Long-term Outcome After Transcatheter Aortic Valve Implantation

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Onassis Cardiac Surgery Center
Δήλωση Συμφερόντων

• Medical Advisory Board for Medtronic, Inc.
Aortic Valve Stenosis

Predominantly a Degenerative Disease

Prevalence
2% of people over 65
3% of people over 75
4% of people over 85

Pathology of Aortic Valve

Healthy Aortic Valve

Stenosed Aortic Valve
ESC/ACC/AHA Guidelines for Treatment of AS

Aortic Valve Replacement (AVR) is a Class I indication in symptomatic patients with severe AS

Why is surgery for aortic stenosis so great?
Patients live longer, feel better, and LV function improves!
At least 30% of Patients with Severe Symptomatic AS are “Untreated”!

**Severe Symptomatic Aortic Stenosis**

Percent of Cardiology Patients Treated

- **AVR:**
  - 41%
  - 60%
  - 48%

- **No AVR:**
  - 59%
  - 40%
  - 52%

Under-treatment especially prevalent among patients managed by primary care physicians.

Reasons for non-treatment: 1. elderly, 2. co-morbidities, 3. patient refusal.
Conclusions—Nonsurgical implantation of a prosthetic heart valve can be successfully achieved with immediate and midterm hemodynamic and clinical improvement.
Bovine pericardial leaflet
Medtronic-Core Valve Bioprosthesis

- Nitinol frame
- Porcine pericardial leaflet
- Self-expandable
- 14 F inner sheath
- 18 F inner sheath
### New TAVI Prosthesis in 2015

<table>
<thead>
<tr>
<th>Device name (manufacturer)</th>
<th>Sheath size (Fr)</th>
<th>Access slit(s)</th>
<th>Valve delivery mechanism</th>
<th>Aneurysm range (mm)</th>
<th>Requirement for temporary pacing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sapien 3 (Edwards)</td>
<td>14</td>
<td>TF, TA, Ao</td>
<td>BE</td>
<td>18–28</td>
<td>Yes</td>
</tr>
<tr>
<td>Centroa (Edwards)</td>
<td>14</td>
<td>TF</td>
<td>SE</td>
<td>18–27</td>
<td>Yes</td>
</tr>
<tr>
<td>Evolut R (Medtronic)</td>
<td>18</td>
<td>TF</td>
<td>SE</td>
<td>18–30</td>
<td>No</td>
</tr>
<tr>
<td>CoreValve (Medtronic)</td>
<td>18, 19</td>
<td>TF, o</td>
<td>SE</td>
<td>22–31</td>
<td>No</td>
</tr>
<tr>
<td>Engager (Medtronic)</td>
<td>30</td>
<td>TA</td>
<td>SE</td>
<td>21–26</td>
<td>No</td>
</tr>
<tr>
<td>Lotus (Bostien Scientific)</td>
<td>18</td>
<td>TF</td>
<td>Mechanical</td>
<td>19–27</td>
<td>No</td>
</tr>
<tr>
<td>Direct Flow (Direct Flow Medical)</td>
<td>18</td>
<td>TF, Ao</td>
<td>Inflatable ring</td>
<td>19–29</td>
<td>No</td>
</tr>
<tr>
<td>Portico (St Jude)</td>
<td>18, 24</td>
<td>TF, Ao</td>
<td>SE</td>
<td>18–25</td>
<td>No</td>
</tr>
<tr>
<td>Jena Valve (Jena Valve)</td>
<td>32</td>
<td>TA</td>
<td>SE</td>
<td>21–27</td>
<td>No</td>
</tr>
<tr>
<td>ACURATE (Symetis)</td>
<td>18, 28</td>
<td>TF, TA</td>
<td>SE</td>
<td>21–27</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Ao, transaortic; BE, balloon-expandable; Fr, French; mm, millimeters; SE, self-expandable; TA, transapical; TF, transfemoral.
TAVR is Available in More Than 65 Countries Around the World

>200,000 total implants to date
Medtronic-Core Valve Bioprosthesis
Edwards - Sapien Bioprosthesis
In-hospital and Short-Term Results: RCT
PARTNER Cohor B (inoperable pts)

All Cause Mortality

\[ \Delta \text{ at 1 yr} = 20.0\% \]
\[ \text{NNT} = 5.0 \text{ pts} \]

HR [95% CI] = 0.51 [0.38, 0.68]
\[ p \text{ (log rank)} < 0.001 \]

**PARTNER Cohort A (high risk pts)**

**All-Cause Mortality**

- HR [95% CI] = 0.93 [0.71, 1.22]
- P (log rank) = 0.62

**Months**

CoreValve US Pivotal Trial
All-Cause Mortality at 2 Years

Δ = 6.5
28.6%

Δ = 4.8
18.9%

Δ = 4.8
14.1%

Δ = 6.5
22.2%

ACC 2015

Months Post-Procedure
## Indications for Transcatheter Aortic Valve Implantation

<table>
<thead>
<tr>
<th>Indication</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAVI should only be undertaken with a multidisciplinary “heart team”</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>including cardiologists and cardiac surgeons and other specialists if</td>
<td></td>
<td></td>
</tr>
<tr>
<td>necessary.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAVI should only be performed in hospitals with cardiac surgery on-site.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>TAVI is indicated in patients with severe symptomatic AS who are not</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>suitable for AVR as assessed by a “heart team” and who are likely to gain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>improvement in their quality of life and to have a life expectancy of</td>
<td></td>
<td></td>
</tr>
<tr>
<td>more than 1 year after consideration of their comorbidities.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TAVI should be considered in high risk patients with severe symptomatic</td>
<td>Ila</td>
<td>B</td>
</tr>
<tr>
<td>AS who may still be suitable for surgery, but in whom TAVI is favoured by</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a “heart team” based on the individual risk profile and anatomic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>suitability.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No mention of euroSCORE or STS

Aortic Stenosis: Choice of Surgical or Transcatheter Intervention

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical AVR is recommended in patients who meet an indication for AVR (listed in Section 3.4) with low or intermediate surgical risk</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>For patients in whom TAVR or high-risk surgical AVR is being considered, members of a Heart Valve Team should collaborate closely to provide optimal patient care</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>TAVR is recommended in patients who meet an indication for AVR for AS who have a prohibitive surgical risk and a predicted post-TAVR survival &gt;12 months</td>
<td>I</td>
<td>B</td>
</tr>
</tbody>
</table>
Aortic Stenosis: Choice of Surgical or Transcatheter Intervention

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TAVR is a reasonable alternative to surgical AVR for AS in patients who meet an indication for AVR and who have high surgical risk</strong></td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Percutaneous aortic balloon dilation may be considered as a bridge to surgical or transcatheter AVR in severely symptomatic patients with severe AS</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>TAVR is not recommended in patients in whom the existing comorbidities would preclude the expected benefit from correction of AS</td>
<td>III: No Benefit</td>
<td>B</td>
</tr>
</tbody>
</table>

ACC/AHA Guidelines 2014
Long Term Results RCT
Five-Year Outcomes of Transcatheter Aortic Valve Replacement (TAVR) in “Inoperable” Patients With Severe Aortic Stenosis: The PARTNER Trial

Samir R. Kapadia, MD
On behalf of The PARTNER Trial Investigators
All-Cause Mortality (ITT)
Landmark Analysis

<table>
<thead>
<tr>
<th>Months</th>
<th>Standard Rx (n = 179)</th>
<th>TAVR (n = 179)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1 Year</td>
<td>HR [95% CI] = 0.50 [0.39, 0.65] p (log rank) &lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>1-3 Years</td>
<td>HR [95% CI] = 0.46 [0.32, 0.66] p (log rank) &lt; 0.0001</td>
<td></td>
</tr>
<tr>
<td>3-5 Years</td>
<td>HR [95% CI] = 0.47 [0.24, 0.94] p (log rank) = 0.028</td>
<td></td>
</tr>
</tbody>
</table>
Repeat Hospitalization (ITT)

<table>
<thead>
<tr>
<th></th>
<th>Standard Rx (n = 179)</th>
<th>TAVR (n = 179)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rehospitalization</td>
<td>53.9%</td>
<td>72.5%</td>
</tr>
<tr>
<td></td>
<td>75.7%</td>
<td>83.0%</td>
</tr>
<tr>
<td></td>
<td>87.3%</td>
<td></td>
</tr>
</tbody>
</table>

HR [95% CI] = 0.40 [0.29, 0.55]
p (log rank) < 0.0001

Repeat Hospitalization (ITT) graph with Kaplan-Meier survival curves for Standard Rx (n = 179) and TAVR (n = 179).
Mean Gradient & Valve Area (AT)

Mean Gradient (mm Hg) vs Valve Area (cm²)

Error bars = ± 1 Std Dev
Five-Year Outcomes after Randomization to Transcatheter or Surgical Aortic Valve Replacement: Final Results of The PARTNER 1 Trial

Michael J. Mack, MD
on behalf of The PARTNER Trial Investigators
All-Cause Mortality (ITT)
All Patients

HR [95% CI]
1.04 [0.86, 1.24]
p (log rank) = 0.76

Error Bars Represent 95% Confidence Limits

67.8%
62.4%
Median Survival All Patients

SAVR

40.6 Months

TAVR

44.5 Months

p (log rank) = 0.76
All Stroke (ITT) : All Patients

HR [95% CI] 1.14 [0.68, 1.93]
p (log rank) = 0.61

Error Bars Represent 95% Confidence Limits

11.3%

10.4%
NYHA Over Time (ITT) : Survivors
Aortic Valve Mean Gradient

No structural valve deterioration that required re-intervention.

Error Bars = ± 1 Std Dev

\[ p < 0.0001 \]
Aortic Valve Area

Error Bars = ± 1 Std Dev

p < 0.0001
Mortality and Post Procedural PVL
TAVR Patients

p (log rank) = 0.0032

75.7%
73.0%
58.6%
Long Term Results: Registries
Long Term Outcomes After TAVI in High-Risk Patients With Severe Aortic Stenosis

The U.K. TAVI Registry

Alison Duncan¹, Peter Ludman², Winston Banya¹, David Cunningham³, Damien Marlee³, Simon Davies¹, Jan Kovac⁴, Thomas Spyt⁴, Neil Moat¹

1: CV BRU Royal Brompton Hospital, London, 2: Queen Elizabeth Hospital, Birmingham
3: University College Hospital, London, 4: University Hospital Leicester,
K-M Survival Curves for UK TAVI cohort implanted 01/01/07 to 31/12/09, censored 01/03/14

3 year survival = 61.2%

5 year survival = 45.5%
## Independent Predictors of Mortality

<table>
<thead>
<tr>
<th>3 years</th>
<th>5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal dysfunction</td>
<td>Renal dysfunction</td>
</tr>
<tr>
<td>Respiratory dysfunction</td>
<td>Respiratory dysfunction</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td>LVEF &lt;50%</td>
<td>LVEF &lt;50%</td>
</tr>
<tr>
<td>Log Euroscore</td>
<td>Log Euroscore</td>
</tr>
<tr>
<td>Age</td>
<td>CAD</td>
</tr>
</tbody>
</table>
Procedural Predictors 5 year Survival after TAVI

No CVA

CVA

Number at risk
No CVA 816 648 584 503 419 154
CVA 33 17 14 12 10 4

p=0.019
Ten Year Follow-Up of TAVI from Vancouver

John Webb MD and Danny Dvir MD
St. Paul’s Hospital, University of BC
Vancouver, Canada

TVT 2016
Total TAVI cases Before May 2011 (n = 463)

- Failed at Baseline (n = 118)
- VIV or Non-Aortic (n = 15)

Mortality < 30 days (n = 35)

Non-Edwards Valves (n = 16)

Insufficient Follow-up (n = 13)

Study patients (n = 266)

Survival time - median 35 months (IQR 12-66 months)
“Structural Valve Degeneration ” has Various Definitions (baseline n=266)

<table>
<thead>
<tr>
<th>SVD definition from the literature</th>
<th># of cases</th>
<th>% of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Stenosis and/or Regurgitation</td>
<td>5</td>
<td>1.9%</td>
</tr>
<tr>
<td>Re-intervention (SAVR or TAVR)</td>
<td>3</td>
<td>1.1%</td>
</tr>
<tr>
<td>Severe AS, severe AR, or Re-intervention</td>
<td>5</td>
<td>1.9%</td>
</tr>
</tbody>
</table>
Structural Valve Deterioration defined as: Freedom from Severe Stenosis, Regurgitation, or Re-intervention

Structural Valve Deterioration defined as: Freedom from Re-intervention
How is durability of surgical valves reported?

Kaplan-Meier freedom from Structural Valve Deterioration

Freedom from Structural Valve Deterioration = freedom from Severe AS/AR or Redo surgery

Expected valve Durability = median survival time without SVD

Very Long-Term Outcomes of the Carpentier-Edwards Perimount Valve in Aortic Position

Thierry Bourguignon, MD, Anne-Lorraine Bouquiaux-Stablo, MD, Pascal Candolfi, PhD, Alain Mirza, MD, Claudia Loardi, MD, Marc-Antoine May, MD, Rym El-Khoury, MD, Michel Marchand, MD, and Michel Aupart, MD

Department of Cardiac Surgery, Tours University Hospital, France, and Department of Biostatistics, Edwards Lifesciences, Nyon, Switzerland
Conclusion

• This is the first documentation of 10 year durability of trans-catheter valves
• Durability exceeds the life expectancy of current patients
• Durability was similar to that reported with common surgical valves
• Clinical follow up exceeds that of some currently available surgical valves
• THV implantation may be a repeatable procedure
• Larger and longer term follow up is needed
The Greek Experience: 4 year Clinical Outcome After Medtronic Core-Valve

Thomopoulou S et al. Age and Ageing 2016
The Greek Experience: 4 year Clinical Outcome After Medtronic Core-Valve

Thomopoulou S et al. Age and Ageing 2016
Valve Performance

Effective Orifice Area increased from $0.66 \pm 0.14$ to $1.87 \pm 0.33 \text{ cm}^2$ after TAVI ($p<0.001$) and remained at $1.23 \pm 0.25 \text{ cm}^2$ at 4 years ($p$ for post TAVI trend $<0.01$)

Mean aortic valve gradient decreased from $50.96 \pm 18.6 \text{ mm Hg}$ to $9.22 \pm 4.6 \text{ mm Hg}$ after TAVI ($p<0.001$) and remained at $15.69 \pm 6.3 \text{ mm Hg}$ at 4 years ($p$ for post TAVI trend $<0.01$)
TAVI Randomized Trials
NOONE Likes Surgery (of any kind)!
Treatment of Aortic Stenosis in the Future

Surgical AVR

TAVI