

# The impact of transcatheter aortic valve implantation on patients' profiles and outcomes of aortic valve surgery programmes: a multi-institutional appraisal<sup>†</sup>

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## Abstract

**OBJECTIVES:** The aim of this retrospective multicenter study was to assess how the development of transcatheter aortic valve implantation (TAVI) influenced the characteristics and outcomes of patients undergoing aortic valve procedures.

**METHODS:** We reviewed 1395 patients who underwent isolated surgical aortic valve replacement (SAVR) or TAVI in three centres with a high-volume TAVI programme. Patients were divided into two groups: 'Pre-TAVI' (395 patients, 28.3%) and 'Post-TAVI' (1000 patients, 71.7%) operated on before and after the introduction of TAVI into clinical practice. We evaluated age, logistic EuroSCORE I (LES) and hospital mortality according to time periods and the procedure performed, whether SAVR or TAVI.

**RESULTS:** 'Post-TAVI' patients were older ( $78.2 \pm 7.8$  vs  $76.8 \pm 6.7$  years;  $P = 0.002$ ) and with a significantly higher LES ( $17.8 \pm 14.7$  vs  $9.1 \pm 9.2$ ;  $P < 0.001$ ) than 'Pre-TAVI' patients. Hospital mortality was not significantly different between groups ('Pre-TAVI' vs 'Post-TAVI': 2 vs 3.4%;  $P = 0.17$ ). Of the 1000 'Post-TAVI' patients, 605 (60.5%) underwent TAVI and 395 (39.5%), SAVR. Patients undergoing TAVI were older ( $79.9 \pm 7.1$  vs  $75.5 \pm 9.2$  years;  $P < 0.001$ ) and with a higher LES ( $22.9 \pm 15.3$  vs  $9.7 \pm 9.3$ ;  $P < 0.001$ ) than 'Post-TAVI' SAVR patients, but their hospital mortality was similar (3.9 vs 2.5%;  $P = 0.22$ ). LES was similar between 'Pre-TAVI' and 'Post-TAVI' SAVR patients ( $9.1 \pm 9.2$  vs  $9.7 \pm 9.3$ ;  $P = 0.26$ ). Furthermore, we did not find significant differences in the overall hospital mortality between SAVR and TAVI patients: 2.3 vs 3.9%,  $P = 0.08$ .

**CONCLUSIONS:** This analysis shows that the development of TAVI has caused an increase in the preoperative risk profile of patients scheduled for aortic valve procedures (SAVR or TAVI) without increasing hospital mortality.

**Keywords:** Heart valve • Transapical • Percutaneous • Aortic valve • Replacement

## INTRODUCTION

Surgical aortic valve replacement (SAVR) is the treatment of choice for severe symptomatic aortic valve stenosis (SSAVS). A European survey has demonstrated that nearly 30% of patients suffering from SSAVS were not referred for surgery by their cardiologist or family physician due to advanced age or severe comorbidities or were considered inoperable by the cardiac surgeon and therefore not accepted for SAVR [1]. For this reason, new therapeutic options for patients with SSAVS were developed and successfully introduced into clinical practice [2]. Transcatheter aortic valve implantation (TAVI) provides good clinical and haemodynamic outcomes both in inoperable patients and in high-risk elderly patients [3], and during the last few years the

number of procedures, as well as performing centres and performing physicians, has rapidly increased. With TAVI, we are now treating patients who were not treated in the past, and as a consequence there has probably been a change in the characteristics of the population of SSAVS patients who undergo a therapeutic procedure on the aortic valve, whether SAVR or TAVI.

The aim of this retrospective multicenter study was to evaluate how the introduction and diffusion of TAVI have influenced the characteristics and outcomes of patients undergoing aortic valve procedures and how this change has impacted on aortic valve surgery programmes.

## PATIENTS AND METHODS

We analysed data from 1395 patients who underwent isolated aortic valve procedures (SAVR or TAVI) from January 2005 to

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November 2011 at three Italian cardiac surgery centres with a high TAVI volume. TAVI and SAVR data were collected in the institutional database of each centre and then retrospectively transferred to an 'ad hoc' database specifically created for this study. Data were then sent anonymized to the University of Padova for storage and analysis. Patients were divided in two groups: 'Pre-TAVI', which included 395 (28.3%) patients who underwent SAVR before the introduction of TAVI in the three participating centres (2005–07) and 'Post-TAVI', which included 1000 (71.7%) patients who received an aortic valve procedure after the introduction of TAVI (2007–11).

Indication for SAVR was SSAVS defined by an aortic valve area  $<0.8 \text{ cm}^2$  and mean transaortic gradient  $>40 \text{ mmHg}$ . Indications for TAVI were as follows: SSAVS; logistic EuroSCORE I (LES)  $>20\%$  and Society of Thoracic Surgeons (STS) score  $>10\%$ ; ascending porcelain aorta. Patients were excluded if their post-procedural life expectancy was  $<1$  year. We did not consider specific age limits for TAVI. Each case was discussed by the local 'TAVI team', which included a cardiac surgeon, an interventional cardiologist and an anaesthesiologist. In this study, we included transfemoral and transapical TAVI. All the three centres follow a 'transfemoral first' policy and, as a consequence, transapical procedures were performed only if the transfemoral approach was not feasible due to narrow and/or calcified aorto-iliac-femoral vessels. TAVI were performed with the Edwards Sapien and Sapien XT balloon expandable bioprosthesis (Edwards Lifesciences, Irvine, CA, USA) and with the CoreValve Revalving system (Medtronic, Minneapolis, MN, USA). We considered age and LES [4] in the two groups of patients and evaluated hospital mortality in the two groups and in patients undergoing SAVR or TAVI. In particular, LES was recalculated in all patients, and those with incomplete data that made LES calculation impossible or unreliable were excluded. All patients gave written informed consent for the procedure (TAVI or SAVR) as well as for the data collection. This study was in accordance with the local ethics committees' guidelines.

## Statistical analysis

Continuous data are expressed as means  $\pm$  one standard deviation. Categorical data are summarized by reporting absolute frequency distribution and percentage. Categorical variables were compared using the  $\chi^2$  test. Student's *t*-test (for unpaired data) or the Mann-Whitney test was used to compare continuous variables, as appropriate. Statistical findings were considered significant if the critical level was  $<5\%$  ( $P < 0.05$ ). Statistical analysis was performed using SPSS (release 13.0 for Windows, Chicago, IL, USA).

## RESULTS

Preoperative clinical characteristics as well as the type of procedure performed and kind of implanted prosthesis of the two groups are listed in Table 1.

### Post-TAVI vs Pre-TAVI

Patients operated on in the 'Post-TAVI' era were older than 'Pre-TAVI' patients ( $78.2 \pm 7.8$  vs  $76.8 \pm 6.7$  years;  $P = 0.002$ ) and with a significantly higher risk profile (LES,  $17.8 \pm 14.7$  vs  $9.1 \pm 9.2\%$ ;  $P < 0.001$ ). However, hospital mortality was 2% (8

**Table 1:** Preoperative age and logistic EuroSCORE of the two study populations and characteristics of the performed procedure

Variable	Pre-TAVI (N = 395)	Post-TAVI (N = 1000)	P-value
Age, years	$76.8 \pm 6.7$	$78.2 \pm 7.8$	0.002
Logistic EuroSCORE I	$9.1 \pm 9.2$	$17.8 \pm 14.7$	$<0.001$
SAVR, n (%)	395 (100)	395 (39.5)	$<0.001$
TAVI, n (%)	0 (0)	605 (60.5)	
TF-TAVI, n (%)		378 (62.5)	
TA-TAVI, n (%)		227 (37.5)	
Sapien/Sapien XT, n (%)		409 (67.6)	
TA-TAVI, n (%)		227 (55.5)	
TF-TAVI, n (%)		182 (44.5)	
CoreValve (TF only), n (%)		196 (32.4)	

SAVR: surgical aortic valve replacement; TAVI: transcatheter aortic valve replacement; TF: trans-femoral; TA: transapical.

patients) in the 'Pre-TAVI' group and 3.4% (34 patients) in the 'Post-TAVI' group; this difference was not statistically significant ( $P = 0.17$ ).

### SAVR vs TAVI

In the 'Post-TAVI' group, 605 (60.5%) patients received a transcatheter bioprosthesis and 395 (39.5%) underwent SAVR. Of these, 378 (62.5%) underwent a transfemoral procedure, while 227 (37.5%) were scheduled for transapical TAVI. Transfemoral procedures were performed with a CoreValve and with a Sapien/Sapien XT device in 196 (51.8%) and 182 (48.2%) patients, respectively. All transapical TAVI were carried out with a Sapien/Sapien XT valve. Globally, of the 605 TAVI patients of the 'Post-TAVI' group, Sapien/Sapien XT and CoreValve bioprostheses were used in 409 (67.6) and 196 (32.4%) patients, respectively. In the 'Post-TAVI' group, patients undergoing TAVI were significantly older than SAVR patients ( $79.9 \pm 7.1$  vs  $75.5 \pm 9.2$  years;  $P < 0.001$ ). Furthermore, TAVI patients had a significantly higher LES compared with those undergoing conventional surgery ( $22.9 \pm 15.3$  vs  $9.7 \pm 9.3\%$ ;  $P < 0.001$ ). In the 'Post-TAVI' group, hospital mortality between TAVI and SAVR was similar. In fact, we observed 24 (3.9%) and 10 (2.5%) deaths in TAVI and in SAVR patients, respectively ( $P = 0.22$ ). Interestingly, we did not observe differences in patients' risk profile between patients undergoing conventional aortic valve replacement both in the 'Pre-TAVI' and in the 'Post-TAVI' era ( $9.1 \pm 9.2$  vs  $9.7 \pm 9.3\%$ ;  $P = 0.26$ ). If we consider all 790 patients who underwent SAVR both in the 'Pre-TAVI' and in the 'Post-TAVI' period, the observed hospital mortality was 2.3% (18 patients), which is not significantly different from the 3.9% mortality of TAVI patients ( $P = 0.08$ ). The rate of mortality of patients undergoing SAVR in the 'Post-TAVI' era was 2.5% (10 patients) and this was similar to that of the 'Pre-TAVI' period (2%; 8 patients).

## DISCUSSION

With this study, our purpose was to analyse how the introduction of TAVI into clinical practice has changed the characteristics of

patients undergoing aortic valve procedures (TAVI and SAVR) and whether this evolution has had any impact on patients' outcomes. The incidence of SSAVS increases with age as a consequence of longer life expectancy. It has been estimated that the prevalence of aortic valve stenosis (at least moderate) is around 2% between 70 and 80 years of age and that it progressively increases after 80 years [5]. The treatment of elderly patients may be challenging due to comorbidities that often increase surgical risk. TAVI in humans was first described by Cribier *et al.* [6] and since then it has undergone a rapid diffusion and technical evolution with promising results [7, 8]. We divided our patients who received an intervention for the treatment of SSAVS according to the era of the procedure whether it was performed before or after the introduction of TAVI. We observed that, after the introduction of TAVI, there was a significant increase in patients' age and risk profile. This was obviously due to the introduction of TAVI into clinical use. In fact, especially at the beginning of the experience, TAVI was mainly dedicated to elderly and extremely sick patients whose LES was particularly high. This policy was supported by international consensus papers [9]. Looking at the 'Post-TAVI' data, we observed that the preoperative risk profile of SAVR patients was significantly lower than TAVI patients and, more importantly, there were no changes between 'Pre-TAVI' and 'Post-TAVI' SAVR patients. In other words, the preoperative risk profile of patients scheduled for SAVR has not changed over time and, in particular, it has not changed after the introduction of TAVI. What makes the global population risk increase is therefore the referral of TAVI patients. LES of TAVI patients of this study was around 23%, and this is consistent with those reported in other TAVI series [10–12]. Although there was a significant increase in LES between groups, we did not observe significant differences in-hospital mortality of patients undergoing aortic valve interventions between the 'Pre-TAVI' era (SAVR only) and the 'Post-TAVI' period (SAVR and TAVI). Thus, according to our data, the introduction of TAVI has led to performing procedures on a generally sicker population without a significant worsening of hospital mortality. The progressive changes in the characteristics of patients suffering from aortic valve disease and undergoing SAVR have already been described by previous studies based on the analysis of large patient populations. A progressive increase in comorbidities and preoperative risk profile over time was described by a large study based on nearly 110 000 patients who underwent isolated SAVR in North America. The authors found that, despite these changes, the rate of observed mortality and major complications like stroke had improved with time and were quite low [13]. This has been confirmed in a paper by Dunning *et al.* who analysed the Society for Cardiac Surgery in the Great Britain and Ireland database in order to assess changes in patients' characteristics over time. They observed a significant increase in age and rate of high-risk patients from 2004 to 2009, but found a significant reduction in mortality that decreased from 4.4% in 2004–05 to 3.7% in 2008–09 (3.2% for isolated SAVR) [14]. The rate of hospital mortality for isolated SAVR reported by these two large studies based on national databases is consistent with that found in our study (2%). Subramanian *et al.* also report low mortality (1.3%) and low rate of complications (stroke, respiratory failure and pacemaker implantation) in 79 high patients screened for TAVI but who finally underwent SAVR [15]. This means that aortic valve surgery may be carried out with excellent outcomes even in high-risk patients. An interesting result of our study is that overall hospital mortality was not different between SAVR and TAVI in the

'Post-TAVI' era, and moreover, it was not different between all SAVR ('Pre-' and 'Post-TAVI') and TAVI, although in this case a trend towards statistical significance was observed. In particular, it is interesting to observe that, despite high EuroSCORE values, the mortality of TAVI is remarkably low. A similar result was found by the OBSERVANT trial investigators, where mortality for TAVI was 3.8%, although in this study, medium-risk patients were analysed. [16]. The limitations of our study are mainly related to the relatively small sample of the population, the participation of only centres with a high TAVI volume and experience, which may lead to optimal TAVI outcomes, the small number of variables that were investigated, which does not allow a comprehensive and global assessment of the characteristics of the examined population and the unmatched nature of the two groups. In spite of these several limitations, this is the first 'real world' analysis of how the features and outcomes of patients referred to the 'aortic team' for the treatment of SSAVS are changing since TAVI has been introduced into clinical practice.

In conclusion, according to our data, after the introduction of TAVI, the risk profile of patients with SSAVS undergoing aortic valve procedures (TAVI or SAVR) has significantly increased, but outcomes are still excellent. The characteristics of patients scheduled for SAVR have not changed over time.

**Conflict of interest:** none declared.

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## APPENDIX. CONFERENCE DISCUSSION

**Dr W. Gomes (São Paulo, Brazil):** You report a large experience and superb short-term outcomes. But in the appraisal of the two different time periods, pre- and post-TAVI introduction, a jump to 60% TAVI use in symptomatic aortic stenosis patients, don't you think that is far above the usual rate of high-risk patients in the overall population? Could you better explain this jump from 0 to 60% use of TAVI in these patients? And do you think, or do you have data on the intermediate or long-term outcomes to endorse these early results and utilization? And next is the issue of cost. With this jump, can your health care system afford this in the event of a more widespread use of TAVI in the coming years?

**Dr D'Onofrio:** Actually, we do not have a 60% TAVI incidence in our surgical population. In fact in this study we included all TAVI patients that were operated on in the three institutions, but not all the surgical patients. We only included isolated aortic valve procedures in which we were able to retrieve all data and to recalculate the logistic EuroSCORE. We are well aware that this is a limitation of this study. However, we did not find any difference in mortality between the pre-TAVI and post-TAVI period, although there was a

majority of TAVI patients included in this cohort. So if we manage to include all conventional aortic valve procedures, this difference will be even smaller. So this is an important message of this study.

Your second question was about the long-term outcomes. Actually I don't have any data. We did not look at this, because it was pretty hard to retrieve all this data from the institutional databases of each centre, so we only looked at 30-day mortality. Anyway, we are now implementing all the databases with follow-up data, especially for conventional AVR patients. So I hope I will be able to answer this question in the near future. And actually cost-effectiveness is a big problem. Fortunately in Italy we don't have 60% of TAVI procedures. At the moment we have, at least in these three centres, around 20% of TAVI out of the total volume of aortic valve procedure patients.

**Dr A. Furnary (Portland, OR, USA):** Your differences in preoperative risk are greatly different between surgical and TAVI, and there is a slight difference in preoperative risk before and after your TAVI programme. What were the differences in observed-to-expected mortality rates rather than raw mortality rates? That would be a better thing to compare rather than raw mortality rates.

**Dr D'Onofrio:** Well, that is true. In the study we realized that actually we are talking about two different patient populations. We have the conventional aortic valve patients against the TAVI patients that have a much higher risk than conventional patients. However, despite these big differences, the observed mortality was quite low. We have to say that these are three high volume TAVI centres, and there is a very strong cooperation in the TAVI team as well as patient selection and discussion of cases. So despite the high risk of these patients, we have only 3.9% mortality.

**Dr Furnary:** Yes, but what was the observed-to-expected ratio? In other words, all you have to do is divide the expected EuroSCORE by the observed and you get an observed-to-expected ratio. That is a much better number rather than saying, well, we looked at it and compared it.

**Dr D'Onofrio:** We had a 22.9% logistic EuroSCORE of the TAVI population versus 3.9% of observed mortality. These are the data.

**Dr Furnary:** You have to do it on a patient-by-patient basis. That should be the basis of your analysis.

**Dr D'Onofrio:** Okay. Thank you for your suggestion. I will do it.

**Dr M. Moz (Leipzig, Germany):** What is the incidence of pacemaker implantation in the Italian Registry of Transapical Aortic Valve Implantation?

**Dr D'Onofrio:** We have a 3.5% rate of implantation of permanent pacemaker in this Registry at the moment out of more than 700 cases.

**Dr J. Andreassen (Aalborg, Denmark):** Have you seen a decrease in the risk profile of the TAVI patients over time, or do you expect this to happen?

**Dr D'Onofrio:** This is a good question. In this paper we included all TAVI patients since the beginning of this experience in Italy. At the start, we included very high-risk patients, but now we are changing our mind and we are no longer including extremely high-risk patients, because we have seen that the outcomes in these patients are not favourable, even with TAVI. Now we include high-risk patients, but not extremely high-risk patients. I didn't look at this data in this paper, but my feeling is that there is a significant decrease in risk profile over time.