Utility vs futility: Any Benefit of TAVI in Patients with severe LV dysfunction or severe COPD

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Disclosures

No financial disclosures related to this talk
The art of risk stratification in TAVI

Nicolas M. Van Mieghem* and Patrick W. Serruys
Utility of TAVI in inoperable Patients

Kapadia SR et al for the PARTNER Trial Investigators. Lancet pub online March15
Improvement of Quality of Life after TAVI in inoperable Patients

KCCQ-Overall Summary

Number available (eligible)

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>Standard Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>170</td>
<td>157</td>
</tr>
<tr>
<td>2</td>
<td>147 (167)</td>
<td>134 (174)</td>
</tr>
<tr>
<td>4</td>
<td>121 (138)</td>
<td>92 (126)</td>
</tr>
<tr>
<td>6</td>
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<td>10</td>
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<tr>
<td>12</td>
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</tbody>
</table>

Futility

The quality of having no useful results: uselessness
American Heritage Dictionary of English Language

„Medical futility means that the proposed therapy should not be performed because available data show that it will not improve the patient‘s medical condition.“
Bernat JL. Neurocrit Care 2005;2(2):198-205
Futility of TAVI

High Risk Patients in the PARTNER Trial - 1 Year Outcomes

Survival

Survival & NYHA

Survival & QoL

Prohibitive Risk Patients in the PARTNER Trial - 1 Year Outcomes

Survival

Survival & NYHA

Survival & QoL

Lindman et al. JACC: Cardiovascular Interventions 2014; 7(7):707-16
The Patient with severe COPD

COPD is a pulmonary condition characterized by chronic airflow limitation that is not fully reversible.

Strong association with smoking, world wide incidence rising.

4th leading cause of death in the USA
Niewoehner D. NEJM 2010;362:1407-1416

COPD is present in 19% of Patients undergoing surgical valve replacement

28-43% of the TAVI Patients have comorbid COPD
Long-Term Outcomes After Transcatheter Aortic Valve Implantation in High-Risk Patients With Severe Aortic Stenosis

The U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry

Table 3 Predictors of Mortality at 1 Year

<table>
<thead>
<tr>
<th>Variables</th>
<th>Alive (n = 684)</th>
<th>Dead (n = 186)</th>
<th>Univariate Model</th>
<th>p Value</th>
<th>Multivariate Model</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edwards SAPIEN</td>
<td>321/680 (47.2)</td>
<td>89/182 (48.9)</td>
<td>1.00</td>
<td></td>
<td></td>
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<tr>
<td>Medtronic CoreValve</td>
<td>359/680 (52.8)</td>
<td>93/182 (51.1)</td>
<td>0.95 (0.70-1.29)</td>
<td>0.75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Route, other</td>
<td>196/684 (28.7)</td>
<td>75/186 (40.3)</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Route, transfemoral</td>
<td>488/684 (71.3)</td>
<td>111/186 (59.7)</td>
<td>0.65 (0.48-0.88)</td>
<td>0.006</td>
<td>0.73 (0.52-1.04)</td>
<td>0.08</td>
</tr>
<tr>
<td>AR moderate/severe</td>
<td>83/674 (12.3)</td>
<td>32/175 (18.3)</td>
<td>1.49 (1.00-2.21)</td>
<td>0.048</td>
<td>1.66 (1.10-2.51)</td>
<td>0.016</td>
</tr>
<tr>
<td>Major vascular complication</td>
<td>39/684 (5.7)</td>
<td>16/185 (8.7)</td>
<td>1.42 (0.82-2.45)</td>
<td>0.21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Permanent pacemaker</td>
<td>108/683 (15.8)</td>
<td>33/184 (17.9)</td>
<td>1.21 (0.83-1.77)</td>
<td>0.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>355/684 (59.9)</td>
<td>101/186 (54.3)</td>
<td>1.19 (0.88-1.61)</td>
<td>0.25</td>
<td></td>
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<tr>
<td>Age, yrs</td>
<td>81.8 ± 7.3</td>
<td>82.3 ± 6.4</td>
<td>1.01 (0.99-1.03)</td>
<td>0.52</td>
<td></td>
<td></td>
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<tr>
<td>AV gradient</td>
<td>81.1 ± 27.1</td>
<td>79.9 ± 27.8</td>
<td>0.996 (0.990-1.002)</td>
<td>0.20</td>
<td></td>
<td></td>
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<tr>
<td>LVEF ≥50%</td>
<td>459/680 (67.5)</td>
<td>94/185 (50.8)</td>
<td>1.00</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>LVEF 30%-49%</td>
<td>169/680 (24.9)</td>
<td>69/185 (37.3)</td>
<td>1.93 (1.40-2.66)</td>
<td>&lt;0.001</td>
<td>1.49 (1.03-2.16)</td>
<td>0.03</td>
</tr>
<tr>
<td>LVEF ≤30%</td>
<td>52/680 (7.6)</td>
<td>22/185 (11.9)</td>
<td>1.89 (1.16-3.07)</td>
<td>0.01</td>
<td>1.65 (0.98-2.79)</td>
<td>0.06</td>
</tr>
<tr>
<td>NYHA functional class I/II</td>
<td>160/680 (23.5)</td>
<td>39/186 (21.0)</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA functional class III/IV</td>
<td>520/680 (76.5)</td>
<td>147/186 (79.0)</td>
<td>1.14 (0.79-1.63)</td>
<td>0.50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary disease</td>
<td>301/653 (46.1)</td>
<td>93/175 (53.1)</td>
<td>1.38 (1.01-1.87)</td>
<td>0.04</td>
<td>1.23 (0.88-1.73)</td>
<td>0.23</td>
</tr>
<tr>
<td>Any previous cardiac surgery</td>
<td>202/667 (30.3)</td>
<td>57/186 (30.7)</td>
<td>1.04 (0.75-1.43)</td>
<td>0.83</td>
<td></td>
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<tr>
<td>PVD</td>
<td>179/654 (27.4)</td>
<td>62/178 (34.8)</td>
<td>1.28 (0.91-1.75)</td>
<td>0.16</td>
<td></td>
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</tr>
<tr>
<td>Diabetes mellitus</td>
<td>146/675 (21.6)</td>
<td>50/136 (26.9)</td>
<td>1.36 (0.98-1.89)</td>
<td>0.07</td>
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<tr>
<td>COPD</td>
<td>176/654 (26.9)</td>
<td>63/180 (35.0)</td>
<td>1.40 (1.02-1.93)</td>
<td>0.04</td>
<td>1.41 (1.00-1.98)</td>
<td>0.05</td>
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<tr>
<td>Creatinine ≥200 mmol/l</td>
<td>38/668 (5.7)</td>
<td>19/185 (10.3)</td>
<td>1.84 (1.14-2.97)</td>
<td>0.012</td>
<td>1.55 (0.90-2.68)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Moat NE et al. JACC 2011;58:2130-8

877 Implants in 870 Patients 2007-2009
69% transfemoral
Mean Log Euroscore 18.5%
Survival 30d 92.9%, 1y 78.6%, 2y 73.7%
Pharmacological implications of coadministration of aspirin and NSAIDs in patients with inflammatory arthritis

Impact of Chronic Obstructive Pulmonary Disease on Valve Academic Research Consortium—Defined Outcomes After Transcatheter Aortic Valve Implantation (from the FRANCE 2 Registry)

Romain Chopard, MD*, Nicolas Meneveau, MD, PhD*, Sidney Chocron, MD, PhD*, Martine Gilard, MD, PhD, Marc Laskar, MD, PhD, Hélène Eltchaninoff, MD, PhD, Bernard Jung, MD, PhD, Pascal Leprince, MD, Emmanuel Teiger, MD, Karine Chevreul, MD, Alain Prat, MD, Michel Lievre, PhD, Alain Leguerrier, MD, Patrick Donzeau-Gouge, MD, PhD, Jean Fajadet, MD, and François Schiele, MD, PhD

3933 Pat. 2010-2011, 895 (22.7%) with COPD, 3038 (77.3%) without

All Cause Mortality at 1y (21.8% vs 18.4%, p<0.03)
NYHA III or IV 13.6% vs 7.3%, p<0.001
Chronic Obstructive Pulmonary Disease in Patients Undergoing Transcatheter Aortic Valve Implantation

Insights on Clinical Outcomes, Prognostic Markers, and Functional Status Changes

319 consecutive Patients, 94(29.5%) with COPD undergoing TAVI
NYHA Class, 6MWT and Duke Activity Index at Baseline, 6 months and 12 months

Definition of Futility: Pat. died or did not improve in NYHA class at 6 months

Similar 30d Mortality in COPD vs. Non-COPD Patients

No difference in VARC Endpoints

COPD Patients had a higher rate of pulmonary complications (27.7% vs 4.5%, p<0.0001)

Sig difference in Mortality after 1year 29.8% vs18.2%, p=0.036) due to higher rate of death by respiratory failure 12.8% vs.0.9%, p<0.001)
Multivariate predictors of mortality in COPD Patients
- eGFR<60ml/min HR 1.87 (0.91-3.84, p=0.089)
- 6MWT HR 1.16 (1.06-1.27, p=0.013)
- Mean aortic Gradient HR 0.98 (0.95-1.01) P=0.109

TAVI treatment was considered futile in 40 COPD Patients (42.5%)
- a distance in the 6MWT <170m was the best predictor of treatment futility (Area under the ROC Curve 0.67)
- TAVI was futile in 59.1% of the patients with <170m vs 28.6% in patients with ≥170m at baseline
All Patients from the PARTNER A+B randomised trials and the continuous Access Registry included (n=2553) were included:

- 1108 with chronic lung disease (272 oxygen dependent)
- 1445 without chronic lung disease
Baseline correlates for 1-year All Cause Death in Patients with CLD post TAVI (multivariate Cox regression analysis)

<table>
<thead>
<tr>
<th>Baseline Correlate</th>
<th>Hazard Ratio (HR)</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Poor patient mobility (6MWT&lt;50m)</td>
<td>1.67</td>
<td>0.0009</td>
</tr>
<tr>
<td>Oxygen dependency</td>
<td>1.44</td>
<td>0.02</td>
</tr>
<tr>
<td>Renal disease</td>
<td>1.43</td>
<td>0.049</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>0.97</td>
<td>0.004</td>
</tr>
<tr>
<td>PAPm (per 10mmHg increase)</td>
<td>1.26</td>
<td>0.008</td>
</tr>
<tr>
<td>Mean aortic valve gradient (per 10mmHg increase)</td>
<td>0.99</td>
<td>0.01</td>
</tr>
</tbody>
</table>

**PBOSS Score (0-5)**
- PAPm≥25mmHg 1 point
- BMI <21kg/m2 1 point
- Oxygen dependency 1 point
- Stress (6MWT 50-199m 1 point, <50m 2 points)

*Dvir D et al. J Am Coll Cardiol 2014;63:269-79*
TAVI in COPD Patients

TAVI Improves Symptoms and reduces mortality in ~60% of Patients with COPD

But ~40% of Patients are dead or have no improvement of symptoms at 6 months

Predictors of bad outcome:
- poor mobility (6MWT)
- pulmonary hypertension
- oxygen dependency
- low body mass index
- poor renal function
- low aortic gradient

-> careful multidisciplinary evaluation of each patient at baseline
Increased mortality after transcatheter aortic valve implantation (TAVI) in patients with severe aortic stenosis and low ejection fraction: A meta-analysis of 6898 patients

26 Studies, enrolling 6898 patients, 30d, 6m and 1y mortality

„Patients with low EF severe aortic stenosis have higher mortality following TAVI compared to normal EF patients.“

TAVI in severely depressed LV Function

Low Flow (SVI≤35mL/m2) but not low LVEF independently predicts Mortality after TAVI

Figure 1

Incidence of 30-Day Mortality According to Flow, Gradient, and Ejection Fraction Status

Le Ven F et al. JACC. 2013;62:782-8
TAVI in severely depressed LV Function

Herrmann et al. Circulation 2013;127:2316-2326
TAVI in severely depressed LV Function

O'Sullivan CJ et al. Eur Heart J 2013 34,3437-3450
TAVI in severely depressed LV Function

Barbash IM et al. Am J Cardiol 2014;113:1536-1542

CASE

78-y old male patient with CAD and severe aortic stenosis, NYHA IV Heart Failure

Left-/right catheterization: LVEF 22%
mean aortic gradient 26mHg
AVA 0.9cm²
LVEDP 30mmHg
mPAP 31mmHg
sig. Ostial RCX Stenosis

-> PCI ostial RCX (DES), Hosp for cardiac recompensation and TAVI Evaluation

-> low dose Dobutamin-stress echocardo showed no LV contractile reserve

-> Cardiac Arrest due to ventricular fibrillation (no stent thrombosis)

-> Transfer to ICU, Treatment with i.v. Dobutamin and Noradrenalin
TAVI in severely depressed LV Function

TAVI in severely depressed LV Function

Contractile Reserve in DSE is not a very good predictor of LV recovery

TAVI in severely depressed LV Function

210 Patients with severe symptomatic Aortic Stenosis referred for Balloonaorticvalvuloplastie(!)  
-> 65 (31%) direct TAVI, 78 (37%) BAV as bridge to TAVI, 67 no interventional Thx.

-> 74% of the BAV pts recievied a valve (TAVI or SAVR)

Saia F et al. Eurointervention 2011;7:723-729
CASE

Balloon valvuloplasty
-> MG 25mmHg -> 19mmHg
-> AVA 0.9 -> 1.1cm²

Cardiac recompensation

Successful TAVI 5w later
(Edwards Sapien3 29mm)
Implantation of ICD

-> no further Events at 8 months
TAVI in severely depressed LV Function

LV Dysfunction is predictor of risk in most of the studies

Low Flow (SVI≤35ml/m2) seems to the better predictor of risk than ejection fraction - invasiv evaluation of all patients

TAVI can be done safely in Patients with depressed LV Function and improves LVEF, symptoms and mortality

In highly-selected, very high risk Patients BAV can be used as a bridge to TAVI
Thank you!
CASE

78-y old male patient referred for possible aortic valve replacement

NYHA IV heart failure, pleural effusion

**Past medical History**

1997 STEMI anterior wall, treated with rtPA

1997 PCI of LAD with BMS

2009 DDDR Pacemaker (Asystolie during Surgery

2009 Squamous Cell Carcinoma distal Esophagus treated with Radio-/Chemotherapy, postactinic pneumonia

2009 traumatic subdural hematoma

2011 Pancreatic adenocarcinoma, treated with Whipple Operation and Chemotherapy
Quality of Life after TAVI at 6 months in the PARTNER B Trial (inoperable Pts)

Quality of Life after TAVI at 1-year in the PARTNER B Trial (inoperable Pts)

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Δ KCCQ</th>
<th>P-Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;85</td>
<td>20.1</td>
<td>0.28</td>
</tr>
<tr>
<td>Age ≤85</td>
<td>31.8</td>
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<tr>
<td>Male</td>
<td>28.6</td>
<td>0.23</td>
</tr>
<tr>
<td>Female</td>
<td>23.6</td>
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</tr>
<tr>
<td>STS Risk &gt;15%</td>
<td>22.7</td>
<td>0.77</td>
</tr>
<tr>
<td>STS Risk 10-15%</td>
<td>24.0</td>
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</tr>
<tr>
<td>STS Risk &lt;10%</td>
<td>29.6</td>
<td></td>
</tr>
<tr>
<td>AV Gradient &gt;40 mmHg</td>
<td>23.4</td>
<td>0.64</td>
</tr>
<tr>
<td>AV Gradient ≤40 mmHg</td>
<td>27.9</td>
<td></td>
</tr>
<tr>
<td>Oxygen Dependent COPD</td>
<td>24.5</td>
<td>0.74</td>
</tr>
<tr>
<td>No Oxygen Dependent COPD</td>
<td>25.8</td>
<td></td>
</tr>
<tr>
<td>Ejection Fraction ≤55%</td>
<td>26.5</td>
<td>0.97</td>
</tr>
<tr>
<td>Ejection Fraction &gt;55%</td>
<td>25.6</td>
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</tr>
<tr>
<td>Valve Area Index ≤0.35</td>
<td>29.4</td>
<td>0.56</td>
</tr>
<tr>
<td>Valve Area Index &gt;0.35</td>
<td>20.9</td>
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</tbody>
</table>

TAVI: Futility?

PARTNER B 2y Follow-up

- STS ≥15%
- Hazard ratio, 0.77 (95% CI, 0.46–1.28)
- P=0.31

- Standard therapy
- TAVR

Makkar RR et al. NEJM2012;366:1996-704

PARTNER B 5y Follow-up

- STS>15%
- P_{log-rank}=0.0749

Kapadia SR et al for the PARTNER Trial Investigators. Lancet pub online March15