TAVI - Update

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Disclosure

Speaker name: Matthias Thielmann

I have the following potential conflicts of interest to report:

☐ Consulting
☐ Employment in industry
☐ Stockholder of a healthcare company
☐ Owner of a healthcare company
☐ Other(s)

☒ I do not have any potential conflict of interest

...except that fact that I am a CV surgeon, experienced in TAVI (~500) as well as sAVR (>1000)
2014 and 2015 TAVI Penetration in Europe

TAVI Procedures/million inhabitants

- Germany
- Switzerland
- France
- Austria
- Netherlands
- Nordics
- Italy
- UK
- Spain
- Greece
- Portugal
- Belgium

EUROSTAT database; TAVI 2014 and 2015 procedures: BIBA medical (independent third party data)
TAVI Reimbursement In EU-Countries

TAVR Reimbursement
- TAVR-specific DRG
- Hospital budget
- SAVR DRG excess from hospital budget
- Trust budget
- Region specific

Source: Adoption of TAVI in Western Europe, N. Piazza London PCR Sept 2013
TAVI in the UK – Adoption and Economic Evidence Jonathan Byrne, PCR 2015
Current TAVI Reimbursement in Germany

DRG for TAVI is currently ~2-3-fold higher in the same AS candidate!

~35,000 Euro
~15,000 Euro
The Dilemma: ‘Indication follows Reimbursement’

Hospital management and physicians are not rewarded for best treatment but rather for best DRG!
Current & Future Indications?

Multidisciplinary ‘Heart Team’

sAVR

TAVI

sutureless AVR
Guideline For Minimal-invasive Heart Valve Interventions
Mutual Resolution By The German Federal Government Commission (G-BA)

Quality guidelines:
- Indication & decision-making
- Institutional treatment

Legal prerequisites:
- structural (heart team)
- institutional (IVC + CVS)
- professionally qualified & skilled
- certified by review committee
State Of The Art In TAVI
Two Different Concepts

**balloonexpandable**
bovine pericardial tissue +
cobalt-cromium stent

**selfexpandable**
Porcine tissue + nitinol stent
2nd & 3rd THV-Generation - Reduction of PVLs

“subannular fixation”

“space filler”
...Via Different Approaches!

- Transfemoral
- Transapical
- Transaxillary
- Transcarotid
- Suprasternal
- Transaortic
- Transfemoral
West-German Heart Center Strategy... so far

Symptomatic Aortic Stenosis

- Contraindications or high-risk surgery
  - Severely compromised LV function or concomitant procedures (e.g. MVR, CABG)
    - Not applicable
    - Yes
  - Poor vascular status
    - Not applicable
    - Yes

- MIS/Sutureless AVR
- Open AVR
- Transfemoral TAVI
- Transaortic TAVI
- Transapical TAVI
West-German Heart Center Strategy...in near future?

Symptomatic Aortic Stenosis

- No
- Contraindications or high-risk surgery
  - Severely compromised LV function or concomitant procedures (e.g. MVR, CABG)
    - No
    - Open AVR
    - MIS/Sutureless AVR
  - Yes
    - Poor vascular status
      - No
      - Transfemoral TAVI
      - Transaxillary TAVI
    - Yes

1st alternative access?
“Standard Operating Procedure” for TAVI practice

West-German Heart Center TAVI Team
(2 Senior Cardiologists, 2 Senior Surgeons)
The German Aortic Valve Registry – GARY
Time-to-event curves for death stratified by the logistic EuroSCORE (n=13639)

Mohr et al. EJCTS 2014;46:808-816
Since 2014 TAVI > sAVR

Strong increase in endovasc TAVI, decrease in transapical TAVI

Decrease in sAVR both isolated and combined with CABG
- Overall decrease in mortality in endovascular TAVI. It is the only access route with a decrease in mortality
- Mortality in endovascular TAVI is getting close to SAVR in-hospital mortality
The German Aortic Valve Registry (GARY)
Mortality of patients undergoing AVR for all four subgroups (n=34063)

Holzhey et al. ATS 2015;101:658-66
‘Minimalist’ Approach: Optimizing Without Compromising!

- Acquiring experience and “mastering” the TAVI procedure
- Local anesthesia as the preferred approach
- Simplifying TAVI procedure
- Standardized care
- Avoiding complications
- Limiting ICU stay
- Optimizing the length of stay
- Understanding optimal reimbursement conditions

Minimalist transcatheter aortic valve replacement: The new standard for surgeons and cardiologists using transfemoral access?

Jensen et al. JTCVS 2015;150:833-9.

Comparison of Transfemoral Transcatheter Aortic Valve Replacement Performed in the Catheterization Laboratory (Minimalist Approach) Versus Hybrid Operating Room (Standard Approach) Outcomes and Cost Analysis


Sedation or general anesthesia for patients undergoing transcatheter aortic valve implantation—does it affect outcome? An observational single-center study

Or Goren MD, Ariel Finkelstein MD, Andrei Gluch MD, Nechama Sheinberg MD, Elia Dery MSc, Idit Matot MD

Evolution of Length of Stay - sAVR vs. TAVI

Source: PMSI-database

Source: AQUA – quality report

Mean length of stay (days)

Germany

France

2012 2013 2014
Vancouver 'Minimalist' Approach in TAVI

Length of stay in 393 consecutive patients discharged after TAVI
May 2012 - October 2014

Early discharge 38.2% !!!

Hottest Current TAVI Data!

Intermediate risk

Lower risk
PARTNER II Cohort A - Intermediate risk

Methods
2,032 patients with severe symptomatic AS and intermediate surgical risk from 55 sites in the US and Canada were included.

Criteria for inclusion
• Severe AS (aortic valve area <0.8 cm or AVA index <0.5 cm/m²)
• Signs of heart failure (NYHA class ≥II)
• Intermediate risk (STS score ≥4 % and decision by a heart team)

Primary endpoint
• Combination of all-cause mortality or disabling stroke at two years

Study design and patient characteristics
Both groups were randomized 1:1 to receive either TAVI or sAVR.

775 patients received transfemoral TAVI and 236 transapical/transaortic TAVI with the SAPIEN XT, while 1,021 received sAVR.

• Mean age: 81.5y (TAVI) vs. 81.7y (sAVR)
• Mean STS score: 5.8 vs. 5.8 %
• NYHA class III or IV: 77.3 vs. 76.1 %
PARTNER II Cohort A - Intermediate risk

Primary Endpoint
All-Cause Mortality or Disabling Stroke

HR [95 % CI]=0.89 [0.73, 1.09]
p (log rank)=0.253

Numbers at risk:
- Surgery: 1,021, 838, 812, 783, 770, 747, 735, 717, 695
- TAVR: 1,011, 918, 901, 870, 842, 825, 811, 801, 774
Conclusions & Limitations - PARTNER II Cohort A

CONCLUSIONS
• The PARTNER II A study shows the non-inferiority of the TAVI procedure with a second-generation prosthesis as compared to surgical valve replacement.
• This cohort demonstrates for the first time that transfemoral TAVI is to be actually superior to surgical AVR.

...but
• Not really intermediate risk patients!
• "...patients are still among the high risk quintile of AS who are candidates for surgery in the US and elsewhere"...
• 26% had previous CABG (redo!), 14% sAVR had concomitant CABG
• 9% sAVR had other concomitant procedures (aortic endarterectomy, aortic root replacement, MVR or tricuspid.

Leon et al. NEJM 2016. 374:1609-1620
PARTNER II S3i - Intermediate risk

Intermediate Risk Symptomatic Severe Aortic Stenosis

Intermediate Risk ASSESSMENT by Heart Valve Team

PII S3i
n=1,077

ASSESSMENT:
Optimal Valve Delivery Access

Transfemoral (TF)

TF TAVR SAPIEN 3

Transapical / TransAortic (TA/TAo)

TA/TAo TAVR SAPIEN 3

PIIIA
n=2,032

ASSESSMENT:
Transfemoral Access

Yes

Transfemoral (TF)

1:1 Randomization

TF TAVR SAPIEN XT VS Surgical AVR

No

Transapical / TransAortic (TA/TAo)

1:1 Randomization

TA/TAo TAVR SAPIEN 3 VS Surgical AVR
PARTNER II S3i - Intermediate risk

Methods
1,077 patients with severe symptomatic AS and intermediate surgical risk from 51 US sites were included.

Criteria for inclusion
• Severe AS 
  (aortic valve area <0.8 cm or aortic valve index <0.5 cm²/m² and aortic valve gradient >40 mmHg or peak velocity >4.0 m/s)
• Intermediate surgical risk (STS score 4-8 or decision by a heart team)

Patient characteristics
The patients received either transfemoral TAVI (89 %), transapical TAVI (7 %) or transaortic TAVI (0.4 %).
• Mean age: 81.9 years
• Mean STS score: 5.2 %
• NYHA class III/IV: 72.6 %

Primary endpoints
• Mortality and stroke rate at 30 days
• Combined endpoint of overall survival, stroke rate and severe/moderate paravalvular regurgitation at one year (Non-inferiority in the propensity score analysis)
PARTNER II S3i - Intermediate risk

All-Cause Mortality and All Stroke (AT)
Unadjusted Time-to-Event Analysis

- PIIA Surgery
- SAPIEN 3 TAVR

Numbers at risk:
- PIIA Surgery: 944, 805, 786, 757, 743
- S3 TAVR: 1,077, 1,012, 987, 962, 930
CONCLUSIONS

• In patients with severe AS and intermediate risk, TAVI with the SAPIEN 3 achieves very good 30-day results with low mortality and stroke rates.
• At one year, TAVI proves to be superior to sAVR in this cohort as shown by propensity score analysis regarding the combined endpoint of mortality, stroke rate and paravalvular regurgitation\(^1,2\).

Kodali S et al. EHJ 2016;pii: ehw112. [Epub ahead of print].
Thourani et al. Lancet 2016;387;2218-2225.
Limitations of PARTNER II S3i Trial

...but – first issue on adjustment!

- Big selection bias of this observational study
- Propensity has to be adjusted at least for MR and LVEF
Limitations of PARTNER II S3i Trial

...but – **second issue on adjustment**!

- No data on concomitant procedures (9.1% in sAVR group)
- No adjustment for concomitant procedures (14.5% sAVR+CABG)
- No data on the number of concomitant procedures

### STS score

<table>
<thead>
<tr>
<th>Procedure: AV Replacement</th>
<th>Risk of Mortality: 0.945%</th>
</tr>
</thead>
</table>

| Procedure: AV Replacement + CAB | Risk of Mortality: 1.347% |

### EuroSCORE

<table>
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<tr>
<th>Operation related factors</th>
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<tbody>
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<td>Urgency 11</td>
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Different Algorithms

Same algorithm, different weights
...but – *third issue on adjustment!*

- Kaplan-Meier survival is non-parametric
- For proper adjustment a propensity score matching, stratification and weighting with regression modeling is necessary

- This appears to be a countersense and these curves are NOT interpretable, as they are simply a first-step evaluation before adjustment.
- Stating the “improtant differences between TAVR and surgery for each endpoint are observed” is inappropriate until data are confirmed by adjusted results.
Quality Criteria for Performing TAVI in Germany

TF-TAVI as 1st choice in all pts (Class-I) with:
- STS ≥4% or
- logES ≥10% or
- age >85y

TA-TAVI as 2nd choice in all pts (Class-I) with:
- STS ≥4% or
- logES ≥10% or
- age >85y

sAVR is only recommended in:
- low risk patients (Class-IIb)
- as 3rd choice in intermediate risk
  (STS >=4% or logES >= 10%)
- only in reasoned cases of high risk
  (STS >8% oder logES >20%)
- only in reasoned cases >85y
Is TAVI Legitimate in Lower risk Patients?

- Predictable procedure (more than PCI)
- Superior hemodynamics (small aortic roots)
- Reduced complications impacting survival: AKI, vascular complications, life-threatening bleeding, disabling stroke
- Reduced atrial fibrillation post-procedure
- Survival benefits (in surgical intermediate-risks)
- Long-term durability?

- Higher rate of AV block ➛ PPI, LBBB
- Higher rate of PVL: endocarditis?
- Bicuspid valves?

NO
Long-term THV Durability?

Ferrari 250 GTO 1962; sold in 2014 for 38 Mio US$
Progression of Mean Gradients 4 years after TAVI; n=1521

Progression of Transvalvular Mean Gradients Following TAVR

- Absence of Anticoagulation Therapy at Discharge
- Valve-in-Valve Procedure (TAVR in a Surgical Valve)
- ≤23 mm Transcatheter Heart Valve
- Greater Body Mass Index

Del Trigo et al. JACC 2016;67:644-55
Long-term Durability of TAVI Valves?

First look at long-term durability of transcatheter heart valves: Assessment of valve function up to 10-years after implantation

Danny Dvir, St. Paul’s Hospital, Vancouver, Canada.

On behalf of coauthors: Helene Eltchaninoff, Jian Ye, Arohumam Kan, Eric Durand, Anna Bizios, Anson Cheung, Mina Aziz, Matheus Simonato, Christophe Tron, Yaron Arbel, Robert Moss, Jonathon Leipsic, Hadas Ofek, Gidon Perlman, Marco Barbanti, Michael A. Seidman, Philippe Blanke, Robert Yao, Robert Boone, Sandra Lauck, Sam Lichtenstein, David Wood, Alain Cribier, John Webb
Long-term Durability of TAVI Valves?

Vancouver TAVI Cases Before May 2011 (n = 462)  
Rouen TAVI Cases Before May 2011 (n = 242)  

Total TAVI cases Before May 2011 (n = 704)  

Failed at Baseline (n = 178)  
VIV/Non-Aortic Position (n = 28)  

Mortality < 30 days (n = 35)  
Non-Edwards Valves (n = 16)  
Insufficient Follow-up (n = 69)  

Study patients (n = 378)
Freedom from THV Degeneration (n=378)

THV degeneration was defined as at least moderate regurgitation AND/OR mean gradient ≥ 20mmHg, which did not appear within 30 days of the procedure and is not related to endocarditis.
Freedom from THV Degeneration (n=378)

Baseline renal failure (GFR<60cc/min) was the strongest correlate for THV degeneration:
HR=3.22, CI 1.45-7.15, p=0.004
Conclusions

- Dramatic continued growth in TAVI worldwide!
- Currently major indication is high-risk or inoperable AS
- TAVI indication is and will be expanded (intermediate/lower risk)
- Current RCTs for intermediate/low-risk pts are biased & most initiated/funded by industry
- Physician-initiated RCTs are necessary – isolated TAVI vs. sAVR
- The TAVI ‘heart-team’ plays a key role in clinical practice
Conclusions II

- TAVI can be performed with high procedural success rates
- There is a (substantial) institutional learning curve
- There are valve-specific complications & limitations
- Long-term durability data are still rare
- *Will CV surgeons play a key role in TAVI?*