# Direct Comparison of Feasibility and Safety of Transfemoral Versus Transaortic Versus Transapical Transcatheter Aortic Valve Replacement

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## ABSTRACT

**OBJECTIVES** The aim of this study was to compare outcomes among transfemoral (TF), transaortic (TAo), and transapical (TA) transcatheter aortic valve replacement (TAVR).

**BACKGROUND** Very few studies have investigated the differences among TF, TAo, and TA TAVR in terms of safety and feasibility.

**METHODS** Between January 2011 and December 2014, 467 consecutive cases of TF TAVR, 289 cases of TAo TAVR, and 42 cases of TA TAVR were analyzed. Baseline characteristics, procedural characteristics, and outcomes were compared between TF and TAo and between TAo and TA approaches.

**RESULTS** Balloon-expandable prostheses were used in 320 cases of TF TAVR (69%), 209 cases of TAo TAVR (72%), and all cases of TA TAVR. The remaining cases were performed using self-expandable prostheses. Patient age and Society of Thoracic Surgeons score were similar (83.8 years vs. 83.7 years vs. 81.3 years and 6.2% vs. 5.8% vs. 7.1%) among all groups. Although nonsignificant, a trend toward lower 30-day mortality (5% vs. 9%; p = 0.057) was observed with TF TAVR compared with TAo TAVR. Kaplan-Meier analysis revealed a trend toward a higher 1-year survival rate (log-rank p = 0.067) with TF TAVR compared with TAo TAVR. There was no significant difference in 30-day mortality between TAo and TA TAVR (9% vs. 14%; p = 0.283). Kaplan-Meier analysis revealed a trend toward a higher 1-year survival rate (log-rank p = 0.154) with TAo TAVR compared with TA TAVR.

**CONCLUSIONS** Although the 30-day mortality and 1-year survival rates were similar between TF and TAo TAVR patients, a trend in favor of the TF approach was observed. In addition, the TAo approach can be considered as an alternative to the TA approach when the TF approach seems unsuitable. (J Am Coll Cardiol Intv 2016;9:2320–5) © 2016 by the American College of Cardiology Foundation.

Transcatheter aortic valve replacement (TAVR) has gained widespread acceptance as a treatment option for patients with severe symptomatic aortic stenosis who are considered at high risk for surgical aortic valve replacement (1–5). Although the transfemoral (TF) approach is recommended as the default approach in many countries, other routes should be considered when the common femoral artery is too small or excessively diseased and especially when it is severely calcified or tortuous. The transapical (TA) approach is used as an alternative route when the TF approach is considered unsafe. However, the TA approach has been reported to be associated with various issues, including myocardial damage, bleeding complications, and slower recovery, especially in patients with chronic pulmonary disease (6–8). The recently developed transaortic (TAo) approach has been reported to be a feasible and safe alternative route to the TA approach (9,10). Although comparative analyses of the TF versus the TA approach have been the subject of several studies, only limited data are available regarding direct comparisons of TF and TAo TAVR and of TAo and TA TAVR. The purpose of this study was, consequently, to compare feasibility and safety between TF and TAo TAVR and between TAo and TA TAVR.

## METHODS

**STUDY DESIGN.** From October 2006, all consecutive high-risk patients with severe symptomatic aortic stenosis treated with TAVR were prospectively included in our dedicated TAVR database. Patients with severe aortic stenosis were considered candidates for TAVR if they were deemed ineligible or at high risk for surgical aortic valve replacement. The decision to proceed with TAVR was made by a dedicated heart team composed of experienced clinical and interventional cardiologists, cardiovascular surgeons, and anesthesiologists. The TAo approach was first used at our center in 2010. However, we decided to retrospectively review patients treated via the TAo approach since January 2011 to exclude the learning period from the analysis. Between January 2011 and December 2014, a total of 816 patients underwent TAVR using balloon-expandable or self-expandable prostheses, 467 via the TF approach, 289 via the TAo approach, and 42 via the TA approach. The other route was subclavian in 18 cases. The TA and subclavian approaches were selected when the TF approach proved difficult because of access issues and when the TAo approach was hampered by the presence of heavy aortic calcifications. Written informed consent was obtained from all patients.

**VASCULAR ACCESS AND VALVE SELECTION.** Patients were selected to undergo TAVR via the TF approach or alternative approaches depending on the size, calcification, and tortuosity of the iliofemoral arterial access. The type and size of the valve prosthesis were selected according to the diameter and shape of the aortic annulus as well as the aortic root characteristics and operator preference.

**PROCEDURE AND POST-PROCEDURAL CARE.** The technical aspects of the TF approach have been described in detail in previous reports (11,12). Almost all TF TAVR cases were performed under conscious sedation with local anesthesia. Furthermore, the closure of the femoral artery was performed using closure devices (13). The procedural techniques of the TAo approach have also been reported elsewhere (14). A straight short manubriotomy down to the second intercostal space was used through a 5-cm skin incision. TA TAVR was performed in a standard fashion, as described previously (15).

Aspirin (75 to 160 mg/day) was recommended prior to TAVR. Clopidogrel was also recommended before the procedure. A bolus of heparin (100 IU/kg) was administered at the start of the procedure to achieve an activated clotting time of 250 to 300 s, and the activated clotting time was measured every 30 min thereafter.

All patients were observed in the intensive care unit for at least 24 h after Edwards valve implantation (Edwards Lifesciences, Irvine, California) or 72 h after CoreValve implantation (patients without previous pacemaker) (Medtronic, Minneapolis, Minnesota). Aspirin was continued indefinitely and clopidogrel for a period of 1 to 6 months. Patients on warfarin therapy received only single-antiplatelet treatment after the procedure, usually aspirin.

**ENDPOINTS.** The main endpoints of this study were 30-day mortality and 1-year survival. All complications were defined according to the Valve Academic Research Consortium 2 criteria (16).

**STATISTICAL ANALYSIS.** All statistical analyses were performed using SPSS version 21.0 (SPSS, Chicago, Illinois). Continuous variables are expressed as mean $\pm$ SD or with the corresponding interquartile range. Normality of distribution was tested using the Shapiro-Wilk test. Dichotomous variables are expressed as counts and percentages. Comparisons of continuous variables with normal distributions were

**TABLE 1** Baseline Clinical Characteristics Stratified by Approach

| | TF (n = 467) | TAo (n = 289) | TA (n = 42) | p Value, TF vs. TAo | p Value, TAo vs. TA |
|---|---|---|---|---|---|
| **Baseline characteristics** | | | | | |
| Age (yrs) | 83.8 ± 7.1 | 83.7 ± 5.6 | 81.3 ± 7.7 | 0.861 | 0.066 |
| Male | 234 (50) | 146 (51) | 30 (71) | 0.912 | 0.011 |
| BMI (kg/m$^2$) | 26.3 ± 4.9 | 26.6 ± 5.1 | 25.3 ± 4.1 | 0.447 | 0.119 |
| BSA (m$^2$) | 1.74 ± 0.20 | 1.74 ± 0.24 | 1.69 ± 0.42 | 0.890 | 0.222 |
| NYHA class III/IV | 422 (90) | 247 (86) | 36 (86) | 0.040 | 0.966 |
| Peripheral artery disease | 49 (11) | 92 (32) | 15 (36) | <0.001 | 0.615 |
| Prior CABG | 39 (8) | 14 (5) | 17 (41) | 0.065 | <0.001 |
| Prior MI | 15 (3) | 17 (6) | 2 (5) | 0.077 | 0.557 |
| Prior stroke | 13 (3) | 16 (6) | 2 (5) | 0.056 | 0.594 |
| Diabetes | 103 (22) | 63 (22) | 11 (26) | 0.922 | 0.523 |
| Hypertension | 320 (69) | 189 (65) | 27 (64) | 0.373 | 0.888 |
| Atrial fibrillation | 132 (28) | 60 (21) | 18 (43) | 0.021 | 0.002 |
| COPD | 59 (13) | 38 (13) | 8 (19) | 0.837 | 0.302 |
| Creatinine clearance | 57.0 ± 23.1 | 60.3 ± 25.5 | 63.2 ± 32.5 | 0.069 | 0.528 |
| Logistic EuroSCORE (%) | 15.9 ± 10.8 | 16.9 ± 11.0 | 22.7 ± 15.7 | 0.272 | 0.033 |
| STS score (%) | 6.2 ± 3.9 | 5.8 ± 3.3 | 7.1 ± 4.2 | 0.192 | 0.081 |
| **Echocardiographic data** | | | | | |
| LVEF (%) | 51.6 ± 14.6 | 54.7 ± 13.8 | 52.9 ± 13.7 | 0.006 | 0.451 |
| Mean gradient (mm Hg) | 48.8 ± 16.5 | 46.1 ± 14.9 | 40.8 ± 11.7 | 0.039 | 0.038 |
| PAP (mm Hg) | 47.4 ± 13.6 | 44.5 ± 12.1 | 43.6 ± 11.5 | 0.009 | 0.660 |
| AR (more than mild) | 67 (14) | 33 (11) | 5 (12) | 0.248 | 0.546 |
| Mean diameter of annulus by CT | 23.7 ± 2.2 | 23.8 ± 2.1 | 24.3 ± 1.8 | 0.481 | 0.296 |

Values are mean ± SD or n (%).

AR = aortic regurgitation; BMI = body mass index; BSA = body surface area; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; CT = computed tomography; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association; PAP = pulmonary artery pressure; STS = Society of Thoracic Surgeons; TA = transapical; TAo = transaortic; TF = transfemoral.

performed using 1-way analysis of variance with Tukey multiple-comparison tests, and categorical variables were analyzed using the chi-square test with Bonferroni adjustment. Survival analyses were performed using Kaplan-Meier analysis. A p value <0.05 was considered to indicate statistical significance.

## RESULTS

### BASELINE PROCEDURAL AND POST-PROCEDURAL CHARACTERISTICS STRATIFIED BY APPROACH.
The main characteristics of the 3 groups are summarized in Table 1. Patient age (83.8 years vs. 83.7 years vs. 81.3 years; p = 0.861 for TF vs. TAo; p = 0.066 for TAo vs. TA) and Society of Thoracic Surgeons score (6.2% vs. 5.8% vs. 7.1%; p = 0.192 for TF vs. TAo; p = 0.081 for TAo vs. TA) were similar. There were more patients with peripheral disease in the TAo and TA groups. Patients in the TF and TA groups had a higher rate of atrial fibrillation compared with those in the TAo group. Logistic European System for Cardiac Operative Risk Evaluation scores were significantly higher in the TA group compared with the TAo group. Regarding echocardiographic findings, patients in the TF group had lower ejection fractions, higher mean pressure gradients, and higher pulmonary artery pressures compared with those in the TAo group.

The main procedural and post-procedural characteristics are summarized in Table 2. Balloon-expandable prostheses were used in 320 cases of TF TAVR (69%), 209 cases of TAo TAVR (72%), and all cases of TA TAVR. The remaining cases were performed using self-expandable prostheses. Procedural success (95% vs. 95% vs. 95%; p = 0.966 for TF vs. TAo; p = 0.660 for TAo vs. TA) was similar, as was the rate of major stroke (2% vs. 2% vs. 5%; p = 0.585 for TF vs. TAo; p = 0.231 for TAo vs. TA). On the contrary, the rate of acute kidney injury was significantly different among the 3 groups (5% vs. 13% vs. 31%; p < 0.001 for TF vs. TAo; p = 0.003 for TAo vs. TA) Although nonsignificant, a trend toward lower 30-day mortality (5% vs. 9%; p = 0.057) was observed with TF TAVR compared with TAo TAVR. There was no significant difference in 30-day mortality between TAo and TA TAVR (9% vs. 14%; p = 0.283).

### 1-YEAR SURVIVAL IN RELATION TO THE APPROACH USED.
The median follow-up period of this cohort was 199 days (interquartile range: 39 to 347 days). The cumulative survival rate of all patients was calculated

using the Kaplan-Meier method and compared using the log-rank test (**Figure 1**). Although nonsignificant, the cumulative 1-year survival rate tended to be higher in the TF group compared with the TAo group (log-rank p = 0.067). Similarly, although nonsignificant, the cumulative 1-year survival rate tended to be higher in the TAo group compared with the TA group (log-rank p = 0.154).

## DISCUSSION

To the best of our knowledge, we report here the results of the first comparison between the TF and TAo approaches in TAVR. In this study, we observed similar outcomes in TF and TAo TAVR patients, with a trend in favor of the TF approach. In addition, our findings confirmed that the TAo approach tended to be associated with better outcomes compared with the TA approach.

Until recently, the TA approach has been selected mainly as an alternative route when the TF approach is not suitable. However, because of its feasibility and given the simplicity of the procedure, the TAo approach has become increasingly used as a preferred approach among non-TF patients (9,10). Reports comparing the TA and TAo approaches have already been published. Lardizabal et al. (17) reported the results of a comparison between the TA (n = 76) and TAo (n = 44) approaches. After propensity matching, 25 patients were compared in each group. There were no significant differences in the incidence of complications including stroke, myocardial infarction, and bleeding events. Although 30-day mortality was not significantly different, 1-year mortality tended to be lower, and 1-year cardiovascular mortality was significantly lower in the TAo group. O'Sullivan et al. (18) reported the results of a meta-analysis comparing the TA (n = 1,543) and TAo (n = 193) approaches and found no significant differences in the incidence of complications including stroke, pacemaker implantation, and bleeding events. In addition, 30-day mortality was similar in the 2 groups. The present study revealed that 30-day mortality tended to be lower and 1-year survival tended to be higher in the TAo group. Consequently, selection of the TAo approach instead of the TA approach as an alternative route seems a reasonable strategy when the TF approach is unsuitable or unsafe.

Several studies have also been carried out to compare the TF and TA approaches (19,20). Blackstone et al. (21) reported the results of a comparison between the TF and TA approaches after propensity matching using data from the PARTNER

(Placement of Aortic Transcatheter Valves) trial. After propensity matching, 501 patients were compared in each group. Adverse procedural events, early mortality, and prolonged recovery were more frequent in patients treated via the TA approach compared with the TF approach.

**TABLE 2  Procedural and Post-Procedural Characteristics Stratified by Approach**

| | TF (n = 467) | TAo (n = 289) | TA (n = 42) | p Value, TF vs. TAo | p Value, TAo vs. TA |
|---|---|---|---|---|---|
| Procedural variables | | | | | |
| Valve type | | | | 0.289 | <0.001 |
| Balloon-expandable valve | 320 (69) | 209 (72) | 42 (100) | | |
| Self-expandable valve | 147 (31) | 80 (28) | 0 (0) | | |
| Post-procedural variables | | | | | |
| Procedural success | 437 (95) | 270 (95) | 40 (95) | 0.966 | 0.660 |
| Major stroke | 7 (2) | 6 (2) | 2 (5) | 0.585 | 0.231 |
| AKI | 21 (5) | 38 (13) | 13 (31) | <0.001 | 0.003 |
| AKI (grade 3) | 2 (1) | 5 (2) | 1 (2) | 0.079 | 0.561 |
| Life-threatening bleeding | 12 (3) | 17 (6) | 3 (7) | 0.021 | 0.479 |
| Annular rupture | 10 (2) | 4 (1) | 0 (0) | 0.584 | 0.580 |
| Pacemaker implantation | 72 (16) | 29 (10) | 3 (7) | 0.032 | 0.408 |
| PVL ≥ grade 2 | 51 (12) | 20 (7) | 2 (5) | 0.071 | 0.424 |
| 30-day mortality | 26 (5) | 27 (9) | 6 (14) | 0.057 | 0.283 |

Values are n (%).

AKI = acute kidney injury; PVL = paravalvular aortic leak; other abbreviations as in **Table 1**.



**FIGURE 1  Survival Curves Stratified by Approach**

TF vs TAo  p=0.067
TAo vs TA  p=0.154

| Number at risk | | | |
|---|---|---|---|
| TF | 467 | 287 | 69 |
| TAo | 289 | 126 | 28 |
| TA | 42 | 25 | 17 |
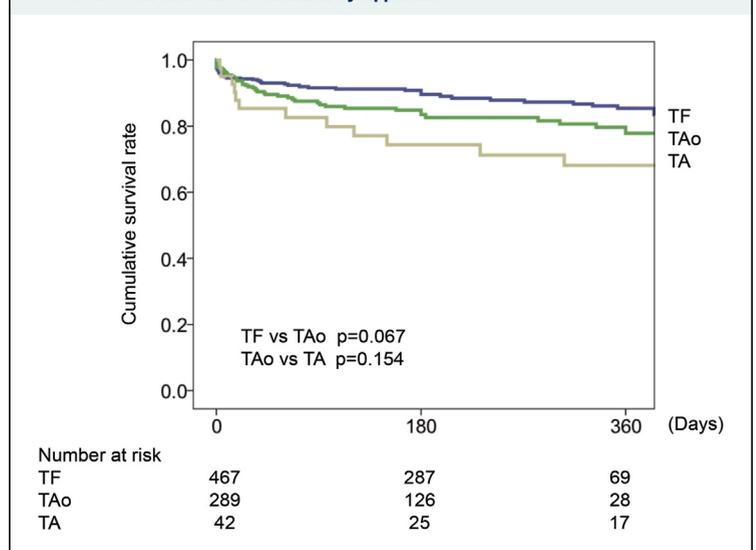
Survival rate was calculated using Kaplan-Meier methods and compared using the log-rank test according to the approach. Although nonsignificant, the cumulative 1-year survival rate tended to be higher in the transfemoral (TF) group compared with the transaortic (TAo) group (log-rank p = 0.067). Similarly, although nonsignificant, the cumulative 1-year survival rate tended to be higher in the TAo group compared with the transapical (TA) group (log-rank p = 0.154).

The findings of our study suggest that the TAo approach is feasible and safe. The adequate volume of procedures performed at our center is 1 of the reasons accounting for the results reported here. The influence of the volume of cases on the outcomes of TA TAVR has been analyzed previously. Kempfert et al. (22) reported that the outcomes of TA TAVR were significantly improved after the first 150 cases. Because the number of TAo TAVR procedures included in this study was in excess of 200, this would appear to be a guarantee of an appropriate level of experience. Another reason is the close collaboration between surgeons and other specialists, including interventional cardiologists, general cardiologists, and imaging specialists. Not only surgical skills but also a sufficient volume of cases and synergy between the experienced members of the heart team are instrumental in ensuring the feasibility of the TAo approach.

The findings of our study also showed a trend in favor of the TF approach. The TF approach is less invasive compared with the TAo approach, including the anesthesia modality. Currently TF TAVR tends to be performed under conscious sedation without transesophageal echocardiography. Frohlich et al. (23) reported the results of a meta-analysis comparing conscious sedation and general anesthesia, which did not show any difference between the outcomes of the 2 study groups.

In conclusion, it seems reasonable that the TF approach should still be the primary choice when anatomically feasible, because of its lesser invasiveness compared with the TAo approach. However, the TAo approach can be considered as an alternative to the TA approach when TF TAVR is unsuitable.

**STUDY LIMITATIONS.** First, the number of cases performed via the TA approach was quite limited compared with the TF and TAo approaches, the surgical team showing a preference for the TAo approach compared with the TA approach after implementing it.

Second, the mean follow-up period was 199 days, and long-term follow-up is needed to investigate the impact of each individual approach on long-term outcomes.

Finally, this was a retrospective observational study conducted at a single center. Further studies and multicenter analysis are required to confirm our findings.

## CONCLUSIONS

Although the 30-day mortality and 1-year survival rates were similar in TF and TAo TAVR patients, we observed a trend in favor of the TF approach. When feasible, the TAo approach can be considered as an alternative to the TA approach when the TF approach seems to be unsuitable.

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### PERSPECTIVES

**WHAT IS KNOWN?** The TF approach in TAVR should be the primary choice when anatomically feasible.

**WHAT IS NEW?** The TAo approach can be considered as an alternative to the TA approach when TF TAVR is unsuitable.

**WHAT IS NEXT?** Further studies with larger cohorts and long-term follow-up are required to investigate the impact of each individual approach on long-term outcomes.

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