Transcarotid Approach for Transcatheter Aortic Valve Replacement With the Sapien 3 Prosthesis

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Transcarotid Approach for Transcatheter Aortic Valve Replacement with the Sapien 3 Prosthesis: A Multicentre French Registry

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ABSTRACT
Background: The transcarotid (TC) approach for transcatheter aortic valve replacement (TAVR) holds the potential to become the optimal alternative to the transfemoral gold standard. Limited data exist regarding safety and efficacy of TC-TAVR using the Edwards Sapien 3 device.
Objectives: We aimed to describe the procedural and clinical outcomes of patients undergoing TC-TAVR with the Edwards Sapien 3 device.
Methods: The French Transcarotid TAVR prospective multicentre registry included patients between 2014 and 2018. Consecutive patients treated in one of the thirteen participating centres, ineligible for transfemoral TAVR were screened for TC-TAVR. Clinical and echocardiographic data were prospectively collected. Peri-operative and 30-day outcomes were reported according to the updated Valve Academic Research Consortium (VARC-2).
Results: 314 patients were included with a median (interquartile range) age of 83 (78-88) years old, 63% were males, STS mortality risk score 5.8% (4-8.3). Most patients presented with peripheral artery disease (64%). TC-TAVR was performed under general anesthesia in 91% of cases, mostly using the left carotid artery (73.6%) with a procedural success of 97%. Three annulus ruptures were reported, all resulting in patient death. At 30 days, rates of major bleeding, new permanent pacemaker, and stroke or transient ischaemic attack were 4.1%, 16%, and 1.6% respectively. 30-day mortality was 3.2%.
Conclusions: TC-TAVR using the Edwards Sapien 3 device was safe and effective in this prospective multicentre registry. The transcarotid approach might be considered, in selected patients, as the first-line alternative approach for TAVR whenever the transfemoral access is prohibited. Sapien 3 device was safe and effective in our multicentre cohort.

KEY WORDS: TAVR, TAVI, transcarotid, Sapien 3

CONDENSED ABSTRACT
Limited data exist regarding the safety of TC-TAVR using the Edwards Sapien 3 device. We conducted a prospective multicentre registry included successive patients between 2014 and 2018. Patients were at intermediate surgical risk (median STS mortality risk score 5.8%) and two-thirds of patients had peripheral artery disease. Procedural success was 97%. Thirty-day mortality, major bleeding, new permanent pacemaker, and stroke or transient ischaemic attack were 3.2%, 4.1%, 16% and 1.6% respectively. In conclusion, TC-TAVR using the Edwards

ABBREVIATIONS AND ACRONYMS
CABG: coronary arterial bypass graft;
CAD: coronary artery disease;
COBP: chronic obstructive bronchopulmonary disease;
LVEF: left ventricle ejection fraction;
MSCT: multislice computed tomography;
STEMI: ST segment elevation myocardial infarction;
STS: Society of Thoracic Surgeons;
TAVR: transcatheter aortic valve replacement;
TC: transcarotid;
THV: transcatheter heart valve

INTRODUCTION

The transcarotid (TC) approach for transcatheter aortic valve replacement (TAVR) has been developed as an alternative to the transfemoral gold standard whenever the latter is precluded. Significant peripheral vascular disease or significant descending aortic disease are some of the anatomical challenges that render the iliofemoral pathway unfeasible(1). Despite an apparent increase over time in the proportion of patients eligible for the transfemoral approach, alternative accesses still represent up to 15% of patients undergoing TAVR in contemporary registries(2–4), with 3.4% of patients treated with the TC approach in the recent FRANCE TAVI registry(3). The TC access has the potential to alleviate some of drawbacks of the other nonfemoral approaches (transapical, subclavian, direct aortic, transcaval)(5–8), given its minimally invasive feature. Previous reports asserting the safety of the TC approach for TAVR focused on the Medtronic Corevalve™ device(9–11)However, data is scarce on TC-TAVR with the Edwards Sapien 3™ (Edwards Lifesciences, Irvine, California) device (9,10,12).

We aimed to describe the procedural and clinical outcomes of patients undergoing TC-TAVR with the Edwards Sapien 3™ device.

METHODS

Patient selection

The French Transcarotid TAVR registry is a collaborative initiative developed by interventional cardiologists and cardiac surgeons performing TC-TAVR. This voluntary database prospectively collected consecutive patient data from 13 French participating centres (Lille University Hospital, Lille; Brabois University Hospital, Vandoeuvre les Nancy, Nancy; Angers University Hospital, Angers; Bordeaux University Hospital; Chirurgie Cardiaque et Vasculaire, Infirmerie Protestante, Lyon; Marie Lannelongue Hospital, Plessis-Robinson; Institut Mutualiste

Montsouris, Paris; Rennes University Hospital, Rennes; Hôpital Européen Georges Pompidou, Paris; Robert Debré University Hospital, Reims; Montpellier University Hospital, Montpellier; centre hospitalo-universitaire de Nîmes; centre hospitalo-universitaire de Perpignan) between January 2014 and April 2018, including patient demographics, clinical and procedural characteristics and outcomes.

Patients suffering from severe symptomatic aortic stenosis were considered for TAVR by the institutional Heart Team whenever deemed to be at high or prohibitive surgical risk. Multimodal vascular imaging was performed in all patients to choose the optimal approach for TAVR. Nonfemoral approach was considered when patient anatomy precluded the transfemoral access: obliterative lower limb arterial disease with severe stenosis, small-calibre iliofemoral vasculature (i.e. diameter <6 mm), heavily calcified vessels, tortuosity or significant descending aortic disease. Peripheral artery disease was defined as history of peripheral arterial surgery or angioplasty, or stenosis ≥50% of the iliofemoral axis. Consecutive patients treated with the Sapien 3 transcatheter heart valve through the TC approach were included in this registry. All patients provided written informed consent for the intervention.

Pre-procedural screening

Vascular anatomy was assessed in all patients eligible for TAVR. Pre-operative multislice computed tomography (MSCT) was used to confirm suitable supra-aortic anatomy. The dimensions of carotid, subclavian, and vertebral arteries were carefully assessed, and Doppler ultrasonography complemented MSCT whenever necessary. Careful assessment of the ipsilateral common carotid artery investigated the presence of minimal luminal diameter ≥6 mm without significant, i.e. ≥50%, stenosis or plaque at high risk of embolization, and the absence of subclavian, vertebral and contralateral carotid stenosis or occlusion, or congenital variants of the

aortic arch (e.g., Bovine arch), which are contraindications for the TC approach. Cerebral magnetic resonance angiography (MRA) screening, if necessary supplemented by a transcranial Doppler ultrasound, was performed to evaluate the circle of Willis and collateral cerebral blood flow to identify patients with the potential for cerebral hypoperfusion. The circle of Willis provides compensation for the reduced blood flow through the ipsilateral carotid during clamping and obstruction by the delivery catheter. Thus, absence of severe stenosis or occlusion of the contralateral carotid or vertebral arteries were verified. All MRAs and transcranial Doppler ultrasounds were interpreted by neurovascular radiologists to inspect adequate collateral cerebral blood flow and evaluate the risk of cerebral hypoperfusion. In all the patients deemed eligible to the TC access, the latter was the approach used for TAVR.

Procedures

All procedures were performed as previously described(13,14). For primary access both common carotid arteries were eligible while the left side was favoured because it provides superior coaxial alignment between the aortic root and the transcatheter heart valve (THV) during deployment. General anaesthesia as well as local anaesthesia with conscious sedation was permitted and left to the decision of the Heart Team. All patients received a loading dose of aspirin (300 mg) and prophylactic antibiotics before the procedure. A temporary pacing wire was inserted through the femoral vein. A 6-French secondary arterial access was inserted through the radial or femoral arteries. Intra-operatively, cerebral perfusion was continually monitored using cerebral oximetry with near infrared spectroscopy (Equanox 7600, Nonin Medical Inc., North Plymouth, Minnesota, USA).

After vertical 2–3 cm incision one or two fingers above the left clavicle, the common carotid artery was carefully dissected to avoid lesion of the vagus nerve. A complementary small

incision 1 cm above the previous one was possible to increase stability for the sheath and the catheter during intravascular navigation. Intravenous heparin was administered to maintain an activated clotting time ≥250 s. A J-tipped soft guidewire was used to guide the JR4 catheter (pigtail or AL1 catheters could have been used, according to crossing difficulties) and then exchanged with a straight-tip guidewire to cross the aortic valve. When the crossing was achieved, the catheter was pushed into the left ventricle, before exchanging the straight guidewire for a stiff guidewire (SAFARI pre-shaped TAVI guidewire 0.035-inch ×300 cm, Boston Scientific Marlborough, MA, USA or Amplatz extra stiff 0.035-inch guidewire, Cook, Inc., Bloomington, Indiana). Pre- and post-dilatation were left to the discretion of the surgeons. After the Edwards-Sapien 3 prosthesis was loaded, the Certitude delivery system, used in all patients, was inserted through the primary carotid access and carefully advanced into the ascending aorta. THV implantation was performed under rapid pacing. Absence of significant peri-prosthetic regurgitation was checked on aortogram before carotid sheath removal. The carotid arterial access was then surgically repaired in a transversal fashion with PROLENE® sutures 5-0 or 6-0, while short clamping proximally and distally to the vascular access. Post-operative transthoracic echocardiography and carotid Doppler ultrasonography were performed before hospital discharge.

Clinical endpoints

Procedural success was defined as a successful implantation of a single THV, in the appropriate aortic position and without aortic rupture. 30-day clinical endpoints are reported according to the updated Valve Academic Research Consortium (VARC-2)(15). All cerebrovascular events were recorded. Whenever stroke and transient ischemic attack was suspected, patients underwent examination by a senior neurologist and underwent diagnostic

neuroimaging whenever indicated according to the neurologist. Stroke and transient ischaemic attack were defined in accordance with the definition of a central nervous system (CNS) type 1 and type 3.a event respectively, as defined by the Academic Research Consortium (ARC)(16).

Statistical analysis

Continuous variables are presented as a median ± interquartile range, and categorical variables are presented as frequencies and percentages. The 30-day survival curve was modelled using the Kaplan-Meier method. Analyses were performed using SPSS 23 software (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp).

RESULTS

Out of the 6680 patients whom underwent TAVR at the 13 participating centers during the study period, a total of 314 patients (4.7%) were included in this multicentre cohort with a median (interquartile range) age of 83 (78-88) years old, two thirds of them were males, with intermediate to high surgical risk (STS mortality risk score 5.8% [4-8.3]), and most of them were severely dyspnoeic with a New York Heart Association functional class III or IV in two thirds of the patients. One third of the patients had atrial fibrillation, two thirds had moderate to severe chronic renal failure, and most of the patients presented with peripheral artery disease (64%).
TC-TAVR was performed under general anaesthesia in 91% of cases in this cohort, mostly through the left carotid (73.6% of cases) and procedural success was achieved in 97% of procedures.

Mortality

Procedure failures (3%) accounted for three patients who required a valve-in-valve procedure for persistent severe angiographic aortic regurgitation, three annulus ruptures, all of

which were fatal: two patients died during the procedure, the third patient died on day 3; 2 patients had conversion to open surgery because of an impossible carotid crossing due to excessive tortuosity; finally, one patient had left-ventricle perforation by the stiff guidewire. 30-day mortality was 3.2% (10 patients).

Morbidity

Major bleeding was observed in 13 patients (4.1%) while major bleeding was related to the carotid access in only one patient who presented a cervical haematoma treated medically, but who needed a transfusion of two units of red blood cells. Three patients (1%) suffered from a tamponade. Five patients (1.6%) presented a major vascular complication, two of which concerned the carotid access. Two patients (0.6%) suffered from per-operative coronary obstruction leading to a ST-segment elevation acute myocardial infarction, resulting in patient death in one of them 6 days after the procedure.

At 30 days 16.2% of patients required a permanent pacemaker. 5.1% of patients had moderate to severe paravalvular leak on the control transthoracic echocardiogram. Furthermore, the median post-implant echocardiographic mean gradient was 11 (8-13) mmHg. The median hospital stay was 7 days (5-10).

Cerebrovascular events

Five patients (1.6%) presented a stroke or transient ischaemic attack (TIA): three strokes occurred within 24 hours after the implantation (one ipsilateral and two contralateral to the carotid access) and two patients presented a TIA 10 and 12 days after the procedure (both contralateral to the carotid access). Of the patients who suffered from peri-operative stroke/TIA,

only one had a history of atrial fibrillation and none had a history of prior stroke or transient ischaemic attack.

DISCUSSION

This descriptive study reports the largest contemporary cohort to date of transcarotid TAVR and demonstrates the safety and efficacy of the transcarotid approach for TAVR with the Edwards Sapien 3™ transcatheter heart valve (THV).

The Certitude delivery system is usually used to deliver the Sapien 3 THV transapically; it is compatible with the low profile 18 French Certitude sheath for the 23 and 26 mm valve and the 21 French Certitude sheath for the 29 mm valve (outer diameter 25 Fr). It has an integrated pusher to streamline the procedure and an articulation feature to facilitate the coaxial positioning. In this cohort the Certitude delivery system was used to implant the THV through both the left and right carotid artery. Major vascular complications have been reported to be inversely correlated with reduced delivery profile(17), although in this cohort we have not witnessed such a relationship for the transcarotid approach since all major vascular complications occurred with 23 or 26 mm Sapien 3 devices, possibly due to the surgical nature of the access that allows direct repair of the access after THV delivery. Furthermore, major bleeding was observed in 4% of patients in this cohort, which is lower than previous data with transfemoral TAVR of the Sapien 3 THV (18).

Stroke is a major concern for the transcarotid approach. This study found a low (1.6%) rate of stroke or transient ischaemic attack at 30 days, which is lower than observed in the PARTNER 2 trial (5.5%) that included predominantly transfemorally treated patients (19) but

comparable to previous observational data with the Medtronic CoreValve™ (2.2%)(10). Extensive pre-operative evaluation of the cerebrovascular anatomy with MSCT, MRA and Doppler in patients eligible for the transcarotid approach might have selected patients at lower risk of cerebrovascular events. Another explanation might be the dislodgement of aortic atherosclerotic plaques by the delivery system by friction during transfemoral TAVR, which is reduced during transcarotid TAVR since the latter allows easier alignment with the aortic annulus. Despite initial reluctance towards this approach due to the proximity to the brain, several reports, including the presented study, reported reassuring data regarding neurological outcomes, which contributed to the acceptance and expansion of this approach(3,9,10). This might be explained by the more extensive experience with the carotid approach amongst cardiovascular surgeons, a less invasive surgery than with the transapical approach that requires thoracotomy, or the transaortic approach that requires sternotomy, and less challenging than the transcaval approach. A recent report from the CoreValve US Pivotal Trial and Continued Access Study substudy analysis provided reassuring data regarding the transaxillary approach, further suggesting that non-transthoracic alternative approaches should be favoured(20,21).

The thirty-day mortality rate remains acceptable with the transcarotid approach in this study (3.2%), comparable to the PARTNER 2 trial intermediate surgical risk cohort (mean STS score 5.8%) and lower than previous observational reports with the transcarotid access in higher risk patients (6-7%)(9,10). The incidence of annulus ruptures in this study is comparable to the incidence reported in the literature (1%). However it is worth noting that the existing literature supports the hypothesis that balloon-expandable valves are at higher risk of annulus rupture and appropriate preventive measures should be observed(22). Two conversions to open surgery were observed in this registry and were due to excessively tortuous carotid anatomy. This observation

emphasizes that excessive tortuosity of the carotid artery should be considered as a contraindication to the TC approach. Also, the TC access should only be attempted after careful evaluation of its' feasibility on pre-operative MSCT. The rate of 30-day moderate to severe perivalvular leak in this cohort (5.1%) is comparable to other recent studies that reported the rates to be between 3 and 10% after TAVR(2,3,19,23). Further research is warranted to investigate if superior coaxial alignment provided with the TC approach could yield lower risk of prosthetic regurgitation that the transfemoral approach. Furthermore, the median duration of hospital stay was 7 [5-10] days. This is shorter than the median 9 days from non-transfemoral TAVR to discharge reported in the FRANCE TAVI registry(3). The observed new pacemaker rate was 16%, which is slightly higher than previous reports(24); this may be due to variations in indications among participating centres, or oversizing practice. Indeed, the rate of new pacemakers varied between 7 and 33%.

Study limitations

This prospective observational study is subject to bias. Only patients treated with the Sapien 3 device were included in the presented study. Outcomes of this study represent those of tertiary high-volume TAVR centres used to the transcarotid approach, thus should be interpreted with caution. Registry data can also be subject to under-reporting of complication rates(25). Furthermore, follow-up was stopped in this study at thirty days and a more extended follow-up might provide further insight regarding long-term outcomes.

CONCLUSION

The transcarotid approach for TAVR using the Sapien 3 transcatheter heart valve was safe and effective in this multicentre French registry. The transcarotid approach could be considered as a safe alternative approach for TAVR when the transfemoral access is prohibited.

PERSPECTIVES

WHAT IS KNOWN?

Previous reports suggested that transcarotid transcatheter aortic valve replacement using self-expandable devices was a safe alternative when transfemoral approach was precluded.

WHAT IS NEW?

Procedural success and 30-day mortality of the transcarotid approach are comparable to those of transfemoral approach reported in randomized trials using the Sapien 3 device, while cerebrovascular and major bleeding events were similar to those reported with the self-expandable devices in spite of design differences of transcatheter heart valves and delivery systems.

WHAT IS NEXT?

Further research is warranted to provide direct comparative evaluation of the transcarotid approach to the transfemoral as well as other alternative approaches such as transsubclavian, transapical, transaortic and transaortic. Also, data on safety of transcarotid transcatheter aortic valve replacement in low risk patients and all comers would allow operators to consider this approach regardless of the risk profile.

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FIGURE LEGEND

Figure 1: Survival curve after TC TAVR.

N°: number; TC: transcarotid; TAVR: transcatheter aortic valve replacement

Table 1: Baseline Characteristics

	N=314
Age	83 (78-88)
Male	197 (62.7)
BMI	25 (23-28.7)
Euroscore I	18.8 (14.4-26.8)
Euroscore II	5.7 (3.7-8.3)
STS score	5.8 (4-8.3)
NYHA class III or IV	209 (66.6)
Atrial fibrillation	107 (34.1)
Diabetes mellitus	84 (26.8)
Diabetes mellitus requiring insulin	28 (8.9)
Peripheral artery disease	201 (64)
Chronic respiratory failure	101 (32.2)
Prior stroke or TIA	36 (11.5)
Prior pacemaker	40 (12.7)
Coronary artery disease	167 (53.2)
Myocardial infarction	57 (18.2)
Prior PCI	123 (39.2)
CABG	63 (20.1)
Cardiac surgery non-CABG	15 (4.8)

Moderate to severe chronic renal failure	191 (60.8)
LVEF pre-TAVR	55 (45-60)
Mean gradient (mmHg)	47 (40-52)
Functional aortic surface (cm^2)	0.8 (0.7-0.9)
Pulmonary hypertension	179 (57)

Table 2: Outcomes

	N=314
General anesthesia	286 (91.1)
Pre-implant balloon valvulopasty	115 (36.6)
Post-implant balloon valvulopasty	45 (14.3)
Left carotid	231 (73.6)
Prosthesis size (mm): - 20 - 23 - 26 - 29	 2 (0.6) 83 (26.4) 147 (46.8) 82 (26.1)
Procedural success	305 (97.1)
Reasons of procedural failure - Valve-in-valve - Annulus rupture - Conversion to open surgery - Left-ventricle perforation	 3 (1) 3 (1) 2 (0.6) 1 (0.3)
Procedural mortality	3 (1)
STEMI	2 (0.6)
Tamponade	3 (1)
Valve malpositioning	0

Major vascular complication	5 (1.6)
Major bleeding	13 (4.1)
Moderate to severe PVL on TTE	16 (5.1)
Post-implant echocardiographic mean gradient	11 (8-13)
New permanent pacemaker	51 (16.2)
Stroke/TIA (30 days)	5 (1.6)
Hospital stay (days)	7 (5-10)
Mortality (30 days)	10 (3.2)