Results of Transfemoral Transcatheter Aortic Valve Implantation

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German Heart Center, Munich, Germany
Division of Cardiac Surgery

Improving TAVI outcomes
TAVI registries
SAVR vs. TAVI
Quality of Life
Market forecast

Transfemoral TAVI Outcomes
“TAVI Pandemonia”

Approximately 20,000 to 25,000 TAVI’s performed in over 60 countries worldwide

European and US TAVI Market

Millenium Research Group
European Heart Valve Market 2009-2010
Relative European numbers - Aortic Tissue Valve Procedures

TAVI 2%  SAVR 10%  Tissue Valve Procedures 25%

# of procedures

<table>
<thead>
<tr>
<th>Year</th>
<th>TAVI</th>
<th>SAVR</th>
<th>Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>2007</td>
<td>609</td>
<td>31990</td>
<td>3140</td>
</tr>
<tr>
<td>2008</td>
<td>3510</td>
<td>33800</td>
<td>33700</td>
</tr>
<tr>
<td>2009</td>
<td>9000</td>
<td>35650</td>
<td>35550</td>
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</tbody>
</table>

Germany, France, Italy, UK,

European Heart Valve Market Forecast

% Procedures

- Tissue 50.1%
- Mechanical 32.3%
- Repair 17.4%
- PHVT 0.2%

2007

PHVT 0.2%  2007  2012  41.1%
Changing practice patterns

German Heart Center Munich

55% Surgical aortic valve replacement

45% Transcatheter aortic valve implantation

PubMed word search
“Transcatheter Aortic Valve Implantation”

Doubling yearly!
Country-based TAVI registries

Presented in Paris at EuroPCR 2010

- Belgium (n=328)
- France (n=244)
- Germany (n=697)
- United Kingdom (n=872)
- Italy (n=772)
Transcatheter aortic valve implantation: early results of the FRANCE (FRench Aortic National CoreValve and Edwards) registry

Hélène Eltchaninoff¹, Alain Prat², Martine Gilard³, Alain Leguerrier⁴, Didier Blanchard⁵, Gérard Fourniel⁶, Bernard Lung⁷, Patrick Donzeau-Gouge⁸, Christophe Tribouilloy⁹, Jean-Louis Debrux¹⁰, Alain Pavie¹¹, and Pascal Gueret¹², on behalf of the FRANCE Registry Investigators

European Heart Journal (2011) 32, 191–197
doi:10.1093/eurheartj/het361

Transcatheter aortic valve implantation: first results from a multi-centre real-world registry

Ralf Zahn¹³, Ulrich Gericke¹³, Eberhard Grube¹³, Axel Linke¹³, Horst Slevogt¹³, Holger Eggebrecht¹³, Rainer Hambrecht¹³, Stefan Sack¹³, Karl Eugen Hauptmann¹³, Gert Richardt¹³, Hans-Reiner Figulla¹⁰, and Jochen Senges¹³, on behalf of the German Transcatheter Aortic Valve Interventions—Registry Investigators

European Heart Journal (2011) 32, 199–204
doi:10.1093/eurheartj/het239

Baseline Characteristics

Age (yrs)

<p>| | | | | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td>83</td>
<td>82</td>
<td>81</td>
<td>83</td>
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</table>

Logistic EuroSCORE (%)

<p>| | | | | |</p>
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<tr>
<td></td>
<td>28</td>
<td>25</td>
<td>21</td>
<td>21</td>
</tr>
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</table>

[Graph showing age distribution and logistic EuroSCORE]
European Registry Results

Relative Usage Ratio

<table>
<thead>
<tr>
<th>Country</th>
<th>MDT CoreValve</th>
<th>Edwards SAPIEN</th>
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</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>57</td>
<td>43</td>
</tr>
<tr>
<td>France</td>
<td>68</td>
<td>32</td>
</tr>
<tr>
<td>Germany</td>
<td>85</td>
<td>15</td>
</tr>
<tr>
<td>UK</td>
<td>47</td>
<td>53</td>
</tr>
<tr>
<td>Italy</td>
<td>100</td>
<td>15</td>
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</table>

30-day mortality

<table>
<thead>
<tr>
<th>Country</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>9%</td>
</tr>
<tr>
<td>France</td>
<td>12.7%</td>
</tr>
<tr>
<td>Germany</td>
<td>7.5%</td>
</tr>
<tr>
<td>UK</td>
<td>6.9%</td>
</tr>
<tr>
<td>Italy</td>
<td>7.2%</td>
</tr>
</tbody>
</table>
European Registry Results
New Permanent Pacemaking

Need for standardization of practice patterns

Word of caution about Registry Data . . .

1. Site selection bias
2. Patient selection bias
3. Physician reporting bias
4. No Core lab involvement
5. Consistency of endpoint definitions
VARC

Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium


European Heart Journal
Quality of Life

5-month follow-up
12-month follow-up

PF=physical functioning; RP=role physical; BP=bodily pain; GH=general health; VT=vitality; SF=social functioning; RE=role emotional; MH=mental health

Marked improvement in all 8 domains of the SF12 questionnaire at early and intermediate-term follow-up.

1. Ussia et al. EHJ 2009;30:1790-1796
2. Pooled REVIVE and REVIVAL data

Quality of Life at 1 year follow-up
German Heart Center Munich (n=186)

Improvement in physical quality of life maintained at 1 year follow-up

No improvement in mental quality of life at 3-months or 1 year follow-up

Krane et al. Am Heart J 2010;160:451-7
Krane et al. submitted 2011
Improving TAVI outcomes

Transfemoral TAVI Outcomes

SAVR vs. TAVI

Quality of Life

Market forecast

TAVI registries

Bern-Rotterdam Risk Adjusted Comparison: TAVI vs. SAVR

30-day mortality outcomes

TAVI = 114
SAVR = 1008

* IPT - inverse probability of treatment weighted


Bern-Munich-Rotterdam
Propensity Score Matched Analysis

**TAVI = 782**
**SAVR = 2884**

Table 1: Baseline characteristics before and after propensity score matching

<table>
<thead>
<tr>
<th>Before PS matching</th>
<th>After PS matching</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TAVI</strong> (n=148)</td>
<td><strong>SAVR</strong> (n=555)</td>
</tr>
<tr>
<td>Age in years, mean(SD)</td>
<td>81.5 (5.5)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>284 (65.9)</td>
</tr>
<tr>
<td>Logistic EuroSCORE, mean(%) (SD)</td>
<td>22.6 (4.2)</td>
</tr>
<tr>
<td>NYHA class, n (%)</td>
<td>1</td>
</tr>
<tr>
<td>II</td>
<td>65 (16.4)</td>
</tr>
<tr>
<td>III</td>
<td>15 (3.8)</td>
</tr>
<tr>
<td>IV</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>198 (32.3)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>191 (31.8)</td>
</tr>
<tr>
<td>Cerebrovascular accident, n (%)</td>
<td>91 (14.9)</td>
</tr>
<tr>
<td>Peripheral vascular disease, n (%)</td>
<td>91 (14.8)</td>
</tr>
<tr>
<td>COPD, n (%)</td>
<td>115 (19.3)</td>
</tr>
<tr>
<td>Pulmonary Hypertension, n (%)</td>
<td>162 (27.2)</td>
</tr>
<tr>
<td>Creatinine, mg/dl (SD)</td>
<td>1.24 (0.8)</td>
</tr>
</tbody>
</table>

**Age 79 years**
**Logistic EuroSCORE 17%**

Cumulative Hazard Ratio
After propensity score matching

**Before matching**

- 30 day mortality: 1.58 (1.12-2.23) p=0.009
- 1 year mortality: 1.72 (1.38-2.15) p<0.001

... in favor of SAVR

**After matching**

- 30 day mortality: 0.94 (0.56-1.55) p=0.80
- 1 year mortality: 1.16 (0.81-1.65) p=0.42

... no significant difference
Leipzig Propensity Score Matched Analysis: TAVI vs. SAVR

1-year survival outcome

TAVI = 100
SAVR = 100

Transapical AVI - 73%

Conventional AVR - 69%

\[ P = 0.547 \]


Hemodynamic Results: TAVI vs. SAVR

Mean Gradient (mmHg)

<table>
<thead>
<tr>
<th></th>
<th>Discharge</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAVI</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>SAVR</td>
<td>13</td>
<td>9</td>
</tr>
</tbody>
</table>

Effective orifice area (cm²)

<table>
<thead>
<tr>
<th></th>
<th>Discharge</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAVI</td>
<td>1.61</td>
<td>1.29</td>
</tr>
<tr>
<td>SAVR</td>
<td>1.38</td>
<td>1.13</td>
</tr>
<tr>
<td>Surgical stentless valve</td>
<td>1.57</td>
<td>1.38</td>
</tr>
</tbody>
</table>

Patient-prosthetic mismatch (%)

<table>
<thead>
<tr>
<th></th>
<th>Discharge</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transcatheter valve</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Surgical stented valve</td>
<td>26</td>
<td>20</td>
</tr>
<tr>
<td>Surgical stentless valve</td>
<td>11</td>
<td>6</td>
</tr>
</tbody>
</table>

Clavel et al. J Am Coll Cardiol 2009; 53:1883-91
TAVI vs. SAVR – Low EF
Propensity score adjusted

LVEF <50%

SAVR  TAVI  P<0.001

Baseline  Discharge  1-year

No. Risk  120  41

LVEF <30%

SAVR  TAVI  P=0.002

Baseline  Discharge  1-year

No. Risk  68  24

Clavel et al. Circulation 2010;122:1928-1936

TAVI vs. SAVR: Low EF

SAVR Group:

TAVI Group:

LVEF >50%

40% LVEF <50%

30% LVEF =50%

20% LVEF =30%

10% LVEF =20%

20% with LVEF > 50%
at 1-year follow-up

TAVI 58% vs. SAVR

Clavel et al. Circulation 2010;122:1928-1936
PARTNER US (Edwards SAPIEN)

Symptomatic Critical Aortic Stenosis

ASSessment

Operable

ACC 2011

2 Trials

Endovascularly Planned Cohorts (Cohort A & B)

TCT 2010

Cohort A

Cohort B

Yes

No

No

Yes

ASSessment Transfemoral Access

PRIMARY ENDPOINT

All-Cause Mortality

Transapical

TAVR Control

TAVR Test

Medical Management Control

Primary

Secondary

Transfemoral

Transapical

Anatomical

Transapical

PRIMARY ENDPOINT

All-Cause Mortality

September 2010

The NEW ENGLAND JOURNAL of MEDICINE

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Ilkoeck, M.D., Robert A. Guyton, M.D., Augusto D. Richard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela C. Douglas, M.D., John L. Petersen, M.D., Jed I. Anderton, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators

September 2010
All Cause Mortality

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

PARTNER US Cohort B

All Cause Mortality

∆ at 1 yr = 20.0%  
NNT = 5.0 pts

PARTNER US Cohort B
Mortality or Major Stroke

HR [95% CI] = 0.58 [0.43, 0.78]
P (log rank) = 0.0003

All-cause mortality or Major Stroke (%)

∆ at 1 yr = 18.3%
NNT = 5.5 pts

PARTNER US Cohort B
Major bleeding
Predictor of Mortality

P (log rank) = 0.0046

No Major Bleed (n=133)

Mortality (%)

43.5%

26.3%

Major bleeding

Predictor of Mortality

Major vascular complications
Predictor of Mortality

P (log rank) = 0.069

No Major Vascular Complication (n=148)

Mortality (%)

47.2%

27.7%
Major stroke Predictor of Mortality

- Major Stroke (n=15)
  - P (log rank) <0.0001

- No Major Stroke (n=184)
  - 27.7%
  - 66.7%

Mortality (%)

Months

PARTNER US Cohort B

Paravalvular Aortic Regurgitation

No changes over time

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

- 6 Month
  - None/Trace: 53%
  - Mild: 40%
  - Moderate: 7%
  - Severe: 0%

- 1 Year
  - None/Trace: 43%
  - Mild: 45%
  - Moderate: 10%
  - Severe: 2%

PARTNER US Cohort B
NYHA class

- Baseline: TAVI Standard Rx
  - Percent: P = 0.68
  - P < 0.0001
  - P < 0.0001
- 30 Day: TAVI Standard Rx
  - Percent: P < 0.0001
  - P < 0.0001
- 6 Month: TAVI Standard Rx
  - Percent: P < 0.0001
- 1 Year: TAVI Standard Rx
  - Percent: P < 0.0001

PARTNER US Cohort B

Partner B Quality of Life
Kansas City Cardiovascular Questionnaire (KCCQ)

- Δ = 13.9
  - P < 0.001
- Δ = 20.7
  - P < 0.001
- Δ = 24.5
  - P < 0.001
Transfemoral TAVI Outcomes

Improving TAVI outcomes

SAVR vs. TAVI

Quality of Life

Market forecast

TAVI registries

Learning Curve

1-year survival outcome (CoreValve System)

18F (n=102) - 84%
21F (n=24) - 80%
25F (n=10) – 60%

Learning Curve

30-day survival outcome
(Edwards THV)

What is the major contributor to the improvements in outcomes?

1. Patient-related factors

1. Procedural- or operator-related factors

1. Device-related factors
### Treatment Options for Aortic Stenosis

**German Heart Center, Munich**

#### Munich TAVI Experience

(n=550)

<table>
<thead>
<tr>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs.)</td>
<td>81</td>
<td>81</td>
<td>80</td>
</tr>
<tr>
<td>Logistic ES (%)</td>
<td>25</td>
<td>19</td>
<td>18</td>
</tr>
<tr>
<td>STS (%)</td>
<td>7</td>
<td>6</td>
<td>5</td>
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</table>
Munich TAVI Experience
(n=550)

<table>
<thead>
<tr>
<th></th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intubation (%)</td>
<td>100</td>
<td>100</td>
<td>73</td>
<td>69</td>
</tr>
<tr>
<td>Contrast use (ml)</td>
<td>156</td>
<td>128</td>
<td>110</td>
<td>104</td>
</tr>
</tbody>
</table>

Unadjusted Cox Proportional Hazard's Model

30-day mortality

- Q4 vs. Q1: HR (95% CI) = 0.33 (0.11-1.00), p-value = 0.053
- 3.8% vs. 11.4%

6-month mortality

- Q4 vs. Q1: HR (95% CI) = 0.49 (0.25-0.95), p-value = 0.035
- 12.4% vs. 22.4%
Adjusted Cox Proportional Hazard’s Model

Baseline characteristics

<table>
<thead>
<tr>
<th>Q4 vs. Q1</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.29 (0.08-1.08)</td>
<td>0.07</td>
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30-day mortality

<table>
<thead>
<tr>
<th>Q4 vs. Q1</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.29 (0.08-1.08)</td>
<td>0.07</td>
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</table>

6-month mortality

<table>
<thead>
<tr>
<th>Q4 vs. Q1</th>
<th>HR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.67 (0.25-1.77)</td>
<td>0.42</td>
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</table>

Obstacles towards “truly” lower risk patients . . .

- Paravalvular regurgitation
- Left bundle branch block & permanent pacemaker
- Long-term Durability
Device-Patient Interface
Post-mortem
(2.8 years)

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

MDT CoreValve 2-year follow-up
18F Safety & Efficacy Study (2006-2008)

EOA (cm²)

Effective Orifice Area
EOA(cm²)

No. at Risk
Baseline (n=109) Discharge (n=73) 1-month (n=60) 1-year (n=52) 2-year (n=37)

Medtronic CoreValve. 18F Safety and Efficacy Study
Edward SAPIEN 3-year follow-up
Vancouver Experience

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Baseline</th>
<th>Post-procedure</th>
<th>12-months</th>
<th>24-months</th>
<th>36-months</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>70</td>
<td>70</td>
<td>57</td>
<td>49</td>
<td>37</td>
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</tbody>
</table>

Effective Orifice Area (EOA) (cm²)

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

Conclusion

We need data from “well-designed” and “appropriately conducted” studies to convince the medical community and reimbursement authorities, and also to better inform patients, about the potential benefits of transcatheter aortic valve implantation.