Transaxillary TAVR Leads to Shorter Ventilator Duration and Hospital Length of Stay Compared to Transapical TAVR

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Abstract: There is an increasing need for alternative access in patients with prohibitive surgical risk who have unsuitable anatomy for transfemoral transcatheter aortic valve replacement (TAVR). Data on differences in periprocedural outcomes via alternative access sites are scarce. We performed a retrospective analysis of patients who underwent Transaxillary (TAX) or Transapical (TAP) TAVR at our center from 2012 to 2019. All data was summarized and displayed as mean ± SD for continuous variables and number of patients in each group. A propensity score was created for each patient in the dataset to determine the probability of axillary vs apical access. We adjusted for propensity score using multivariate logistic regression. A total of 102 patients underwent TAVR via alternative access: 28 patients (27%) via TAX and 74 patients (73%) via transapical (TAP)

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access. The average time to extubation in the TAX group was 5.3 ± 3.5 hours vs 9.1 ± 8.8 hours in the TAP patients ($P = 0.03$). None of the TAX patients required reintubation compared to 23% of TAP TAVR ($P = 0.003$). The average hospital length of stay for TAX was 2.4 ± 2.0 days compared to 6.9 ± 3.3 days ($P < 0.0001$) for TAP. TAX TAVR patients had significantly lower re-intubation rates, shorter time to extubation and in-hospital length of stay, but higher pacemaker implantation rates. TAX TAVR had improved periprocedural outcomes compared to TAP TAVR and remains the preferred TAVR alternative access. (Curr Probl Cardiol 2021;46:100624.)

Introduction

Transcatheter aortic valve replacement (TAVR) has become one of the widely accepted options to treat patients with severe aortic stenosis across all surgical risk profiles.[1-5] Transfemoral (TF) access remains the gold standard for TAVR as it is the most studied access site, easiest for the operator and well tolerated by patients.[6-9] An estimated 15% of patients are unable to undergo TAVR secondary to unfavorable aorto-iliofemoral anatomy or tortuosity, advanced calcifications, small caliber vessels, or prior vascular surgery.[10] Fanaroff et al, identified peripheral arterial disease as an independent predictor of higher 1-year all-cause mortality in patient undergoing TF TAVR.[11] Initially, the antegrade transapical (TAP) approach was the only alternative TAVR access for the balloon expandable TAVR valves.[12]

The evolution of the newer generation of TAVR valves and need for improved outcomes have led to multiple new alterative access sites including transcaval, TAP, transcarotid, transaxillary (TAX), and transaortic with limited and variable periprocedural outcome data reported.[13-18] Outcomes for TAP TAVR have been inferior to other alternative access sites in prior studies, resulting in higher mortality, major or life-threatening bleeding, acute kidney injury, and longer hospital length of stay.[19,20] Prior literature has not reported detailed differences in intensive care unit (ICU) length of stay, complications, and reintubation rates in TAX vs TAP. This is a single center, retrospective analysis on the peri-procedural and mid-term procedural outcomes in 2 non-TF TAVR access approaches utilizing both self-expandable CoreValve system (Medtronic Inc, Minneapolis, MN) and balloon-expandable Sapien valve (Edwards Lifesciences, Irvine, CA).

Methods

Patient Selection

Our analysis includes 102 consecutive patients with severe AS receiving either TAX or TAP TAVR between December, 2012 and October, 2019 at Ochsner Medical Center in New Orleans, Louisiana. All patients had previously been declined for surgical aortic valve (AV) replacement due to high surgical risk and were ineligible for TF TAVR secondary to unfavorable anatomy. An interdisciplinary heart team determined eligibility for TAVR and agree upon either a TAX or TAP access route. Preprocedural work-up included transthoracic, coronary angiography and contrast-enhanced multislice computed tomography for access site assessment and aortic root measurements.

Procedural Aspects

All procedures were performed under general anesthesia by an interdisciplinary heart team. TAX access was obtained via a left subclavicular cut-down. Based on surgeon preference, the left axillary artery was accessed via an arteriotomy and temporary attachment of a Gore-Tex conduit (W. L. Gore & Associates, Inc, Flagstaff, AZ) or surgically opened longitudinally and closed via a double purse-string suture (Fig 1, Fig 2). The TAVR procedure itself was performed in accordance with the individual manufacturer recommendations. After valve implantation, adequate vessel closure was verified by angiography. The TAP TAVR was performed via an anterior thoracotomy and if needed, partial rib removal. The pericardium was exposed, purse-string sutures were placed at the apex. The apex was accessed via a needle and a TAVR valve was deployed over a wire (Fig 3). The apex was closed with purse-string sutures at the apex and left thorax drain was placed at time of chest closure. All patients received a temporary venous pacemaker during the procedure and it was removed the next day if no significant conduction abnormalities occurred. All patients were extubated either immediately post procedure or in the ICU per our center's extubation criteria protocols. Patients were transferred to a cardiac step-down floor when clinically appropriate and discharged once criteria were met. Dual antiplatelet therapy was prescribed with aspirin 81 mg and clopidogrel 75 mg daily for at least 6 months, followed by aspirin 81mg daily for life. Patients on oral anticoagulation were bridged with intravenous unfractionated heparin and resumed oral anticoagulation shortly after the procedure.

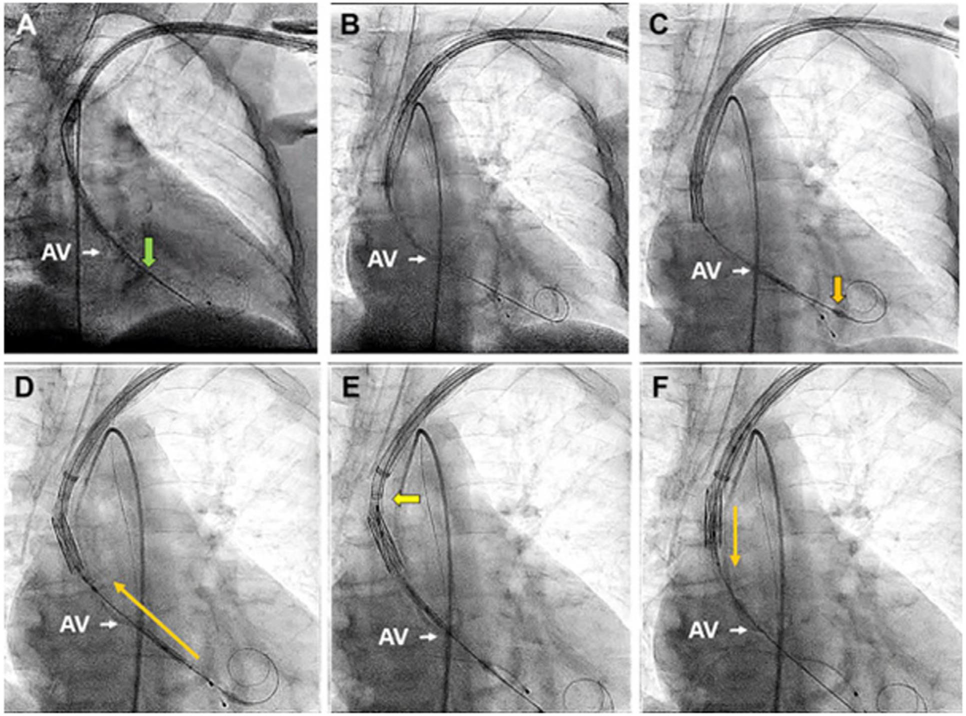

FIG 1. Maneuvers of the SAPIEN 3 Valve System in TAX TAVR. Maneuvers of the SAPIEN 3 Valve System in Transaxillary TAVR – Radiographic pictures. The dilator tip (green arrow) of Edwards sheath crosses the aortic valve (AV) (A). As the delivery system is advanced forward for the S3 valve to exit the sheath (B), the nose cone would be in the left ventricle (orange arrow) (C). The balloon is then pulled back (orange arrow) toward the S3 valve (D), which may result in the catheter bending (yellow arrow) requiring adjustments to be done in a stepwise fashion (E). Final step advances the valve forward (orange arrow) to mount it onto the balloon (F). AV, aortic valve; TAVR, transcatheter aortic valve replacement; TS, transaxillary/subclavian. Bapat V, Tang GHL. Axillary/Subclavian Transcatheter Aortic Valve Replacement: The Default Alternative Access? JACC Cardiovasc Interv. 2019 Apr 8;12(7):670-672.

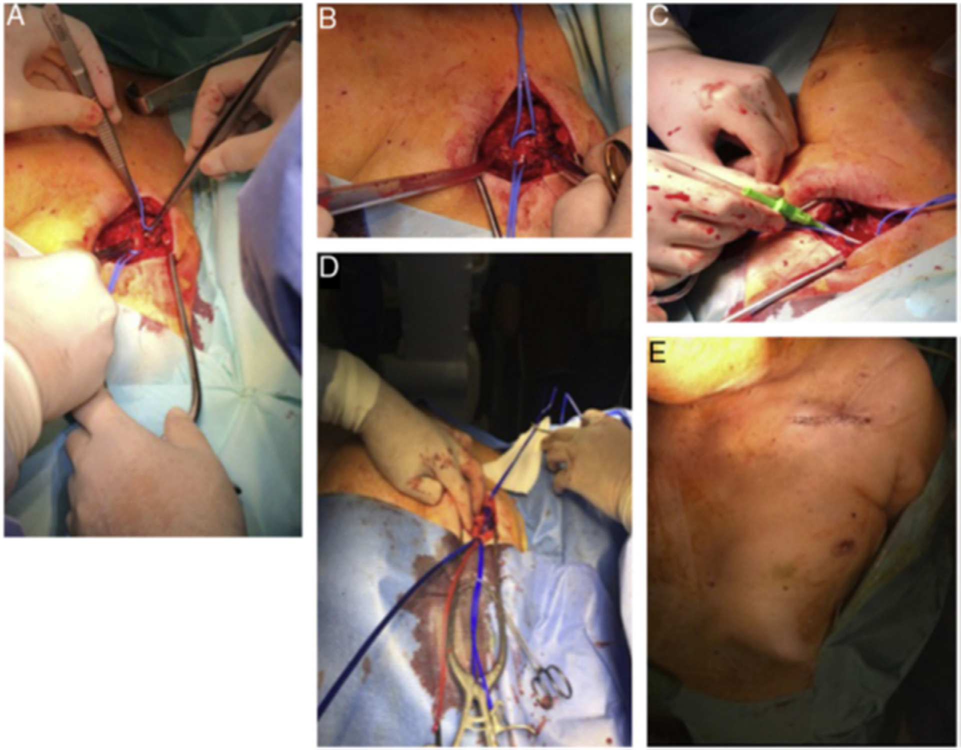

FIG 2. Surgical technique for Transaxillary TAVR. Surgical technique for Transaxillary TAVR. A: cut down to expose the right axillary artery. B: purse-string suture of the axillary artery. C: 6-Fr sheath in the axillary artery after puncture. D: Portico valve in the axillary artery delivered without a sheath, using an extra support guidewire. E: closure of the surgical wound. Cardenal Piris RM, Araji Tiliani O, Díaz Fernández JF, et al, Sheathless transaxillary transcatheter aortic valve implantation using the Portico valve system. Initial experience of a real-world "Heart Team". Rev Esp Cardiol (Engl Ed). 2020 Feb;73(2):178-180.

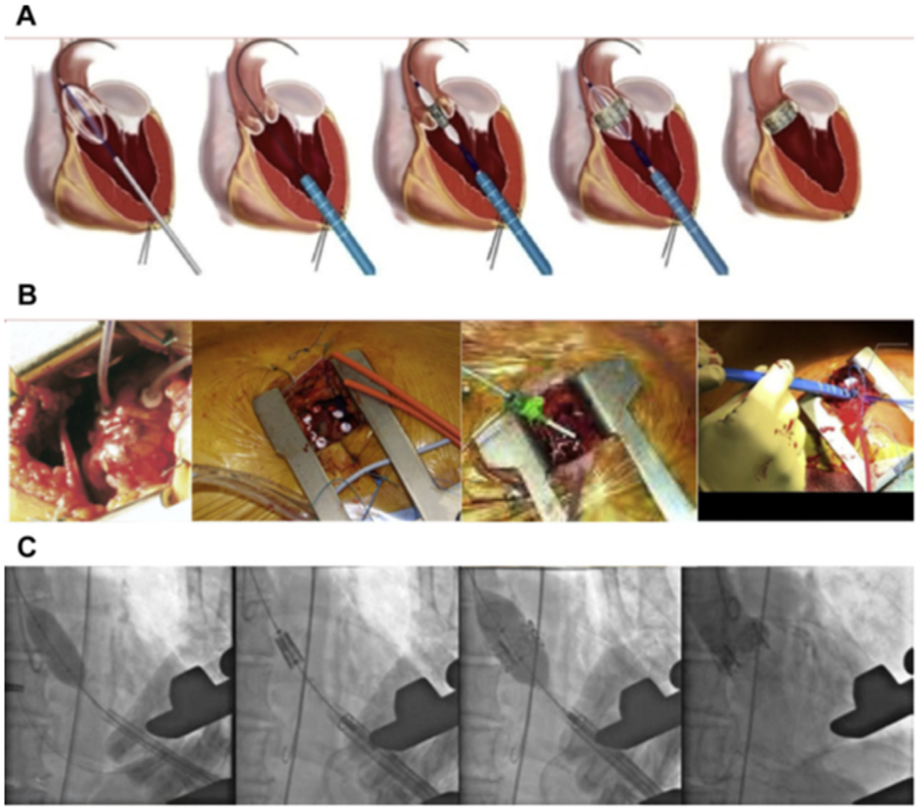

FIG 3. Transapical TAVR implantation. Transapical (TA-TAVR): (A) concept, (B) access and closure, (C) valve deployment. Sarkar K, Sarkar M, Ussia GP. Current status of transcatheter aortic valve replacement. Med Clin North Am. 2015 Jul;99(4):805-33.

Data Management and Follow Up

Our study was designed as a retrospective analysis of data from a single center experience with TAVR in 102 consecutive patients. All relevant baseline, procedural, and follow-up data were collected in a dedicated database. After hospital discharge 30-day data were collected at an in-clinic visit and 1-year mortality follow up data were collected via chart review.

Statistics

All data were summarized and displayed as mean ± SD for continuous variables and as counts (proportions) for categorical variables. Student's t-test and Pearson chi-square test or Fisher's exact test were used to evaluate statistical significance between continuous and categorical variables, respectively. Differences in outcomes confounded by baseline characteristics were assessed using propensity matching for each patient in TAP and TAX TAVR data sets.

The variables included in the multivariate logistic regression model were age, sex, body mass index, New York Heart Association class, Society of Thoracic Surgery score, left ventricular ejection fraction, smoking status, presence of permanent pacemaker, AV area, AV mean gradient, peak velocity and the presence of each of the following comorbidities - CAD, Diabetes, Hypertension, PAD, Atrial Fibrillation, and Stroke. The propensity score was adjusted using multivariate logistic or linear regression, as appropriate. All analyses were performed using STATA version 15 (StataCorp, College Station, Texas). Statistical significance was defined as 2-tailed P value of <0.05.

Results

Baseline Characteristics

A total of 102 patients underwent TAVR via alternative access. 28 patients (27%) via TAX and 74 patients (73%) via TAP access. The mean age in the TAX group was 75.2 ± 8.2 and 75.9 ± 8.3 in the TAP group. Peripheral vascular disease was present in 75% of patients in the TAX group and in 84% of the TAP group. Significantly more patients had diabetes in the TAX group compared to the TAP group (60.7% vs 37.8%, $P = 0.05$)

Baseline characteristics and demographic information is summarized in Table 1.

Table 1. Baseline characteristics

	Transaxillary n (%) N = 28	Transapical n (%) N = 74	*P* value
Age (SD), years	75.2 (8.2)	75.9 (8.3)	0.7
Age, Median (IQR), years	75 (69-83)	76 (71-82)	
Male sex	21 (75)	41 (55)	0.12
NYHA 3-4	21(75)	50 (68)	0.63
BMI (SD) Kg/m^2	28.6 (6.2)	27.1 (2.2)	0.07
BMI, Median (IQR) Kg/m^2	26.7	27	
STS (SD)	5.5 (3.7)	6.9 (4.0)	0.11
STS, Median (IQR)	4.9	6.3	
CAD	26 (93)	65 (88)	0.72
DM II	17 (61)	28 (38)	0.05
HTN	25 (89)	73 (99)	0.06
PAD	21 (75)	62 (84)	0.39
AF	14 (50)	29 (39)	0.37
LVEF (SD) EF%	48.7 (15)	50.5 (13.5)	0.56
LVEF Median (IQR)	52.5	55	
CVA	7 (25)	14 (19)	0.58
CABG	13 (46)	37 (50)	0.82
PCI	17 (61)	33 (45)	0.18
Hx of Smoking	25 (89)	62 (84)	0.75
COPD	16 (57)	34 (46)	0.37
ESRD	0	0	1.0
Prior PPI	1 (3.6)	9 (12)	0.27
Valve Type			
BEV	6 (21.4)	74 (100)	
SEV	22 (78.6)	0	
Valve Size, mm			
	23-2	23-38	
	26-6	26-26	
	29-21	29-9	
		20-1	
AVA (SD) cm^2	0.87 (0.8)	0.69 (0.2)	
AV Mean Gradient (SD) mmHg	48.1 (15.7)	45.9 (12.9)	
PV (SD) m/s	4.3 (0.8)	4.35 (0.75)	

AF, atrial fibrillation; AV, aortic valve; AVA, aortic valve area; BEV, balloon expandable valve; BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; DM II, diabetes mellitus type II; ESRD, end stage renal disease; HTN, hypertension; Hx, history; IQR, interquartile range; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; PPI, permanent pacemaker insertion; PV, peak velocity; SD, standard deviation; SEV, self-expanding valve; STS, Society of Thoracic Surgery.

Periprocedural Characteristics

There was a trend toward shorter procedural time in TAX TAVR, but it did not meet statistical significance compared to TAP (109.8 ± 43.6 minutes vs 123.8 ± 30.7 minutes; *P*= 0.07). Post procedural balloon aortic valvuloplasty was needed in 7.1% of TAX patients and 5.4% of TAP patients to optimize valve placement. Only 1 TAX patient needed a second valve secondary to severe paravalvular leak post procedure. Only 1 patient (1.4%) was put on cardiopulmonary bypass in the TAP cohort.

Short and Mid-term Clinical outcomes

The average time to extubation in the TAX group was 5.3 ± 3.5 hours vs 9.1 ± 8.8 hours in the TAP patients (P= 0.03). None of the TAX patients required reintubation compared to 23% of TAP TAVR (P= 0.003).

The average hospital length of stay for TAX was 2.4 ± 2.0 days compared to 6.9 ± 3.3 days (P< 0.0001) for TAP. Twenty-eight percent of patients in the TAX group needed new pacemaker implantation vs 9.5% of patients in the TAP group (P = 0.02).

More patients post TAX TAVR required permanent pacemaker insertion (PPI) compared to TAP TAVR (28.6% vs 9.5%, P= 0.003). There was no significant difference in strokes, paravalvular leak, or 30-day Mortality.

After adjusting for propensity score, the difference in hospital LOS remained robust (unadjusted −4.47 95%CI [−5.84, −3.1), P value <0.001 vs adjusted −4.52 95%CI [−6.25, −2.80], P value <0.001). The difference in new PPM was no longer significant after including the propensity score in the logistic regression model (unadjusted OR 3.77 95%CI [1.22, 11.69], P value 0.021 vs adjusted OR 1.70 95%CI [0.40, 7.19], P value 0.469). No difference was observed in 30-day mortality and stroke even after adjusting for propensity score (Table 3). Periprocedural characteristics and outcomes are summarized in (Table 2) and (Fig 4).

Discussion

We have shown in this retrospective analysis good outcomes for TAP TAVR and even better outcomes for TAX TAVR. This is driven by shorter ventilator duration, ICU LOS, and lower rates of reintubation in the TAX TAVR patients.

Ventilator Duration and Hospital Length of Stay

In our study, all patients in this cohort were electively intubated prior to procedure. Patients who underwent TAX had a shorter time to extubation compared to a TAP approach and none of the TAX patients required reintubation compared to 23% of TAP TAVR (P= 0.003). There is limited data on prior published cohorts on the duration of mechanical ventilation and ICU LOS between the 2 approaches. Dahle et al reported

Table 2. Procedural characteristics and outcomes of transaxillary compared to transapical TAVR

	Transaxillary n (%) N = 28	Transapical n (%) N = 74	*P* value
General anesthesia	1 (100)	74 (100)	1.0
BAV post	2 (7.1)	4 (5.4)	0.66
LOS (SD)	2.4 (2.0)	6.9 (3.3)	<0.0001
LOS, median	2 (1-3)	6 (5 -8.2)	
ICU LOS (hrs)	45.7 (31)	61.7 (47)	0.1
ICU LOS, Median	32 (6-51)	41.5 (29-94)	
Time to extubation (hours)	5.3 (3.5)	9.1 (8.8)	0.03
Median time to extubation (hours)	3.5	7	
Procedure time, median	108 (86.6-130)	123.5 (97-147)	
Cardio-Pulm bypass	0	1 (1)	
VIV TAVR	0	0	
Emergent need for second valve	1 (3.5)	0	
30-day endocarditis	0	0	
New LBBB	10 (36)	14 (19)	0.12
Post TAVR PPI	8 (28.5)	7 (9.5)	0.026
Reintubation	0	17 (9.5)	0.003
Vascular Injury	1 (3.5)	0	1.0
30-day need for dialysis	1 (3.5)	5 (7)	1.0
30-day post MI	0	8 (11)	0.1
Post MG	8.5 (4.3)	11.1 (3.7)	0.003
Post MG, median	8	11	
Post PV	1.5 (0.6)	2.2 (0.5)	<0.0001
Minor bleed	7 (25)	7 (9.5)	0.055
Major bleed	1 (3.5)	5 (7)	1.0
30-day CVA	1 (3.5)	1/68 (1.5)	0.5
30-day TIA	0	1/68 (1.5)	1.0
GFR pre	52.2 (11.8)	51 (11.9)	0.64
GFR post	52.2 (11.3)	50.6 (12.5)	0.55
CVA type			
Ischemic	1 (3.5)	1 (1.4)	
Hemorrhagic	0	0	
Cause of death (30-day)			
Renal Failure	0	2 (2.7)	
VT Arrest	0	1 (1.4)	
Cardiac arrest	0	2 (2.7)	
Withdrawal of care	0	1 (1.4)	
Unknown	2 (7.1)	1 (1.4)	
Device success	28 (100)	64/67 (86.5)	0.55
PVL			
0	6	44	
1	5	14	
2	8	14	
3	2	2	
4	0	0	
Intra-procedural Mortality	0	0	
30- day mortality	2/28 (7.1)	7/73 (9.5)	1.0
1-yr mortality	0/14 (0)	13/70 (17.6)	0.11

AF, atrial fibrillation; BAV, balloon angioplasty aortic valve; CVA, cerebrovascular accident; GFR, glomerular filtration rate; ICU, intensive care unit; LBBB, left bundle-branch block; LOS, length of stay; MG, mean gradient; MI, myocardial infarction; PV, peak velocity; PVL, paravalvular leak; TAVR, transcatheter aortic valve replacement; TIA, transient ischemic attack; VIV, valve-in-valve; VT, ventricular tachycardia.

Table 3. Logistic regression: propensity score adjustment using regression analysis

Outcome	Unadjusted OR (95%CI)	*P* value	Adjusted OR (95%CI)	*P* value
30-day mortality	0.73 (0.14, 3.72)	0.700	1.06 (0.14, 7.88)	0.951
New PPI	3.77 (1.22, 11.69)	0.021	1.70 (0.40, 7.19)	0.469
Stroke	2.48 (0.15, 41.11)	0.526	3.48 (0.11, 115.22)	0.484
	Unadjusted (95%CI)		Adjusted (95%CI)	
Hospital LOS	−4.47 (−5.84, −3.1)	<0.001	−4.52 (−6.25, −2.80)	<0.001

CI, confidence interval; LOS, length of stay; OR, odds ratio; PPI, permanent pacemaker insertion.

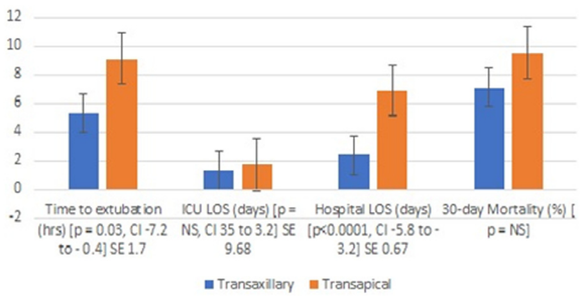

FIG 4. Periprocedural Outcomes in TAX vs TAP TAVR.

significantly shorter ICU stay in TAX vs TAP TAVR, 26.3 hours vs 37 hours respectively.[13] Kirker et al, noted ICU stay median 47.4 hours (26.6-73.5) (interquartile range) and ventilator median 6 hours (4.5-7.0) (interquartile range) in TAP TAVR.[21] Our study showed a non-significant trend toward shorter ICU LOS, 45.7 hours for TAX TAVR compared to TAP TAVR 61.7 hours. Thourani et al reported ICU stay mean 107 ± 181 hours and ventilator mean time 56 ± 175 hours for TAP TAVR.[22] The longer intubation time among TAP patients may be explained by a more invasive procedure which includes a thoracotomy and resultant hemodynamic changes associated with these invasive procedures including chest tube placement. Additionally, there is likely an increased need for opioid control for analgesia with the more invasive intrathoracic approach of TAP compared to TAX which could lead to delayed time to patient extubation. Conscious sedation with local anesthesia, in lieu of general anesthesia, is an evolving method to perform TF TAVR with lower ICU LOS, fewer complications, and lower mortality.[23] This is currently applicable to TF TAVR, but there is not enough data to draw conclusions concerning TAX or TAP TAVR. TAX access has previously resulted in lower 30-day mortality, shorter lengths of ICU and hospital stay compared with TAP and transaortic access.[17,24] In our study, TAX had a significantly shorter hospital length of stay compared to TAP approach (2.4 ± 2.0 days, 6.9 ± 3.3 days, P value <0.0001).

Permanent Pacemaker Insertion

TAVR carries an increased risk of conduction disturbances, notably new-onset left bundle-branch block and advanced atrioventricular block.[25] A study reported an incidence of high-degree atrioventricular block/complete heart block to be in 7.4% intraoperatively with persistent complete heart block occuring in 4.7% of those patients.[26]

In our study, patients who underwent TAX TAVR had a relatively high (29.6%) new PPI rate compared to TAP TAVR patients (10.4%). The higher PPI rate could be explained by the high initial implantation rate of self-expandable valves. The incidence of conduction disturbances in our TAX approach while statistically higher than TAP, was consistent with previously reported PPI rates.[27,28] This finding of higher PPI among TAX TAVR patients compared to the TAP patients could be attributed to valve depth and/or increased valve manipulation during implantation in the TAX approach. Currently, with improving operator experience and increased use of balloon-expandable valves, we could see further decreases in future TAX TAVR postprocedural PPI rates.

Vascular Complications

Despite limited data and limited experience with the TAX approach, procedural success is high with a low vascular complication rate.[13] All TAX TAVR in our study were preformed via a subclavian surgical cut down. Percutaneous access of the subclavian artery has also been reported but prior studies have shown a high complication rate, with 1 series reporting a 29% subclavian artery stenting rate for failed arterial closure devices.[29] The concern for the percutaneous approach arises around adequate closure of the axillary artery due to its anatomical location and difficulties performing manual compression of the arteriotomy site, and difficulty using arterial closure devices.[30] The proximity and posterior orientation of the axillary artery to the axillary vein increases the risk of vascular injury with a percutaneous approach. Post procedural hemostasis is crucial to eliminate the occurrence of major access site complications.[30]

Implantable Cardiac Defibrillator and Myocardial Infarctions

The previous presence of a pacemaker/implantable cardiac defibrillator or a patent left internal mammillary artery (LIMA) graft were not considered as a contraindication to TAX vascular access provided that the diameter of the subclavian artery was >7 mm.[31] Patients with previous pacemaker/implantable cardiac defibrillator implants did not result in a limitation or result in difficulty obtaining TAX access. There is an inherent concern of compromising coronary perfusion in patient with a patent LIMA graft.[31] However, our study showed no occurrence of peri-procedural myocardial infarction in TAX patients, including 13 patients with prior coronary artery bypass graft. TAX access safety is further supported by Modine, et al who studied 19 high-risk patients with previous LIMA grafts who underwent TAX TAVR without any occurrence of LIMA obstruction.[32]

Stroke and Use of Cerebral Protection Devices

Prior registries showed the TAX approach has a higher 30-day stroke 6.5% vs 3.5% vs a TF approach and 6.3% in TAX compared to 3.1% a TAP approach (P value < 0.001).[13,14] In our cohort, stroke occurred within 30 days post procedure in 2 patients, 1 in both TAP and TAX TAVR approach ($P = 0.5$). The higher occurrence of stroke TAX TAVR in prior studies compared to TAP TAVR could be attributed to micro-emboli to the carotid arteries from catheter manipulation and calcifications from preballoon dilation of the stenotic AV prior to TAVR. The current literature has not been able to adequately address whether there is a differential stroke risk for a left vs a right axillary artery access site. A potential future stroke prevention technique could be to use a cerebral protection device via a right radial artery approach which would allow for an unobstructed left subclavian artery for left TAX access.[33] Currently, there is no data supporting the use of cerebral embolic protection systems during TAVR and their benefits during TAVR access remain unclear.

Limitations

The following limitations are inherent in our study. (1) The study includes various transcatheter heart valves with different sample sizes of each individual valve, not allowing a comparative analysis of procedural efficacy. (2)

Data is from a single center, but with multiple experienced operators. (3) Data was collected retrospectively and overall had a small sample size. (4) We electively choose to intubate all the patients in the study. Time to extubation and re-intubation results may not therefore be applicable to centers that do not choose to intubate this patient population.

Conclusions

TAX TAVR has impressive outcomes and should be first line for alternative access TAVR. We showed high device success rate and low periprocedural complication rates. TAX TAVR compared to TAP had shorter ICU and overall hospital length of stay and shorter ventilator duration

REFERENCES

1. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;364:2187–98.
2. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363:1597–607.
3. Waksman R, Rogers T, Torguson R, et al. Transcatheter aortic valve replacement in low-risk patients with symptomatic severe aortic stenosis. *J Am Coll Cardiol* 2018;72:2095–105.
4. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med* 2019;380:1695–705.
5. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med* 2019;380:1706–15.
6. Gilard M, Eltchaninoff H, Iung B, et al. Registry of transcatheter aortic-valve implantation in high-risk patients. *N Engl J Med* 2012;366:1705–15.
7. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. *N Engl J Med* 2014;370:1790–8.
8. Holmes DR, Brennan JM, Rumsfeld JS, et al. Clinical outcomes at 1 year following transcatheter aortic valve replacement. *JAMA* 2015;313:1019–28.
9. Reardon MJ, Van Mieghem NM, Popma JJ, et al. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2017;376:1321–31.
10. Takagi H, Hari Y, Nakashima K, Kuno T, Ando T. ALICE (All-Literature Investigation of Cardiovascular Evidence) Group. Comparison of early and midterm outcomes after transsubclavian/axillary versus transfemoral, transapical, or transaortic transcatheter aortic valve implantation. *Heart Lung J Crit Care* 2019;48:519–29.
11. Fanaroff AC, Manandhar P, Holmes DR, et al. Peripheral artery disease and transcatheter aortic valve replacement outcomes: a report from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Therapy Registry. *Circ Cardiovasc Interv* 2017;10:e005456.

12. Fröhlich GM, Baxter PD, Malkin CJ, et al. Comparative survival after transapical, direct aortic, and subclavian transcatheter aortic valve implantation (data from the UK TAVI registry). *Am J Cardiol* 2015;116:1555–9.
13. 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;12:662–9.
14. Gleason TG, Schindler JT, Hagberg RC, et al. Subclavian/axillary access for self-expanding transcatheter aortic valve replacement renders equivalent outcomes as transfemoral. *Ann Thorac Surg* 2018;105:477–83.
15. Greenbaum AB, Babaliaros VC, Chen MY, et al. Transcaval access and closure for transcatheter aortic valve replacement: a prospective investigation. *J Am Coll Cardiol* 2017;69:511–21.
16. Wee IJY, Stonier T, Harrison M, Choong AMTL. Transcarotid transcatheter aortic valve implantation: a systematic review. *J Cardiol* 2018;71:525–33.
17. Allen KB, Chhatriwalla AK, Cohen D, et al. Transcarotid versus transapical and transaortic access for transcatheter aortic valve replacement. *Ann Thorac Surg* 2019;108:715–22.
18. Debry N, Delhaye C, Azmoun A, et al. Transcarotid transcatheter aortic valve replacement: general or local anesthesia. *JACC Cardiovasc Interv* 2016;9:2113–20.
19. Ciuca C, Tarantini G, Latib A, et al. Trans-subclavian versus transapical access for transcatheter aortic valve implantation: a multicenter study. *Catheter Cardiovasc Interv Off J Soc Card Angiogr Interv* 2016;87:332–8.
20. Chekrallah Chamandi, Ramzi Abi-Akar, Josep Rodés-Cabau, et al. Transcarotid compared with other alternative access routes for transcatheter aortic valve replacement. *Circ Cardiovasc Interv* 2018;11:e006388.
21. Kirker EB, Hodson RW, Spinelli KJ, Korngold EC. The carotid artery as a preferred alternative access route for transcatheter aortic valve replacement. *Ann Thorac Surg* 2017;104:621–9.
22. Thourani VH, Li C, Devireddy C, et al. High-risk patients with inoperative aortic stenosis: use of transapical, transaortic, and transcarotid techniques. *Ann Thorac Surg* 2015;99:817–23. discussion 823-825.
23. Toppen W, Johansen D, Sareh S, et al. Improved costs and outcomes with conscious sedation vs general anesthesia in TAVR patients: time to wake up? *PloS One* 2017;12:e0173777.
24. 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;123:1501–9.
25. Houthuizen P, Van Garsse LAFM, Poels TT, et al. Left bundle-branch block induced by transcatheter aortic valve implantation increases risk of death. *Circulation* 2012;126:720–8.
26. Junquera L, Freitas-Ferraz AB, Padrón R, et al. Intraprocedural high-degree atrioventricular block or complete heart block in transcatheter aortic valve replacement recipients with no prior intraventricular conduction disturbances. *Catheter Cardiovasc Interv Off J Soc Card Angiogr Interv* 2020;95:982–90.

27. Zhan Y, Saadat S, Soin A, Kawabori M, Chen FY. A meta-analysis comparing trans-axillary and transfemoral transcatheter aortic valve replacement. *J Thorac Dis* 2019;11:5140–51.
28. Biondi-Zoccai G, Peruzzi M, Abbate A, et al. Network meta-analysis on the comparative effectiveness and safety of transcatheter aortic valve implantation with CoreValve or Sapien devices versus surgical replacement. *Heart Lung Vessels* 2014;6:232–43.
29. Schäfer U, Ho Y, Frerker C, et al. Direct percutaneous access technique for transaxillary transcatheter aortic valve implantation: "the Hamburg Sankt Georg approach.". *JACC Cardiovasc Interv* 2012;5:477–86.
30. Schäfer U, Deuschl F, Schofer N, et al. Safety and efficacy of the percutaneous transaxillary access for transcatheter aortic valve implantation using various transcatheter heart valves in 100 consecutive patients. *Int J Cardiol* 2017;232:247–54.
31. Petronio AS, De Carlo M, Bedogni F, et al. 2-year results of CoreValve implantation through the subclavian access: a propensity-matched comparison with the femoral access. *J Am Coll Cardiol* 2012;60:502–7.
32. Modine T, Sudre A, Collet F, et al. Transcutaneous aortic valve implantation using the axillary/subclavian access with patent left internal thoracic artery to left anterior descending artery: feasibility and early clinical outcomes. *J Thorac Cardiovasc Surg* 2012;144:1416–20.
33. Ndunda PM, Vindhyal MR, Muutu TM, Fanari Z. Clinical outcomes of sentinel cerebral protection system use during transcatheter aortic valve replacement: a systematic review and meta-analysis. *Cardiovasc Revascularization Med Mol Interv* 2019. S1553-8389(19)30257-X.