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The Transaortic Approach for Transcatheter Aortic Valve Replacement

Initial Clinical Experience in the United States

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Objectives This study sought to investigate the technical feasibility and safety of the transaortic (TAO) transcatheter aortic valve replacement (TAVR) approach in patients not eligible for transfemoral (TF) access by using a device commercially available in the United States.

Background A large proportion of candidates for TAVR have inadequate iliofemoral vessels for TF access. The transapical route (TAP) is the current alternative but is associated with less favorable outcomes. Other access options need to be explored.

Methods Forty-four consecutive patients with inoperable, severe aortic stenosis underwent TAO TAVR in our institution. Procedural and 30-day clinical outcomes data were compared with data from 76 consecutive patients who underwent TAP TAVR at our site. Technical learning curves were assessed by comparing outcomes of the first 20 cases with the subsequent patients who underwent each procedure.

Results The TAO and TAP TAVR groups were similar in terms of device success according to Valve Academic Research Consortium criteria (89% vs. 84%; $p = 0.59$) and rates of the 30-day combined safety endpoint of all-cause mortality, myocardial infarction, major stroke, disabling bleeding, severe acute kidney injury, and valve reintervention (20% vs. 33%; $p = 0.21$). The TAO approach, compared with TAP TAVR, was associated with lower combined bleeding and vascular event rate (27% vs. 46%; $p = 0.05$), shorter median intensive care unit length of stay (3 vs. 6 days; $p = 0.01$), and a favorable learning curve.

Conclusions TAVR via the TAO approach is technically feasible, seems to be associated with favorable outcomes, and expands the current alternative options for access sites in patients with inoperable aortic stenosis who are ineligible for TF TAVR. (J Am Coll Cardiol 2013;61:2341–5) © 2013 by the American College of Cardiology Foundation

Transcatheter aortic valve replacement (TAVR) has revolutionized the management of severe aortic stenosis (AS) in patients who are at high risk or ineligible for surgical aortic valve replacement (SAVR). The Edwards SAPIEN (Edwards Lifesciences, Irvine, California) transcatheter heart valve (THV) with its RetroFlex 3 delivery system, the first clinically available TAVR device in the United States, was approved by the US Food and Drug Administration for transfemoral (TF) TAVR in patients with inoperable, severe AS. However, a significant proportion of patients who would otherwise qualify for TAVR (up to 30% in the PARTNER [Placement of Aortic Transcatheter Valves] trial [1]) are excluded because of inadequate iliofemoral vascular access. In these patients, the transapical (TAP) route was the alternative method of device delivery. Unfortunately, early experience with TAP TAVR suggests a trend toward less favorable periprocedural outcomes (2) and a steep learning curve (3). Thus, other access strategies need to be explored. We describe our initial experience with the transaortic (TAO) TAVR approach for the treatment of these patients.

Methods

Forty-four consecutive patients underwent TAO TAVR between January 2012 and June 2012 at our site and

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Abbreviations and Acronyms

AS = aortic stenosis
CV = cardiovascular
ICU = intensive care unit
LOS = length of stay
SAVR = surgical aortic valve replacement
TAO = transaortic
TAP = transapical
TAVR = transcatheter aortic valve replacement
TF = transfemoral
THV = transcatheter heart valve

were enrolled in a prospective database. All patients had symptomatic (New York Heart Association class II to IV), inoperable, severe AS and inadequate TF vascular access. Severe AS was defined according to PARTNER trial criteria (4), as was inoperability that was formally determined by at least 2 cardiothoracic surgeons. Iliofemoral access was deemed inadequate if the minimum vessel diameter was <7 mm for a 23-mm valve (<8 mm for a 26-mm valve) or if there were vascular anatomic abnormalities that precluded TF device delivery.

The TAO TAVR procedure was performed in a hybrid cardiac catheterization laboratory under general anesthesia (Fig. 1). The operative steps are listed in Table 1.

Study outcomes. The main study outcomes were Valve Academic Research Consortium–defined acute technical device success and 30-day combined safety endpoint. Acute technical device success was defined as successful vascular access, successful delivery and deployment of a single valve at the correct anatomic position, and appropriate prosthetic valve function without significant (moderate or severe) perivalvular regurgitation or stenosis; these assessments were made by using echocardiography immediately after valve deployment and before hospital discharge. The combined safety outcome is a hierarchical composite of all-cause mortality, major stroke, disabling bleeding, severe (stage 3) acute kidney injury, postprocedure myocardial infarction, major vascular complication, and repeat procedure for valve-related dysfunction.

To evaluate the technical learning curve, the hierarchical composite of intraprocedural adverse events (procedural death, rescue cardiac surgery, valve reintervention, life-threatening hemorrhage, major vascular complications, myocardial infarction, and major stroke) was used to compare the first 20 cases with the subsequent patients who underwent the operation. Length of stay (LOS) at the intensive care unit (ICU) and total hospital LOS were also recorded. All events were adjudicated by using the Valve Academic Research Consortium criteria (5).

Comparator cohort. To evaluate the effect of the technical learning curve and clinical safety of the TAO TAVR approach, outcomes data were compared with data from 76 consecutive patients who underwent TAP TAVR at our site from May 2009 to June 2012. TAP TAVR was performed by using the SAPIEN THV and its dedicated Ascendra delivery system, as described elsewhere (1).

Statistical analysis. Absolute numbers, percentages, and medians were calculated to describe the population. For

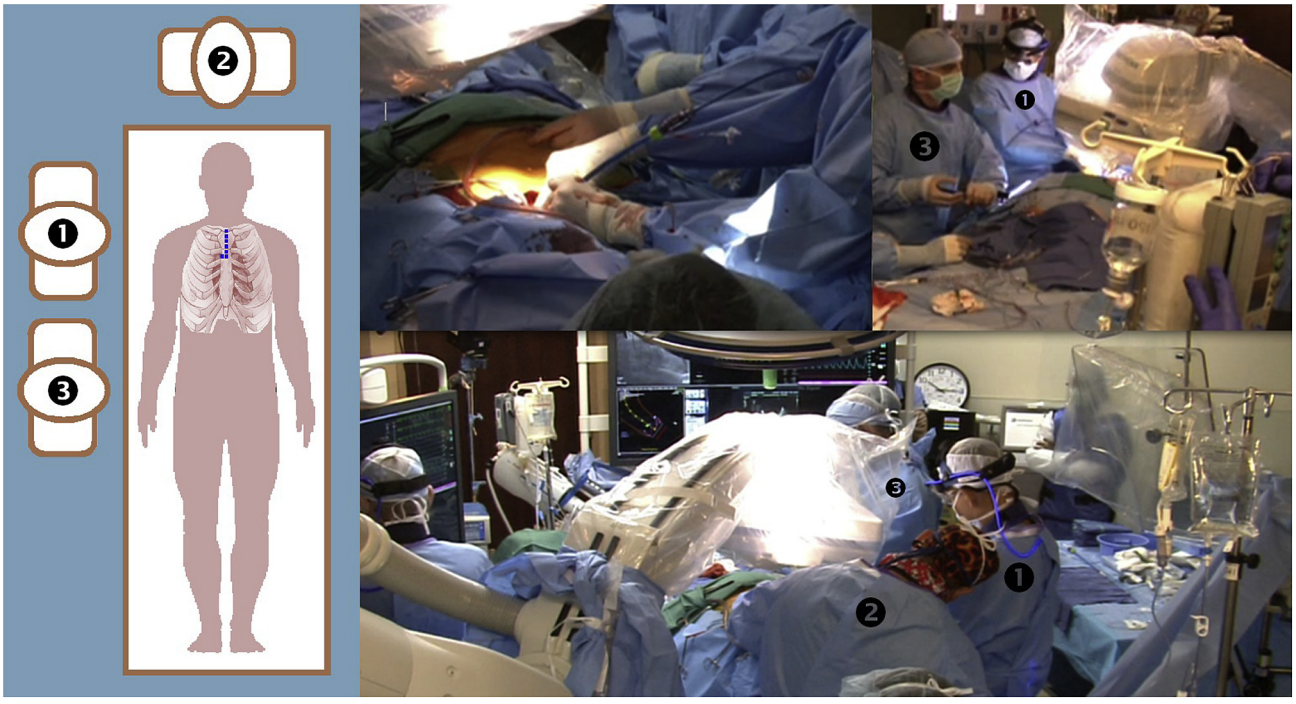

Figure 1 The Transaortic Transcatheter Aortic Valve Replacement Procedure

The layout of the hybrid cardiac catheterization laboratory and the position of the operators are shown. **(1)** A cardiac surgeon secures the delivery sheath, **(2)** an interventional cardiologist directs the delivery catheter, and **(3)** a second interventional cardiologist deploys the valve.

Table 1 Step-by-Step Description of the TAO TAVR Procedure

A 2-inch midline skin incision was made on the chest just below the sternal notch.
A limited, upper "mini-J" sternotomy was performed at the second intercostal space.
The innominate vein was identified and mobilized to expose the ascending aorta below.
A suitable, noncalcified area for aortotomy was identified.
A double purse-string suture of 4-0 Prolene was placed over the aortotomy site.
Intravenous heparin was administered for anticoagulation.
An 18-gauge needle was used to puncture the ascending aorta at the aortotomy site.
A short 7-F sheath was inserted through the aortotomy over a guidewire.
The aortic valve was crossed with a 6-F pigtail catheter.
The catheter was exchanged with a 0.035-inch Amplatz Extra-Stiff guidewire*.
The 7-F sheath was exchanged with the RetroFlex 3 introducer sheath.
The introducer tip was advanced about 1 cm into the ascending aorta.
Balloon aortic valvuloplasty was performed by using an Edwards 23 × 30 mm balloon catheter.
The transcatheter aortic valve prosthesis was deployed by using the RetroFlex 3 delivery catheter.
The introducer sheath was removed, and the purse-string sutures were tied to seal the aortotomy.
A chest tube was inserted in the pericardium left of the aorta, exiting through the right chest.

*Before insertion, the distal end of the stiff guidewire was bent into a large semicircular shape to reduce risk of ventricle perforation.

TAO = transaortic; TAVR = transcatheter aortic valve replacement.

comparisons between groups, the Mann-Whitney *U* test for continuous variables and the chi-square test or Fisher exact test for categorical variables were used. A 2-tailed p value of 0.05 was considered to indicate statistical significance.

Results

The baseline demographic and clinical profiles of patients in both groups were generally similar (Table 2). The TAP group had a higher median Society of Thoracic Surgeons (STS) score, driven by a higher proportion of patients who had previous coronary artery bypass graft and stroke. All patients in the TAO group were deemed inoperable, whereas most patients in the TAP group were eligible for SAVR.

THV implantation was successful in all patients in the TAO and TAP groups. Thirty-nine patients (89%) in the TAO group met the Valve Academic Research Consortium–defined criteria for acute technical device success, compared with 64 (84%) in the TAP group (p = 0.59). The proportion of patients with significant residual perivalvular regurgitation was also similar between groups (Table 3). In the TAP group, 3 cases (4%) of valve malposition/embolization occurred, and 5 patients (7%) required rescue valve-in-valve TAVR. No such device-related complications were reported in the TAO group.

One patient in the TAO group and 2 patients in the TAP group died during the procedure. Two of these deaths (1 in each group) resulted from aortic root perforation during valve deployment. The other intraoperative mortality in the TAP group was due to myocardial infarction resulting from obstruction of the left coronary ostium by the implanted prosthesis.

Table 2 Baseline Characteristics of Patients

Characteristic	TAO (n = 44)	TAP (n = 76)	p Value
Median age (yrs)	85 ± 5.6	87 ± 5.8	0.18
Male	19 (43)	40 (53)	0.34
Median STS score	8.0 ± 3.8	10.8 ± 3.7	0.01
Inoperable for surgical AVR	44 (100)	10 (13)	0.01
NYHA class III or IV	39 (89)	64 (84)	0.59
Diabetes mellitus	10 (23)	19 (25)	0.83
Previous myocardial infarction	8 (18)	18 (24)	0.50
Previous coronary artery bypass graft	9 (20)	38 (50)	0.01
Cerebrovascular disease	13 (30)	53 (70)	0.01
Peripheral vascular disease	32 (73)	57 (75)	0.83
Chronic obstructive pulmonary disease	22 (50)	31 (41)	0.35
Baseline creatinine ≥2.0 mg/dl	3 (7)	14 (18)	0.10
Atrial fibrillation	11 (25)	28 (37)	0.23
Pulmonary hypertension	9 (20)	10 (13)	0.31
Median aortic valve area (cm^2)	0.65 ± 0.15	0.61 ± 0.44	0.42
Median LV ejection fraction (%)	60 ± 14	58 ± 14	0.45

Values are mean ± SD or n (%).

AVR = aortic valve replacement; LV = left ventricular; NYHA = New York Heart Association; STS = Society of Thoracic Surgeons; TAP = transapical route; other abbreviation as in Table 1.

At 30 days, the combined safety endpoint was similar between the TAO and TAP groups (20% vs. 33%, respectively; p = 0.21). Rates of all-cause death were identical between

Table 3 Procedural and Clinical Outcomes by TAVR Approach

Outcome	TAO (n = 44)	TAP (n = 76)	p Value
Device-related event			
Acute technical device success	39 (89)	65 (86)	0.78
Implantation success	44 (100)	76 (100)	0.99
Moderate or severe final residual periprosthetic regurgitation	5 (11)	9 (12)	0.99
Leaflet entrapment/malcoaptation	0 (0)	2 (3)	0.53
Malposition/embolization	0 (0)	3 (4)	0.29
Implantation of 2 valves	0 (0)	5 (7)	0.16
Rescue surgical AVR	0 (0)	0 (0)	0.99
Procedural death	1 (2)	2 (3)	0.99
30-day clinical events			
Combined clinical safety endpoint	9 (20)	22 (29)	0.50
All-cause death	6 (14)	11 (14)	0.99
CV mortality	1 (2)	9 (12)	0.09
Myocardial infarction	0 (0)	2 (2)	0.53
Major stroke	0 (0)	1 (1)	0.99
Minor stroke	1 (2)	0 (0)	0.37
Severe AKI (stage 3)	1 (2)	1 (1)	0.99
New atrial fibrillation	6 (14)	15 (20)	0.32
New permanent pacemaker	1 (2)	5 (7)	0.41
Rescue cardiac surgery	3 (7)	1 (1)	0.14
Life-threatening bleeding	6 (14)	10 (13)	0.99
Major bleeding	5 (11)	21 (28)	0.04
Major vascular complications	1 (2)	4 (5)	0.65
Total bleeding and vascular events	12 (27)	35 (46)	0.05

Values are n (%).

AKI = acute kidney injury; AVR = aortic valve replacement; CV = cardiovascular; other abbreviations as in Table 2.

groups. Only 1 (17%) of the 6 deaths in the TAO group was cardiovascular (CV)-related (intraprocedural mortality), whereas 9 (82%) of the 11 deaths in the TAP group were adjudicated as CV mortality (p = 0.02). Causes of non-CV deaths in the TAO group were pneumonia-related respiratory failure (4 cases) and *Clostridium difficile* sepsis (1 case).

The incidence of life-threatening/disabling bleeding did not differ between groups. However, the rate of major bleeding was higher in the TAP group compared with the TAO group (28% vs. 11%, respectively; p = 0.04), as was the incidence of total bleeding and vascular complications (46% vs. 27%, respectively; p = 0.05). On average, patients in the TAP group stayed twice as long in the ICU as the TAO group (6 vs. 3 days; p = 0.01). Median hospital LOS was also lower in the TAO group, but this finding was not statistically significant (Fig. 2).

The rates of composite intraprocedural adverse events did not differ between the first 20 cases and the subsequent 56 patients who underwent TAP TAVR (15% vs. 14%, respectively; p = 0.99). However, procedural adverse events occurred exclusively in the first 20 patients who underwent TAO TAVR (20% vs. 0%; p = 0.04), suggesting a more favorable technical learning curve (Fig. 3).

Discussion

Although the TAP approach is an effective option for TAVR (6), the need for alternative access strategies remains. In the FRANCE 2 (French Aortic National CoreValve and Edwards) Registry (7) of nearly 3,200 TAVR patients, TAP access was an independent predictor of decreased survival. Also, a trial that sought to compare TAP TAVR with conventional SAVR was prematurely terminated due to excess adverse events with the TAP approach (2).

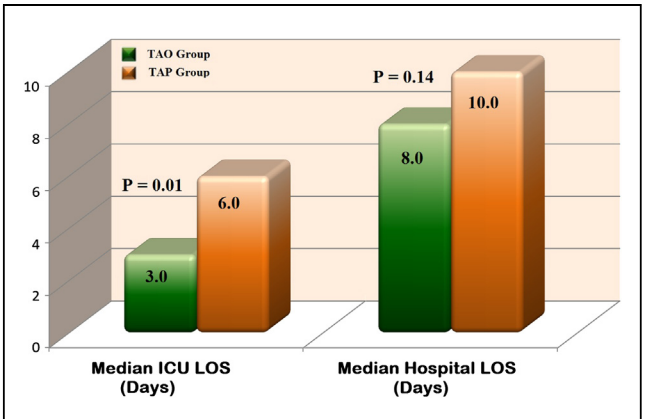

Figure 2 Length of Stay

The intensive care unit (ICU) and hospital lengths of stay (LOS) using the transcatheter aortic valve replacement (TAVR) approach are displayed. ICU LOS was significantly lower in the transaortic (TAO) group than in the transapical route (TAP) group. There was also a nonsignificant trend toward lower total hospital LOS with TAO TAVR.

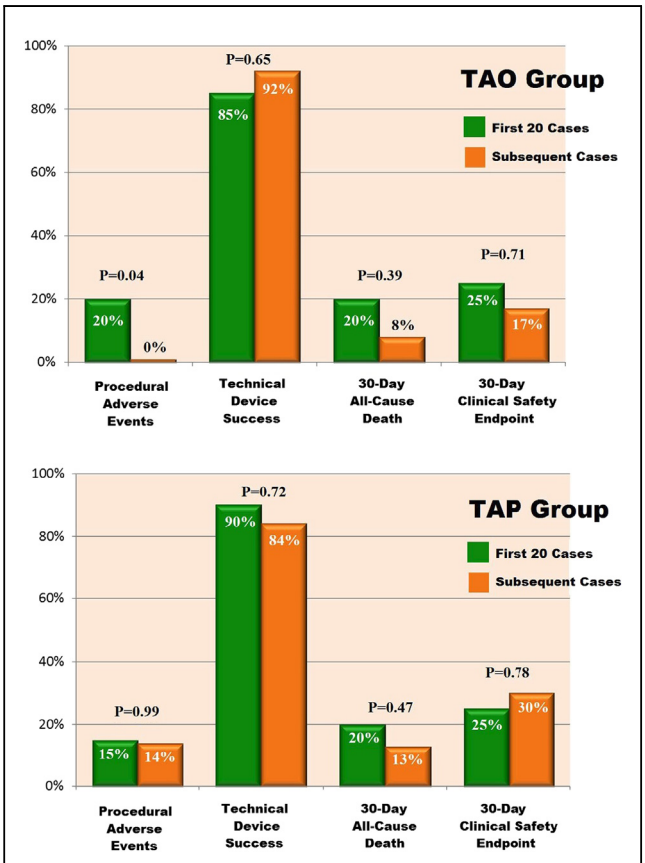

Figure 3 Learning Curve

The procedural learning curve outcomes according to the TAVR approach are presented. In the TAO group **(top)**, procedural adverse events were significantly reduced after the first 20 cases. This observation was not seen in the TAP group **(bottom)**. Abbreviations as in Figures 1 and 2.

Our findings demonstrate that the TAO approach is technically feasible in patients with inoperable, severe AS who are ineligible for TF TAVR. In our cohort, TAO TAVR was associated with lower bleeding rates, shorter ICU stay, and more favorable learning curve compared with the TAP approach.

Multiple transfusions during cardiac surgery are associated with increased mortality and morbidity (8). Efforts to reduce operative blood loss are likely as important in TAVR. In 28% of TAP patients in our series, significant blood loss occurred during access site closure. In the TAP approach, hemostasis at the left ventricular apex was sometimes difficult to attain by using purse-string sutures. This does not seem to be an issue with the TAO approach, as the double purse-string sutures provided excellent seal of the aortotomy (a routine maneuver for cardiothoracic surgeons who are experienced with cannulating the aorta). This success contributed to a significant 61% relative reduction in perioperative blood transfusions in TAO TAVR compared with TAP TAVR.

A cost-effectiveness analysis of the PARTNER trial found that TAP TAVR was associated with substantially

higher overall costs compared with SAVR because of minimal reduction in ICU and hospital LOS (9). This information is vital for any institution starting a TAVR program. In our series, ICU LOS was significantly longer in TAP TAVR patients, owing to a longer duration of severe surgical site pain and higher incidence of significant post-thoracotomy pleural effusion that complicated postoperative pulmonary function.

As with other new devices and modalities, TAVR requires a certain period for operator training and familiarization. In our study, the technical learning curve for TAO TAVR seemed favorable, as major intraprocedural adverse events were effectively averted after the first 20 cases. There was also a trend toward a reduction in clinical events and mortality in the TAO group with increasing operator experience. This pattern was not observed with TAP TAVR, implying a steeper learning curve and a larger number of procedures required for proficiency. A significant learning effect was previously demonstrated in a cohort of approximately 300 TAP TAVR patients, in whom a sharp decline in morbidity and mortality was noted after the first 150 cases (3).

Device malposition was reported in 3 patients and need for second THV implantation was required in 5 patients, all in the TAP group. Left ventricular contractions induced significant movement of the introducer sheath in the TAP route, which made manipulation and positioning of the THV across the native valve difficult. Conversely, we observed very little movement of the introducer sheath with TAO access, resulting in more stable and controlled positioning and deployment of the THV.

To the best of our knowledge, our series is the largest cohort of patients who underwent TAO TAVR in the United States to date. A similar preliminary experience was reported in Europe with comparable clinical outcomes (10). However, the European study used a newer-generation THV (SAPIEN XT) and delivery system (Ascendra2), which were not available in the United States at the time of the study. Our TAO TAVR program was discontinued with implementation of the 2012 Medicare national coverage determinations for TAVR (11). Our study was completed before the Ascendra delivery system (the original TAP platform) was approved by the U.S. Food and Drug Administration for clinical use in the United States, and therefore comparative data between the use of TF and TAP delivery devices in TAO TAVR are lacking. Finally, the use of delivery systems not specifically designed for TAO TAVR can lead to technical issues during device delivery (12). Therefore, development of a dedicated delivery system for TAO TAVR is recommended to improve the safety and efficacy of this procedure.

Study limitations. This was a nonrandomized, single-center registry study that is subject to unmeasurable confounders. The comparison of patients was taken from 2 different time periods, which may have influenced the learning curve for the TAO procedure. The TAP group also had a higher median STS score compared with the TAO group, and this finding could also have potentially influenced the outcomes. Larger randomized clinical trials are necessary to confirm our results.

Conclusions

TAVR via the TAO approach, using the device commercially available in the United States, is technically feasible and seems to be associated with favorable outcomes in patients with inoperable, severe AS who are not candidates for TF access. The TAO approach expands the current alternative options for TAVR access sites, and development of a dedicated delivery platform is recommended to further improve its efficacy and safety.

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Key Words: direct aortic ■ transcatheter aortic valve replacement ■ transaortic.