 10 studies comprising 1,736 patients between 2012 and 2013, where they compare TA to TAo access. Results showed pooled success rates of 96.3% for TAo compared to 93.7% for TA, and there were no significant differences in 30-day mortality, stroke/TIA, major bleeding, heart block requiring pacemaker insertion, or paravalvular regurgitation (38).

The TAo approach has also been favored in some cases over the TA as well as the TF approach, even when their access is feasible. The ROUTE registry prospectively enrolled 301 patients undergoing TAVR at 18 European centers from February 2013 to February 2015, where 74.4% of patients were deemed suitable candidates for TAo as well as TA and/or TF-TAVR, however 48% of those patients were chosen for TAo access due to center preference (39).

The TAo route also offers advantages to percutaneous routes by decreasing the risk of complications related to vessel injury, avoiding smaller arteries like the iliofemoral or subclavian through the insertion of a large-bore sheath directly in a large-caliber vessel (40). Additionally, direct visualization of the aorta facilitates positioning of the valve prosthesis for ease of deployment, and cardiac surgeons are familiar with accessing and cannulating the aorta for conventional procedures, therefore many of the skills are transferable.

Similarly to the TA route, the primary drawback of the TAo approach is in its more invasive nature, accessing the ascending aorta through a sternotomy or thoracotomy (16). The primary contraindication is porcelain aorta and careful evaluation must be taken when considering patients with previous sternotomy or bypass grafts that overlie the aorta (2).

Until recently, there were few publications showing results of TAo-TAVR procedures in larger series, and it remained less frequently used in most centers. However, it has been reported as more favorable to TA-TAVR in order to avoid myocardial injury and can be considered for patients who cannot undergo a percutaneous TF or SC-TAVR (14,23).

### *Subclavian/axillary TAVI*

The first article reporting a case of TAVR via subclavian access was published in 2008 by Ruge and colleagues (41). Since that time, numerous reports have described its use in those who are not candidates for TF, TA, or TAo approaches with some centers reporting its use in ranges from 6–20% of TAVR cases (5,16).

The SC/transaxillary approach has been described as a preferential non-TF route due to lower invasiveness, shorter procedure time, and decreased need for general anaesthesia (5). This reduces possible complications related to weaning of respiratory support or post-operative delirium, and can decrease length of patients' hospital stay (42,43). Like the traditional TF approach, SC access can provide a percutaneous delivery of the transcatheter heart valve making it a more suitable option for elderly, frail, debilitated patients. This approach can also be done through a standard cut-down technique (5,44). Additionally, the procedure itself is very similar to the femoral approach and subclavian artery access is familiar to most cardiac surgeons (40,45).

Reported drawbacks to this route include increased risk of vascular complications since the subclavian artery wall is thinner and frailer than the femoral artery (45,46). Subclavian access is also restricted by similar limitations in vessel caliber and presence of calcification as in the TF approach, and the procedure is not advised for patients with significantly tortuous or calcified vessels, or an artery diameter less than 6–7 mm (47). Patient factors to consider include those with a patent left internal mammary artery (LIMA) graft because of the risk of an occlusive sheath in the subclavian artery (16). Some reports have stated that SC access is not advisable in these patients, yet others have demonstrated that the procedure can safely be performed if attention is given to avoid advancing the sheath across the LIMA origin (48,49). Another procedural concern in the percutaneous rather than the surgical cut-down approach is adequate closure of the axillary artery due to

 

manual compression of the puncture site being anatomically challenging and often inefficient to control bleeding (5). Additionally, increased risk of neurological complication is also present with this approach due to the close proximity of the brachial plexus (50). It has also been suggested that patients with unsuitable left subclavian anatomy would not be good candidates for SC-TAVR since the right side often has an unfavorable implantation angle (42), however, right subclavian access has been successfully reported in a select number of cases (41).

Valve device is an additional consideration with SC-TAVR. It is not very common to use balloon-expandable valves for this approach, and the CoreValve prosthesis is primarily used due to its small introducer sheath, whereas an adequate straight portion of artery would be needed to place the crimped Edwards Sapien valve onto the balloon, making the procedure more complex (16). However, Jarrett 2017 reports that SC access has become the preferred non-TF route at their center, even when using balloon expandable valves (51).

The US CoreValve High-Risk study reported a numerically lower 30-day mortality with SC (8.6%) than with transthoracic (TAo/TA) access (13.6%), likely relating to invasiveness (52), and data from the UK registry showed SC access to be the only non-TF approach for which survival was not significantly different from TF, potentially representing the safest non-TF access route (14). In this same study, TA and TAo approaches were associated with almost identical survival, both significantly lower than after TF or SC-TAVR. These findings are consistent with Italian CoreValve Registry data where comparable procedural and 2-year results after SC and TF-TAVR were found, and authors then concluded that SC access may also be considered a valid option even if TF access is difficult but feasible (43). The Italian Registry study compared 141 SC-TAVRs with 141 TF-TAVRs, showing no significant differences in procedural success and mortality, even though pre-operative risk was significantly higher in the SC group due to higher prevalence of coronary, cerebral, and peripheral artery disease. More recently in 2017, Gleason and colleagues reported on a SC-TAVR cohort of patients within the CoreValve US Pivotal Trial and Continued Access Study, compared to a cohort of TF patients from the same trials. Authors concluded in their analysis of the clinical trial with the largest reported cohort of SC-TAVR patients to date, that results demonstrated no significant differences in outcomes, with 30-day and 1-year mortality rates equivalent to TF-TAVR procedures (7).

Based on these results, many researchers believe that TF access will remain the standard approach for TAVR due to its familiarity and the progression towards reduction in device size making vascular access more easily achievable. However, there will remain a subset of patients unsuitable for femoral access, and with evidence emerging towards the non-inferiority of the SC approach, it should be determined if TF-TAVR should continue to be the first choice treatment for inoperable patients with severe AS.

### *Brachiocephalic TAVR*

There currently exists two single-center case series that have evaluated the potential of a brachiocephalic approach to TAVR, gaining access either through an upper partial sternotomy or a suprasternal cut-down approach. Capretti and colleagues reported 1 major stroke and 3 access-site related vascular complications in their series of 26 patients, with no deaths at 30 days and 2 deaths within a mean follow-up of 317 days (53). Philipsen and colleagues performed the procedure on 20 patients, with 6 and 12-month survival rates of 85% and 75% respectively (54).

Though further studies are needed to confirm the feasibility of brachiocephalic TAVR and compare it to other approaches, these small case-series provide preliminary evidence towards adding another option to current alternatives in patients for which other TAVR approaches are contraindicated.

### *Carotid TAVR*

In 2010, Modine and colleagues published the first case report on TAVR via carotid access (55), and in 2012 reported results from a series of 12 patients who successfully underwent TC-TAVR with the CoreValve prosthesis (56). Their only significant adverse effect was one incidence of transient ischemic attack (TIA). Having demonstrated the feasibility and short-term success of this new approach, those authors concluded that the TC access adds another potential option to the available TAVR procedures.

In 2016, Stonier and colleagues conducted an in depth literature review assessing the feasibility and safety of TC-TAVR (57). Data on 72 patients from 16 studies were analyzed, all whom were considered unfit for standard TF access as well as TA, TAo, and SC routes. Overall mortality across the studies was 4.1%. There was 1 intraoperative death due to aortic annulus rupture during balloon valvuloplasty, and 2 deaths within 30-day post-

 

procedure, one from multi-system organ failure and one from haemopericardium (58,59). Adverse effects included 2 TIA's (56,59), 10 patients requiring transfusion of 2 or more units of packed red cells (8,60), one with acute kidney injury requiring new dialysis (8), and one intraoperative dissection that subsequently resolved (55). The need for permanent pacemaker insertion was the most common event, required in nine cases (60-62).

It has been recommended that patients considered for this technique require a common carotid artery diameter greater than 8mm without evidence of calcification, stenosis, or severe tortuosity (2). Comprehensive neurovascular workup is also necessary to rule out significant atherosclerotic disease and assess patency of the Circle of Willis. If those criteria are met, the procedure is described as being a relatively straightforward procedure with similarities to a carotid endarterectomy (63). Passive antegrade carotid perfusion through a temporary shunt into the common carotid has been used to ensure adequate cerebral perfusion during the procedure.

Limitations to available data include heterogeneous follow-up across studies, and small sample sizes that raise the possibility of bias in neglecting to report poor outcomes in the early stages of this procedures' use. Authors nevertheless suggest that in accepting limitations of their systematic review, carotid access is a potential alternative route for TAVR and further research should seek to support these findings. Nonetheless, since limited experience exists with this procedure, currently the most popular view is that it should only be considered when all other access sites are contraindicated (2,63).

Contrary to this however, are recent experiences in high-volume centers reporting promising outcomes (64,65). Notably, a 2017 publication from Kirker and colleagues reports on their use of TC-TAVRs in a high volume US center whose approach favors carotid access over other non-TF routes. Authors report faster procedure times, shorter length of stay, and comparable or better 30-day and 1-year outcomes between their TC, TA, and TF patients, concluding that at their institution, TC-TAVR is faster and safer than TA, with outcomes comparable to standard TF access (65).

### *Transcaval TAVR*

The most recent development in alternative TAVR procedures is the transcaval approach. Greenbaum and colleagues describe a technique of transfemoral venous access by passing through the inferior vena cava (IVC) to enter the adjacent abdominal aorta (66). Reasoning for this approach was due to the inferiority of transthoracic access over femoral artery access, suggesting exploration of an alternative TF option.

The first experience with their novel approach took place in 2013, treating 19 high-risk patients using Edwards Sapien valves (66). Successful caval-aortic access was achieved in all patients, with successful TAVR procedure completed in 17 patients. One death occurred during attempted surgical retrieval of an embolized valve into the left ventricle. Subsequent to their early experience, authors presented results of 100 patients from an initial prospective, multicenter study of participants ineligible for TF access and at high or prohibitive risk for thoracic access (67). The study's primary endpoint was device success, defined as successful transcaval access and closure device deployment. Device success occurred in 99 of 100 patients with inpatient and 30-day survival rates of 96% and 92% respectively, and a median hospital stay length of 4 days. Retroperitoneal bleeding was the main complication to be considered. Hematomas were shown on computed tomography (CT) scans in 24% of patients pre-discharge and 5% of patients at 30-day follow-up, though most were small to moderate. It was inferred that because the intrinsic retroperitoneal pressure exceeds that of the IVC, aortic bleeding decompresses into the venous hole. This theory was initially suggested in their preclinical data where in animal models it was shown that aorto-caval fistulas were well tolerated without repair (68). Furthermore, authors suggest that bleeding may be reduced with the development of purpose-built closure devices.

Limitations to the data include the generalizability of results due to the small cohort of patients and short-term follow up. Additionally, criteria for determining eligibility for transcaval access, and non-eligibility for other non-TF TAVR procedures were not detailed. While patients in this series were said to be unsuitable for TF, TA, and TAo-TAVR procedures, consideration of TC or SC access was not mentioned and it is possible that a number of these patients could have benefited from approaches that are more established (5,43,57).

A review of Greenbaum and colleagues' experience suggests that this data should not yet affect clinical practice, but that further studies should aim to build on their findings towards establishing its feasibility as an alternative TAVR approach within select high-risk patients with no alternative options (69).

 

## Discussion/future perspectives

Over the course of the last decade, TAVR has emerged as a novel treatment option, providing successful outcomes in patients with severe AS and prohibitive surgical risk. Given its success and less invasive nature when compared to SAVR, hypotheses emerged as to whether or not TAVR would be indicated for patients with moderate or perhaps even low surgical risk.

In recent years, the PARTNER II and SURTAVI trials aimed to evaluate the potential for TAVR in intermediate-risk patients, both trials showing promising results of non-inferiority of TAVR versus SAVR in intermediate-risk patients (70,71). However, the promising results seemed to be isolated to the femoral route, and longer-term follow-up is needed to assess the sustainability of the quality-of-life improvements in the treated patients. SURTAVI researchers also noted that it is still unknown whether TAVR is suitable for patients in the low-risk category (71). In 2012, an initial attempt was made in the STACCATO trial to evaluate this patient population, but was prematurely terminated due to poor results for patients in the TAVR group (72). Investigators stated that TAVI should not be considered in patients who are at a low surgical risk due to the well-established successful outcomes offered by SAVR. Authors also noted however, that the inferior results for TAVR in low-risk versus high-risk patients have the potential to change with future developments of improved devices and pre-operative assessments. It is also of note that the STACCATO comparison was between SAVR and TA-TAVR. Given that TA access is increasingly being recognized as a higher risk and less favorable approach to percutaneous non-TF TAVR routes, it is possible that these routes could lead to better outcomes and be applicable to low-risk operative patients in the future. These recent developments provide insight into the future of TAVR and the potential to expand its indications to a wider patient population.

In our center, the transfemoral approach is used in the great majority of cases, with direct transaortic access reserved for patients with unsuitable peripheral access. Every procedure is done with the presence of a cardiologist and a cardiac surgeon. All potential patients are seen at the TAVI clinic by the cardiologist, the cardiac surgeon and the TAVI nurse. In some cases, the input of a vascular surgeon is also obtained. Furthermore, these patients are thoroughly discussed weekly at TAVI rounds following a "heart team" approach. Preoperative imaging, namely coronary angiogram, peripheral angiogram, cardiac CT scan, transesophageal echocardiograms are reviewed in detail in order to decide on the access site, the type of valve needed and its size.

A final point of discussion is to mention the potential limitations of current data. Given that publications primarily consist of data obtained from centers who chose to publish their results in case reports or registries, it is possible that favorable data is selectively published over unfavorable data. Unsuccessful cases, such as those in the STACCATO trial, provide valuable information to both researchers and clinicians in order to allow for learning opportunities and to gain an accurate representation of the state of TAVR in order to guide current treatment practices.

## Conclusions

Although femoral access remains the standard, alternate access sites have proven to be safe and successful for patients unsuitable for TF-TAVR. The most current consensus statement approved by numerous professional societies does not give general recommendation for access site selection, and given that PARTNER trial data includes only TF and TA cases, it is suggested that use of these approaches be maintained until adequate data is obtained (1). However, the value of data from non-clinical trials should not be discounted, and there is an important role in increasing the use of TAVR registries to provide up to date data on current clinical practice.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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