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Bioprosthetic structural valve deterioration: How do TAVR and SAVR prostheses compare?☆

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ABSTRACT

Background: The durability of TAVR prostheses has come under major scrutiny since the move towards lower risk patients. We sought to compare the rate of structural valve deterioration (SVD) over time between transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR).
Methods: We included all TAVR and SAVR patients (age ≥ 75 years) that were performed in our centre from 2005 until 2015. Applying the internationally "agreed on" definitions of SVD, we surveyed all available serial echocardiographic follow-ups.
Results: We included 269 TAVR and 174 SAVR cases. Post-intervention, TAVR patients had lower mean and peak gradients but higher rate of mild aortic regurgitation. SAVR patients had longer follow-up (in months, SAVR: 53 (30, 85) Vs TAVR: 33.4 (23, 52)). SVD as per Valve Academic Research Consortium-2 (VARC-2) was similar between the two groups (TAVR 28% Vs SAVR 31%; $P = 0.593$) but moderate haemodynamic SVD (European Association of Percutaneous Cardiovascular Intervention (EAPCI) criteria) was more common among SAVR cases (TAVR 11.5% Vs SAVR 20.7%; $P = 0.007$). Using Kaplan-Meier estimates, the rate of SVD over time was not different between the two groups as per VARC-2 criteria but different when moderate haemodynamic SVD criteria were applied (Log Rank $P = 0.022$) in favour of TAVR. The mean gradient rose steadily over time but more so post-SAVR ($\beta = 0.52 \pm 0.24$ in comparison to TAVR at every given time point; $P = 0.032$).
Conclusion: Structural valve deterioration is common on long-term follow-up post-TAVR. The rate is similar to post-SAVR cases according to VARC-2 criteria but less according to the moderate haemodynamic SVD criteria.

1. Introduction

Trans-catheter aortic valve replacement (TAVR) now has an indisputable evidence base as the 'Gold Standard' treatment for aortic stenosis (AS) in inoperable and high risk patients and the literature supporting its use in intermediate risk patients is evolving fast [1–3]. As such, the procedure is being widely applied across the world. The issue of whether TAVR prostheses will behave in the same way as surgical bioprostheses over longer-term follow-up has been increasingly debated as the number of patients treated increases. Moreover, as lower risk and potentially younger patients are exposed to this technique, the question of prosthesis durability becomes more important.

Bench side testing and finite element analysis suggested shorter durability of TAVR prostheses [4]. Despite the widespread adoption of TAVR, clinical data about TAVR prostheses durability have been slow to emerge. Patients receiving TAVR prostheses were high risk or inoperable - all of whom were elderly with significant co-morbidity - and died within few years of their index procedure [5]. As such, the literature on long-term follow-up was limited by the fact that these patients did not survive long enough for detailed analysis of this issue. There have been some studies examining prosthesis deterioration after TAVR, but the majority are considered 'mid-term' (up to 5 years).

This issue was brought in to sharp focus when data was presented by Dvir et al. [6] in May 2016 describing raw data from Rouen and Vancouver which suggested that there was an important prosthesis failure rate and much debate followed. Until then, there were various definitions and cut-offs used for structural valve deterioration (SVD); Valve Academic Research Consortium – 2 (VARC – 2) definition being the most widely accepted. However, responding to unmet need, the European

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Association of Percutaneous Cardiovascular Interventions (EAPCI) published a consensus statement to standardize the definition of SVD and valve failure for future reporting (July 2017) [7].

The first Edwards Sapien prosthesis (Edwards Lifesciences, Irvine, California) TAVR in the UK was performed at King's College Hospital in 2007 - we are primarily an Edwards Sapien prosthesis centre - and we were therefore able to exploit our long TAVR history by examining our entire patient cohort to address this question. We sought to study the rate of prosthesis deterioration post-TAVR in this population and compare it to a population of patients post-surgical aortic valve replacement (SAVR) during the same period.

2. Methods

2.1. Study population

We studied all patients who underwent TAVR in our centre since 2007 and compared them to a comparator group undergoing SAVR with bioprostheses during the same period. Considering that age at time of implantation is a significant predictor of SVD, SAVR patients' age was limited to 75 years or above [5]. Recruited patients (TAVR or SAVR) had to have at least one echocardiographic follow-up (at our centre) 30 days after the index procedure to be included. We only included SAVR cases that were implanted due to aortic stenosis; other indications such as aortic regurgitation and infective endocarditis were excluded. Patients with a mean gradient of ≥20 mm Hg or moderate or severe aortic regurgitation (AR) with either TAVR or SAVR within 30 days of the index procedure (early failure) were also excluded. In addition, patients that developed infective endocarditis during follow-up were excluded to allow the study to focus on prosthesis deterioration with time.

2.2. Data collection

Data from serial echocardiographic follow-ups were collected as per the definitions described below. Mean transprosthetic valve gradient was calculated using modified Bernoulli equation. Effective orifice area (EOA) was calculated using the continuity equation and when it had to be calculated multiple times at different time points; the same left ventricular outflow tract (LVOT) diameter was used for all studies for that case. Baseline characteristics were collected prospectively and stored on a national database for both TAVRs and SAVRs. Mortality data were censored from an up-to-date national database (National Health Service Spine Portal). All patients gave written consent prior to the index procedure.

2.3. Definition of outcomes

Considering how dynamic the topic of SVD is, we thought to report on all the "agreed on" definitions so far and compare outcomes according to these definitions:

- VARC-2 definition (any of the following) [8]:
  - Transprosthetic valve gradient ≥ 20 mm Hg
  - Effective orifice area (EOA) ≤ 0.9 for body surface area (BSA) < 1.6 cm^2 and EOA ≤ 1.1 cm^2 for BSA ≥ 1.6 cm^2
  - DVI < 0.35 m/s,
  - Moderate or severe prosthetic valve regurgitation
- Moderate haemodynamic SVD (any of the following) [7]:
  - Mean transprosthetic gradient > 20 mm Hg and < 40 mm Hg
  - Mean transprosthetic gradient > 10 and <20 mm Hg change from baseline
  - Moderate intra-prosthetic AR*
  - New or worsening AR (>1+/4+) from baseline
- Severe haemodynamic SVD (any of the following) [7]:
  - Mean transprosthetic gradient > 40 mm Hg
  - Mean transprosthetic gradient > 20 mm Hg change from baseline
  - Severe intra-prosthetic AR*
  - New or worsening AR (>2+/4+) from baseline

  * We included both intra- and para-prosthetic AR as differentiating between these two entities can be difficult on trans-thoracic echocardiography (TTE).
- Dvir el al definition (any of the following):
  - Mean transprosthetic valve gradient ≥ 20 mm Hg
  - Moderate or severe AR
- Morphological SVD and bioprosthetic valve failure (BVF) were defined as per the recent EAPCI consensus statement [7].

2.4. Statistical analysis

Continuous variables are expressed as means and standard deviation when data are normally distributed and as median and interquartile when distribution was skewed. Categorical variables are expressed as percentages and compared using Fisher exact test or Chi-Square test. Parametric and non-parametric tests were used to compare the groups as per data's normality distribution. Mortality and SVD rates over time were compared using Kaplan-Meier (KM) estimates. Event-free analysis was based on first documented event (mortality or SVD depending on the subject of analysis) per patient only. The KM survival graph was truncated to 5 years to allow for the rule of thumb that KM survival curves should be truncated when the sample size reaches 10% of the original sample. Considering the baseline differences between the 2 groups, we propensity matched 2 cohorts (1:1 propensity matching with a calibre of 0.2) and re-run the SVD rate comparison using Kaplan-Meier estimates again. To compare changes over time for repeat measures, we used linear mixed model after identifying best fit model (based on lowest Akaike's information criterion (AIC) and number of parameters). A two-sided P value of <0.05 was considered significant.

3. Results

3.1. Follow-up data

As per the exclusion criteria, 41 and 310 cases were excluded from TAVR and SAVR groups due to no local follow-up after 30 days from the index procedure. The case selection flowchart in Supplementary material demonstrates how between 2007 and 2015, 269 TAVR cases met the study inclusion criteria; whilst 174 SAVR cases met the inclusion criteria between 2005 and 2015. The total follow-up in months was longer among SAVR cases. Yet, 815 TAVR echocardiographic follow-ups were censored over a total of 36.5 years, whilst 399 SAVR cases follow-up were censored over a total of 41.6 years, Table 4 in Supplementary material give details for every follow-up time point.

3.2. Baseline and procedural characteristics

As per Table 1, the baseline differences between the 2 groups reflect the clinical case selection variance. Unsurprisingly, TAVR patients were older (82.4 (6.6) years Vs 79.8 (3.6); $P < 0.001$), more symptomatic and had a higher logistic EuroSCORE (20.5% (11) Vs 12.2% (9); $P < 0.001$). More TAVR patients were in atrial fibrillation (27.1% Vs 17.8%; $P = 0.015$) and had pulmonary disease. TAVR patients had smaller body surface area (1.79cm^2 (0.23) Vs 1.87 (0.22); $P < 0.001$) but received larger valves (valve size 25 mm (2) Vs 22.9 (1.9); $P < 0.001$). The type of prostheses used is reported in Table 2, of note, 96% of the TAVR cohort received an Edwards Sapien prosthesis (Edwards Lifesciences, Irvine, California). Other characteristics such as gender, baseline creatinine,

Table 1
Baseline characteristics.

Variable	TAVR	SAVR	*P* value
Number of cases	269 (60.7%)	174 (39.3%)	N/A
Age (years)	82.4 (6.6)	79.8 (3.6)	0.001
Female	135 (50%)	80 (45%)	0.221
NYHA ≥ III	171 (63.6%)	49 (28.2%)	0.001
Current smoker	9 (3.3%)	8 (4.6%)	0.334
Hypertension	210 (78.1%)	142 (81.6%)	0.218
Pulmonary disease	74 (27.5%)	23 (13.2%)	0.001
Neurological disease	39 (14.5%)	24 (13.8%)	0.476
Extra-cardiac arteriopathy	96 (35.7%)	35 (20.1%)	0.001
AF	73 (27.1%)	31 (17.8%)	0.015
Severe LVSD	12 (4.5%)	6 (3.4%)	0.396
Serum creatinine (μmol/L)	109 (90)	98 (30)	0.063
Logistic ES (%)	20.5 (11)	12.2 (9)	0.001
BSA (m^2)	1.79 (0.23)	1.87 (0.22)	0.001
BMI (kg/m^2)	26.7 (5.7)	27.6 (4.9)	0.071
Urgent intervention	55 (20.4%)	44 (25.3%)	0.141
Valve size (mm)	25 (2)	22.9 (1.9)	0.001
Peak gradient (mm Hg)	75 (25)	70 (27)	0.066
Trans-femoral	175 (65%)	N/A	N/A
SAVR plus	N/A	94 (54%)	N/A
Bypass time (minutes)	N/A	89 (41)	N/A
Cross-clamp time (minutes)	N/A	65 (29)	N/A
Mean ICU stay (days)	1.24 (1.39)	9.3 (85)	0.278
Median ICU stay (days)	1 (1, 1)	1 (1, 1)	0.278
Mean days in hospital (days)	6 (4, 10)	8 (6, 11)	0.054

AF = atrial fibrillation, BMI = body mass index, BSA = body surface area, ES = EuroScore, ICU = intensive care unit, LVSD = left ventricular systolic dysfunction, NYHA = New York Heart Association, SAVR = surgical aortic valve replacement, TAVR = transcatheter aortic valve replacement.