Different impact of sex on baseline characteristics and major periprocedural outcomes of transcatheter and surgical aortic valve interventions: Results of the multicenter Italian OBSERVANT Registry

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Background: Despite the widespread use of transcatheter aortic valve implantation (TAVI), the role of sex on outcome after TAVI or surgical aortic valve replacement (AVR) has been poorly investigated. We investigated the impact of sex on outcome after TAVI or AVR.

Methods: There were 2108 patients undergoing TAVI or AVR who were enrolled in the Italian Observational Multicenter Registry (OBSERVANT). Thirty-day mortality, major periprocedural morbidity, and transprosthetic gradients were stratified by sex according to interventions.

Results: Female AVR patients showed a worse risk profile compared with male AVR patients, given the higher mean age, prevalence of frailty score of 2 or higher, New York Heart Association class of 3 or higher, lower body weight, and preoperative hemoglobin level ($P \leq .02$). Similarly, female TAVI patients had a different risk profile than male TAVI patients, given a higher age and a lower body weight and preoperative hemoglobin level ($P \leq .005$), but with a similar New York Heart Association class, frailty score, EuroSCORE ($P =$ NS), a better left ventricular ejection fraction and a lower prevalence of left ventricular ejection fraction less than 30%, porcelain aorta, renal dysfunction, chronic obstructive pulmonary disease, arteriopathy, and previous cardiovascular surgery or percutaneous coronary intervention ($P \leq .01$). Women showed a smaller aortic annulus than men in both populations ($P < .001$). Female sex was an independent predictor in the AVR population for risk-adjusted 30-day mortality (odds ratio [OR], 2.34; $P = .043$) and transfusions (OR, 1.47; $P = .003$), but not for risk-adjusted acute myocardial infarction, stroke, vascular complications, permanent atrioventricular block ($P =$ NS). Female sex was an independent predictor in the TAVI population for risk-adjusted major vascular complications (OR, 2.92; $P = .018$) and transfusions (OR, 1.93; $P = .003$), but proved protective against moderate to severe postprocedural aortic insufficiency ($P = .018$).

Conclusions: Female sex is a risk factor for mortality after aortic valve replacement, for major vascular complications after TAVI, and for transfusions after both approaches. (J Thorac Cardiovasc Surg 2014;147:1529-39)

Transcatheter aortic valve implantation (TAVI) has been reported as an effective treatment option for severe aortic stenosis in patients at high risk for current surgical aortic valve replacement (AVR).[1] However, few studies have investigated the impact of sex-related differences on periprocedural outcomes after TAVI, although the role of sex on short- and long-term outcome after cardiac surgery has been addressed extensively and female sex has been shown as a risk factor for perioperative mortality in both the EuroSCORE and Society of Thoracic Surgeons Risk Score.[2,3] As far as TAVI is concerned, contradictory results have been reached: some investigators have shown improved survival in female patients after TAVI,[1,4,5] other investigators have found an increased risk for major vascular complications together with a higher rate of blood transfusions.[6] These studies, however, came from retrospective analyses of single-center experiences.[4-6]

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Abbreviations and Acronyms

AV = atrioventricular
AVR = aortic valve replacement
LVEF = left ventricular ejection fraction
NYHA = New York Heart Association
OBSERVANT = Observational Study of Appropriateness, Efficacy, and Effectiveness of AVR-TAVI procedures for the treatment of severe symptomatic aortic stenosis
OR = odds ratio
PARTNER = Pivotal Placement of Aortic Transcatheter trial
TAVI = transcatheter aortic valve implantation

Therefore, the aim of this study was to investigate the role of sex on both clinical presentation and postprocedural outcomes after TAVI and AVR. The analysis was performed from a prospective series of patients enrolled in the Italian National Institute of Health Observational Multicenter Registry (Observational Study of Appropriateness, Efficacy, and Effectiveness of AVR-TAVI procedures for the treatment of severe symptomatic aortic stenosis [OBSERVANT]), a prospective registry aimed at evaluating the efficacy and effectiveness of TAVI versus AVR procedures for the treatment of severe symptomatic aortic stenosis.

METHODS

Study Design and Data Collection

In December 2010, the Italian National Health Institution in cooperation with the Italian Ministry of Health, the National Agency for Regional Health Services, Italian regions, and Italian scientific societies representing the professionals involved in the management of patients with severe aortic stenosis launched OBSERVANT.[7] Enrollment started in January 2011 and ended in June 2012. However, the present analysis refers to the first 6 months of OBSERVANT data collection. The study protocol was approved by the local ethics committees. All patients enrolled in the database provided informed consent in an anonymous form. A detailed description of the study protocol has been reported previously.[7]

Study Population

On the basis of established criteria, the study included all symptomatic adult patients admitted to hospitals with a diagnosis of severe symptomatic aortic stenosis (defined as an aortic valve area <1 cm^2, a maximum aortic velocity >4 m/s, or a mean pressure gradient >40 mm Hg) and requiring an aortic valve procedure.[7] Treatment allocation always came from the review of the local multidisciplinary heart team involving cardiologists, surgeons, and anesthesiologists, as per current guidelines.[8]

Because of the observational nature of the registry, there was no standardization of clinical protocols: accordingly, techniques for TAVI and AVR were left to the discretion of each participating center. Each interventional team could choose to implant 1 of the 2 commercially available valves: the balloon-expandable Edwards Sapien or Sapien XT prosthesis (Edwards Lifesciences, Irvine, Calif) or the self-expandable CoreValve (Medtronic, Minneapolis, Minn). Sapien devices were implanted by either the transfemoral or transapical route, and CoreValve devices were implanted by the transfemoral or transaxillary approach. Antiplatelet regimens and anticoagulation protocols similarly were based on individual institutional policies. Surgery, management of cardiopulmonary bypass, cardioplegic techniques, and anesthetic techniques were all left to each individual center's discretion, although they were based on well-established institutional policies.[7]

End Points and Follow-up Evaluation

Overall hospital mortality was the primary end point of the OBSERVANT study, whereas secondary end points included overall mortality within 12 and 24 months and the incidence of in-hospital major adverse cardiac and cerebrovascular events, as already reported.[7]

For the purpose of this study, differences in preoperative characteristics between women and men in both TAVI and AVR populations were investigated. Hospital mortality was considered the primary end point and was stratified by sex according to interventions. Acute myocardial infarction, stroke, major cardiovascular complications, transfusions, permanent atrioventricular (AV) block, and transprosthetic gradients were secondary end points and similarly stratified by sex according to interventions.[7] Definitions of end points already have been reported.[7] End points were adjudicated by 2 independent investigators at each participating center.

Statistical Analysis

All the analyses were performed stratifying by type of intervention and sex.

Continuous variables are presented as mean $\pm$ standard deviations and were compared by the Student t test; categoric variables are presented as counts and percentages and were compared by the chi-square test or the Fisher exact test when appropriate. The unadjusted effects of sex on periprocedural outcomes and 30-day mortality were estimated by univariate logistic regression models for dichotomous outcomes and by linear regression models for continuous outcomes. For each considered end point a specific stepwise procedure was used to identify the independent predictors (exclusion probability, 0.10; inclusion probability, 0.20). Sex was used as the determinant, whereas all the measured potential confounders, including variables related to the multicenter nature of the study (ie, volume of cases by center, surgeon experience, management of anesthesiology/surgery/percutaneous procedures), were offered to the model as independent variables. For each considered end point a specific multivariable logistic regression or linear regression model was implemented using age plus the variables selected by the stepwise procedures. Risk-adjusted odds ratio (OR) or exponentiation of the beta coefficient (dependent variable variation in women vs men) and corresponding P values are presented for AVR and TAVI separately. Intercorrelation between independent variables was checked with appropriate tests, and co-linearity was avoided by selecting the most relevant variable (based on statistical and clinical considerations) between 2 co-linear variables.

All the analyses were performed using the statistical package STATA version 11 (Stata Corp, College Station, Tex). A P value less than .05 was considered significant.

RESULTS

Population Enrolled and Participating Centers

A total of 101 centers (60 cardiac surgery units and 41 catheter laboratories) participate in the registry. Between January 2011 and June 2011 the population comprised 2108 patients, 1383 (65.6%) of whom underwent surgical