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Sex-Based Differences in Outcomes With Transcatheter Aortic Valve Therapy

TVT Registry From 2011 to 2014

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ABSTRACT

BACKGROUND A differential impact of sex has been observed in transcatheter aortic valve replacement (TAVR) outcomes from small observational studies and subgroup analyses of randomized trials.

OBJECTIVES The goal of this study was to compare the in-hospital and 1-year outcomes in male and female subjects from the U.S. nationwide TAVR registry.

METHODS National data from the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry were used for in-hospital outcomes, and data linked from the Centers for Medicare & Medicaid Services were used to provide 1-year events. Multivariable logistic regression adjustment was performed for in-hospital outcomes. Fine-Gray models were used for nonfatal 1-year outcomes to account for the competing risk of death.

RESULTS From 2011 to 2014, a total of 11,808 (49.9%) women and 11,844 (51.1%) men underwent TAVR. Compared with male patients, female patients were older, with a lower prevalence of coronary artery disease, atrial fibrillation, and diabetes but a higher rate of porcelain aorta, lower glomerular filtration rate, and higher mean Society of Thoracic Surgeons score (9.0% vs. 8.0%; all $p < 0.001$). Women were treated more often by using nontransfemoral access than men (45.0% vs. 34.0%). Despite using smaller device sizes, women achieved valve cover index ≥8% more often than men (66% vs. 54%). In-hospital vascular complications were higher in women (8.27% vs. 4.39%; adjusted hazard ratio [HR]: 1.70; 95% CI: 1.34 to 2.14; $p < 0.001$) and a trend toward higher bleeding (8.01% vs 5.96%; adjusted HR: 1.19; 95% CI: 0.99 to 1.44; $p = 0.06$) was observed; however, 1-year mortality was lower (21.3% vs. 24.5%; adjusted HR: 0.73; 95% CI: 0.63 to 0.85; $p < 0.001$) in women than in men.

CONCLUSIONS Female patients undergoing TAVR had a different risk profile compared with male patients. Notwithstanding a greater adjusted risk for in-hospital vascular complications, 1-year adjusted survival was superior in female patients. (J Am Coll Cardiol 2016;68:2733–44) © 2016 by the American College of Cardiology Foundation.

Transcatheter aortic valve replacement (TAVR) has increasingly been adopted as the definitive treatment for severe symptomatic aortic valve stenosis in patients at extreme high risk for surgery (1,2). Unlike percutaneous coronary intervention, approximately 50% of patients undergoing TAVR are female (3,4). Female subjects are at higher risk of procedural complications compared with male subjects, particularly bleeding and vascular complications (4,5). These events have been associated with increased post-TAVR rehospitalization and mortality (4,6,7).

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ABBREVIATIONS AND ACRONYMS

CI = confidence interval

CMS = Centers for Medicare & Medicaid Services

GFR = glomerular filtration rate

HR = hazard ratio

MACE = major adverse cardiac events

MI = myocardial infarction

NACE = net adverse cardiac events

NYHA = New York Heart Association

OR = odds ratio

STS/ACC = Society of Thoracic Surgeons/American College of Cardiology

TAVR = transcatheter aortic valve replacement

TVT = Transcatheter Valve Therapy

VARC = Valve Academic Research Consortium

Heart teams typically use algorithmic scores such as the European System for Cardiac Operative Risk Evaluation score and the Society of Thoracic Surgeons (STS) score to determine the 30-day mortality and morbidity risks, as an aid to decision-making for selection of optimal therapies (TAVR, surgical aortic valve replacement, or medical therapy). However, these scores were designed to predict surgical, not TAVR risk (8,9). Moreover, because these scores attribute a higher risk to female sex (10), early risks may be overestimated and potentially result in underutilization of definitive valve replacement.

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The longer term clinical outcomes after TAVR in female subjects compared with male subjects have not been extensively studied. Several observational studies and a recent meta-analysis have indicated improved survival in female patients undergoing TAVR than male patients (4,5,11,12). However, given the higher rate of procedural complications in female patients, the reasons for this finding are not fully understood. The 1-year post-TAVR clinical outcomes in female patients are of significant interest because they can influence expert consensus statements and recommendations for selection of patients for TAVR. We therefore sought to examine the sex-based differences in patients undergoing TAVR from the large national Transcatheter Valve Therapy (TVT) registry of the STS/American College of Cardiology (ACC). This registry is one of the largest of valve patients to date, receiving prospectively collected data on patients undergoing TAVR from 348 centers nationwide. All patients undergoing commercial TAVR in the United States with an approved valve device are routinely entered into this registry per the mandate of the U.S. Centers for Medicare & Medicaid Services (CMS) (1).

METHODS

The STS/ACC TVT Registry was established in 2011 in accordance with the CMS National Coverage Determination requirements for TAVR reimbursements. The registry is periodically audited and includes comprehensive baseline information, as well as 30-day and 1-year follow-up data. The registry data are linked with Medicare administrative claims for detection of events requiring hospitalization. This methodology of data acquisition, event ascertainment, and analysis in the STS/ACC TVT Registry has been previously published in detail (3).

ENDPOINTS AND DEFINITIONS. Endpoints were assessed in the hospital and at 1 year. In-hospital events included all-cause death, myocardial infarction (MI), stroke, major bleeding, and major vascular complications as per the Vascular Academic Research Consortium (VARC)-2 definition (13). Major adverse cardiac events (MACE) were defined as the composite of death, MI, or stroke. Net adverse cardiac events (NACE) were defined as the composite of in-hospital MACE, major bleeding, or major vascular complication. Other endpoints included composite death or stroke and death or MI.

One-year individual endpoints included time to event occurrence of death, MI, stroke, and clinically significant bleeding. Composite endpoints included MACE, death or stroke, death or MI, and a composite of MACE or clinically significant bleeding.

In-hospital events were validated at the site level before submission into the TVT Registry. In-hospital VARC-2 major bleeding was defined as in-hospital bleeding or a vascular event with hemoglobin drop or need for transfusion. VARC-2 major vascular complication was defined as the composite of major vascular access site complication or unplanned vascular surgery, annular rupture, aortic dissection, or perforation with or without tamponade. One-year events were derived from CMS data. One-year clinically significant bleeding was a composite of International Classification of Diseases-9th Revision-Clinical Modification, codes derived from CMS claims data (Online Appendix).

STATISTICAL ANALYSIS. Groups were compared according to sex. Categorical data are presented as frequencies (percentages) and were compared by using the Pearson chi-squared test. Continuous variables are presented as mean ± SD or median (interquartile range) and were compared by using the Wilcoxon rank-sum test. Estimated odds ratios for in-hospital outcomes were generated by using logistic regression with generalized estimating equations to account for within-center clustering. One-year event rates were calculated by using the Kaplan-Meier method or as the cumulative incidence for nonfatal events. Because in-hospital events were derived from registry data and 1-year events were derived from CMS data, time-to-event curves represent a combination of the 2 data sources. Estimated hazard ratios (HRs) and confidence intervals (CIs) were generated by using a Cox model, with robust variance estimation to account for within-center clustering. Nonfatal events were analyzed by using the Fine-Gray method for competing risks (1,14). All analyses were performed in SAS version 9.4 (SAS Institute, Inc., Cary,