Early and late outcomes after transcatheter versus surgical aortic valve replacement in obese patients

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Abstract

Introduction: Data on the early and late outcome following transcatheter aortic valve implantation (TAVI) and surgical aortic valve replacement (SAVR) in obese patients are limited. We investigated whether TAVI may be superior to SAVR in obese patients.

Material and methods: Obese patients (body mass index ≥ 30 kg/m²) who underwent either SAVR or TAVI were identified from the nationwide OBSERVANT registry, and their in-hospital and long-term outcomes were analysed. Propensity score matching was employed to identify two cohorts with similar baseline characteristics.

Results: The propensity score matching provided 142 pairs balanced in terms of baseline risk factors. In-hospital and 30-day mortality did not differ between SAVR and TAVI obese patients (4.6% vs. 3.3%, p = 0.56, and 5.2% vs. 3.2%, p = 0.41, respectively). Obese SAVR patients experienced a higher rate of renal failure (12.4% vs. 3.6%, p = 0.0105) and blood transfusion requirement (60.3% vs. 25.7%, p < 0.0001) in comparison with TAVI patients. A higher rate of permanent pacemaker implantation (14.4% vs. 3.6%, p = 0.0018), and major vascular injuries (7.4% vs. 0%, p = 0.0044) occurred in the TAVI group. Five-year survival was higher in the SAVR group compared to the TAVI patient cohort (p = 0.0046), with survival estimates at 1, 3 and 5 years of 88.0%, 80.3%, 71.8% for patients undergoing SAVR, and 85.2%, 69.0%, 52.8% for those subjected to TAVI procedures.

Conclusions: In obese patients, both SAVR and TAVI are valid treatment options, although in the long term SAVR exhibited higher survival rates.

Key words: transcatheter aortic valve implantation, aortic valve replacement, obesity, mortality.
Introduction

Recent data demonstrated an overall increase in patients referred for either transcatheter aortic valve implantation (TAVI) or surgical aortic valve replacement (SAVR) [1, 2]. These patients present a severe comorbidity profile, including obesity [1, 3–7]. Although obesity is a severe chronic health condition predisposing to coronary artery disease (CAD) and other adverse cardiovascular events, there is a paucity of data comparing the effectiveness of TAVI vs. SAVR in this patient population [3, 5]. The purpose of the present study was to analyse and compare the early and late outcomes of obese patients undergoing TAVI and SAVR from a nationwide prospective cohort study.

Material and methods

Patients and study design

The OBSERVANT (Observational Study of Effectiveness of SAVR–TAVI Procedures for Severe Aortic Stenosis Treatment) is a national prospective observational cohort study that enrolled consecutive patients affected by severe aortic stenosis at 93 Italian centres between December 2010 and June 2012. Briefly, the study was run by the Italian National Institute of Health in collaboration with the Italian Ministry of Health, the National Agency for Regional Health Services, Italian Regions, and Italian scientific cardiologic and cardiac surgery societies [8, 9]. The complete list of the executive working group, participating centres and investigators is reported in the Supplementary Table S1.

The detailed protocol with patient eligibility criteria and data collection modalities have been previously reported in detail [6]. Data were collected prospectively and underwent robust validation to ensure high data quality, with systematic review of administrative and medical chart audits in order to correct clinical and temporal conflicts and/or discrepancies [8]. Data on patient characteristics, demographics, comorbidities, intraoperative factors, and postoperative outcomes were collected in a standardized online datasheet on a password-protected website, stored and analysed at the Italian National Institute of Health [6]. Information on survival and in-hospital events was obtained through a record linkage with the National Hospital Discharged Records database (Ministry of Health) and with the Tax Registry Information System, respectively. This study was approved by the Regional or Institutional Review Board (IRB) of the participating centres. All patients provided written informed consent for their participation and follow-up evaluations.

The study population included all consecutive adult patients requiring TAVI and SAVR for severe aortic valve stenosis. Body mass index (BMI) was defined as the weight in kilograms divided by the square of the height in metres (kg/m²) [10], and according to the World Health Organization (WHO) classification [11], obese patients were defined as those having a BMI ≥ 30 kg/m². Only obese patients were included for the purpose of the present study (Supplementary Figure S1). The choice of SAVR technique and the type of prosthesis as well as the type of TAVI valve and approach were left to the physician’s discretion and individual institutional practice.

Primary outcome measures were 30-day and 5-year mortality from intervention. Secondary outcomes included in-hospital adverse events, such as in-hospital mortality, cardiac tamponade, perioperative acute myocardial infarction (AMI), stroke, renal failure, permanent pacemaker (PM) implantation, vascular complications, blood transfusion, infections, and intensive care unit (ICU) stay. Outcome definitions have been previously reported in detail [8].

This study complies with The REporting of studies Conducted using Observational Routinely collected health Data (RECORD) statement (Supplementary Table SII) [12].

Statistical analysis

Statistical analysis was performed using the SAS statistical package, version 9.4 (SAS Institute Inc., Cary, NC, USA). The normal distribution of continuous variables was tested with the Kolmogorov-Smirnov test. Variables with a skewed distribution were compared using Wilcoxon rank sum tests. The t-test, χ² or Fisher’s exact test was used to compare frequencies among groups of treated patients, as appropriate. Exploratory analyses showed that the TAVI cohort had a significantly higher operative risk compared to the SAVR cohort. Therefore, a propensity score was calculated by non-parsimonious logistic regression and employed for one-to-one matching of patients undergoing SAVR and TAVI using the nearest neighbour method and a caliper of 0.2 of the standard deviation of the logit of the propensity score. The t-test for paired sample for continuous variables, the McNemar test for dichotomous variables, the Stuart-Maxwell test for categorical variables and the analysis of the standardized differences after matching were used to evaluate the balance between the matched groups. The same tests were used to test differences in the early adverse events of propensity score matched groups. When a patient of a pair was lost to follow-up and the matched patient was still alive, the time of observation of both patients was truncated at the time of the last observation of the lost patient in order to warrant the comparability of the study groups. Differences in the outcomes at 5 years
were evaluated by the Kaplan-Meier method with the Klein-Moeschberger stratified log rank test. Tests were two-sided and a $p < 0.05$ was considered statistically significant.

**Results**

Among a total of 7618 consecutive patients enrolled in the OBSERVANT cohort study, 1463 obese patients who underwent SAVR ($n = 1213$) or TAVI ($n = 250$) were identified and retained for this analysis. Baseline characteristics, including demographic data, comorbidities and cardiac status are summarized in Table I. Briefly, in the SAVR group, 957 (78.9%) patients were classified as obese class I (BMI 30 – < 35 kg/m$^2$), 205 (16.9) as obese class II (BMI 35 – < 40 kg/m$^2$), and 51 (4.2%) as obese class III (BMI $\geq$ 40 kg/m$^2$), while in the TAVI group, 179 (71.6%) were classified as obese class I, 54 (21.6%) as obese class II, and 17 (6.8%) as obese class III. Patients in the TAVI cohort tended to be older, frail, and more frequently affected by heart failure and severe comorbidities (Table I).

After propensity score-matching analysis, 142 pairs of SAVR and TAVI patients were obtained and postmatching standardized differences for all measured covariates were less than 10%, suggesting substantial covariate balance across groups (Supplementary Figures S2 and S3). This was confirmed by a balance in the European System for Cardiac Operative Risk Evaluation (EuroSCORE) II ($4.7 \pm 5.8\%$ vs. $4.5 \pm 4.7\%$, $p = 0.73$; Table I). In the matched population, in-hospital mortality during the index admission and 30-day mortality did not differ between the two groups (3.6% vs. 4.3%, $p = 0.76$, and 4.2% vs. 3.5%, $p = 0.76$, respectively). Obese SAVR patients experienced a higher rate of renal failure (12.4% vs. 3.6%, $p = 0.0105$) and blood transfusion (60.3% vs. 25.7%, $p < 0.0001$) in comparison with TAVI obese patients. Conversely, a higher rate of permanent pacemaker implantation (14.4% vs. 3.6%, $p = 0.0018$), and major vascular injuries (7.4% vs. 0%, $p = 0.0044$) was registered in the TAVI cohort. No differences in other outcomes of interest were recorded between the two groups, including length of stay in the intensive care unit (Table II). Transcatheter aortic valve implantation was associated with significantly lower 5-year survival than SAVR ($p = 0.0046$). Actuarial survival estimates at 1, 3 and 5 years were 88.0%, 80.3%, 71.8% after SAVR, and 85.2%, 69.0%, 52.8% after TAVI (Figure 1).

**Discussion**

In this large nationwide prospective cohort study, we observed that in obese patients (BMI $\geq$ 30 kg/m$^2$): 1) both SAVR and TAVI had comparable in-hospital and 30-day mortality; 2) in-hospital complications including renal failure and blood transfusion requirement were more frequent in patients who underwent SAVR, while permanent PM implantation and major vascular injury rates were higher in those who underwent TAVI; and 3) TAVI was associated with lower 5-year survival than SAVR.

Our findings are of interest in light of the increased number of high-risk patients referred for either SAVR or TAVI procedures [1, 2]. Over a 5-year period, Brennan et al. [2] documented an overall increase in patients undergoing SAVR, analysing data from 800 cardiac surgery centres across the United States, and observing an even more pronounced trend among institutions offering on-site TAVI procedures. In-hospital mortality for all SAVR procedures at TAVI sites significantly declined from 3.4% to 2.9%, with the greatest declines among intermediate and high-risk SAVR patients [3]. Consonant data have been reported in patients undergoing TAVI, including improved survival and other postoperative outcomes [3, 13, 14]. As a consequence, a non-negligible stratum of obese patients is potentially referred for either SAVR or TAVI. In our study, the prevalence of obese patients was 21% and 13% in SAVR and TAVI groups, respectively. Similar data have been observed from other registries [1, 3–5]. However, although obesity is a cluster of related risk factors including hypertension, diabetes, dyslipidaemia and renal dysfunction [15], comparative data on early and late outcomes in obese patients undergoing SAVR and TAVI are lacking. Ando and colleagues [3] using the National Inpatient Sample (NIS) data from a US community hospital, analysed in-hospital mortality and adverse events occurring in obese (BMI $\geq$ 30 kg/m$^2$) patients following SAVR and TAVI procedures. In this series, TAVI portended similar in-hospital mortality and a lower rate of perioperative myocardial infarction, renal failure, and other end-organ complications [3]. However, no mid- or long-term survival data comparing SAVR and TAVI procedures in obese patients were presented [3]. Only the U.S. pivotal trial and NOTION trial in unadjusted sub-group analyses evaluated the 2-year survival between obese patients treated with SAVR versus TAVI, and no differences were observed [16, 17].

The present study is the first comparing 5-year mortality between SAVR and TAVI in obese patients, documenting that both procedures achieved goods early results, but with a higher 5-year mortality for TAVI patients. This possibly highlights a technique-related late survival benefit of SAVR in the obese patient cohort. Certainly, this result is in contrast with the 5-year outcome data of the PARTNER 1 study [18], where risk of death was 67.8% in the TAVI group compared with 62.4%
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Table I. Baseline characteristics of obese patients in pre- and post-matched treatment cohorts

| Clinical and operative variables | Overall series | Propensity score matched pairs |
|----------------------------------|---------------|--------------------------------|
|                                  | SAVR (N = 1213) | TAVI (N = 250) | P-value | SAVR (N = 142) | TAVI (N = 142) | P-value |
| Demographic:                     |               |                  |         |               |                  |         |
| Age [years]                      | 72.2 ±8.8     | 80.6 ±5.4       | < 0.0001| 79.7 ±5.2     | 79.5 ±5.7       | 0.78     |
| Female                           | 589 (48.6)    | 172 (68.8)      | < 0.0001| 92 (64.8)     | 94 (66.2)       | 0.81     |
| BMI [kg/m²]                      | 33.2 ±3.3     | 33.9 ±4.2       | 0.02    | 33.3 ±3.2     | 33.7 ±3.7       | 0.30     |
| BMI classes [kg/m²]:             |               |                  |         |               |                  |         |
| 30–35                            | 957 (78.9)    | 179 (71.6)      | 0.03    | 110 (77.5)    | 107 (75.4)      | 0.56     |
| 35–40                            | 205 (16.9)    | 54 (21.6)       | 0.02    | 27 (19.0)     | 25 (17.6)       | 0.03     |
| > 40                             | 51 (4.2)      | 17 (6.8)        | 0.02    | 5 (3.5)       | 10 (7.0)        | 0.02     |
| Haemoglobin [mg/dl]              | 12.6 ±1.8     | 11.7 ±1.6       | < 0.0001| 12.1 ±1.7     | 11.9 ±1.6       | 0.26     |
| Albumin [mg/dl]                  | 3.7 ±1.03     | 3.7 ±0.7        | 0.40    | 3.6 ±1.3      | 3.7 ±0.6        | 0.24     |
| eGFR [mg/min/1.73 m²]            | 68.5 ±22.0    | 55.5 ±21.6      | < 0.0001| 56.9 ±18.8    | 58.0 ±21.3      | 0.65     |
| Cardiac status:                  |               |                  |         |               |                  |         |
| LVEF < 50%                       | 176 (15.7)    | 58 (23.4)       | 0.00    | 30 (21.1)     | 25 (17.6)       | 0.42     |
| NYHA class III–IV                | 497 (41.2)    | 166 (67.5)      | < 0.0001| 84 (59.2)     | 88 (62.0)       | 0.61     |
| Unstable angina                  | 45 (3.8)      | 10 (4.1)        | 0.82    | 5 (3.5)       | 3 (2.1)         | 0.41     |
| Urgent status                    | 43 (3.5)      | 6 (2.4)         | 0.36    | 4 (2.8)       | 6 (4.2)         | 0.41     |
| Concomitant CAD                  | 385 (31.7)    | 56 (22.4)       | 0.00    | 29 (20.4)     | 31 (21.8)       | 0.77     |
| Prior AMI                        | 119 (10.0)    | 25 (10.1)       | 0.95    | 8 (5.6)       | 10 (7.0)        | 0.62     |
| Pulmonary hypertension           | 52 (4.6)      | 36 (14.8)       | < 0.0001| 16 (11.3)     | 12 (8.5)        | 0.45     |
| Prior PCI                        | 152 (12.5)    | 68 (27.2)       | < 0.0001| 25 (17.6)     | 26 (18.3)       | 0.87     |
| Prior BAV                        | 14 (1.2)      | 38 (15.2)       | < 0.0001| 1 (0.7)       | 19 (13.4)       | < 0.0001|
| Peak aortic gradient [mm Hg]     | 79.9 ±21.3    | 82.0 ±22.3      | 0.19    | 80.9 ±24.3    | 83.0 ±21.6      | 0.47     |
| Mean aortic gradient [mm Hg]     | 50.0 ±14.5    | 50.4 ±15.4      | 0.73    | 50.8 ±16.9    | 50.7 ±14.1      | 0.94     |
| Comorbidities:                   |               |                  |         |               |                  |         |
| COPD                             | 136 (11.2)    | 92 (37.1)       | < 0.0001| 37 (26.1)     | 36 (25.4)       | 0.89     |
| Diabetes mellitus                | 396 (32.6)    | 102 (40.8)      | 0.01    | 57 (40.1)     | 57 (40.1)       | 1.00     |
| Long-term dialysis               | 9 (0.7)       | 2 (0.8)         | 0.92    | 1 (0.7)       | 1 (0.7)         | 1.00     |
| Neurological dysfunction         | 22 (1.8)      | 18 (7.2)        | < 0.0001| 8 (5.6)       | 10 (7.0)        | 0.62     |
| Peripheral arteriopathy          | 172 (14.4)    | 48 (19.7)       | 0.04    | 26 (18.3)     | 26 (18.3)       | 1.00     |
| Chronic liver disease*           | 17 (1.5)      | 5 (2.0)         | 0.52    | 4 (2.8)       | 3 (2.1)         | 0.71     |
| Smoking history                  | 218 (18.7)    | 23 (9.8)        | 0.00    | 18 (14.0)     | 14 (10.9)       | 0.47     |
| Frailty score, moderate-severe   | 65 (5.4)      | 70 (28.0)       | < 0.0001| 29 (20.4)     | 32 (22.5)       | 0.67     |
| Active neoplastic disease        | 7 (0.6)       | 16 (6.5)        | < 0.0001| 5 (3.5)       | 5 (3.5)         | 1.00     |
| Oxygen dependency                | 8 (0.7)       | 25 (10.0)       | < 0.0001| 3 (2.1)       | 4 (2.8)         | 0.71     |
| Critical preoperative status     | 13 (1.1)      | 5 (2.0)         | 0.22    | 5 (3.5)       | 3 (2.1)         | 0.48     |
| Prior aorto-iliac surgery        | 31 (2.6)      | 9 (3.6)         | 0.36    | 5 (3.5)       | 4 (2.8)         | 0.74     |
| Prior cardiac surgery            | 43 (2.5)      | 29 (11.6)       | < 0.0001| 11 (7.7)      | 12 (8.5)        | 0.83     |
| EuroSCORE II [%]                 | 2.7 ±1.1      | 5.5 ±5.4        | < 0.0001| 4.7 ±5.8      | 4.5 ±4.7        | 0.73     |

Data are reported as mean and standard deviation or counts and percentages. *Child-Pugh class B or C. SAVR – surgical aortic valve replacement, TAVI – transcatheter aortic valve implantation, BMI – body mass index, LVEF – left ventricle ejection fraction, NYHA – New York Heart Association, CAD – coronary artery disease, AMI – acute myocardial infarction, PCI – percutaneous coronary intervention, BAV – balloon aortic valvuloplasty, COPD – chronic obstructive pulmonary disease, eGFR – estimated glomerular filtration rate.
in the SAVR group. However, in this randomized study only high-risk patients were enrolled, including a limited number of obese patients, possibly not entirely reflecting the unique characteristics of this patient population. As a matter of fact, the prognostic impact in late survival exerted by obesity was different between the TAVI group (hazard ratio (HR) = 0.96, and 95% confidence interval (CI): 0.93–0.98) and the SAVR group (HR = 0.97, 95% CI: 0.95–1.00) [18]. More favourable survival rates in SAVR vs. TAVI have also been observed in other specific patient subgroups, including low-risk patients and those with preoperative chronic kidney disease [19, 20].

Another interesting finding of our analysis is that the present data also challenge the current practice whereby obese patients are rejected for SAVR and TAVI procedures [5, 21]. Interestingly, in the current series no difference in the rate of postoperative infections, including sepsis, was observed. This finding also suggests that obesity should not be considered as a discriminatory element in the choice between SAVR and TAVI in obese patients.

Our study has a number of limitations. First, observational data routinely collected have inaccuracies, and this registry is not an exception, despite the extensive validation as part of the OB- Servant governance programme with rigorous methods and quality assurance practices [8, 9]. Second, we adopted BMI as a surrogate of the body fat composition, although other potential aspects of body composition such as visceral fat or fat distribution were not explored. Third, it remains distinctly possible that obese patients with a more severe profile of comorbidities considered at high risk for a cardiac and interventional operation were refused for either SAVR or TAVI, therefore contributing to selection of a spurious group of obese patients fit for invasive treatment. Fourth, this study is limited by the small number of enrolled patients, but this is the only comparison specifically addressing the possible differences in the long-term outcome in obese patients. Finally, this analysis referred only to patients undergoing transfemoral TAVI, and whether these results could be applied to trans-apical, trans-aortic or trans-axillary approaches remains unknown. In addition, in our study new and emerging sur-

**Table II.** Early outcomes in the propensity score-matched cohorts

| Outcomes                  | SAVR (n = 142) | TAVI (n = 142) | P-value |
|---------------------------|----------------|----------------|---------|
| In-hospital mortality     | 5 (3.6)        | 6 (4.3)        | 0.76    |
| 30-day mortality          | 6 (4.2)        | 5 (3.5)        | 0.76    |
| Stroke                    | 1 (0.7)        | 4 (2.9)        | 0.18    |
| Acute kidney injury       | 17 (12.4)      | 5 (3.6)        | 0.01    |
| Permanent pacemaker       | 5 (3.6)        | 20 (14.4)      | < 0.0001|
| Myocardial infarction     | 0 (0.0)        | 1 (0.7)        | 1.00    |
| Cardiac tamponade         | 2 (1.4)        | 6 (4.3)        | 0.16    |
| Major vascular injury     | 0 (0.0)        | 10 (7.4)       | < 0.0001|
| Emergency PCI             | 0 (0.0)        | 1 (0.7)        | 1.00    |
| Postoperative infection:  |               |                | 0.71    |
| Wound infection           | 3 (2.2)        | 2 (1.5)        |         |
| Lung or other organ infections | 5 (3.7)   | 3 (2.2)        |         |
| Sepsis                    | 4 (2.9)        | 2 (1.5)        |         |
| Blood transfusion         | 82 (60.3)      | 35 (25.7)      | < 0.0001|
| ICU stay [days]           | 4.0 ±9.3       | 3.2 ±5.8       | 0.42    |

Data are reported as mean and standard deviation or counts and percentage. SAVR – surgical aortic valve replacement, TAVI – transcatheter aortic valve implantation, PCI – percutaneous coronary intervention, ICU – intensive care unit.

**Figure 1.** Five-year survival estimates after SAVR and TAVI procedures in obese (body mass index ≥ 30 kg/m²) patients

SAVR – surgical aortic valve replacement, TAVI – transcatheter aortic valve implantation. Confidence intervals are provided.
gical techniques using a minimally invasive or sutureless approach were not considered. Therefore, another possible comparison between the two populations that is much more grounded in reality than the comparison presented is missed. The literature clearly shows that a mini-sternotomy approach and rapid deployment valves are associated with better early and late outcomes in comparison with conventional surgical approaches and an aortic prosthesis [22, 23].

In conclusion, in obese patients both SAVR and TAVI are valid treatment options, with comparable early mortality results. SAVR was associated with better 5-year survival than TAVI. Obese patients should not be refused for SAVR or TAVI procedures, and further studies are needed to clarify the real long-term benefit of SAVR compared with TAVI in this specific cohort of patients.

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Conflict of interest

The authors declare no conflict of interest.

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