Measuring the risk in valve patients

Lessons learnt from the TAVI story?

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Faculty disclosure

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I disclose the following financial relationships:

Consultant for Abbott, Boehringer Ingelheim, Valtech

Paid speaker for Edwards Lifesciences
Management of severe aortic stenosis

Severe AS

Symptoms

LVEF < 50%

Physically active

Exercise test

Presence of risk factors and low/intermediate individual surgical risk

Re-evaluate in 6 months

Contraindication for AVR

High risk for AVR

Short life expectancy

TAVI

Med Rx

No

Yes

No

Yes

No

Yes

AVR

AVR or TAVI

Risk scores and contraindication for surgery

- **Contraindication for surgery (Partner B)**
  - 358 patients
  - Logistic Euroscore: 28%
  - STS score: 12%
  

- **High risk for surgery, but operable (Partner A)**
  - 699 patients
  - Logistic Euroscore: 29%
  - STS score: 12%

Risk scores in valve surgery

• Good discrimination (low vs. high risk)
  C-index 0.75-0.80

• But poor calibration (predicted vs. observed risk)


• Euroscore II
  improved calibration, but no specific data in high-risk patients
EuroSCORE I and II: external validation

- Good discrimination (c-index 0.82)

Better calibration than Euroscore I only for low and intermediate risks

(Barili et al. Eur Heart J 2013;34:22-9)
EuroSCORE II: validation in valvular diseases

- 2931 consecutive patients operated on for valvular surgery in Bichat Hospital during a 5-year period
- 30-day mortality: 5.5%

(Bouleti et al. ESC 2013)
EuroSCORE II: validation in valvular diseases

- 239 patients operated on for valvular surgery with Euroscore I ≥ 20% (mean 35±16)
- 30-day mortality: 25%

(Bouleti et al. ESC 2013)
EuroSCORE and TAVI

- 250 patients treated with TAVI
- Mean age $83 \pm 7$ years
- 190 transfemoral, 60 transapical
- 30-day mortality 7.6%
- c-index
  - ES I 0.63
  - ES II 0.66
  - STS 0.58

*(Durand et al. Am J Cardiol 2013;111:891-7)*
Risk Score for TAVI

- France 2 registry (01 Jan 2010 - 31 Dec 2011)
- 3933 patients in 34 centres
- Exclusion of 100 patients (missing procedure data or valve-in-valve)

- 3833 patients
  - Random sampling
    - Derivation cohort: 2552 patients
    - Validation cohort: 1281 patients

- 382 deaths at 30 days or in hospital (10%)

*Iung et al. Heart 2014;100:1016-23*
# Predictive model and score

<table>
<thead>
<tr>
<th></th>
<th>Adjusted odds-ratio [95% CI]</th>
<th>( p )</th>
<th>Points for score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 90</td>
<td>1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>( \geq 90 )</td>
<td>1.53 [1.02-2.30]</td>
<td>0.04</td>
<td>1</td>
</tr>
<tr>
<td><strong>Body mass index</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \geq 30 )</td>
<td>1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>18.5-30</td>
<td>1.51 [1.01-2.27]</td>
<td>0.05</td>
<td>1</td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>2.27 [1.09-4.74]</td>
<td>0.03</td>
<td>3</td>
</tr>
<tr>
<td><strong>NYHA class IV</strong></td>
<td>1.79 [1.26-2.54]</td>
<td>0.001</td>
<td>2</td>
</tr>
<tr>
<td>( \geq 2 ) acute pulmonary edemas last year</td>
<td>1.61 [1.12-2.30]</td>
<td>0.01</td>
<td>2</td>
</tr>
<tr>
<td><strong>Pulmonary hypertension</strong> (sPAP ( \geq 60 ) mmHg)</td>
<td>1.45 [1.08-1.94]</td>
<td>0.01</td>
<td>1</td>
</tr>
<tr>
<td><strong>Critical state (Euroscore)</strong></td>
<td>2.39 [1.42-4.02]</td>
<td>0.001</td>
<td>3</td>
</tr>
<tr>
<td><strong>Respiratory insufficiency</strong></td>
<td>1.64 [1.22-2.20]</td>
<td>0.001</td>
<td>2</td>
</tr>
<tr>
<td><strong>Dialysis</strong></td>
<td>2.88 [1.46-5.66]</td>
<td>0.002</td>
<td>4</td>
</tr>
<tr>
<td><strong>Approach</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfemoral or subclavian</td>
<td>1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Transapical</td>
<td>2.02 [1.47-2.78]</td>
<td>&lt;0.0001</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>2.18 [1.11-4.28]</td>
<td>0.02</td>
<td>3</td>
</tr>
</tbody>
</table>
Prediction and Calibration

C-index

Derivation cohort
0.67 [0.64-0.71]

Validation cohort
0.59 [0.54-0.64]
Calibration
(Predicted vs. Observed Mortality)

Development cohort

Validation cohort
Frailty in patients with aortic stenosis

- **Prevalence in patients undergoing TAVI**
  - 25% in a multicentre Canadian series of 339 patients  
  - 17% in the TAVI German Registry (697 patients)  
    (*Zahn et al. Eur Heart J* 2011, 32:198-204)
  - 23% in the Partner B Cohort (358 patients)  

- **Impact of indices of functional performance / frailty**
  - Karnofsky index was predictive of 30-day MACCE/death  
    (*Buellesfeld et al. Eur Heart J* 2010:31:984-91)
  - Independent predictor of 5-year survival  
    (*Rodes Cabau et al. J Am Coll Cardiol* 2012;60:1864-75)
Impact of Frailty / Disability Indices

- 152 patients aged ≥70 undergoing CABG and/or valve surgery (mean Euroscore I 10.4%)
- 37 (24%) in-hospital mortality or major morbidity (STS)
- Discrimination (c-index)
  - Euroscore I 0.65
  - STS PROM 0.67
  - STS PROMM 0.68
- C-index of STS PROMM increased from 0.68 to 0.73 when adding:
  - Nagi scale
  - 5-meter gait speed

(Afilalo et al. Circ Cardiovasc Qual Outcomes 2012;5:222-8)
Impact of Frailty / Disability Indices

• 2137 patients from the PARTNER trial/registry
• 6-month poor outcome (death or impaires Qol as assessed by the Kansas city Cardiomyopathy Questionnaire)
• 33% poor outcome at 6 months
• 10 predictive factors, including MMSE and 6-min walk test
• Discrimination (c-index)
  – Derivation sample 0.66
  – Validation sample 0.64

(Arnold et al. Circulation 2014;129:2682-90)
Indications for transcatheter aortic valve implantation

<table>
<thead>
<tr>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>C</td>
</tr>
</tbody>
</table>

TAVI should only be undertaken with a multidisciplinary “heart team” including cardiologists and cardiac surgeons and other specialists if necessary.

TAVI should only be performed in hospitals with cardiac surgery on-site.

TAVI is indicated in patients with severe symptomatic AS who are not suitable for AVR as assessed by a “heart team” and who are likely to gain improvement in their quality of life and to have a life expectancy of more than 1 year after consideration of their comorbidities.

TAVI should be considered in high risk patients with severe symptomatic AS who may still be suitable for surgery, but in whom TAVI is favoured by a “heart team” based on the individual risk profile and anatomic suitability.

« In the absence of a perfect quantitative score, the risk assessment should mostly rely on the clinical judgement of the ‘heart team’, in addition to the combination of scores. »

High Surgical Risk?
Decision between TAVI and AVR?

- EuroScore ≥ 20%
- STS score > 10%
- Fraility
- Chest radiation
- Porcelain aorta
- Re-operation

HEART TEAM DECISION
2.5. Evaluation of Surgical and Interventional Risk
See Table 5 for risk assessment combining STS risk estimate, frailty, major organ system dysfunction, and procedure-specific impediments.

Table 5. Risk Assessment Combining STS Risk Estimate, Frailty, Major Organ System Dysfunction, and Procedure-Specific Impediments

<table>
<thead>
<tr>
<th></th>
<th>Low Risk (Must Meet ALL Criteria in This Column)</th>
<th>Intermediate Risk (Any 1 Criterion in This Column)</th>
<th>High Risk (Any 1 Criterion in This Column)</th>
<th>Prohibitive Risk (Any 1 Criterion in This Column)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STS PROM*</td>
<td>&lt;4% AND</td>
<td>4% to 8% OR</td>
<td>&gt;8% OR</td>
<td>Predicted risk with surgery of death or major morbidity (all-cause) &gt;50% at 1 y OR</td>
</tr>
<tr>
<td>Frailty†</td>
<td>None AND</td>
<td>1 Index (mild) OR</td>
<td>≥2 Indices (moderate to severe) OR</td>
<td></td>
</tr>
<tr>
<td>Major organ system compromise not to be improved postoperatively‡</td>
<td>None AND</td>
<td>1 Organ system OR</td>
<td>No more than 2 organ systems OR</td>
<td>≥3 Organ systems OR</td>
</tr>
<tr>
<td>Procedure-specific impediment§</td>
<td>None</td>
<td>Possible procedure-specific impediment</td>
<td>Possible procedure-specific impediment</td>
<td>Severe procedure-specific impediment</td>
</tr>
</tbody>
</table>
Conclusion

- Risk-stratification faces limitations when applied to TAVI.
- This is mainly due to a moderate discrimination of predictive models of short and mid-term outcome.
- The same findings apply to valvular surgery when performed in high-risk patients.
- No score threshold can be used to reliably identify patients who will not benefit from TAVI.
- The inclusion of indices of cognitive or functional capacity may improve the performance of future scores.
- Current guidelines therefore privilege the heart team approach in decision-making.
Frailty

« A syndrome of decreased reserve and resistance to stressors, resulting from multiple declines across multiple physiologic systems leading to vulnerability to adverse outcomes »

≥ 3 criteria among: weakness, weight loss, exhaustion, low physical activity, and slowed walking speed


Katz index of independence

A – Independent in feeding, continence, transferring, toileting, dressing, and bathing
B – Independent in all but one of these functions
C – Independent in all but bathing and one additional function
D – Independent in all but bathing, dressing, and one additional function
E – Independent in all but bathing, dressing, toileting, and one additional function
F – Independent in all but bathing, dressing, toileting, transferring, and one additional function
G – Dependent in all six functions

(Katz et al. JAMA 1963;185:914-919. )
The Expanded Heart Team

General practitioner

Referring physician

Clinical cardiologist (non interventional)

Geriatrician

Pneumologist

Cardiac surgeon

Nephrologist

Interventional cardiologist

Rehabilitation specialist

Anesthesiologist

Diabetologist

Neurologist

The patient with complex CAD and comorbidity

European Heart Journal (2010) 31, 2501-2555
European Journal of Cardio-thoracic Surgery (2010) 38, S1-S52

www.escardio.org/guidelines
Refining clinical indications for TAVI

- **Patients who are not candidates to any intervention**
  - Poor expected life expectancy / QoL
  - Need for better identification
    (improved risk scores, assessment of comorbidities, functional and psychometric evaluation…)

- **TAVI in patients at low(er) risk for AVR**
  - Concerns on durability, residual AR
  - Comparative evaluation with the results of AVR
    (randomised trials)
Impact of comorbidities on life expectancy

- Causes of death (30 days to 1 Year) in the Source Registry
- 1038 patients (TAVI using Sapien valve)
- Half of deaths were of non-cardiac cause

(Thomas et al. Circulation 2011;124:425-33)
At the present stage, TAVI should not be performed in patients at intermediate risk for surgery and trials are required in this population.  

(ESC/EACTS Guidelines 2012)
Epidemiology of valvular disease

- High prevalence of valvular disease in the elderly
- Predicted increase
- Decision-making issues:
  - Risk of interventions
  - Life expectancy, QoL
  - Patient selection

(Nkomo et al. Lancet 2006;368:1005-11)

(Iung and Vahanian Heart 2012;98:iv7–iv13)
Limitations of risk scores in high-risk patients

- Population characteristics
- Change in techniques (surgery, percutaneous techniques, anaesthesia)
- Choice and coding of variables
- Relative or absolute contraindications for surgery
  - Porcelain aorta
  - Chest radiation
  - Hepatic insufficiency
- Complex conditions requiring an individual approach
  - Active endocarditis
  - Cancer
  - Frailty

*(Rosenhek et al. Eur Heart J 2012;33:822-8)*
Frailty and management of AS

Pegaso study: 928 octogenarians with severe AS
Mean age 84±3 yrs, 59% female
49% were independent (Katz index A)

Planned management

<table>
<thead>
<tr>
<th></th>
<th>AVR (n=244 26%)</th>
<th>TAVI (n=261 28%)</th>
<th>Conservative (n=423 46%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>82±2</td>
<td>85±3</td>
<td>85±4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Log. Euroscore I</td>
<td>21±13</td>
<td>31±18</td>
<td>33±17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Katz index A (%)</td>
<td>70</td>
<td>48</td>
<td>39</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

(Martínez-Sellés et al. ESC 2012)
Frailty and management of AS

Pegaso study: 928 octogenarians with severe AS
Predictive factors of the absence of surgery (TAVI or conservative management)

<table>
<thead>
<tr>
<th></th>
<th>OR [95% CI]</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>1.3 [1.2-1.4]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Log. Euroscore I</td>
<td>1.02 [1.01-1.04]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Katz index A (%)</td>
<td>1.5 [1.3-1.7]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Max. gradient (mm Hg)</td>
<td>0.99 [0.98-0.99]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic PAP (mm Hg)</td>
<td>1.03 [1.01-1.05]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV EF &lt; 40%</td>
<td>2.0 [1.1-3.7]</td>
<td>0.05</td>
</tr>
</tbody>
</table>

(Martínez-Sellés et al. ESC 2012)