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Transcatheter or surgical treatment of severe aortic stenosis and coronary artery disease: A comparative analysis from the Italian OBSERVANT study

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ABSTRACT

Background: To assess clinical outcomes of patients with concomitant severe aortic stenosis (AS) and coronary artery disease (CAD) who underwent transcatheter aortic valve implantation (TAVI) and percutaneous coronary intervention (PCI) or surgical aortic valve replacement (SAVR) and coronary artery bypass grafting (CABG).
Methods: Data were extracted from the multicenter OBSERVANT study. For the purposes of the present analysis, we included only patients with established stable CAD meeting any of the following inclusion criteria: 1) TAVI patients with CAD undergoing staged PCI or TAVI and PCI in the same session; 2) SAVR patients undergoing combined SAVR and CABG in the same session.
Results: After propensity-score matching, a total of 472 patients (236 per group) were identified. Among TAVI patients, PCI was performed prior to the procedure in 217 patients (92.0%), whereas concomitant TAVI and PCI were performed in 19 patients (8.0%). At 3-year, there was no difference in survival between the two groups (KM estimate of freedom from death for SAVR and TAVI patients of 0.742 and 0.650, respectively; log-rank *p*-value of 0.105). The rate of MACCE was comparable between the two groups (KM estimate of freedom from MACCE for SAVR and TAVI patients of 0.683 and 0.582, respectively; log-rank *p*-value of 0.115).
Conclusions: In patients with associated severe AS and CAD, percutaneous treatment (TAVR and staged or concomitant PCI) was comparable to surgical treatment (SAVR and concomitant CABG) with respect to the early and mid-term risk of death from any cause, myocardial infarction, stroke and unplanned revascularization.

1. Introduction

Coronary artery disease (CAD) is common in patients with severe aortic stenosis (AS), which does not surprise because these two pathologies share many causative factors [1]. The presence of concomitant CAD has been associated with adverse procedural outcomes in aortic valve replacement [2, 3].

If in surgical patients the current standard of care for patients with concomitant AS and CAD is to combine coronary artery bypass grafting (CABG) with surgical aortic valve replacement (SAVR) in the same session [4, 5], optimal management of CAD in the context of transcatheter aortic valve implantation (TAVI) is highly debated due to the lack of comprehensive and consistent data on this topic [6, 7]. However, in clinical practice, prophylactic percutaneous coronary intervention (PCI) or concomitant TAVI and PCI of coronaries supplying large myocardial areas are the most adopted approaches [7–10].

The comparative efficacy of TAVI and SAVR has been extensively investigated in large randomized trials [11–14] and propensity matched-based observational studies [15]. However, patients with CAD requiring coronary revascularization were excluded from the majority of

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randomized trials or poorly investigated, thus creating an important gap in the current evidence [11–14].

To shed light on this controversial area, we report on the mid-term clinical outcomes of a large series of patients with concomitant severe AS and CAD who underwent TAVI and PCI or SAVR and CABG and were recruited in the Italian national multicenter OBSERVANT (Observational Study of Effectiveness of SAVR-TAVI Procedures for Severe Aortic Stenosis Treatment) study.

2. Methods

2.1. Study design and data quality assessment

OBSERVANT is a national observational, prospective, multicenter, cohort study that enrolled consecutive patients undergoing TAVI or SAVR for severe aortic valve stenosis at 93 Italian cardiology/cardiac surgery centers. Details on the study design, patient eligibility criteria, and data collection modalities of the OBSERVANT registry have been reported elsewhere [16, 17]. This study was coordinated by the Italian National Institute of Health and led in cooperation with the Italian Ministry of Health, the National Agency for Regional Health Services, Italian Regions, and Italian scientific societies and federations representing Italian professionals involved in the management of severe AS. In the participating hospitals, both SAVR and TAVI were available options. Techniques and choice of the prosthesis were left to the operator's discretion according to local pre-interventional workout and institutional practice. The Ethical Committee of each participating center approved the study protocol, and patients gave their informed consent to participate in the study.

2.2. Patient population

Invasive coronary angiography was mandatory in all patients and was assessed by the local heart team. In case of significant CAD (i.e., >50% diameter stenosis on visual assessment of the coronary angiogram), the treatment strategy and completeness of revascularization was determined based on consensus decision before TAVI or SAVR at each participating center. For the purposes of the present analysis, we included only patients with established stable CAD (i.e., documented by coronary angiography) meeting any of the following inclusion criteria: 1) TAVI patients with CAD undergoing PCI prior to the procedure (<6 months before TAVI) or combined TAVI and PCI in the same session; 2) SAVR patients undergoing combined SAVR and CABG in the same session. Inoperable patients (i.e. porcelain aorta and hostile thorax) and patients undergoing hybrid PCI and CABG procedures, concomitant interventions in other valves, or those undergoing TAVI non-transfemoral access were excluded.

2.3. Outcomes of interest

The primary outcomes of interest were all-cause mortality and the composite of death, myocardial infarction, stroke and unplanned revascularization at 30 days, 1, 2 and 3 years from SAVR or TAVI. Unplanned revascularization was defined as any revascularization procedure (CABG or PCI) performed at least 30 days after the index intervention or as revascularization for acute myocardial infarction at any time point.

2.4. Follow up

As part of the OBSERVANT study, an administrative follow-up has been set up for each enrolled patient through a record linkage with the National Hospital Discharged Records (HDR) database (for in-hospital events: re-hospitalization, stroke, acute myocardial infarction, PCI and CABG) and with the Tax Registry Information System (TRIS) (for information on life status). Specific quality assessment activities were arranged to evaluate the reliability and coherence of the OBSERVANT database. In particular, independent observers, following specific standard operating procedures, monitored the participating hospitals to assess the completeness of the enrolled cohort and to compare the collected data to those reported in the original clinical charts.

2.5. Statistical analysis

Continuous variables are reported as mean and standard deviation (SD) while dichotomous parameters as frequencies and percentages (%). The normal distribution of continuous parameters was tested with the Kolmogorov-Smirnov test. Variables with a skewed distribution were compared with the use of Wilcoxon rank sum tests. *t*-Test, Chi-square or Fisher exact tests were used to compare frequencies among groups, as appropriate. Unadjusted event rates at follow-up were plotted according to the Kaplan-Meier method and differences in survival were tested with the log-rank test. We used the cumulative incidence function to account for the competing risk of death with other events of interest (e.g. MI, stroke and unplanned revascularization). We then compared the cumulative incidence functions between SAVR and TAVI groups using the Gray test.

2.6. Propensity score matching

To account for the non-randomized design of our study, a propensity score has been estimated using a logistic regression model according to a non-parsimonious approach [18]. The following clinical pre-procedural variables were included in the model: age, gender, chronic obstructive pulmonary disease, diabetes, history of myocardial infarction, left ventricular ejection fraction, neurological disease, creatinine and hemoglobin levels, dialysis, Euroscore II-estimated risk of 30-day mortality, frailty, New York Heart Association functional class III or IV at presentation, moderate-to-severe mitral regurgitation, peripheral artery disease, mean gradient, pulmonary hypertension. Pairs of SAVR and TAVI patients having the same probability score (nearest neighbor method; caliper = 0.25 * SD (logitPs)) have been matched with a 1:1 ratio. Standardized mean differences before and after matching were calculated and a standardized difference below 10% was considered as a criterion of balance between the study cohorts. In addition to weighting, a simultaneous multivariate adjustment (doubly robust estimate) was performed for covariates included in the propensity score model with an absolute standardized difference >10% after weighting. Finally, predicted probabilities of survival from the adjusted Cox-model were obtained and plotted for the principal outcomes of interest.

All tests performed in the current analysis are two-tailed and a p-value < 0.05 has been considered statistically significant. All statistical analyses were conducted in R statistical software (version 3.2.1) equipped with the "twang" and "survival" packages.

3. Results

A total of 7618 consecutive patients with severe AS were enrolled in the OBSERVANT study between December 2010 and June 2012. All patients underwent either SAVR ($n = 5707$) or TAVI ($n = 1911$) between December 2010 and June 2012. From this unselected cohort, a total of 1719 patients (1420 SAVR and 299 TAVI patients) met the inclusion/exclusion criteria for this post-hoc analysis and were included in the study. Administrative linkage was carried out in 100% of patients and follow-up was complete in all patients.

Clinical characteristics between the SAVR and TAVI groups are shown in Table 1. As expected, before matching there was a marked unbalance in covariates between the two groups.

3.1. Propensity scores balance

After matching, a total of 236 pairs of patients were identified. Differences between TAVI and SAVR patients were well corrected for most of covariates, except for creatinine, dialysis and low LVEF (<30%), with standardized differences slightly above 10% (12.6, 10.8 and 11.6%, respectively). To take into account this imbalance, all the outcome estimate provided below have been adjusted for these three covariate following the doubly robust estimate approach.

3.2. Procedural characteristics of the matched cohorts

All TAVI procedures were performed using the third-generation, self-expanding CoreValve prosthesis (Medtronic Inc., Galway, Ireland) or the balloon-expandable Edwards SAPIEN XT (Edwards Lifescience, Irvine, CA). Among TAVI patients, PCI was performed prior to the procedure in 217 patients (92.0%), whereas concomitant TAVI and PCI were performed in 19 patients (8.0%). All SAVR patients underwent concomitant valve replacement and CABG.

3.3. Periprocedural and in-hospital outcomes

Moderate or severe paravalvular regurgitation (0.6% vs. 14.3%, $p < 0.001$), vascular complications (0.8% vs. 9.3%, $p < 0.001$) and high degree conduction disturbances requiring pacemaker implantation (3.0% vs. 17.4%, $p < 0.001$) were more frequently encountered in TAVI patients. Conversely, acute kidney injury (14.0% vs. 2.5%, $p \leq 0.001$) and bleeding requiring >4 units of RBCs (15.3% vs. 3.4%, $p < 0.001$) were more frequently reported in the surgical cohort.

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