Prevalence, clinical characteristics and outcomes of high-risk patients treated for severe aortic stenosis prior to and after transcatheter aortic valve implantation availability

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Abstract

OBJECTIVES: Transcatheter aortic valve implantation (TAVI) has emerged as an effective treatment for high-risk patients with severe aortic stenosis (AS). The aim of our study was to compare the prevalence, characteristics and outcomes of high-risk patients treated prior to and after the availability of TAVI in our high-volume surgical institution.

METHODS: Among 879 consecutive patients treated 2 years before ('pre-TAVI era') and after ('modern era') the availability of TAVI in our institution, 83 patients were at high risk [defined by logistic EuroSCORE >20%].

RESULTS: Among all patients treated for severe AS, the prevalence of high-risk patients was higher in the modern era (12.7 vs 4.9%, P < 0.0001). In the modern era, high-risk patients were treated by TAVI in 89% of cases. Despite similar logistic EuroSCORE (34.9 vs 34%, P = 0.96), the clinical characteristics of these patients have evolved: high-risk patients in the modern era were older (85.3 ± 5.9 vs 78.5 ± 6.5 years, P = 0.0005) and presented more frequently with New York Heart Association class III–IV (92.3 vs 61.1%, P = 0.003), while high-risk patients treated by surgical aortic valve replacement in the pre-TAVI era presented more frequently with a critical preoperative status (33.3 vs 7.7%, P = 0.01), lower left ventricular ejection fraction (41 ± 14 vs 49 ± 15%, P = 0.05) and a history of recent myocardial infarction (27.8 vs 6.1%, P = 0.02). The overall 1-year survival was not different for high-risk patients treated in the pre-TAVI era or in the modern era (61 ± 11 vs 68 ± 6%, P = 0.52).

CONCLUSIONS: The availability of TAVI has increased the prevalence of high-risk patients treated for severe AS and changed the clinical features of this kind of patients who were rarely surgically treated before. The 1-year survival was similar between pre-TAVI and modern eras.

Keywords: Aortic stenosis • Transcatheter aortic valve implantation • Aortic valve replacement • High risk

BACKGROUND

Patients with severe aortic stenosis (AS) and symptoms have a poor prognosis in the absence of treatment [1]. For decades, conventional surgical aortic valve replacement (SAVR) was the only available curative treatment. Although SAVR reduces symptoms and improves survival, at least one-third of patients with a legitimate surgical indication were denied SAVR because of a high estimated operative risk [2–4].

Transcatheter aortic valve implantation (TAVI) has emerged in a few years as the reference curative treatment for patients with severe AS who cannot undergo surgery [5] and as a valuable alternative to SAVR for high-risk patients, with a similar survival rate [6]. This less invasive procedure has recently gained rapid expansion. The aim of this study was to compare the prevalence, the characteristics and outcomes of high-risk patients treated prior to and after the availability of TAVI.

METHODS

This retrospective study included all consecutive patients treated for native severe AS in our high-volume surgical centre during a
4-year period (from January 2008 to December 2011). Criteria for inclusion were patients aged >18 years treated by SAVR or TAVI for severe AS during this period. According to guidelines, severe AS was defined as an aortic-valve area of <1 cm² or a mean aortic-valve gradient of ≥40 mmHg [7].

Patients were excluded if severe AS was associated with more than moderate (≥grade 3/4) mitral or aortic regurgitation, if SAVR was associated with mitral repair or replacement, or tricuspid repair.

Patients who underwent SAVR or TAVI in our institution during this period were identified throughout two national prospective registries: the EPICARD® database and the French Aortic National CoreValve® and Edwards (FRANCE2) registry, respectively. The characteristics of patients treated by SAVR in our centre were extracted from the EPICARD® database of the French Society for Thoracic and Cardiovascular Surgery that gathers all cardiac surgeries performed in 61 centres in France. TAVI has been available in our centre since January 2010. Our hospital was one of the 33 French centres authorized to perform TAVI by the French Ministry of Health and all the characteristics and outcomes of our patients treated by TAVI were included in the FRANCE2 Registry [8].

We assessed the prevalence of treated patients with AS among all cardiac surgeries performed in our centre by calculating the ratio: all treated patients for AS (by SAVR or TAVI)/all patients treated by SAVR + TAVI + other cardiac surgeries during the same period.

Two periods were defined according to the availability of TAVI in our hospital: a ‘pre-TAVI era’ from January 2008 to December 2009 and a ‘modern era’ from January 2010 to December 2011.

To assess the risk of death at the time of intervention, we used the logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) that was systematically calculated at the time of SAVR or TAVI with the use of a logistic regression equation. Scores range from 0 to 100%, with higher scores indicating greater risk. As previously reported, we defined high-risk patients as patients presenting with a logistic EuroSCORE higher than 20% [8].

In the pre-TAVI era period, the only therapeutic option for all patients with severe AS was SAVR. In the modern era, a multidisciplinary approach was systematically performed for each high-risk patient referred to our centre, including a referring cardiologist, interventionist cardiologist, cardiothoracic surgeon, intensivist, echocardiographer, imaging specialist and anesthesiologist. After a collegial decision of this ‘heart team’, TAVI or SAVR was performed. TAVI was also performed for non-high-risk patients (logistic EuroSCORE <20%) for patients with ascending porcelain aorta or with comorbidities but considered too frail to undergo SAVR.

The balloon-expandable Edwards SAPIEN® or SAPIEN XT prosthesis ( Edwards Lifesciences) or the self-expandable CoreValve® (Medtronic) were used for TAVI. The trans-femoral approach was the first therapeutic option. Apical or subclavian accesses were used in case of impossibility of the trans-femoral route [9].

The following parameters were extracted from the two prospective registries: clinical records, including demographics, baseline clinical characteristics, functional status assessed by New York Heart Association (NYHA) class, coexisting conditions, logistic EuroSCORE, existence of a critical status before TAVI or SAVR (defined by the existence of one or more of the following events: ventricular tachycardia or fibrillation, aborted sudden death, preoperative cardiac mass, preoperative ventilation before arrival in the anaesthetic room, preoperative inotropic support, intra-aortic balloon counterpulsion or preoperative acute renal failure, need of urgent TAVI or SAVR before the beginning of the next working day), baseline echocardiographic data [aortic valve area (AVA), mean aortic valve pressure gradient (MPG), left ventricular ejection fraction (LVEF), systolic pulmonary artery pressure], details of the procedure (SAVR or TAVI), post-procedure in-hospital adverse outcomes (including survival at discharge from hospital), intensive care unit (ICU) and hospital length of stay.

Follow-up

The long-term follow-up was achieved for all high-risk patients by contacting patients or referring physicians, in order to assess survival and functional status at last contact.

Statistical analysis

Continuous variables are presented as mean ± SD, except for the length of the follow-up, which is expressed as median [25th–75th percentiles]. Continuous variables were compared using the Wilcoxon rank sum test. The Wilcoxon rank sum test was chosen because of the small sample size of patients. Categorical variables are presented as absolute values and percentages, and compared using Fisher’s exact test. Late survival was analysed for high-risk patients using the Kaplan–Meier method and survival rates are given with their standard errors. A P value of <0.05 was considered to indicate a statistically significant difference. Analyses were conducted with the JMP 7.0.1 software (SAS Institute, 2007).

RESULTS

Global population characteristics

The study population included 879 consecutive patients (460 men and 419 women, mean age 74.5 ± 9.3 years, range 27–96 years) with severe AS (mean AVA 0.7 ± 0.2 cm², MPG 50 ± 15 mmHg, LVEF 58 ± 11%). According to the period of treatment, 367 patients were treated by SAVR in the pre-TAVI era and 512 patients were treated in the modern era: 404 by SAVR and 108 by TAVI. Among all patients treated by TAVI, 54% [58 of 108] were classified as high risk according to their logistic EuroSCORE.

The prevalence of SAVR among all cardiac surgeries was 25% [367/1467] in the pre-TAVI era and 28% [404/1416] in the modern era (P = 0.03). When considering all treated patients by cardiac surgery or TAVI, the prevalence of patients treated for severe AS increased in the modern era (34% [512/1524] vs 25% [367/1467] in the pre-TAVI era, P < 0.0001), Fig. 1.

High-risk patients

In the study population, 83 high-risk patients (9.4%) were identified. The prevalence of high-risk patients treated for severe AS was significantly higher in the modern era than in the pre-TAVI era (12.7% [65 of 512] vs 4.9% [18 of 367], respectively, P < 0.0001), Fig. 2.

Clinical and echocardiographic baseline characteristics of high-risk patients in both periods are detailed in Table 1.

In the pre-TAVI era, 18 high-risk patients were treated: the mean age was 78.5 ± 6.5 years (range, 65–88 years), 44.4% were women, the mean logistic EuroSCORE was 34.9 ± 13.6% and the mean AVA was 0.6 ± 0.1 cm². Treatment consisted of SAVR with a bioprosthesis in
Conversely, high-risk patients in the pre-TAVI era had more frequently a history of recent myocardial infarction (27.8 vs 6.1%, respectively, \( P = 0.02 \)), presented more frequently with a critical preoperative status (33.3 vs 7.7%, respectively, \( P = 0.01 \)) and with a lower LVEF (41 ± 14 vs 49 ± 15%, respectively, \( P = 0.05 \)). The 6 patients with critical status in the pre-TAVI era presented initially with myocardial infarction in 2 patients, aborted sudden death due to ventricular fibrillation in 1, preoperative ventilation before arrival in the anaesthesia room in 1, preoperative inotropic support in 5, intra-aortic balloon counter-pulsation in 2, need of urgent SAVR before the beginning of the next working day in 2 cases. These high-risk patients presenting with critical status in the pre-TAVI era were 76.2 ± 9 years old and presented with a significantly lower LVEF than high-risk patients without critical status (28 ± 10 vs 49 ± 12%, respectively, \( P = 0.003 \)). Finally, 5 patients (27.8%) with severe AS were admitted initially for myocardial infarction, which led to discovery of a previously unknown severe AS and performing of SAVR + CABG in 2 patients with critical status. Thus, SAVR in high-risk patients was planned and performed in stable conditions (no critical status, no recent myocardial infarction) for 9/18 patients (50%) in the pre-TAVI era versus 8/65 patients (12%) in the modern era, \( P = 0.014 \).

Finally, logistic EuroSCORE and all other coexisting conditions were similar during these two periods (all \( P > 0.05 \)).

Non-high-risk patients

During the pre-TAVI era, 349 non-high-risk patients underwent SAVR (278 bioprosthesis and 71 mechanical valves). In the modern era, 447 non-high-risk patients were treated for severe AS: 397 patients underwent SAVR (320 bioprosthesis and 77 mechanical valve), whereas 50 patients were treated by TAVI (trans-femoral in 45 patients and apical in 5 patients). Baseline clinical and echocardiographic characteristics of non-high-risk patients (EuroSCORE ≤20%) were not significantly different in the modern era when compared with the pre-TAVI era (all \( P > 0.05 \)).

Thirty-day adverse outcomes and survival for high-risk patients

In-hospital outcomes are detailed in Table 2. Need of renal replacement therapy, transfusions and heart failure were significantly more frequent in the pre-TAVI era than in the modern era (all \( P < 0.05 \)). There was a trend to statistically more frequent vascular complications in the modern era than in the pre-TAVI era (18.5% vs 0% in the pre-TAVI era, \( P = 0.06 \)). Strokes occurred only in the modern era in 2 patients: 1 transient ischaemic stroke occurred after trans-femoral TAVI in a 91-year-old patient and 1 stroke with disabling sequelae after SAVR in a 75-year-old patient. The length of stay in the ICU was significantly shorter in the modern era than in the pre-TAVI era (6.5 ± 7.5 vs 13.6 ± 16.7 days, respectively, \( P = 0.005 \)).

The all-cause 30-day mortality rate was similar during both eras: 22% in the pre-TAVI era versus 13.8% in the modern era, \( P = 0.46 \). In the pre-TAVI era, in-hospital deaths were mainly due to cardiogenic shock and multiorgan failure after SAVR. In the modern era, 1 patient died immediately after trans-femoral TAVI (ventricular fibrillation). The other in-hospital deaths were due to non-cardiovascular causes, including respiratory cause (3 patients), multiorgan failure (3 patients), renal insufficiency (1 patient) and infection (1 patient).
One-year survival in high-risk patients

The 1-year follow-up was completed for all patients. The 2-year follow-up was available for all patients treated by TAVI but not for all patients treated by SAVR in the modern era. Hence, a comparative 2-year survival analysis could not be performed. The median follow-up was 25.1 months (range: 12–50.6 months) [3.2–37.7].

During the follow-up, 21 deaths occurred after discharge from hospital for patients treated in the modern era: 13 due to extracardiac causes; 3 due to heart failure and 5 from unknown causes. The overall 1-year survival rate for all high-risk patients was 66 ± 5%. One-year survival rates were 61 ± 11% for high-risk patients in the pre-TAVI era and 68 ± 6% in the modern era (P = 0.52); Fig. 3. When considering the type of treatment...
The main results of the present study are as follows: (i) the prevalence of high-risk patients treated for severe AS increased with the emergence of TAVI; (ii) despite similar logistic EuroSCORE between both eras, the clinical features of these patients have considerably changed towards older age and more stable condition; (iii) in real life, TAVI was the first therapeutic option in high-risk patients, performed in 89% of this population; (iv) 1-year survival rate was similar between high-risk patients treated in the pre-TAVI era and in the modern era.

In our study, only 18 high-risk patients underwent surgery in the pre-TAVI era, representing 4.9% of all patients treated by SAVR during this period. Among this subgroup, 6 patients (33.6%) presented initially with a critical preoperative status with poor LVEF, cardiogenic shock, resuscitated ventricular fibrillation and need for intra-aortic balloon counter-pulsation. Urgent surgery was then performed in order to rescue these relatively young patients (76.2 ± 9 years) who were haemodynamically unstable. Furthermore, 5 patients were admitted initially for acute myocardial infarction leading to discovery of severe AS and severe coronary disease requiring SAVR and CABG. Thus, in the pre-TAVI era, SAVR was planned and performed in only 9 high-risk patients without critical status or recent myocardial infarction (2.4% of all SAVR in this period), illustrating the remarkably very low number of high-risk patients referred to our centre and treated by SAVR before TAVI became available. Brennan et al. [10] reported a prevalence rate of 7.5% of high-risk patients among all SAVR (n = 103500) performed in 962 centres between 1999 and 2007 in North America. These results highlighted the rarity of high-risk patients with severe AS treated before the emergence of TAVI.

Whereas SAVR was rarely performed and considered often as a rescue surgery for high-risk patients in the pre-TAVI era, the emergence of TAVI has changed the clinical features of treated high-risk patients. These high-risk patients in the modern era were older and presented more frequently with class III or IV NYHA class. There was also a trend for more patients with significant renal insufficiency. Previous studies have shown that one-third of patients with symptomatic severe AS did not undergo SAVR, mainly because of advanced age, left ventricular dysfunction, comorbidities or perceived prohibitive operating risk [3]. The high-risk patients treated in the modern era in our study shared some characteristics with patients denied SAVR in the Euro Heart Survey: age >80 years, frequently in NYHA class III or IV and decreased LVEF [2]. Interestingly, the absolute number of SAVR in our centre did not decrease in the modern era. Furthermore, the prevalence of treated patients with severe AS increased and represented, in the modern era, one-third of cardiac interventions performed in our centre. One explanation may be that the availability of TAVI permitted to offer curative treatment to more patients with severe AS, both to high-risk patients and non-high-risk patients. Bach et al. [3] have shown that, among unoperated patients with severe AS, only one-third of patients were referred to a cardiac surgeon to confirm the impossibility of SAVR because of a too-high operative risk. The possibility to treat high-risk patients by TAVI probably increased the global chart flow of patients with severe AS and enabled cardiologists to refer their patients in a tertiary centre for an accurate and global evaluation, in order to suggest the most suitable treatment.

The PARTNER trial (ClinicalTrials.gov number, NCT00530894) demonstrated that TAVI was non-inferior, but not superior, to SAVR for 1-year survival in high-risk patients [6]. Nevertheless, our results showed that, in daily practice, TAVI was the preferential method to treat high-risk patients, as previously reported [11]. Many reasons may explain why TAVI was the first-choice treatment for these patients. First, TAVI is perceived as a less invasive method, probably more adapted to frail and elderly patients.

**DISCUSSION**

We report here a study comparing the management of high-risk patients with severe AS in the pre-TAVI and the modern era. The main results of the present study are as follows: (i) the prevalence independently of the period of treatment, 1-year survival rates were similar between high-risk patients treated by SAVR or TAVI: 68 ± 9 vs 66 ± 6%, respectively (P = 0.91); Fig. 4.

**Functional status at last follow-up**

While 85% of high-risk patients [71 of 83] were in NYHA class III or IV before intervention, 72% of survivors [37 of 51] were in class I or II at the last follow-up. There was no significant difference in functional status of survivors treated in the pre-TAVI or in the modern era with, respectively, 62.5 and 74% of survivors in NYHA class I–II at the last follow-up (P = 0.67).

![Figure 3: Kaplan–Meier 1-year survival of high-risk patients treated in the pre-TAVI era compared with the modern era.](https://example.com/figure3)

![Figure 4: Kaplan–Meier 1-year survival of high-risk patients treated by SAVR or TAVI, independently of the period of treatment.](https://example.com/figure4)
Secondly, TAVI has become available in our centre since January 2010 and the previously published promising results with this method encouraged its widespread use [11, 12]. Finally, the decision-making systematically included the opinion of the heart team and of the referring cardiologist, generally favourable to TAVI for these patients who would have probably not been referred to our centre a few years ago.

The postoperative morbidity rate was high during both eras, related to patient severity and to the type of treatment. However, we showed that the postoperative course was less complicated in the modern era. First, these elements may be explained by the predominant use of the TAVI technique itself for high-risk patients in the modern era. Conversely, in the pre-TAVI era, more need of renal replacement or transfusions, more episodes of heart failure and a higher length of stay in the ICU may be explained as consequences of a more severe preoperative status and decreased LVEF. Morbidity was lesser in patients treated by TAVI despite an increased complexity of clinical profile, but some complications specifically related to the TAVI procedure emerged, such as major vascular access-related complications (13.2%), in relation to transfemoral access, with an incidence similar to previous studies [13, 14]. Conversely, strokes and permanent pacemaker placement rates were comparable in both eras with rates in accordance with previous studies [15].

In-hospital mortality rates were high (22% before the TAVI era and 13.8% during the modern era) but not significantly different in both eras and related to the severity of patients with a mean logistic EuroSCORE at 34%. The overall 1-year survival for all high-risk patients was 66 ± 5% and was similar in both eras despite differences in clinical characteristics. In the modern era, patients were younger but their ‘high-risk’ status was mainly due to a more critical preoperative status and lower LVEF while the high-risk status calculated by EuroSCORE in the modern era was mainly due to age and comorbidities. The survival rate at 1 year in our study was slightly inferior to the survival rates in the PARTNER study: 75.6% for TAVI and 73.2% for SAVR in cohort A, and 69.3% for the TAVI group in cohort B (inoperable patients) [5, 6]. This difference in survival could be attributed to the higher logistic EuroSCORE of our high-risk patients (34.9% in our study vs 29.0% in PARTNER). This survival rates should be interpreted in the light of the high mortality rate observed in the group ‘standard treatment’ (49.7%) at one year for the inoperable patients of the PARTNER study (cohort B arm) [6]. Interestingly, 1-year survival of high-risk patients was similar irrespective of the era (pre-TAVI or modern) and type of treatment (SAVR or TAVI), despite an increased number of more frail and aged patients who were not treated before TAVI availability. These results are consistent with the main result of the PARTNER Trial (cohort A) showing that TAVI and SAVR were associated with similar rates of one-year survival. It suggests that TAVI could be a credible alternative to SAVR. Moreover, Fairbairn et al. [16] have shown that TAVI was cost-effective compared with SAVR over a 10-year horizon, mainly due to lower post-procedure costs and shorter length of stay in the postoperative period, as also reported in our study.

Finally, in our study, most deaths occurred after discharge from hospital and were related to baseline comorbidities as in the SOURCE registry [13].

Limitations

The first limitation is the definition of a high-risk patient for cardiac surgery, a definition that remains arbitrary. Preoperative multivariable scoring systems have been developed in order to help the clinician in the operative decision. Logistic EuroSCORE is known to overestimate the operative risk, in particular for high-risk patients [17] and the Society of Thoracic Surgeons (STSs) Score may be more accurate for patients at the highest risk undergoing SAVR [18]. Osnabrugg et al. [19] have recently reported that logistic EuroSCORE II may be more accurate for predicting outcomes after SAVR. However, in our study, only the logistic EuroSCORE was available. Furthermore, the mean logistic EuroSCORE of our high-risk patients was higher than in previous studies [6, 8], allowing us to consider our patients as high risk.

Secondly, the two cohorts were compared without matching, making it a descriptive two-cohort study. Thus, we cannot conclude that SAVR or TAVI was the most adapted treatment for high-risk patients. However, the aim of this study was not to compare SAVR to TAVI but to describe the evolution of the prevalence and the clinical features of treated high-risk patients according to the availability of each treatment.

Thirdly, frailty was evaluated in our study by our ‘heart team’ without using specific scores or tools of frailty. Evaluation of frailty is difficult and there are many different definitions and methods. However, frailty has been identified as a risk factor for postoperative morbidities, an independent risk factor of in-hospital mortality, prolonged institutional care and shorter mid-term survival after cardiac surgery [20]. In addition to a classical score (STS or EuroSCORE), an objective evaluation using a validated score would enable one to improve the stratification of patients for surgery or TAVI.

Fourthly, in the modern era, the decision to propose SAVR or TAVI for a high-risk patient was taken after a multidisciplinary approach (Heart Team). There are no findings in our database to explain this individual decision, most often in favour of TAVI. However, this decision was taken on multiple arguments: age, comorbidities, frailty, good results of first TAVI procedures, desire of patient and of referring cardiologists.

Finally, the results of this single-centre retrospective study should be confirmed in multicentric studies. However, in our high-volume centre, more than 30 physicians were involved in the screening, decision-making, intervention and post-procedure management, enabling one to avoid individual decisions concerning the type of treatment (to operate or not, TAVI or SAVR).

CONCLUSIONS

The emergence of TAVI has allowed us to offer effective treatment to patients with severe AS previously not referred to a tertiary centre or denied surgery. In the pre-TAVI era, high-risk patients were rarely treated and SAVR was often considered as a rescue surgery. In the modern era, the clinical features of treated high-risk patients have evolved with stable older patients, more frequently in NYHA class III or IV. Although the clinical features of these patients were different, 1-year survival was similar for high-risk patients treated before and during the modern era, by SAVR or TAVI.

Conflict of interest: none declared.

REFERENCES


