Durability of Balloon-Expandable Heart Valves

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship                  Company

- Consulting Fees/Honoraria                        - Edwards Lifesciences
Transcatheter valves durability is one of the major remaining issues in the context of extension of TAVI to younger patients.

It is well known that surgical bioprosthesis have a limited durability.

Bioprosthetic durability can be altered by structural valve deterioration (SVD) but also by thrombosis and endocarditis.

When deterioration is severe, it can lead to hemodynamic and clinical deterioration and require re-intervention (common surgical definition of SVD).

Data on durability of transcatheter valves are still scarce.
Durability of TAVI vs SAVR at 5 years

From the randomized PARTNER 1 Trial

- Unchanged AVA & gradient comparable to SAVR
- No valve deterioration

M Mack et al. PARTNER 1
Lancet 2015:385(9986):2477-84
A clash of thunder at EuroPCR 2016

PUBLIC RELEASE: 17-MAY-2016

EuroPCR 2016: Half of transcatheter heart valves show degeneration within 10 years of TAVI

First study of long-term durability shows high rates of valve degeneration

Danny DVIR
Standardized definitions of structural deterioration and valve failure in assessing long-term durability of transcatheter and surgical aortic bioprosthetic valves: a consensus statement from the European Association of Percutaneous Cardiovascular Interventions (EAPCI) endorsed by the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Davide Capodanno, Anna S. Petronio, Bernard Prendergast, Helene Eltchaninoff, Alec Vahanian, Thomas Modine, Patrizio Lancellotti, Lars Søndergaard, Peter F. Ludman, Corrado Tamburino, Nicolò Piazza, Jane Hancock, Julinda Methilli, Robert A. Byrne, Andreas Baumbach, Arie Pieter Kappetein, Stephan Windecker, Jeroen Bax, and Michael Haude


Standardized Definition of Structural Valve Degeneration for Surgical and Transcatheter Bioprosthetic Aortic Valves

Danny Dvir, Thierry Bourguignon et al

Circulation 2018;137:388-399
**Durability of bioprosthetic valves**

Need for standardized definitions

- Intrinsic permanent changes of the prosthetic valve: stenosis, regurgitation or both
- Any abnormality not intrinsic to the valve itself (mismatch, paravalvular AR ..)
- Thrombus development
- Endocarditis

1% / Pt / yr

Clinical: 1%
SVD: New Standardized Definitions

Moderate SVD (any of the following):
Mean gradient $> 20 \text{ and } < 40 \text{mmHg}$
Mean change from baseline $> 10 \text{ and } < 20 \text{mm Hg}$
Moderate central AR, new or worsening $> 1$

Severe SVD (any of the following):
Mean gradient $> 40 \text{mmHg}$
Mean change from baseline $> 20 \text{mm Hg}$
Severe central AR, new or worsening $> 2$

Morphological SVD (any of the following):
Leaflet integrity/function abnormality (i.e. torn or flail leaflet)
Leaflet structure abnormality (i.e. patchy calcification causing valvular stenosis or central regurgitation)
Leaflet function abnormality (i.e. impaired motion, stenosis and/or central regurgitation)
Strut/frame abnormality (i.e. fracture)
Haemodynamic and morphological SVD
Bioprosthetic Valve Failure (BVF) directly patient related

**Autopsy findings**

Autopsy findings of bioprosthetic valve dysfunction, likely related to the cause of death, or valve-related death (i.e. any death caused by bioprosthetic valve dysfunction or sudden unexplained death following diagnosis of bioprosthetic valve dysfunction)

**Repeat intervention**

Repeat intervention (i.e. valve-in-valve TAVI, paravalvular leak closure or SAVR) following confirmed diagnosis of bioprosthetic valve dysfunction

**Severe hemodynamic SVD**

Mean transprosthetic gradient ≥40 mmHg
Mean transprosthetic gradient ≥20 mmHg change from baseline
Severe intra-prosthetic aortic regurgitation, new or worsening (>2+/4+) from baseline
Recent data on durability beyond 5 years 2018-2019 data

ESC/EACTS Standardized definitions except for NOTION

<table>
<thead>
<tr>
<th>Valve type</th>
<th>N°</th>
<th>Period</th>
<th>Valve type</th>
</tr>
</thead>
<tbody>
<tr>
<td>BE: 100%</td>
<td>378</td>
<td>2002-12</td>
<td>Eltchaninoff <em>Euro Interv 2018</em></td>
</tr>
<tr>
<td>SE:71% / BE: 29%</td>
<td>300</td>
<td>2007-09</td>
<td>Deutch et al <em>Euro Interv 2018</em></td>
</tr>
<tr>
<td>SE:100%</td>
<td>152</td>
<td>2007-11</td>
<td>Holy et al <em>Euro Interv 2018</em></td>
</tr>
<tr>
<td>SE: 83% / BE: 17%</td>
<td>288</td>
<td>2007-12</td>
<td>Barbanti et al <em>AHA 2018</em></td>
</tr>
<tr>
<td>SE:64% / BE 36%</td>
<td>241</td>
<td>2007-2011</td>
<td>UK Registry <em>J Am Coll Cardiol 2019</em></td>
</tr>
<tr>
<td>SE:100%</td>
<td>1 45</td>
<td>2009-2013</td>
<td>NOTION 2 <em>J Am Coll Cardiol 2019</em></td>
</tr>
<tr>
<td>SE:16% / BE:84%</td>
<td>1403</td>
<td>2002-2011</td>
<td>French Registry <em>Circulation Intv 2019 in press</em></td>
</tr>
</tbody>
</table>
**Recent data on durability beyond 5 years 2018-2019 data**

ESC/EACTS Standardized definitions except for NOTION

<table>
<thead>
<tr>
<th></th>
<th>7-y survival (KM)</th>
<th>7-y/8-y Total SVD</th>
<th>7/8-y Severe SVD</th>
<th>7-y/8-y Re-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eltchaninoff</td>
<td>18%</td>
<td><strong>3.2%</strong></td>
<td>1%</td>
<td>0.6%</td>
</tr>
<tr>
<td><em>Euro Interv 2018</em></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Deutch et al</td>
<td>23.2%</td>
<td>14.9%</td>
<td></td>
<td>4 Pts (%)</td>
</tr>
<tr>
<td><em>Euro Interv 2018</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Holy et al</td>
<td>35%</td>
<td>0%</td>
<td>3.3% (not for SVD)</td>
<td></td>
</tr>
<tr>
<td><em>Euro Interv 2018</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barbanti et al</td>
<td></td>
<td>8.2%</td>
<td>2.4%</td>
<td>0.7%</td>
</tr>
<tr>
<td><em>AHA 2018</em></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>UK Registry* *6 yrs</td>
<td>8.7%</td>
<td>0.4%</td>
<td></td>
<td>0%</td>
</tr>
<tr>
<td><em>JACC 2019</em></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>NOTION 2*</td>
<td>58%</td>
<td>4.3%</td>
<td>0.7%</td>
<td>2.2%</td>
</tr>
<tr>
<td><em>JACC 2019</em></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>French Registry</td>
<td>18%</td>
<td><strong>11.2%</strong></td>
<td>4.2%</td>
<td>1%</td>
</tr>
<tr>
<td><em>Circulation Interv 2019</em></td>
<td></td>
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</table>

*Re-intervention: 0.7 – 1%*
According to this definition, the rate of SVD at 6 years after SAVR is lower but remains greater than after TAVR.
Assessment of Structural Valve Deterioration of Transcatheter Aortic Bioprosthetic Balloon-Expandable Valves Using the New Consensus Definition. The Rouen Study

378 Pts: From 2002 to 2012
Compassionate / Inoperable / High-risk

Baseline characteristics

<table>
<thead>
<tr>
<th>Age, years</th>
<th>83.3±6.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA Class III-IV</td>
<td>75.1%</td>
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</table>

<table>
<thead>
<tr>
<th>Condition</th>
<th>Count (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension, n (%)</td>
<td>253 (65.5%)</td>
</tr>
<tr>
<td>PVD, n (%)</td>
<td>82 (21.2%)</td>
</tr>
<tr>
<td>Renal failure, n (%)</td>
<td>289 (74.9%)</td>
</tr>
<tr>
<td>MI, n (%)</td>
<td>91 (23.6%)</td>
</tr>
<tr>
<td>AF, n (%)</td>
<td>148 (38.3%)</td>
</tr>
<tr>
<td>Stroke, n (%)</td>
<td>23 (6.0%)</td>
</tr>
<tr>
<td>Pacemaker, n (%)</td>
<td>48 (12.4%)</td>
</tr>
<tr>
<td>PCI, n (%)</td>
<td>105 (27.2%)</td>
</tr>
<tr>
<td>CABG, n (%)</td>
<td>71 (18.4%)</td>
</tr>
</tbody>
</table>

Logistic Euroscore 22.8±13.1%

SURVIVAL (KM)
The Rouen Study
100% Balloon Expandable Valves

Exhaustive Echocardiographic Follow-up Obtained in 98% of Pts

Unchanged mean gradient and valve area
The Rouen Study
100% Balloon Expandable Valves

« Structural Valve Deterioration »

Free from SVD 87% at 8 years

Total SVD at 8 years 9 Pts

Kaplan Meyer Analysis

Moderate SVD:
Mean gradient ≥ 20 and < 40mmHg, or
Mean change from baseline ≥ 10 and < 20mm Hg
Moderate central AR, new or worsening > 1

Severe SVD:
Mean gradient ≥40mmHg, or
Mean change from baseline ≥ 20mm Hg
Severe central AR, new or worsening ≥ 2

At 8 years:
Severe SVD in 3 Pts only
Re-intervention in 2: 0.58%
What about SVD post-SAVR?

Very Long-Term Outcomes of the
Carpentier-Edwards Perimount Aortic Valve in Patients Aged 60 or Younger

Thierry Bourguignon, MD, Rym El Khoury, MD, Pascal Candolfi, PhD, Claudia Loardi, MD, Alain Mirza, MD, Julie Boulanger-Lothion, MD, Anne-Lorraine Bouquiaux-Stablo-Duncan, MD, Fabien Espitalier, MD, Michel Marchand, MD, and Michel Aupart, MD

Ann Thorac Surg 2015; 100:853-9

1984-2003
373 Pts
CE Perimount
Mean FU = 8.6±5.9 yrs

Actuarial freedom from reintervention
10 yrs: 88±2%
15 yrs: 71±4%
20 yrs: 38±6%
Recent data with SAVR using echocardiographic assessment

Rate, Timing, Correlates, and Outcomes of Hemodynamic Valve Deterioration After Bioprosthetic Surgical Aortic Valve Replacement

Circulation. 2018;138:971-985

Hemodynamic valve deterioration defined by:
1) an increase in mean gradient $> 10$ mm Hg with a decrease in EOA or worsening of trans-prosthetic aortic regurgitation $> 1/3$ and at least moderate on FU and;
2) abnormalities of leaflets morphology and motion

1387 Pts
70+-8 yrs
Baseline TTE
4.1 mth (1.3-6.5)

926 TTE at 5 yrs

385 TTE at 10 yrs

Repeat TTE at $> 2$ yrs
Recent data with SAVR using echocardiographic assessment

HVD during the total echo follow-up = 30.9% (428 Pts)

Among Pts with HVD, only 37% (159 Pts) underwent re-intervention
Conclusions

- Severe structural valve deterioration after TAVI is rare in an elderly population and the need for re-intervention is very low (< 1 %) at 7-8 y
- This is particularly true with the first generations of Balloon Expandable Valve as shown in the Rouen series (0.5% reintervention at 8 years)
- Sub-clinical SVD is more frequent and exists in both surgical and percutaneous bioprosthetic valves
- Recent data and extension of TAVI emphasize the need for annual assessment of all bioprosthetic valves using echo (and CT +/-PET-Scan when necessary to eliminate thrombus or endocarditis) using standardized definitions
- The incidence of SVD with TAVI Valves in a lower-risk and younger population remains unknown.
- The incidence of SVD with the new generation (SAPIEN 3) Balloon Expandable valve will deserve further assessment on long-term