Axillary Transcatheter Aortic Valve Replacement in Patients With Peripheral Vascular Disease

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The axillary artery seems an interesting alternative in nonfemoral transaortic valve replacement (TAVR) patients. This study describes our experience with this technique and its short-term follow-up results. This is a retrospective single center study. All axillary TAVR performed in our department between 2015 and 2017 were included in the study. Mean follow-up was 13.2 ± 9.5 months. All reporting was done according to the VARC-2 criteria. During the period covered, 43 patients had an axillary TAVR. Most patients were men (62.7%), had a mean age of 83.9 ± 5.3 years and presented with EuroSCORE I, II, and STS score of 27.9 ± 13.5%, 5.6 ± 4.9%, and 7.7 ± 4.05%, respectively. Vascular access was successful in all patients with a higher frequency of left approach (69.7%, $n = 30$). Both Medtronic CoreValve 37.2% ($n = 16$) and Edwards Sapien3 62.8% ($n = 27$) valves were used. An apical Certitude delivery system was preferentially used (24/27) in the latter group. There were no reported instances of valve migration or need for a second valve implantation. A single case (2.3%) of arterial vascular complication was reported. Central neurologic morbidity was 2.3%. No patient experienced brachial plexus injury. A pacemaker was implanted in 18.6% of cases ($n = 8$), with no significant difference between the 2 valves patient groups (S3 14.8% vs CV 25%, P 0.67). The 30-day mortality was 6.9% ($n = 3$) and 1-year survival was 86% [95% CI 72.6, 93.4]. Axillary TAVR is associated with acceptable morbidity, mortality, and leads to satisfactory short-term clinical outcomes. It has the potential to become the main alternative access route in nonfemoral TAVR patients.

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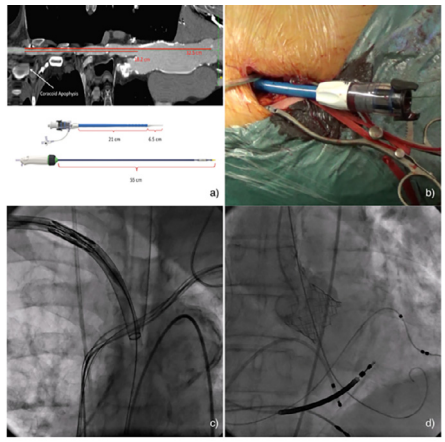
Keywords: TAVR, Axillary artery, Alternative TAVR



Planning and procedure of a right transaxillary TAVR.

Central Message

Axillary artery seems to be an interesting option for an alternative arterial route in patients unfit for femoral TAVR.

Perspective Statement

This study shows that transaxillary TAVR is a viable option, and supports previous suggestions about reliability of this access route. Because it is extrathoracic and spares cerebral vessels this procedure is particularly suitable for fragile patients. Additional independent studies, with longer follow-up periods and larger patient populations will be required to further confirm these results.

Abbreviations: TAVR, transaortic valve replacement; TF, transfemoral; TAx, transaxillary; PAD, peripheral arterial disease; NYHA, New York Heart Association; COPD, chronic obstructive pulmonary disease; BMI, body mass index; LVEF, left ventricular ejection fraction; RVD, right ventricular dysfunction; TAPSE, tricuspid annular plane systolic excursion; PCM, pacemaker; VARC, Valve Academic Research Consortium

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OBJECTIVE

Transcatheter aortic valve replacement (TAVR) procedures are growing exponentially worldwide. This is an established technique often used in high-risk patients, with good long-term outcomes.[1,2] More recently TAVR is being increasingly considered for intermediate risk patients with a growing body of literature reporting on good results.[3,4] Transfemoral (TF) approach remains the gold standard; however, presence of significant comorbidities in a subgroup of approximately 10–20% of the patients, in particular with severe peripheral arterial disease (PAD), will be a counterindication to the TF approach. Several alternative access routes are currently being

considered, with no clear consensus emerging as an optimal second choice. The transaxillary (TAx) approach is one of them; it is less invasive than intrathoracic procedures and has the advantage of a direct and short arterial route. Evidence about its practicality and safety is growing since it was first proposed and appears an interesting route in nonfemoral fragile patients.[5] This study describes our experience with this technique and its short-term results.

MATERIALS AND METHODS

Patients and Statistical Evaluation

The study was approved by the Institutional Review Board of the French Society of Thoracic and Cardio-Vascular Surgery (CERC-SFCTCV-2018-2-19-13-35-7-HyII). This is a retrospective single center study. All patients who deemed unfit for surgery were considered for TAVR by the heart team of our department. Whenever possible a geriatric evaluation was done with specific scores, evaluation of the nutritional status and estimation of the self-sufficiency with the family of the patient. Since 2015, of all patients considered for TAVR, those with severe PAD (a TF contraindication) were recommended for TAx TAVR as the first choice and they were prospectively included in France TAVR registry up to 2017. These data were used in our study and the results are reported according to the VARC-2 criteria.[6] All patients included in this study presented with severe calcified aortic stenosis but no associated significant aortic insufficiency. During the 2-year span of the study, 262 TAVR procedures were performed in our center (including the patients of this study) mostly through the transfemoral route. For nontransfemoral patients ($n = 48$) the following access were used: axillary artery ($n = 43$), whose outcomes are the main focus of this study: apical ($n = 2$), innominate ($n = 2$), and carotid ($n = 1$). Right ventricular dysfunction was defined as a TAPSE measured by echo <15 mm. Follow-up information after release from the hospital were collected through telephone interviews with the patients' attending physicians or cardiologists. Statistical analyses were performed using Statistique Epidémiologie Médicine software. Graphics were produced using the GraphPad software. Continuous variables are described using mean values ± standard deviation and categorical values are described using percentages. Survival was defined as the time lapsed from the date of TAVR until the date of death or the end of the follow-up. Complete and uniform information was obtained for all patients; none of them was lost during the follow-up. Characteristics of subjects were compared with chi-square or Fisher's tests for categorical variables and with Student's t tests for continuous variables. Survival was studied using the Kaplan-Meier statistic and significance estimated using the log-rank test.

TAVR Procedure

All patients had a gated aortic CT scan as part of their pre-TAVR work-up. If the TF route was excluded, axillary arteries preferably left and if not available right were considered. Axillary arteries were deemed unsuitable if the patient had an ipsilateral pacemaker (PCM) or a patent internal thoracic coronary graft. All procedures were performed in the catheterization laboratory, under general anesthesia, except for 2 patients with previous history of severe respiratory failure, who were implanted under conscious sedation and local anesthesia. The axillary artery was accessed through a 4−6-cm incision at the level of the deltopectoral groove as described elsewhere.[7,8] A simple step-by-step dissection was always performed (Video 1). The TAVR procedure was carried out as usual. Both, balloon-expendable (Sapien3, Edwards Lifesciences Inc, Irvine) and self-expendable (CoreValve Evolut R, Medtronic Inc, Minneapolis) valves were used. When balloon-expendable valves were used, preference was given to the Certitude apical delivery system, in which the valve is directly positioned at the tip of the balloon. Self-expendable valves were introduced sheathless directly in the artery. An angiogram and a transthoracic echo were performed in the catheterization laboratory to seek evidence of eventual aortic regurgitation. Artery hemostasis was achieved with a polypropylene purse-string suture. The wound was closed without drainage as standard and surgical glue was applied on the skin. The patient was not given any particular wound care subsequently and shower was allowed after 5 days.

RESULTS

During this 2-year period, 43 patients had a TAx TAVR in our department. The mean follow-up of the entire cohort was 13.2 ± 9.5 months. The mean age when undergoing the procedure was 83.9 years and the majority of patients were men (62.7%). The mean body mass index was 26.6 ± 3.7 kg/m^2. Clinical preoperative characteristics are shown in Table 1. Almost half of the patients (41.8%, $n = 18$) had a clinical frailty, as assessed in the majority of cases (10/18 patients) by geriatric evaluation. Most of the patients were highly symptomatic with NYHA stage III or IV dyspnea.

Vascular access was successful in all patients and was primarily from the left (69.7%, Table 2). Both types of valves were used: Medtronic CoreValve ($n = 16$) and Edwards Sapien3 ($n = 27$). For the latter patients, the apical Certitude delivery system was mostly used (24/27). There were no reports of valve migration or need for a second implantation. Postdilatation was rare (4 patients) and no patient left the catheterization laboratory with a worse than a grade II aortic regurgitation (15 patients with no aortic regurgitation, 26 patients with grade I, and 2 patients with grade II aortic regurgitation). There were 2 episodes of major complications. One involved a cardiac tamponade following a tear of the right ventricle by the external femoral pace probe, which was successfully managed by an emergent surgical Marfan incision. The other complication was a fatal arterial vascular rupture at the level of a heavy calcified innominate artery, during a right Sapien3 29 mm TAx TAVR, insertion using a Certitude delivery system.

Table 3 summarizes the morbidity and mortality observed among our patients. Neurologic morbidity tares were of 2.3%

Table 1. Preimplant Characteristics

	43 Patients, mean ± SD/% (*n*)
Age	83.9 ± 5.3 years
Men	62.7% (27)
NYHA	II (13.9% 6)
	III (74. 4% 32)
	IV (11.6% 5)
EuroScore I	27.9 ± 13.5
EuroScore II	5.6 ± 4.9
STS score	7.7 ± 4.05
Redo	32% (14)
	CABG 11
	VIV 3
Ischemic cardiomyopathy	44.1% (19)
COPD	37.2% (16)
Stroke	18.6% (8)
Diabetes mellitus	34.8% (15)
Anticoagulated atrial fib	41.8% (18)
Urgent	6.9% (3)
Mean gradient	46.7 ± 15.5 mm Hg
Surface	0.7 ± 0.1 cm^2
LVEF	55.4 ± 11.9 %
RVD	13.9% (6)

BMI, body mass index; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; RVD, right ventricular dysfunction; VIV, valve in valve.

(1 patient with subsequent full clinical recovery). The PCM rate was 18.6% (n = 8), but no significant difference was seen between the patients in the 2 different valve groups (P 0.67). The median length of postoperative hospitalization was 9 days (range 0−33 days). Two patients (4.6%) were prescribed on a double antiplatelet plus anticoagulant therapy upon discharge; 1 was readmitted 2 weeks later with a local hematoma requiring surgical revision. The procedural mortality was 2.3% (1 patient

Table 2. TAVR Procedure Characteristics

	43 Patients, mean ± SD/% (*n*)
Predilatation	34.8% (15)
Valve	S3 62.8% (27)
	CV 37.2% (16)
Valve size	23 mm 20.9% (9)
	26 mm 46.5% (20)
	29 mm 27.9% (12)
	31 mm 4.6 (2)
Left TAx TAVR	69.7% (30)
Postdilatation	9.3% (4)
AR > 2	0
Amount of contrast	105.5 ± 32.9 mL
X-ray time	23.1 ± 7.4 min
Major complications	1 Ax rupture
	1 Tamponnade

AR, aortic regurgitation.

Table 3. Outcomes of Axillary TAVR

	43 Patients, mean ± SD/ % (*n*)
Stroke	2.3% (1)
Mean gradient	11.2 ± 4.1 mm Hg
Surface	1.6 ± 0.3 cm^2
LVEF	54.8 ± 11.6%
PCM	18.6% (8)
	S3 4/23 14.8%
	CV 4/16 25%
30-Day mortality	6.9% (3)
In-hospital mortality*	13.9% (6)*

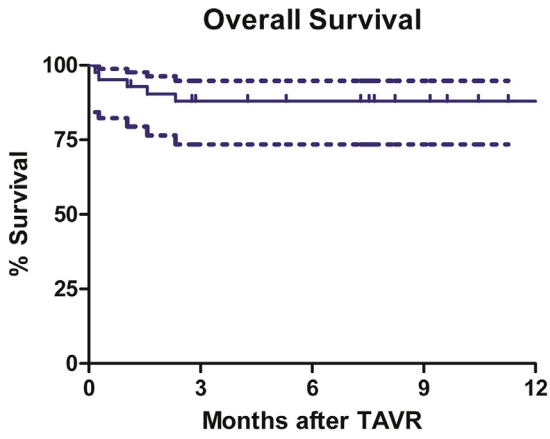
LVEF, left ventricular ejection fraction; PCM, pacemaker, S3 = Sapien3, CV = Corevalve.
*Three patients died before 30 days and 3 others died after 30 days but without leaving the hospital.

with vascular rupture, as mentioned above). The 30-day mortality rate was 6.9% (3 patients, all from cardiovascular causes, including the previously mentioned vascular rupture) and the in-hospital mortality rate was 13.9% (n = 6, 3 patients died in the hospital before 30 days and 3 others died after 30 days but without leaving the hospital). Among these patients, 4 died as a result of cardiovascular causes and 2 of severe pulmonary infections.

One-year overall survival was of 86% [72.6; 93.4] (Fig. 1). The only factor that significantly affected 1-year survival was preimplant clinical frailty 96% [80.4, 99.2] vs 72.2% [49.1, 87.5], log-rank P = 0.03 (Fig. 2). Other factors such as pre-TVAR right ventricular dysfunction (P 0.13), urgent TAVR (P 0.49), or implant of a PCM (P 0.86), were not significantly associated with 1-year survival.

DISCUSSION

As the TAVR-eligible patient pool is globally growing, an increasing number of severe PAD patients with TAVR indication are presenting at the preoperative work-up. The transfemoral access remains contraindicated in patients with small and tortuous femoral vessels or iliofemoral stenosis, because of associations with higher rates of procedural failure and vascular complications. Alternative routes have been proposed for such cases, but their application is primarily based on local surgical expertise and subjective preferences. The different access routes are intrathoracic or extrathoracic.[9] The intrathoracic TAVR includes transapical, transinnominate artery, and transaortic, by either upper ministernotomy or minithoracotomy. The transapical approach was historically the first alternative route. Although this technique can be successfully used in some difficult cases, it is too invasive and associated with higher mortality than TF TAVR.[1] The transinnominate artery offers a direct access to the aortic arch and may be considered as an extrathoracic approach in cases of thin patients where it can be very near to the sternal notch.[10] Nevertheless, routine surgical exposure of the innominate artery can be very challenging, especially in obese patients, as this artery is often



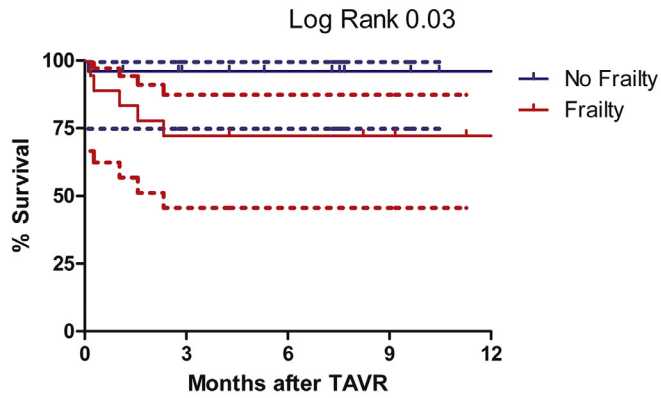
Months	3	6	9	12
Nr at risk	33	30	26	21

Figure 1. Overall 1-year survival.

located under the sternal manubrium. Similar to the intrathoracic access, the transaortic approach is more invasive than extrathoracic options, as it involves opening of the sternum or the pleural space and requires chest tube drainage at the end of the procedure.[11]

The extrathoracic TAVR may follow the transcarotid, transcaval or trans-subclavian routes. The transcarotid one, especially from the left, is very interesting. Also it may be performed under local anesthesia. The risk of cerebral events however is non-negligible (6.3%) as it was reported recently.[12] The transcaval approach has been reported with promising results,[13] but experience remains limited with few publications in the literature. The subclavian approach, first described in 2008,[5] presents 2 major advantages: absence of intrathoracic entry and safeguard of the cerebral vessels. Initial reports were promising[14,15] and recent publications generally agree that this access route has better survival rates than transaortic or transapical TAVR[16,17] with the short and mid-term results comparable to TF TAVR.[18,19] Some authors performing a fully-percutaneous subclavian approach have even proposed "to switch from lower extremity to upper extremity as the preferred approach for TAVI procedure in a near future."[20]

In our clinics, we prefer the surgical dissection of the axillary artery at the level of the deltopectoral groove. Here the artery is more superficial and dissection is very easy and reproducible with good outcomes even in severe obese patients.[21] The artery can be dissected under local anesthesia if needed. The inner diameter of the axillary artery usually allows the introduction of an 18- or 20-Fr cannula for general cardiovascular procedures, suggesting it as a good access for TAVR. Percutaneous access to this artery may be however challenging; one study reports a 29% rate of stenting for failed arterial closure devices. Although it leads to good clinical results in patients with patent



Months	3	6	9	12
Nr at risk No Frailty	20	18	14	13
Nr at risk Frailty	13	12	9	8

Figure 2. Survival with respect to preimplant frailty.

left internal thoracic grafts,[22] we tend to avoid TAx TAVR in these patients, due to the risk of graft dissection or occlusion during the procedure. In our cohort, the left axillary artery was the preferred access route, because of a more favorable angle for sheath progressing toward the aortic valve. The right axillary artery may also be helpful, especially when the left internal mammary artery has been used for previous coronary revascularization, or when a cardiac PCM is implanted on the left side. Although several authors express no preference between the right and the left subclavian routes,[23] right access may have some degree of kinking and especially posterior innominate calcifications. Indeed, we experienced an innominate rupture with a patient presenting with a severe isolated calcification at this level. Despite the large diameter of arteries, heavy posterior parietal calcifications limited the arterial elasticity, which led to a fatal complication. As a result we now evaluate meticulously preoperative CT scans in all right TAx TAVR candidates and, in doubt, we always consider alternatives for access.

Subclavian TAVR has been mostly performed with the Medtronic CoreValve devices or in some cases using transfemoral Edwards Sapien3, which requires additional manipulations in the ascending aorta in order to insert the balloon at the level of the valve. In our clinics, we prefer an off-label apical Edwards Sapien3 Certitude delivery system, which is simple to use with the valve already crimped on the balloon and crucially avoids additional manipulations and reduces the risk of embolic events secondary to displacement of atherosclerotic material. However, as this sheath has a diameter of 18 Fr, it cannot be suitable for all patients and one needs to consider that in fragile small axillary arteries, especially in women, the transfemoral sheath may be better indicated. To our knowledge, this is the first published description of use of the Edwards Sapien3 Certitude delivery system through an axillary approach.

Intrathoracic TAVR is increasingly falling out of favor. The TAx TAVR, does not require the intrathoracic entry, wound drain, and in some cases no general anesthesia, follows the same direction that the TF TAVR, and leads to rapid postimplantation rehabilitation and discharge.

CONCLUSION

Axillary TAVR is feasible, and associated with acceptable morbidity and mortality as well as satisfactory short-term results. In our opinion, this approach has the potential to become a major alternative access in nonfemoral TAVR patients.

Acknowledgment

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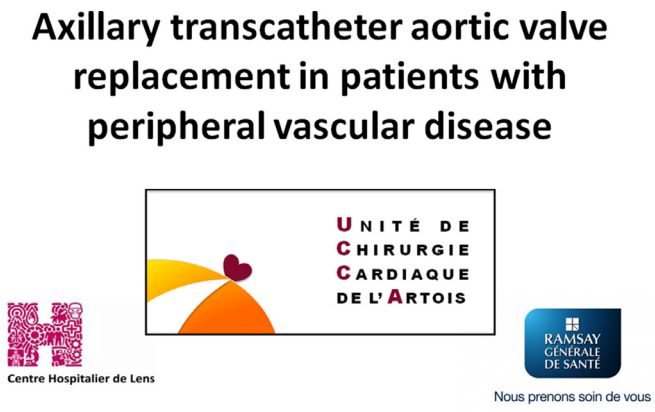
SUPPLEMENTARY MATERIAL

The following is the supplementary data to this article:



Video 1. Video showing a right axillary transcatheter procedure with an initial dissection of the artery at the level of the deltopectoral groove.

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