ΤΑVR
Σύγχρονες ενδείξεις

Νάσος Μαγγίνας, MD
FACC, FESC
Νοσοκομείο Mediterraneo
Γλυφάδα
Σύγκρουση συμφερόντων

• Καμία σχετικά με αυτή την παρουσίαση
Trans-catheter aortic valve implantation: Contemporary practice and the future

Omar Aldalati, Philip MacCarthy, Rafal Dworakowski
Kings College Hospital, London, United Kingdom

TAVI implants per million; difference between 2008 and 2011

X 3-4

Cardiology Journal
German Institute for Quality Assurance and Transparency in Healthcare (IQTIG)

Number of procedures

In-Hospital mortality
TAVR in Greece

Germany

Greece

X 3.3

X 2.5
SAVR/TAVR in Greece/Germany

Per million population in 2018

- Greece: 167 SAVR, 51 TAVR
- Germany: 181 SAVR, 115 TAVR
Expected growth in the next decade
SAVR risk assessment: the Heart Team

STS PROM < 4%  4-8%  8-50%  >50%

Low  Moderate  High  Inoperable
Prohibitive risk

TAVR reasonable for patients with contraindications to SAVR:

Absolute: Porcelain aorta, hostile chest, radiation damage, previous severe thoracotomy complications
Relative: frailty, cirrhosis, CABG/vulnerable grafts, severe PHTN, severe RV failure
Risk scores for TAVR
(STS PROM)

Predicted 30 d. mortality
Observed 30 d. mortality
# RCTs in TAVR

<table>
<thead>
<tr>
<th></th>
<th>STS PROM</th>
<th>RCTs</th>
<th>Observational, Registries, Meta-analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inoperable</td>
<td>&gt; 50%</td>
<td>PARTNER B</td>
<td>CoreValve extreme risk</td>
</tr>
<tr>
<td>High risk</td>
<td>8-50 %</td>
<td>PARTNER A</td>
<td>STS, France Registries UK, Asian Registries GARY, Australian Registries</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US CV high risk Study</td>
<td></td>
</tr>
<tr>
<td>Moderate risk</td>
<td>4-8 %</td>
<td>PARTNER 2A</td>
<td>S3, Thourani, Lancet 2016</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SURTAVI</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>US Pivotal NOTION</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>STACCATO (TA)</td>
<td></td>
</tr>
<tr>
<td>Low risk</td>
<td>&lt; 4 %</td>
<td>NOTION</td>
<td></td>
</tr>
</tbody>
</table>
Five year mortality PARTNER IB Inoperable patients

Standard treatment group

TAVR group

HR 0.50, 95% CI 0.39–0.65; \( p_{\text{log-rank}} < 0.0001 \)

Number at risk

Standard treatment group

TAVR group

93.6%

71.8%

STS 11 to 12

Kapadia S et al, Lancet 2015;385:2485
Five year mortality PARTNER I
High surgical risk

HR 1.04, 95% CI 0.86-1.24; p=0.76

STS 11 to 12

67.8%
62.4%
CoreValve high risk group

1 year mortality

3 year mortality/CVA

Adams DH et al, NEJM 2014;370:1790

Deeb GM et al, JACC 2016;67:2565
Intermediate risk patients

PARTNER 2 (STS 5.8%)       SURTAVI (STS 4.5%)

Leon M et al, NEJM 2016;374:1609

Reardon MJ et al, NEJM 2017;376:1321
## TAVR: current indications

<table>
<thead>
<tr>
<th>Symptomatic AS</th>
<th>2017 ACC/AHA</th>
<th>2017 ESC/EACTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe symptomatic AS and <strong>prohibitive risk</strong> (STS&gt;50%), with survival &gt; 12 months</td>
<td>TAVR IA</td>
<td></td>
</tr>
<tr>
<td>Severe symptomatic AS and <strong>high risk</strong> (STS&gt;8-50%), depending on patient and procedural risks</td>
<td>TAVR vs SAVR IA</td>
<td>TAVR vs SAVR IB</td>
</tr>
<tr>
<td>Severe symptomatic AS and <strong>intermediate risk</strong> (STS 4-8%), depending on patient and procedural risks</td>
<td>TAVR vs SAVR IIA</td>
<td>TAVR vs SAVR IB</td>
</tr>
<tr>
<td>Severe symptomatic AS and <strong>low risk</strong> (STS &lt;4%), depending on patient and procedural risks</td>
<td>SAVR IB</td>
<td>SAVR IB</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Asymptomatic AS</th>
<th>2017 ACC/AHA</th>
<th>2017 ESC/EACTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe AS</td>
<td>SAVR IB</td>
<td>SAVR IC with + EST, low EF</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SAVR IIA with vel&gt;5,5, PHTN, BNP</td>
</tr>
</tbody>
</table>
### 2017 ESC/EACTS Guidelines for the management of valvular heart disease

#### B) Choice of intervention in symptomatic aortic stenosis

Aortic valve interventions should only be performed in centres with both departments of cardiology and cardiac surgery on site and with structured collaboration between the two, including a Heart Team (heart valve centres).

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>C</th>
</tr>
</thead>
</table>

The choice for intervention must be based on careful individual evaluation of technical suitability and weighing of risks and benefits of each modality (aspects to be considered are listed in Table 7). In addition, the local expertise and outcomes data for the given intervention must be taken into account.

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>C</th>
</tr>
</thead>
</table>

SAVR is recommended in patients at low surgical risk (STS or EuroSCORE II < 4% or logistic EuroSCORE I < 10%\(d\) and no other risk factors not included in these scores, such as frailty, porcelain aorta, sequelae of chest radiation).\(^93\)

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>B</th>
</tr>
</thead>
</table>

TAVI is recommended in patients who are not suitable for SAVR as assessed by the Heart Team.\(^91,94\)

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>B</th>
</tr>
</thead>
</table>

In patients who are at increased surgical risk (STS or EuroSCORE II ≥ 4% or logistic EuroSCORE I ≥ 10%\(d\) or other risk factors not included in these scores such as frailty, porcelain aorta, sequelae of chest radiation), the decision between SAVR and TAVI should be made by the Heart Team according to the individual patient characteristics (see Table 7), with TAVI being favoured in elderly patients suitable for transfemoral access.\(^91,94-102\)

<table>
<thead>
<tr>
<th></th>
<th>I</th>
<th>B</th>
</tr>
</thead>
</table>

Balloon aortic valvotomy may be considered as a bridge to SAVR or TAVI in haemodynamically unstable patients or in patients with symptomatic severe aortic stenosis who require urgent major non-cardiac surgery.

<table>
<thead>
<tr>
<th></th>
<th>IIb</th>
<th>C</th>
</tr>
</thead>
</table>

Balloon aortic valvotomy may be considered as a diagnostic means in patients with severe aortic stenosis or other potential causes for symptoms (i.e. lung disease) and in patients with severe myocardial dysfunction, pre-renal insufficiency or other organ dysfunction that may be reversible with balloon aortic valvotomy when performed in centres that can escalate to TAVI.

| | IIb | C |
# 2017 ESC/EACTS Guidelines for the management of valvular heart disease

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Favours TAVI</th>
<th>Favours SAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>STS/EuroSCORE II &lt;4% (logistic EuroSCORE I &lt;10%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>STS/EuroSCORE II ≥4% (logistic EuroSCORE I ≥10%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Presence of severe comorbidity (not adequately reflected by scores)</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Age &lt;75 years</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Age ≥75 years</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Frailty&lt;sup&gt;b&lt;/sup&gt;</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Restricted mobility and conditions that may affect the rehabilitation process after the procedure</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Suspicion of endocarditis</td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>
# 2017 ESC/EACTS Guidelines for the management of valvular heart disease

<table>
<thead>
<tr>
<th>Anatomical and technical aspects</th>
<th>Favours TAVI</th>
<th>Favours SAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Favourable access for transfemoral TAVI</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Unfavourable access (any) for TAVI</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Sequelae of chest radiation</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Porcelain aorta</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Presence of intact coronary bypass grafts at risk when sternotomy is performed</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Expected patient–prosthesis mismatch</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Severe chest deformation or scoliosis</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Short distance between coronary ostia and aortic valve annulus</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Size of aortic valve annulus out of range for TAVI</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Aortic root morphology unfavourable for TAVI</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Valve morphology (bicuspid, degree of calcification, calcification pattern) unfavourable for TAVI</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Presence of thrombi in aorta or LV</td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>
Low risk patients: TAVR yet not indicated

Transcatheter Versus Surgical Aortic Valve Replacement in Patients With Severe Aortic Valve Stenosis
1-Year Results From the All-Comers NOTION Randomized Clinical Trial

STS 2.9%
EuroSCORE 8.4%
TAVR=142
SAVR=134
TAVR vs SAVR in low risk patients

Non randomized
TAVR, N=200
SAVR, N=719
STS<3%

<table>
<thead>
<tr>
<th>Observed</th>
<th>TAVR</th>
<th>SAVR</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay post-procedure, days</td>
<td>2.0 ± 1.1</td>
<td>6.4 ± 3.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VARC 2 life-threatening or major bleeding*</td>
<td>5/200 (2.5)</td>
<td>74/719 (10.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VARC 2 major vascular complications</td>
<td>5/200 (2.5)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Acute kidney injury†</td>
<td>0/200 (0.0)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>All-cause death</td>
<td>0/200 (0.0)</td>
<td>5/719 (0.7)</td>
<td>0.591</td>
</tr>
<tr>
<td>Stroke</td>
<td>0/200 (0.0)</td>
<td>4/719 (0.6)</td>
<td>0.582</td>
</tr>
<tr>
<td>MI</td>
<td>0/200 (0.0)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>0/200 (0.0)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>New-onset atrial fibrillation</td>
<td>6/200 (3.0)</td>
<td>293/719 (40.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>New PPM implantation</td>
<td>10/200 (5.0)</td>
<td>32/719 (4.5)</td>
<td>0.742</td>
</tr>
<tr>
<td>Coronary artery obstruction</td>
<td>1/200 (0.5)</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

FIGURE 3 Total Aortic Regurgitation in the TAVR Cohort

(J Am Coll Cardiol 2018;72:2095-105)
Moderate/severe structural valve deterioration (SVD) was defined as a mean gradient ≥20 mm Hg, an increase in mean gradient ≥10 mm Hg from 3 months post-procedure, or more than mild intraprosthetic aortic regurgitation (AR) either new or worsening from 3 months post-procedure.

Nonstructural valve deterioration (NSVD) similar. Bioprosthetic valve failure (BVF) similar.

Severe SVD: 1) mean gradient ≥40 mm Hg and/or ≥20 mm Hg increase from baseline; AND/OR 2) peak velocity ≥4 m/s and/or ≥2 m/s increase from baseline; AND/OR 3) severe new or worsening intraprosthetic aortic regurgitation (AR).

Moderate SVD: 1) mean gradient ≥20 and <40 mm Hg and/or ≥10 and <20 mm Hg increase from baseline; AND/OR 2) peak velocity ≥3 and <4 m/s and/or ≥1.5 and <2 m/s increase from baseline; AND/OR 3) moderate new or worsening intraprosthetic AR.
Asymptomatic AS

Death/AVR

ACC 2017  ESC 2017

SAVR

IB  IC  IIA

# Upcoming RCTs in TAVR

<table>
<thead>
<tr>
<th>Trial</th>
<th>Objective</th>
<th>Date of completion</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARTNER 3</td>
<td>To determine safety and effectiveness of Sapien 3 in low risk patients in comparison to sAVR</td>
<td>2027</td>
</tr>
<tr>
<td>UK TAVI</td>
<td>To determine clinical effectiveness and cost-utility of TAVI in comparison to sAVR (high and intermediate risk)</td>
<td>2016</td>
</tr>
<tr>
<td>ACTIVATION</td>
<td>Percutaneous coronary intervention prior to TAVI</td>
<td></td>
</tr>
<tr>
<td>GALILEO</td>
<td>Effect of rivaroxaban anticoagulation strategy in comparison to dual anti-platelet therapy</td>
<td>2018</td>
</tr>
<tr>
<td>TAVR UNLOAD</td>
<td>To determine safety and efficacy of TAVI in patients with moderate aortic stenosis and heart failure in comparison to optimal medical therapy</td>
<td>2020</td>
</tr>
<tr>
<td>STEP for patients prior</td>
<td>Whether supervised exercise would improve frailty status of TAVI patients</td>
<td>2017</td>
</tr>
<tr>
<td>to undergoing TAVR</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Ongoing RCTs:
TAVR presently not indicated

<table>
<thead>
<tr>
<th>Trial ID</th>
<th>PARTNER 3</th>
<th>Evolut R low risk</th>
<th>NOTION 2</th>
<th>EARLY TAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NCT02675114</td>
<td>NCT02701283</td>
<td>NCT02825134</td>
<td>NCT03042104</td>
</tr>
<tr>
<td>Number of patients</td>
<td>1328</td>
<td>1200</td>
<td>992</td>
<td>1109</td>
</tr>
<tr>
<td>Comparator</td>
<td>SAVR</td>
<td>SAVR</td>
<td>SAVR</td>
<td>Clinical surveillance (no intervention)</td>
</tr>
<tr>
<td>Design</td>
<td>Randomized, non-inferiority</td>
<td>Randomized, non-inferiority</td>
<td>Randomized, non-inferiority</td>
<td>Randomized</td>
</tr>
<tr>
<td>Definition of low risk</td>
<td>Heart Team predicted peri-operative mortality &lt;2% (STS &lt;4%)</td>
<td>Heart Team predicted 30-day SAVR mortality &lt;3% (STS &lt;3%)</td>
<td>STS &lt;4%, age ≤75 years</td>
<td>Asymptomatic patient</td>
</tr>
<tr>
<td>Transcatheter heart valve in TAVI arm</td>
<td>SAPIEN 3 only, transfemoral approach</td>
<td>Evolut R or CoreValve</td>
<td>Any CE approved transcatheter heart valve, only transfemoral approach</td>
<td>SAPIEN 3</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Up to 10 years</td>
<td>Up to 5 years</td>
<td>Up to 5 years</td>
<td>2 years</td>
</tr>
<tr>
<td>Primary endpoint</td>
<td>All-cause mortality, all stroke, and rehospitalization at 1 year</td>
<td>All-cause mortality or disabling stroke at 2 years</td>
<td>All-cause mortality, MI, and stroke at 1 year</td>
<td>Non-hierarchical composite of all-cause mortality, all stroke, and unplanned CV hospitalization</td>
</tr>
</tbody>
</table>
Exploratory TAVR indications

- Younger, low risk patients
  - No data for <70 y.o.
  - Long life expectancy
    - TAVR durability
      - 3.2% at 8 years, Eltchaninoff H, et al, EuroIntervention 2018;14:e264–e271
    - Future TAVR interventions?
    - Silent CVAs
    - Long term effect of mild AR
    - Long term effect of PPM
    - Coronary access
  - Extension to low risk group is expected to increase patient number by ~ 50%
  - Antithrombotic regimen?
Exploratory TAVR indications

- Bicuspid AV
  - Similar mortality
  - More PVL
  - Less PPM
  - Aortopathy?

- ViV
  - Careful patient/bioprosthesis selection
  - Prosthesis mismatch
  - More coronary obstruction 2.3%
  - Valve fracture
  - ESC/EACTS 2017, IIaC

- Paradoxical low-flow, low-gradient AS
Greek data

- Low TAVR use compared to EU
- Central approval strict, due to financial constraints, using EuroSCORE > 20% and STS > 5%
- ESC/EACTS suggest EuroSCORE > 10% or STS > 4%
- Lack of detailed database (in progress)
Conclusions

- TAVR is a revolutionary treatment for AS and is indicated in:
  - Inoperable (extreme surgical risk) patients
  - High surgical risk patients
  - Moderate surgical risk patients
- Several clinical, anatomical and technical parameters may change the final recommendation and should be discussed with the patient
- TAVR is increasingly used clinically in specific subsets (bicuspid AV, ViV)
- Extension to other cohorts under RCT investigation
• Ευχαριστώ
gia tηn προσοχή σας