Long-Term Outcomes Associated with the Transaortic Approach to Transcatheter Aortic Valve Replacement

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Objective: We investigated the long-term safety, efficacy and clinical outcomes associated with transaortic (TAO) transcatheter aortic valve replacement (TAVR) in the United States. Background: We previously reported the technical feasibility and short-term safety of TAO TAVR. Compared to transapical (TAP) access, the TAO approach was associated with shorter median intensive care unit (ICU) length of stay (LOS) and more favorable technical learning curve. However, outcomes data beyond 30 days were lacking and the longer-term clinical consequences of this strategy were unknown. Methods: Mortality outcomes at 1 year (and longer) of 44 consecutive patients who underwent TAO TAVR in our institution were compared with that of 76 consecutive patients who underwent TAP TAVR at our site. Risk-adjusted analysis was performed in propensity-matched patients (25 from each group) to account for baseline differences. Results: TAO TAVR was associated with a trend towards lower all-cause mortality at 1 year compared to TAP TAVR (18% vs. 34%, P=0.09 in the overall sample; 12% vs. 40%, P=0.05 in the matched cohort). The higher probability of survival with TAO TAVR persisted after a median follow-up period of 23 months (hazard ratio [HR]=1.96, P=0.06 in the overall sample; HR=3.4, P=0.01 in the matched cohort). Cardiovascular mortality at 1 year was lower with TAO TAVR (2% vs. 22%, P=0.01 in the overall sample; 4% vs. 28%, P=0.05 in the matched cohort). ICU LOS (shorter in the TAO group) and implantation of second prosthetic valve (higher incidence in the TAP group) were independent predictors of long-term mortality. Conclusion: The outcomes associated with TAO TAVR compare favorably with TAP TAVR. Our results appear to corroborate the long-term safety and efficacy of the TAO approach in TAVR patients with inadequate iliofemoral access.

Key words: Aortic Stenosis; Heart Valve Surgery; Structural Heart Disease; Interventional Cardiology

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Conflict of Interest: Dr. Cohen has served as a consultant for Accumed Systems Inc., Edwards Lifesciences, and Medtronic. Dr. Heldman reports he has received research funds from Edwards Lifesciences. Dr. W. O’Neill reports he has served as consultant to Medtronic, he is an owner of Accumed Systems Inc., and he owns stock in Synacor Inc. and Syntheon Cardiology. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Received 22 May 2014; Revision accepted 30 November 2014
DOI: 10.1002/ccd.25785
Published online 3 February 2015 in Wiley Online Library (wileyonlinelibrary.com)

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BACKGROUND

We previously described the novel transaortic (TAO) approach to the implantation of the Edwards SAPIEN® (Edwards Lifesciences, Irvine, California) transcatheter heart valve (THV) in inoperable patients with severe aortic stenosis (AS) who were not eligible for transfemoral (TF) transcatheter aortic valve replacement (TAVR) [1]. Compared to the transapical (TAP) route which was the standard strategy for these patients, the TAO approach was associated with favorable procedural and short-term outcomes, including an advantageous technical learning curve, and shorter intensive care unit (ICU) length of stay (LOS). However, the long-term clinical implication of this strategy is unknown. We report the 1-year (and longer) outcomes of patients who underwent TAO TAVR in the United States (US).

METHODS

Forty-four consecutive patients who underwent TAO TAVR in our institution from January until June 2012 were enrolled in a prospective database, and were compared with 76 consecutive patients who underwent TAP TAVR at our site between May 2009 and June 2012. The patient selection criteria and description of the TAVR procedures were previously reported [1]. All 110 patients had severe, symptomatic aortic stenosis and inadequate TF access. All patients in the TAO group and 10 patients in the TAP group were formally determined to be inoperable by at least 2 cardiothoracic surgeons. Sixty-six of the 76 patients in the TAP group were eligible for conventional surgical aortic valve replacement (SAVR), but were deemed to be at high risk for operative complications or death on the basis

| TABLE I. Baseline Demographic Characteristics of Subjects and Short-Term Clinical Events by TAVR Approach | OVERALL SAMPLE | MATCHED COHORT |
| DEMOGRAPHICS | TAO (n = 44) | TAP (n = 76) | P-Value | TAO (n = 25) | TAP (n = 25) | P-Value |
| Median Age (years) | 85 | 87 | 0.18 | 86 | 87 | 0.41 |
| Male Gender | 19 (43%) | 40 (53%) | 0.34 | 13 (52%) | 14 (56%) | 0.99 |
| Median STS Score | 8.0 | 10.8 | 0.01 | 8.4 | 8.6 | 0.90 |
| Inoperable for Surgical AVR | 44 (100%) | 10 (13%) | 0.01 | 17 (68%) | 16 (64%) | 0.99 |
| NYHA Class 3 or 4 | 39 (89%) | 64 (84%) | 0.59 | 23 (92%) | 19 (76%) | 0.25 |
| Diabetes Mellitus | 10 (23%) | 19 (25%) | 0.83 | 6 (24%) | 4 (16%) | 0.73 |
| Previous Myocardial Infarction | 8 (18%) | 18 (24%) | 0.50 | 4 (16%) | 4 (16%) | 0.99 |
| Previous CABG | 9 (20%) | 38 (50%) | 0.01 | 5 (20%) | 7 (28%) | 0.74 |
| Cerebrovascular Disease | 13 (30%) | 53 (70%) | 0.01 | 7 (28%) | 14 (56%) | 0.09 |
| Peripheral Vascular Disease | 32 (73%) | 37 (57%) | 0.83 | 25 (100%) | 22 (88%) | 0.24 |
| Any COPD | 22 (50%) | 31 (41%) | 0.35 | 14 (56%) | 9 (36%) | 0.27 |
| Baseline Creatinine ≥2.0 | 3 (6%) | 14 (18%) | 0.10 | 2 (8%) | 6 (24%) | 0.25 |
| Atrial Fibrillation | 11 (25%) | 28 (37%) | 0.23 | 7 (28%) | 7 (28%) | 0.99 |
| Pulmonary Hypertension | 9 (20%) | 10 (13%) | 0.31 | 7 (28%) | 3 (12%) | 0.29 |
| Frailty | 26 (59%) | 36 (47%) | 0.26 | 0.70 | 0.61 | 0.71 |
| Median Aortic Valve Area (cm2) | 0.65 | 0.61 | 0.42 | 55 | 60 | 0.29 |
| Median LV Ejection Fraction (%) | 60 | 58 | 0.45 | 86 | 87 | 0.41 |

30-DAY CLINICAL EVENTS

Device Success | 39 (89%) | 65 (86%) | 0.78 | 23 (92%) | 21 (84%) | 0.67 |
| Moderate or Severe Final Residual Periprosthetic Regurgitation Implantation of 2 THV | 0 (0%) | 5 (7%) | 0.16 | 0 | 3 (12%) | 0.23 |
| Myocardial Infarction | 0 (0%) | 2 (2%) | 0.53 | 0 | 1 (4%) | 0.35 |
| Stroke | 1 (2%) | 1 (1%) | 0.99 | 0 | 0 | 0.99 |
| Life-Threatening Bleeding | 6 (14%) | 10 (13%) | 0.99 | 3 (12%) | 1 (4%) | 0.61 |
| Major Bleeding | 5 (11%) | 21 (28%) | 0.04 | 4 (16%) | 5 (20%) | 0.99 |
| Total Bleeding Events | 11 (25%) | 31 (41%) | 0.11 | 7 (28%) | 6 (24%) | 0.99 |
| Major Vascular Complications | 1 (2%) | 4 (5%) | 0.65 | 0 | 1 (4%) | 0.99 |
| Severe AKI (Stage 3) | 1 (2%) | 1 (1%) | 0.99 | 0 | 1 (4%) | 0.99 |
| New Atrial Fibrillation | 6 (14%) | 15 (20%) | 0.32 | 4 (16%) | 7 (28%) | 0.50 |
| New Permanent Pacemaker | 1 (2%) | 5 (7%) | 0.41 | 0 | 1 (4%) | 0.99 |
| Rescue Cardiac Surgery | 3 (7%) | 1 (1%) | 0.14 | 2 (8%) | 0 | 0.49 |
| Median Hospital LOS (days) | 8.0 | 10.0 | 0.14 | 7.0 | 12 | 0.05 |
| Median ICU LOS (days) | 3.0 | 6.0 | 0.01 | 3.0 | 6.0 | 0.03 |

STS – Society of Thoracic Surgeons; AVR – Aortic Valve Replacement; NYHA – New York Heart Association; CABG – Coronary Artery Bypass Grafting; COPD – Chronic Obstructive Pulmonary Disease; LV – Left Ventricle; AKI – Acute Kidney Injury; THV – Transcatheter Heart Valves; LOS – Length of Stay; ICU – Intensive Care Unit.
of comorbid conditions that were associated with at least 15% risk of 30-day postoperative mortality.

OUTCOMES

The main endpoint was all-cause mortality at 1 year. Secondary outcomes included all-cause and cardiovascular (CV) mortality at 30 days and 1 year, and probability of long-term survival. Clinical endpoints were adjudicated using the updated Valve Academic Research Consortium (VARC) criteria [2].

STATISTICAL ANALYSIS

Absolute numbers, percentages, and medians were calculated to describe the population. For 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. Multivariate logistic regression analysis was used to identify clinical variables which were independently predictive of outcomes. Time-to-event analysis was performed using Kaplan–Meier estimates using THV implantation time as landmark, and was compared between groups with the use of the log-rank test. A 2-tailed p value of 0.05 was considered to indicate statistical significance.

A risk-adjusted analysis using propensity matching was performed to account for differences in baseline characteristics between groups. Weighted scores were obtained from regression data and greedy algorithm was utilized to identify 25 matched patients from each group.

RESULTS

The baseline demographic and clinical profiles of patients in both groups were generally similar (Table I). In the overall sample, the TAP group had a higher median Society of Thoracic Surgeons (STS) score compared to the TAO group (10.8 vs. 8.0, respectively; \( P = 0.01 \)), driven by a higher proportion of patients who had previous coronary artery bypass grafting (CABG; 9% vs. 38%; \( P = 0.01 \)) and stroke (30% vs. 70%; \( P = 0.01 \)). Procedural and 30-day clinical outcomes between groups were similar, except for longer median ICU and hospital LOS in the TAP group for both overall sample and the propensity-matched cohort.

All-cause mortality at 30 days was identical between groups (14% vs. 14%). Most of deaths in the TAP group was CV-related, while majority of deaths in the TAO group was from non-CV causes (Table II). CV mortality at 1 year was significantly higher in the TAP compared to the TAO group, both in the overall sample (22% vs. 2%, respectively; \( P = 0.01 \)) and stroke (30% vs. 70%; \( P = 0.01 \)). Procedural and 30-day clinical outcomes between groups were similar, except for longer median ICU and hospital LOS in the TAP group for both overall sample and the propensity-matched cohort.

All patients were followed for at least 21 months.
After a median follow-up period of 23 months, Kaplan-Meier analysis (Fig. 1) showed a persistent trend towards higher probability of long-term survival in the TAO compared to the TAP group (hazard ratio [HR] = 1.96, \( P = 0.059 \) in the overall sample; HR = 3.4, \( P = 0.01 \) in the matched cohort).

On multivariate regression analysis, none of the demographic variables was independently predictive of long-term mortality. Among the periprocedural clinical variables, the need for second THV implantation/valve-in-valve procedure (odds ratio [OR] 1.16, confidence interval [CI] 1.04–1.30), stage 3 acute kidney injury (OR 3.79, CI 1.50–9.58), and ICU LOS (OR 2.68, CI 2.65–2.71) were found to be independent predictors of 1-year mortality.

**DISCUSSION**

Up to 30% of patients with severe AS who are eligible for TAVR have inadequate iliofemoral access [3]. In these patients, alternative delivery routes for the THV include axillary/subclavian, TAP, TAO, and antegrade transseptal, among others [4,5]. Among the non-TF approaches, TAP TAVR is by far the most widely utilized (accounting for 80% in the US [6]) owing to the long worldwide experience with the technique, and abundant data regarding its safety and efficacy. Although effective, clinical outcomes with TAP TAVR have not been as favorable as that of TF access. For example, several international registries [7–9] have shown significantly higher mortality and morbidity associated with TAP compared to TF TAVR, both in the short- and long-term, prompting a search for other viable vascular access options.

We previously demonstrated the safety and technical feasibility of TAO TAVR in TF-ineligible patients. The technique is gaining popularity, and was utilized in 4% of all TAVR procedures during the first 18 months of its clinical introduction in the US [6]. However, data on TAO TAVR are limited, and information on clinical outcomes beyond 30 days are lacking. Our study provides a first glimpse at the longer-term safety and efficacy of TAO approach.

The all-cause mortality rate of TAO TAVR in our series was 18% at 1 year, which compares favorably with historical mortality data from the inoperable (30.7%) and high-risk (24.2%) cohorts of the PARTNER (Placement of Aortic Transcatheter Valves) trial [3,10], as well as the French national registry (24%) [7].

Our data point to a trend towards better overall survival with the TAO compared to the TAP group at 1 year and longer follow-up. Also, a higher incidence of CV mortality was observed in the TAP group. At 1 year, only 1 of the 7 deaths in the TAO group was CV-related (i.e., procedural mortality); the rest were deemed to be associated with the patient’s chronic comorbid conditions (i.e., pneumonia, sepsis, and chronic respiratory failure).

It is possible that the mortality difference between groups was due to the higher median STS score and rates of prior CABG and stroke in the TAP group; however, these variables were not predictive of mortality on regression analysis. Furthermore, the observed long-term differences between groups were essentially unchanged after propensity-matched adjusted analysis.

Interestingly, the need for a second THV implantation and ICU LOS were found to be independent predictors of 1-year mortality.
predictors of 1-year mortality in our series. A total of 5 TAP TAVR patients required valve-in-valve procedures (vs. none in the TAO group), presumably because THV delivery was more technically-challenging with TAP access.

Overall, TAP TAVR patients required a median 3 days longer ICU stay compared to TAO TAVR in our series. It was previously shown that prolonged ICU stay after cardiac surgery was associated with significantly worse overall outcomes. In one study, prolonged ICU LOS was an independent predictor of higher in-hospital mortality, and those who were discharged alive had worse long-term survival [11].

Our findings support the long-term safety and efficacy of TAO TAVR in patients with inoperable AS. Our data also suggest a trend towards better clinical outcomes compared to the TAP approach. These results, along with a more favorable technical learning curve, imply that the TAO route may be considered as the preferred alternative in patients with inadequate TF access.

LIMITATIONS

This was a nonrandomized, single-center registry study and the comparison between groups occurred over different time periods which may have introduced unmeasurable confounders. The dissimilarities in baseline characteristics, including higher risk profile of the TAP patients, could have accounted for the observed difference in outcomes between groups. Our cohort may not be directly comparable to that of prior trials and registries for this same reason. Our sample size is small, and larger, adequately powered randomized studies are required to make definitive conclusions.

CONCLUSION

The outcomes associated with TAO TAVR compare favorably with TAP TAVR. Our results appear to corroborate the long-term safety and efficacy of the TAO approach in TAVR patients with inadequate ilio-femoral access.

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