TAVR 2013 - Where are We Going?

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I have the following financial relationships to disclose:

Edwards
Boston Scientific

Type of relation:

Proctor
TAVR – the First Decade

Severe Symptomatic Aortic Stenosis

Percent of Cardiology Patients Treated

- Bouma 1999: 59% AVR, 41% No AVR
- Iung* 2004: 68% AVR, 32% No AVR
- Pellikka 2005: 70% AVR, 30% No AVR
- Charlson 2006: 40% AVR, 60% No AVR
- Spokane (prelim): 52% AVR, 48% No AVR
- Bach: 69% AVR, 31% No AVR
- Vannan (Pub. Pending): 55% AVR, 45% No AVR

TAVR targeted patients Inoperable / High-risk for SAVR

April 16, 2002
TAVR for Inoperable / High-risk for SAVR - CoreValve

2-years survival

79% 81.6% 85.1% 82.8%
Belgian¹ n=141
UK² n=460
Italian³ n=772
Meta-analysis⁴ n=2156

74% of patients sustained improvement of at least one functional class at 2 years (P<0.01)

NYHA Classification
- Improved 3 levels
- Improved 2 levels
- Improved 1 level
- No change
- Worsened 1 level
- Worsened 2 levels
- Worsened 3 levels

Effective orifice area and mean gradient

Follow-up Visit

Baseline
Discharge
30 Days
6 Months
1 Year
2 Years

Effective orifice area mm²
Mean gradient mmHg
TAVR for Inoperable / High-risk for SAVR – Edwards

All cause Mortality or Stroke

EQ-5D Utilities
New (Off-Label) Indications for TAVR

Since 2002 (FIM), TAVR has emerged as a good alternative to surgical AVR in patients with severe aortic stenosis who are at high risk or inoperable.

TAVR is currently indicated for patients with tri-cuspid aortic valve stenosis.

Many patients with other aortic and mitral pathologies are also at high surgical risk and may benefit from TAVR.
New TAVR Indications

Aortic Regurgitation

Failed Bioprosthetic Valves
TAVI Registry for Pure Native AR

14 European Centers


- St George’s Hospital NHS Trust, London, UK
- Royal Sussex County Hospital, Brighton, UK
- St Georg Hospital Hamburg, Germany
- Sheba Medical Center, Tel Hashomer, Israel
- Kercoff Heart Center, Bad Nauheim, Germany
- CHU Rangueil, Toulouse, France
- University of Pisa, Pisa, Italy
- University Hospital, Antwerp, Belgium
- Royal Brompton Hospital, London, UK
- Hôpital Cardiologique, Lille, France
- German Heart Center, Munich, Germany
- Silesian Medical Center, Katowice, Poland
- Leipzig Heart Center, Germany
- University Hospital of Asturias, Spain
<table>
<thead>
<tr>
<th>Principle causes of AR</th>
<th>Count</th>
</tr>
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<tbody>
<tr>
<td>Degenerative</td>
<td>28</td>
</tr>
<tr>
<td>Post-endocarditic</td>
<td>6</td>
</tr>
<tr>
<td>Aortic aneurysm</td>
<td>4</td>
</tr>
<tr>
<td>Post radiotherapy</td>
<td>2</td>
</tr>
<tr>
<td>Chronic aortic dissection</td>
<td>1</td>
</tr>
<tr>
<td>Cusp restriction due to</td>
<td></td>
</tr>
<tr>
<td>Takayasu’s disease</td>
<td>1</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>43</td>
</tr>
</tbody>
</table>
TAVI for Pure Native Valve AR

Access

- Transfemoral: 81.4%
- Left Subclavian: 9.3%
- Direct Aortic: 7.0%
- Carotid: 2.3%
Results
TAVI for Pure Native Valve AR

• Successful implantation in 42/43 patients (97.7%).

* 1 open heart surgery and valve replacement
Results
TAVI for Pure Native Valve AR

- 2nd Valve required 8 (18.6%)
- Paravalvular Leakage Grade ≤ 1 34 (79.1%)
  Grade 2 7 (16.3%)
  Grade ≥ 3 2 (4.7)*

*1 open heart surgery and valve replacement

- According to Valve Academic Research Consortium (VARC) definitions, procedural success was 76.8%
Results
TAVI for Pure Native Valve AR

• All 8 patients (18.6%) who required a second valve had **absent** annular calcification on CT or Echo (p=0.014)
### Results - VARC Outcomes
#### TAVI for Pure Native Valve AR

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day mortality</td>
<td>4 (9.3%)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>1 (2.3%)</td>
</tr>
<tr>
<td>30-day stroke</td>
<td>2 (4.7%)</td>
</tr>
<tr>
<td>Major</td>
<td>2 (4.7%)</td>
</tr>
<tr>
<td>Minor</td>
<td>0</td>
</tr>
<tr>
<td>1-year mortality</td>
<td>6/28 (21.4%)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>3/28 (10.7%)</td>
</tr>
</tbody>
</table>
30 Day NYHA Functional Class

Number of Patients

Deaths
Class 4
Class 3
Class 2
Class 1

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

0 30 day
Bioprosthetic valves are increasingly implanted in aortic-valve replacement open-heart surgeries.

• These valves commonly fail within 10-15 years, resulting in a need for a high risk “redo” operation.

• Transcatheter valve implantation inside a degenerated bioprosthetic valve (“valve in valve”, VIV) is a less-invasive alternative approach*. 
Transcatheter Aortic Valve Replacement for Degenerative Bioprosthetic Surgical Valves
Results From the Global Valve-in-Valve Registry

Dvir et al Circulation 2012
A, Stented bioprosthesis with leaflets mounted inside the frame struts.

Tuzcu E M et al. Circulation 2012;126:2280-2282
Analysis of high postprocedural gradients (mean gradients ≥20 mm Hg) after valve-in-valve procedures, according to surgical bioprosthesis size: large (internal diameter ≥23 mm), intermediate (≥20 and <23), and small (<20)

Dvir D et al. Circulation 2012;126:2335-2344
Kaplan–Meier survival curve of patients undergoing transcatheter aortic valve replacement for degenerated bioprosthetic valve (valve-in-valve).

Dvir D et al. Circulation 2012;126:2335-2344
Clinical and hemodynamic results of patients undergoing transcatheter aortic valve replacement for degenerated bioprosthetic valves (valve-in-valve).

Dvir D et al. Circulation 2012;126:2335-2344
Case examples of device malposition and ostial coronary obstruction during aortic valve-in-valve implantations
Case examples of valve-in-valve procedures performed inside small surgical bioprostheses.
Are all Inoperable or high risk patients for SAVR, should be candidates for TAVR?

TAVR for moderate/low risk AS patients – Are we ready?
Frailty Phenotype

Syndrome of multisystem impairment associated with aging that results in decreased physiologic reserve and increased vulnerability to stressors.

Frailty increases the risk of functional decline after TAVR

Functional decline = loss of independence in 1 or more ADL*

*Schoenenberger AW, Eur Heart J 2012

*activities of daily living
Frailty: Increased mortality after TAVR

*J Am Coll Cardiol Intv.* 2012;5(9):974
**TAVR: Futility**

**Futility**: Inability to survive one year despite AVR

<table>
<thead>
<tr>
<th>Frailty Assessments</th>
<th>&lt; 80 Yrs</th>
<th>80-90 Years</th>
<th>&gt; 90 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt; 21</td>
<td>4%</td>
<td>5%</td>
<td>6%</td>
</tr>
<tr>
<td>Albumin &lt; 3.3</td>
<td>4%</td>
<td>5%</td>
<td>7%</td>
</tr>
<tr>
<td>Wheelchair Bound</td>
<td>7%</td>
<td>8%</td>
<td>10%</td>
</tr>
<tr>
<td>Does Not Live Independently</td>
<td>5%</td>
<td>6%</td>
<td>9%</td>
</tr>
</tbody>
</table>

**TAVR PARTNER B Two Year Outcome**

- **STS ≥15**
- **STS 5-14.9**
- **STS <5**
Inoperable or high risk patients for SAVR, might **not** be candidates for TAVR either. It is difficult to accept, but some patients are beyond invasive therapy!

TAVR for moderate/low risk AS patients – Are we ready?
## TAVR for Inoperable / High-risk Patients for SAVR - Outcomes

<table>
<thead>
<tr>
<th>First Generation Aortic TCVs</th>
<th>Edwards</th>
<th>CoreValve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure success</td>
<td>95 - 97.8 %</td>
<td></td>
</tr>
<tr>
<td>Valve Embolization</td>
<td>1 %</td>
<td>0 %</td>
</tr>
<tr>
<td>Annulus rupture</td>
<td>1 %</td>
<td>0.2 %</td>
</tr>
<tr>
<td>Valve Dislodgment</td>
<td>0 %</td>
<td>3 %</td>
</tr>
<tr>
<td>Need for additional valve (2/3 valves)</td>
<td>2 - 3 %</td>
<td></td>
</tr>
<tr>
<td>Paravalvular leak Grade ≥ 2</td>
<td>6 -10 %</td>
<td></td>
</tr>
<tr>
<td>Coronary occlusion or sub-occlusion</td>
<td>1 %</td>
<td>&lt;0.3%</td>
</tr>
<tr>
<td>Pacemaker requirement</td>
<td>5 %</td>
<td>35 %</td>
</tr>
<tr>
<td>Major vascular complications</td>
<td>~10%</td>
<td>~8 %</td>
</tr>
<tr>
<td>Stroke</td>
<td>3 - 6 %</td>
<td></td>
</tr>
<tr>
<td>Valve Durability</td>
<td>bench model tests</td>
<td></td>
</tr>
</tbody>
</table>
Moderate/Severe periprosthetic AR post TAVR

- **Blue**: Medtronic CoreValve
- **Green**: Edwards-SAPIEN
Impact of peri-AR on 1-year survival

Sinning, Grube, et al., JACC 2012
## Explanations for Procedure Complications

<table>
<thead>
<tr>
<th>Valve Embolization</th>
<th>Low or Too High + mm *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valve Dislodgment</td>
<td>Technical error + Too High</td>
</tr>
<tr>
<td>Need for additional valve</td>
<td>Too Low or Too High</td>
</tr>
<tr>
<td>Paravalvular leak Grade ≥ 2</td>
<td>Too Low + mm *</td>
</tr>
<tr>
<td>Coronary occlusion</td>
<td>Too High + mm *</td>
</tr>
<tr>
<td>Pacemaker requirement</td>
<td>Too Low + mm *</td>
</tr>
</tbody>
</table>

Wrong measurements* / Valve position / Valve design

*measurement mistakes: undersizing, oversizing
SAVR is an excellent therapy for symptomatic patients with severe aortic stenosis (class I indication) – it improves survival and quality of life with acceptable procedural complications.

TAVR for moderate/low risk AS patients – What should be done to be ready?
TAVR Procedures in 2013 (the 2\textsuperscript{nd} decade) will have to Address:

- Pervialvular Leak
- Coronary Occlusion
- Control and Accuracy of Positioning
- Pacemaker Need
- Stroke
- Major Vascular Complications
**Next Generation Aortic TCVs**

<table>
<thead>
<tr>
<th>Event</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedure success</td>
<td>&gt; 98 %</td>
</tr>
<tr>
<td>Valve Embolization</td>
<td>none</td>
</tr>
<tr>
<td>Annulus rupture</td>
<td>&lt; 0.1 %</td>
</tr>
<tr>
<td>Valve Dislodgment</td>
<td>none</td>
</tr>
<tr>
<td>Need for additional valve (2/3 valves)</td>
<td>none</td>
</tr>
<tr>
<td>Paravalvular leak Grade ≥ 2</td>
<td>&lt; 1 %</td>
</tr>
<tr>
<td>Coronary occlusion or sub-occlusion</td>
<td>none</td>
</tr>
<tr>
<td>Pacemaker requirement</td>
<td>5 - 8 %</td>
</tr>
<tr>
<td>Major vascular complications</td>
<td>&lt; 1 %</td>
</tr>
<tr>
<td>Stroke</td>
<td>&lt; 2 %</td>
</tr>
<tr>
<td>Valve Durability</td>
<td>6-12 years</td>
</tr>
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</table>
TAVR Procedure in 2013 will Require

- Advanced Imaging Modalities
- New TAVR Systems
- Cerebral Embolic Protection Devices
- Access and Closure Strategies
Better Imaging Pre/Post Procedure

CT Annular Measures Can Predict PV Leak

Willson et al JACC 2012
3D TE Echo (IC?)

3D TEE (Qlab): Defining the basal (annular) plane

3d Qlab: Coronal axis

3d Qlab: Cross-section

3d Qlab: Long axis
The Optimal TAVR Procedural Suite

Integrated CT/Angio Systems

Rotation, 3D reconstruction, image fusion
New Transfemoral TAVR Systems

Direct Flow  Boston Sci. Lotus  St. Jude Portico

Aortex  Heart Leaflet Technologies  EndoTech
New Transapical TAVR Systems

Jena Valve

Medtronic Engager

Symetis Accurate
Two New Edwards Valve Platforms

*Edwards SAPIEN 3 Valve*

**Adaptive Seal**
conformability to irregular anatomical surfaces, and to minimize paravalvular leaks

Balloon Expandable

*Edwards CENTRA Valve*

Self Expandable
New CoreValve Evolut Platforms

CoreValve Evolut Recaptureable
23/26/29/31 mm
18 mm to 29 mm Annulus Size Range to Avoid Patient Prosthesis mismatch
Boston Scientific Sadra Lotus™ Valve System

Bovine Pericardium
Proven durability

Nitinol Frame
for retrieval and repositioning

Adaptive Seal
conformability to irregular anatomical surfaces, and to minimize paravalvular leaks
Stroke in TAVR

Etiology of Strokes

• During TAVR: TCD has shown that the majority of procedural embolic events occurred during BAV, manipulation of catheters across the aortic valve, and valve implantation.
• During AVR, TCD evidence of emboli during insertion of an aortic cannula at the start of CPB and after declamping the aorta
• Late embolic events post-AVR are presumably caused by debris from the prosthesis, and development of AF
>51% Periprocedural


- Acute events (≤ 24 hours) independently predicted by balloon postdilation and valve dislodgement/embolization
- Subacute events (1-30 days) predicted by new onset A-fib, while late events (> 30 days) associated with chronic A-fib, PVD, and cerebrovascular disease
- Major stroke predicts mortality both early (OR 7.43; 95% CI 2.45-22.53) and late (HR 1.75; 95% CI 1.01-3.04)

**Implications:** Among TAVR patients, early stroke events are connected to procedural factors and late events to comorbidities.
Embolic Protection Devices for TAVR

Keystone - Deflector
• Clinical Phase
• 9F Transfemoral delivery

Claret Medical - Dual Filter (Montage)
• Clinical Phase
• 6F Transradial or brachial delivery

Edwards/Embrella - Deflector
• Clinical Phase
• 6F Transradial or brachial delivery
Major Vascular Complications

Additional Access/Approaches

- 24 FR (EDW RetroFlex)
- 22 FR (EDW RetroFlex)
- 20 FR (EDW NovaFlex)
- 18 FR (CoreValve)
- 16 FR (CoreValve)

- Direct aortic
- Subclavian
- PC TransApical
- Transfemoral
InSeal ATUM Vascular Closure Device

Sealing membrane (biodegradable)

Vessel wall
APICA: Standardize the approach to apical cannulation
Performing TA TAVI

Percutaneous procedure

Robust Sealing
Valve Durability

Freedom from Structural Valve Deterioration – Perimount Valve

Figure 6: Freedom from Explant Due to SVD

Patients ≥ 60 Years

- Actuarial freedom at 20 years is 77.1 ± 7.2%
Valve Durability: A Lesson from Surgical Valves

• Maintaining Proper Leaflet Motion is Critical to Long Term Valve Durability
• Leaflet bending/folding during valve operation induces high stresses on leaflets. High bending stresses on leaflets can lead to bending fatigue and potentially delamination, calcification, and/or valve failure.\(^1\)
• Misalignment, leaflet prolapse, asynchrony, poor cooptation, high commissure stress, pinwheeling/bending may lead to early failure.
Valve Durability

TAVR Durability - ?????
Studies / Registries will tell
Thank You