TAVI-PM
Post-mortem observation study of TAVI

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University Heart Center Hamburg

Late breaking TAVI registries
Conflicts of Interest

- Member of the Drug Commission of the German Medical Association
- Member of the Ethics Committee Hamburg/ Germany
- Research grants: Vifor Pharma
- Previous honoraria: Amgen, Astra-Zeneca, Novartis, Sanofi-Aventis, Vifor (2016-2018)
TAVI proved benefit in subjects with severe and symptomatic aortic stenosis.

<table>
<thead>
<tr>
<th>STS: &lt;4%</th>
<th>STS: 4-8%</th>
<th>STS: &gt;8%</th>
<th>Inoperable</th>
<th>Too sick „futile“</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log. Euroscore I: &lt;10%</td>
<td>Log. Euroscore I: 10-20%</td>
<td>Log. Euroscore I: &gt;20%</td>
<td>Current SAVR patients</td>
<td>Current TAVI patients</td>
</tr>
</tbody>
</table>

Current TAVI patients

Conservative management
Assessing long-term durability of TAVI/SAVR –
2017 Consensus statement of EAPCI, ESC, EACTS

Background

Bioprosthetic Valve Dysfunction

- **Structural Valve Deterioration**
  - Calcification, leaflet fibrosis, tear/fail – degeneration and/or hemodynamic dysfunction

- **Nonstructural Valve Deterioration**
  - Intra/para-prosthetic regurgitation, malposition, patient-prosthesis mismatch, late embolism – degeneration and/or dysfunction

- **Thrombosis**
  - Thrombus development on structure of prosthetic valve – dysfunction with/without thromboembolism

- **Endocarditis**
  - Infection on prosthetic valve – perivalvular access, dehiscence, pseudoaneurysms, fistulae, vegetation, cusp rupture

adapted from Eur Heart J 2017;38:3382-90
Objectives

- To systematically explore TAVI prosthesis post mortem
- To assess TAVI post mortem immunohistologically
Overall study flow

- 451 TAVI patients (implanted 2007 – 2018) with informed consent for post-mortem, implanted or medically treated at our site
- 39 post mortem TAVIs examined so far
- 451 TAVI patients (implanted 2007 – 2018) with informed consent for post-mortem, implanted or medically treated at our site

- 39 post mortem TAVIs examined so far
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<th>Characteristics</th>
<th>Value</th>
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<td>Age (years)</td>
<td>81.1 ± 7.2</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>44 %</td>
</tr>
<tr>
<td>Insulin-dependent diabetes mellitus</td>
<td>26 %</td>
</tr>
<tr>
<td>Hypertension</td>
<td>74 %</td>
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<td>Renal insufficiency</td>
<td>35 %</td>
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<td>Atrial fibrillation</td>
<td>48 %</td>
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<td>64 %</td>
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<td>Log Euro-Score</td>
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## Preliminary results - Characteristics

**Characteristics (n=39)**

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**Time from implantation to death & post mortem assessment**

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<th>Time Interval</th>
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<tr>
<td>&lt; 1 year</td>
<td>14</td>
</tr>
<tr>
<td>1-2 years</td>
<td>9</td>
</tr>
<tr>
<td>2-4 years</td>
<td>8</td>
</tr>
<tr>
<td>&gt; 4 years</td>
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</tr>
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**Valve Type**

<table>
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<tr>
<td>Self-expandable</td>
<td>27</td>
</tr>
<tr>
<td>Balloon-expandable</td>
<td>12</td>
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Preliminary results – Overview structural valve deterioration

Bioprosthetic Valve Dysfunction

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- Infection on prosthetic valve – perivalvular abscess, dehiscence, pseudoaneurysms, fistulae, vegetation, cusp rupture
Preliminary results – structural valve deteriorations

TAVIs post-mortem: Immunohistochemistry

H&E (general morphology-fibrosis)
Preliminary results – Histological scoring (fragmentation/irregularity)

1 – no/low fragmentation
2 – low/high fragmentation
3 – high fragmentation
Preliminary results – Histological scoring (fragmentation/irregularity)

1 – no/low fragmentation
2 – low/high fragmentation
3 – high fragmentation

Apex of leaflet
Base of leaflet

< 1 year  1-2 years  2-4 years  > 4 years
Preliminary results – structural valve deteriorations

1- no/low deteriorations
2- low/medium deteriorations
3- single leaflet deteriorated
4 - all leaflets deteriorated

ESC Congress
Munich 2018
Macroscopic scoring deterioration (mean)

1- no/low deteriorations
2- low/medium deteriorations
3- single leaflet deteriorated
4- all leaflets deteriorated

< 1 year ▼ 1-2 years ▼ 2-4 years ▲ > 4 years
Preliminary results – Overview beyond structural valve deterioration

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    - fragmentation and irregularity

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ESC Congress Munich 2018
Preliminary results – Overview beyond structural valve deterioration

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- Intra/para-prosthetic regurgitation, malposition, patient-prosthesis mismatch, late embolism – degeneration and/or dysfunction
  - Grade 3/4 regurgitation
  - Prosthesis malposition: 1
  - Prosthesis mismatch:

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Endocarditis
- Infection on prosthetic valve – perivalvular abscess, dehiscence, pseudoaneurysms, fistulae, vegetation, cusp rupture
  - Perivalvular abscess
  - Dehiscence:
  - Vegetations:
  - Perforation: 1

ESC Congress Munich 2018
Limitations

- Preliminary results and limited sample size
- Hemodynamic relevance of deteriorations observed have yet to be assessed (post-mortem CT analyses and pulse-duplicator tests to follow)
- Subanalyses to be performed (medication, inflammatory status)
- Comparative analysis with surgical bioprosthetic valves on its way
- TAVI valves show fragmentation and irregularity, confirming previous experimental in vitro reports, but this does not result in increased valve dysfunction

- Possible correlation of morphological changes observed on clinical outcome remains unclear

- Hemodynamic relevance of deterioration in bioprosthetic valves remains unclear

- Further research, in particular comparative analyses with surgical bioprosthetic valves is needed

Conclusion