Transcatheter Aortic Valve Implantation: Should we go to lower risk patients?

Alec Vahanian
Bichat Hospital, Paris
The Devices for TAVI

Medtronic CoreValve® TAV

Edwards SAPIEN™ THV

CE mark 2007

CE mark 2007

>25000 patients treated
Current Indications for TAVI

# Patients

Surgery

TAVI

Risk
Proposed Management of Severe Aortic Stenosis in the TAVI era

Inclusion Criteria for TAVI

After assessment by the ‘Team’

- Severe AS
- Symptomatic
- Life expectancy >1year
- Contra indications for surgery, or
  - High Risk for Surgery :
    - Clinical judgement +
      - EuroScore (logistic) > 20% ; STS Score>10%
  - AND/OR
    - Porcelain aorta
    - History of thoracic irradiation
    - Severe thoracic deformity
    - Patent coronary by pass

Logistical Euroscore distribution
AVR vs. TAVI in Bichat Hospital (2008)
Logistical Euroscore distribution
AVR vs. TAVI in Leipzig (2008)
Results of TAVI
# National TAVI Registries

<table>
<thead>
<tr>
<th>%</th>
<th>Belgian (n=279)</th>
<th>French (n=244)</th>
<th>Spanish (n=108)</th>
<th>UK (n=872)</th>
<th>Germany (n=833)</th>
<th>Italian (n=1248)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Devices</td>
<td>E/MCV</td>
<td>E/MCV</td>
<td>-</td>
<td>MCV/E</td>
<td>MCV/E</td>
<td>MCV</td>
</tr>
<tr>
<td>Procedural success</td>
<td>97</td>
<td>97</td>
<td>98.1</td>
<td>-</td>
<td>95.6</td>
<td>99</td>
</tr>
<tr>
<td>1 month survival</td>
<td>91</td>
<td>87.3</td>
<td>92.6</td>
<td>93.1</td>
<td>92.5 (in hosp)</td>
<td>94.6</td>
</tr>
</tbody>
</table>

Courtesy of J Bosmans (Belgian Registry); H Eltchaninoff (French Registry); A.S. Petronio (Italian Registry); Paul Avanzas (Spanish Registry) (EuroPCR 2010)
PARTNER: Inoperable patients
All Cause Mortality

HR [95% CI] = 0.54 [0.38, 0.78]
P (log rank) < 0.0001

Numbers at Risk

<table>
<thead>
<tr>
<th></th>
<th>TAVI</th>
<th>Standard Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 months</td>
<td>179</td>
<td>179</td>
</tr>
<tr>
<td>6 months</td>
<td>138</td>
<td>121</td>
</tr>
<tr>
<td>12 months</td>
<td>122</td>
<td>83</td>
</tr>
<tr>
<td>18 months</td>
<td>67</td>
<td>41</td>
</tr>
<tr>
<td>24 months</td>
<td>26</td>
<td>12</td>
</tr>
</tbody>
</table>
## Transfemoral Aortic Valve Implantation
### 30-Day Complications

<table>
<thead>
<tr>
<th></th>
<th>Edwards Sapien</th>
<th>Medtronic CoreValve</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Webb (146) PARTNER (179)</td>
<td>Source (946)</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurological complicity</td>
<td>8 5 7.5</td>
<td>12 5.4</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2 0 1</td>
<td>2 0</td>
</tr>
<tr>
<td>Permanent pacemaker</td>
<td>4 3.4 7</td>
<td>25 17</td>
</tr>
<tr>
<td>Vascular complications</td>
<td>8 16 11</td>
<td>NA 2</td>
</tr>
<tr>
<td>AR &gt; 2/4</td>
<td>5 1* 6</td>
<td>2 6</td>
</tr>
</tbody>
</table>

*severe
PARTNER
Paravalvular Regurgitation

30 Day
- None/Trace: 1%
- Mild: 12%
- Moderate: 35%
- Severe: 52%

6 Month
- None/Trace: 7%
- Mild: 53%
- Moderate: 40%

1 Year
- None/Trace: 2%
- Mild: 10%
- Moderate: 45%
Follow-up After TAVI

(Gurvitch R et al. Circulation 2010;122:1319-1327.)

(Walther, Leipzig)
Functional Improvement 2 years after TF TAVI

(Gurvitch R et al. Circulation 2010;122:1319-1327.)
PARTNER: Quality of Life

Primary Endpoint: KCCQ Overall Summary

Δ = 13.9
P < 0.001

Δ = 20.7
P < 0.001

Δ = 24.5
P < 0.001

MCID = minimum clinically important difference
Valve Function after TAVI

(Gurvitch R et al. Circulation 2010;122:1319-1327.)
Comparison of Outcomes for Transapical TAVI vs. Conventional Aortic Valve Replacement

(Walther et al. Euro Heart J 2010;31:1398-1403.)
The PARTNER US Trial

Population: High Risk/Non-Operable Symptomatic, Critical Calcific Aortic Stenosis

Cohort A

ASSESSMENT: Operability

Total n= 1040

ASSESSMENT: Transfemoral Access

Cohort A TF Powered Independently

Cohort A TA Powered to be Pooled with TF

Primary Endpoint: All Cause Mortality (Non-inferiority)

April 2011
The Situation Today
Growing TAVI Experience in Europe

1.2% → 6.5% → 13% → 20%

<table>
<thead>
<tr>
<th>Year</th>
<th>TAVI # of Procedures</th>
<th>SAVR # of Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>609</td>
<td>48850</td>
</tr>
<tr>
<td>2008</td>
<td>3510</td>
<td>51400</td>
</tr>
<tr>
<td>2009</td>
<td>9000</td>
<td>59390</td>
</tr>
<tr>
<td>2010</td>
<td>12000</td>
<td>61000</td>
</tr>
</tbody>
</table>
Screening in Bichat among 380 High-risk Patients Referred for TAVI

EuroSCORE ≥ 20% - STS PROM ≥ 10% / CI to AVR

Medical Rx 118 (31%)

TAVI 225 (59%)

Conventional AVR 37 (10%)
Severe Symptomatic AS in the Elderly

Severe AS: Valve Area $\leq 0.6 \text{ cm}^2/\text{m}^2$ BSA or Mean Gradient $\geq 50 \text{ mmHg}$

Symptomatic AS: NYHA Class III or IV or Angina

Aortic Stenosis $\geq 75$ years
N=408

No Severe AS (n=114)

Severe AS (n=284)

No Symptoms N=68

Symptoms N=216

No Intervention N=72 (33%)

Intervention N=144 (67%)

NYHA III : 106

NYHA IV : 36

Angina : 148

(Iung et al. Eur Heart J 2005;26:2714-20)
### Management of High-Risk Patients with AS in the TAVI Era

<table>
<thead>
<tr>
<th>Location</th>
<th>N</th>
<th>TAVI (%)</th>
<th>AVR (%)</th>
<th>Med. Therapy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dallas</td>
<td>71</td>
<td>21</td>
<td>14</td>
<td>65</td>
</tr>
<tr>
<td>Rotterdam</td>
<td>77</td>
<td>18</td>
<td>14</td>
<td>68</td>
</tr>
<tr>
<td>Cleveland</td>
<td>92</td>
<td>20</td>
<td>21</td>
<td>59</td>
</tr>
<tr>
<td>Vancouver</td>
<td>112</td>
<td>43</td>
<td>18</td>
<td>39</td>
</tr>
<tr>
<td>Milano *</td>
<td>220</td>
<td>45</td>
<td>14</td>
<td>41</td>
</tr>
<tr>
<td>Bichat *</td>
<td>273</td>
<td>54</td>
<td>12</td>
<td>34</td>
</tr>
</tbody>
</table>

* * ESC 2009
BUT !!!!

- Systematic analysis of medical records in Rotterdam (2004-2007)

- 179 patients with severe AS and symptoms
  - 56% received medical treatment:
    - Perceived high operative risk 34% (LES=11%)
    - Symptoms perceived as mild 19%
    - AS perceived as non-severe 14%
    - Patient preference 9%

(Van Geldrop, Eur J CardiothoracSurg 2009, 35:905)
Indications for TAVI

# Patients

Surgery

TAVI

Risk

?
Availability of Percutaneous Intervention is Attractive

- Less invasive:
  - Less painful
  - Shorter hospital stay
  - Faster recovery
  - Less influenced by patient’s comorbidity
Food and Drug Administration modernization act of 1997

« nothing in the act shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship »

50 to 65% of DES are classified as off label but these implantations are now considered as standard care !!!
Decision-making for intervention

- Prognosis according to the severity and consequences of valvular disease
- Risks and late consequences of intervention
- Patient life expectancy and quality of life
- Patient wishes after information: **Self referral!**
- Local resources, in particular results of surgery

*(ESC Guidelines, Eur Heart J 2007;28:230-68)*
Logistic EuroSCORE in TAVI Series

(Mean+/−SD)
« if you don’t come up with good evidence people will still continue to expand the indication »

P Kappetein Eur Heart J , Jan 2011
Inclusion Criteria for TAVI

After assessment by the ‘Team’

- Severe AS
- Symptomatic
- Life expectancy >1 year
- Contra indications for surgery, or
  High Risk for Surgery:
  - Clinical judgement +
    - EuroScore (logistic) > 20%; STS Score > 10%
  AND/OR
  - Porcelain aorta
  - History of thoracic irradiation
  - Severe thoracic deformity
  - Patent coronary by pass
  - ......................

Risk Scores

- Good discrimination (low vs. high risk)
- But poor calibration (predicted vs. observed risk)

<table>
<thead>
<tr>
<th>N. of Patients</th>
<th>N. of Factors</th>
<th>Area under the ROC curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>STS score (Edwards et al.) (J Am Coll Cardiol 2001)</td>
<td>49073 val</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>43463 val+CABG</td>
<td>20</td>
</tr>
<tr>
<td>Ambler et al. (Circulation 2005)</td>
<td>32839</td>
<td>13</td>
</tr>
<tr>
<td>EuroSCORE (Roques et al.) (J Heart Valve Dis 2001)</td>
<td>5672</td>
<td>17</td>
</tr>
<tr>
<td>EuroSCORE tested in the Euro Heart Survey</td>
<td>1269</td>
<td>17</td>
</tr>
</tbody>
</table>

The “Ideal” Model for the Prediction of the Risk of AVR @ TAVI

- Specific evaluation in valve patients
- Tested in a subset representative of the global patient population and practices
- Prospective and external validation
- Easy to use
- Prediction of long-term outcome, morbidity, costs
- “Use-by-date”
Inclusion Criteria for TAVI

After assessment by the ‘Team’

- Severe AS
- Symptomatic
- Life expectancy >1 year
- Contra indications for surgery, or
  - High Risk for Surgery:
    - Clinical judgement +
      - EuroScore (logistic) > 20% ; STS Score>10%
  AND/OR
    - Porcelain aorta
    - History of thoracic irradiation
    - Severe thoracic deformity
    - Patent coronary by pass
    - .....................

Porcelain Aorta

Cyphoscoliosis

Patent grafts

Chest radiation
## SOURCE REGISTRY
Demographics and Risk Factors – Overall Group <20 & >20

**Why TAVI for < LES 20?**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>All Treatments &lt; 20 (N=908)</th>
<th>All Treatments &gt;= 20 (N=1429)</th>
<th>All Treatments p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA Class IV</td>
<td>83 (9.14%)</td>
<td>244 (17.07%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Female</td>
<td>523 (57.60%)</td>
<td>815 (57.03%)</td>
<td>0.6345</td>
</tr>
<tr>
<td>Age &gt;= 80 Years</td>
<td>526 (57.93%)</td>
<td>1016 (71.10%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Smoking</td>
<td>207 (22.80%)</td>
<td>263 (18.40%)</td>
<td>0.0110</td>
</tr>
<tr>
<td>Coronary Artery Disease</td>
<td>396 (43.61%)</td>
<td>838 (58.64%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Congestive Heart Failure</td>
<td>218 (24.01%)</td>
<td>499 (34.92%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>99 (10.90%)</td>
<td>262 (18.33%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Carotid artery stenosis (over 50%)</td>
<td>63 (6.94%)</td>
<td>218 (15.26%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Porcelain Aorta</td>
<td><strong>91 (10.02%)</strong></td>
<td>95 (6.65%)</td>
<td>0.0037</td>
</tr>
<tr>
<td>Mitral valve disease</td>
<td><strong>260 (28.85%)</strong></td>
<td>448 (31.35%)</td>
<td>0.1803</td>
</tr>
<tr>
<td>Cancer</td>
<td><strong>182 (20.04%)</strong></td>
<td>186 (13.02%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Pulmonary disease</td>
<td>206 (22.69%)</td>
<td>389 (27.22%)</td>
<td>0.0149</td>
</tr>
<tr>
<td>Pulmonary disease: FEV1 less than 1.0</td>
<td>32 (3.52%)</td>
<td>29 (2.03%)</td>
<td>0.0327</td>
</tr>
<tr>
<td>Renal insufficiency / Failure</td>
<td>195 (21.48%)</td>
<td>476 (33.31%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Post thoracic radiation therapy</td>
<td><strong>14 (1.54%)</strong></td>
<td>6 (0.42%)</td>
<td>0.0396</td>
</tr>
<tr>
<td>Peripheral vascular disease (non carotid)</td>
<td>123 (13.55%)</td>
<td>346 (24.21%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>PTCA / stent</td>
<td>203 (22.36%)</td>
<td>420 (29.39%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>CABG</td>
<td>108 (11.89%)</td>
<td>392 (27.43%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Carotid endarterectomy / Carotid stent</td>
<td>20 (2.20%)</td>
<td>70 (4.90%)</td>
<td>0.0009</td>
</tr>
<tr>
<td>Prior surgical aortic bioprosthesis in place? (VIV)</td>
<td>6 (0.66%)</td>
<td>20 (1.40%)</td>
<td>0.0166</td>
</tr>
</tbody>
</table>
Risk-Benefit Assessment

“The key element to establish whether patients are high risk for surgery is clinical judgement, which should be used in association with a more quantitative assessment, based on the combination of several scores”

The Key role of the “Heart team”

Coronary Artery Disease

Decision based on
- Symptoms, clinical presentation
- Location of lesions
- Myocardium at risk
- Suitability for PCI

Options
- TAVI + medical Rx ?
- PCI pre / per TAVI ?
- Reconsideration of surgery ?
- Give up any intervention ?
Bicuspid valve

We need more data!

Case by case decision
- annulus: shape/diameter
- amount/distribution of Ca

Dedicated devices?
Follow-up after TAVI

No structural dysfunction but we need a longer follow-up to know the timing and mode of valve failure.
‘Valve-in-a-Valve’: The Solution if Valve Failure Occurs?
Danish TAVI trials
Operable patients, age ≥75 yrs with aortic valve stenosis

Apical TAVI, n: 100
Primary end-point
1-month death, stroke, renal failure

CoreValve, n = 140
Primary end-point
12-month death, stroke, AMI

Identical CRF
Identical CRF
Identical CRF
Identical CRF

SAVR, n = 100
SAVR, n = 140

(Courtesy of Leif Thuesen)
Patient referred for severe aortic stenosis with indication for aortic valve replacement

‘All-comers’ trial
1. Documentation of risk scores
2. Clinical judgment based on ‘State of the Art’ by the Heart Team

Moderate-High risk
Randomise (1100pts)
TAVI (transfemoral, subclavian, retroperitoneal, transapical) vs. SAVR

Surgical AVR registry
Low risk

TAVI registry
Inoperable

End Point: death or major stroke at 1 year (Courtesy of Patrick Serruys)
<table>
<thead>
<tr>
<th></th>
<th>2002</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery Cath</td>
<td>25/24/22F</td>
<td>18F</td>
</tr>
<tr>
<td>Surgical cut-down</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Cardiac Support</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>Full</td>
<td>Local</td>
</tr>
</tbody>
</table>
Navigation and Positioning
Progress in Technology

- Bovine Pericardial Tissue
- ThermaFix™ anti-calcification process
- Leaflets matched for both deflection and thickness
- Cobalt-Chromium Frame
- Scalloped leaflet design
- Size extension

Cribier-Edwards™ THV
Edwards SAPIEN® THV 23mm, 26mm
Edwards SAPIEN® XT THV 23mm, 26mm,
Conclusions

- Today, TAVI is only indicated in high risk patients with severe AS and severe symptoms

- Further research on:
  - Risk stratification models for AVR and TAVI and implementation of their use in conjunction with the other elements in decision-making
  - Evaluation of TAVI (safety, durability, feasibility of subsequent intervention) in single centre series, comprehensive registries, and randomised trials
  - Technology

- It is only then that indications could be expanded to lower risk patients