Διαδερμική αντικατάσταση αορτικής βαλβίδας (TAVI)

Διαταραχές αγωγής. Ενδείξεις μόνιμης βηματοδότησης

ΕΜΜ. Ν. ΣΗΜΑΝΤΗΡΑΚΗΣ
ΚΑΘΗΓΗΤΗΣ ΚΑΡΔΙΟΛΟΓΙΑΣ
Disclosures

None
Conduction Disturbances after TAVR

- New *LBBB* occurs in 19% to 55% of patients
- New *high-degree atrioventricular block* in approximately 10% of patients
- New *RBBB* in 2% and *LAHB* in 2%
- Up to half of new bundle branch block and complete heart block can be expected to *resolve before discharge*
- The likelihood of new conduction disturbances depends on *patient and procedural factors*
- *Rate of PPI* after TAVR is ≈17% (range 18%–49%) after self-expanding CoreValve implantation and ≈6% (0%–12%) after balloon-expandable Edwards valve implantation
AV Conduction Failure after TAVR

Macroscopic and Histological View of the Conduction System, JACC. Cardiovascular Interventions. DOI: 0.1016/j.jcin.2012.03.004.
Mechanisms of TAVR-induced LBBB

1. Encroachment of conduction system by the prosthesis itself. (Permanent Block!)

2. Mechanical disruption by calcium displacement during valve deployment. (Permanent Block!)

3. Tissue edema and reaction to ischemia, inflammation related to TAVI. (maybe Temporary Block!)

**NOP-LBBB incidence:**

Self-expandable (MD CV) > 40%
Balloon valve (ES) > 10%

*Preservation of the aortic leaflets, often calcified...*
2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>I) High degree or complete AV block after cardiac surgery and TAVI. A period of clinical observation up to 7 days is indicated in order to assess whether the rhythm disturbance is transient and resolves. However, in case of complete AV block with low rate of escape rhythm this observation period can be shortened since resolution is unlikely.</td>
<td>I</td>
<td>C</td>
</tr>
</tbody>
</table>

## New-Onset LBBB and Mortality

### All cause mortality

<table>
<thead>
<tr>
<th>Study name</th>
<th>Hazard ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-Value</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nazif 2014</td>
<td>0.900</td>
<td>0.559</td>
<td>1.448</td>
<td>-0.434</td>
<td>0.664</td>
</tr>
<tr>
<td>Carrabba 2015</td>
<td>0.975</td>
<td>0.308</td>
<td>3.088</td>
<td>-0.043</td>
<td>0.966</td>
</tr>
<tr>
<td>Houthuzien 2014</td>
<td>1.490</td>
<td>1.097</td>
<td>2.024</td>
<td>2.551</td>
<td>0.011</td>
</tr>
<tr>
<td>Urena 2014</td>
<td>0.928</td>
<td>0.732</td>
<td>1.176</td>
<td>-0.618</td>
<td>0.537</td>
</tr>
<tr>
<td>Schymik 2015</td>
<td>1.835</td>
<td>1.172</td>
<td>2.874</td>
<td>2.653</td>
<td>0.008</td>
</tr>
<tr>
<td>Franzoni 2015</td>
<td>1.442</td>
<td>0.592</td>
<td>3.512</td>
<td>0.806</td>
<td>0.420</td>
</tr>
<tr>
<td>Testa 2013</td>
<td>0.880</td>
<td>0.691</td>
<td>1.121</td>
<td>-1.034</td>
<td>0.301</td>
</tr>
</tbody>
</table>

### Meta Analysis

LBBB post TAVR: A predictor of SCD

Late Cardiac Death in Patients Undergoing Transcatheter Aortic Valve Replacement
Incidence and Predictors of Advanced Heart Failure and Sudden Cardiac Death

✓ **3.729** patients who underwent TAVR (balloon 57% / self-expanding 43%)
✓ F-up 22 ± 18 months

✓ Endpoint: **SCD**

✓ 3 groups: NO NOP-LBBB, NOP-LBBB (12.6%), NOP-LBBB + PMK (2.5%)

→ New-onset persistent LBBB following TAVR (**RR of SCD x2.5**)
→ New-onset persistent LBBB and a QRS duration **>160 ms** (**RR of SCD x5!!!**)
→ New-onset persistent LBBB + PMK (during hospitalization) (RR=1 !!!)

Marina Urena et al. JACC 2015
LBBB post TAVR: A predictor of SCD

Late Cardiac Death in Patients Undergoing Transcatheter Aortic Valve Replacement (TAVR)

Incidence and Predictors of Advanced Heart Failure and Sudden Cardiac Death

<table>
<thead>
<tr>
<th>NOP-LBBB:</th>
<th>471</th>
<th>352</th>
<th>284</th>
<th>229</th>
<th>195</th>
</tr>
</thead>
<tbody>
<tr>
<td>No NOP-LBBB:</td>
<td>3,068</td>
<td>2,086</td>
<td>1,679</td>
<td>1,327</td>
<td>1,043</td>
</tr>
</tbody>
</table>

C

Log rank: <0.001

<table>
<thead>
<tr>
<th>QRS duration &gt;160 msec:</th>
<th>48</th>
<th>31</th>
<th>24</th>
<th>19</th>
<th>16</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRS duration ≤160 msec:</td>
<td>330</td>
<td>262</td>
<td>212</td>
<td>174</td>
<td>146</td>
</tr>
</tbody>
</table>

Patients at risk:

<table>
<thead>
<tr>
<th>0</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both:</td>
<td>56</td>
<td>31</td>
<td>23</td>
<td>18</td>
</tr>
<tr>
<td>LVEF ≤40%:</td>
<td>603</td>
<td>388</td>
<td>308</td>
<td>231</td>
</tr>
<tr>
<td>NOP-LBBB:</td>
<td>415</td>
<td>321</td>
<td>261</td>
<td>211</td>
</tr>
<tr>
<td>None:</td>
<td>2,465</td>
<td>1,697</td>
<td>1,371</td>
<td>1,051</td>
</tr>
</tbody>
</table>

Log rank: 0.010

TABLE 6: Electrocardiographic Predictors of Sudden Cardiac Death in Patients With New-Onset Persistent Left Bundle-Branch Block Following TAVR (n=471)

<table>
<thead>
<tr>
<th>Univariate HR (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1.01 (0.98-1.04)</td>
</tr>
<tr>
<td>PR &gt;200 ms</td>
<td>—</td>
</tr>
<tr>
<td>Discharge</td>
<td></td>
</tr>
<tr>
<td>QRS duration</td>
<td>1.02 (0.99-1.05)</td>
</tr>
<tr>
<td>QRS &gt;160 ms</td>
<td>4.78 (1.56-14.63)</td>
</tr>
<tr>
<td>PR &gt;200 ms</td>
<td>0.26 (0.03-2.20)</td>
</tr>
</tbody>
</table>
LBBB post TAVR

A 1-year RR of permanent pacemaker implantation

Risk to receive a PMK within $1^{st}$-y: 200%

B 1-year RR of cardiac death

Risk of cardiac Death within $1^{st}$-y: 150%

C 1-year RR of all-cause death

Risk of all cause death within $1^{st}$-y: 130%
If you implant Pmk for LBBB post TAVI

Risk of Cardiac death within 1st-y: -30%!

Risk of all cause death within 1st-y: NS
### Pacemaker implantation and Mortality

#### 1-year RR of all-cause death

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>PPI following TAVR</th>
<th>No PPI following TAVR</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Houthuizen, et al. 2012</td>
<td>20 events, 118 total</td>
<td>140 events, 679 total</td>
<td>0.82 [0.54, 1.26]</td>
</tr>
<tr>
<td>D’Ancona, et al. 2011</td>
<td>3 events, 20 total</td>
<td>51 events, 302 total</td>
<td>0.89 [0.30, 2.60]</td>
</tr>
<tr>
<td>Urena, et al. 2014</td>
<td>46 events, 239 total</td>
<td>272 events, 1317 total</td>
<td>0.93 [0.70, 1.23]</td>
</tr>
<tr>
<td>Mouillet, et al. 2015</td>
<td>41 events, 252 total</td>
<td>98 events, 581 total</td>
<td>0.96 [0.69, 1.35]</td>
</tr>
<tr>
<td>Biner, et al. 2014</td>
<td>6 events, 58 total</td>
<td>18 events, 172 total</td>
<td>0.99 [0.41, 2.37]</td>
</tr>
<tr>
<td>De Carlo, et al. 2012</td>
<td>6 events, 44 total</td>
<td>16 events, 125 total</td>
<td>1.07 [0.44, 2.55]</td>
</tr>
<tr>
<td>Pereira, et al. 2013</td>
<td>5 events, 19 total</td>
<td>9 events, 37 total</td>
<td>1.08 [0.42, 2.78]</td>
</tr>
<tr>
<td>Buellesfield, et al. 2012</td>
<td>19 events, 98 total</td>
<td>37 events, 207 total</td>
<td>1.08 [0.66, 1.79]</td>
</tr>
<tr>
<td>Kawaguchi, et al. 2015</td>
<td>10 events, 28 total</td>
<td>40 events, 132 total</td>
<td>1.18 [0.67, 2.06]</td>
</tr>
<tr>
<td>Nazif, et al. 2015</td>
<td>45 events, 173 total</td>
<td>374 events, 1800 total</td>
<td>1.25 [0.96, 1.64]</td>
</tr>
<tr>
<td>Schymik, et al. 2015</td>
<td>13 events, 69 total</td>
<td>85 events, 565 total</td>
<td>1.25 [0.74, 2.12]</td>
</tr>
</tbody>
</table>

Total (95% CI) 1118 events, 5917 total

Total events 214 events, 1140 total

Heterogeneity: $\chi^2 = 4.64$, df = 10 (P = 0.91); $I^2 = 0\%$

Test for overall effect: $Z = 0.46$ (P = 0.64)

Regueiro et al., Circ Cardiovasc Interv. 2016;9:e003635
PPI post TAVI: Clinical impact

The PARTNER (Placement of AoRtic Transcatheter Valves) Trial and Registry

1973 patients who underwent TAVR (balloon valve only)
Rate of PPMI = 8.8%

- NOP-LBBB had higher risk of PPI
- PPI ~ was NOT associated with a higher risk of death
- PPI ~ repeated risk of all cause death + re-hospitalization

Evolution of LVEF

Tamim Nazif et al. JACC Cardiovascular Intervention 2015
Dizon JM et al. Heart 2015
Complications after PM implantation

FOLLOWPACE Study

N=1’517
FU 5.8 years

Age an independent predictor of complications, both within 2 months and during FU.
Monitoring: How long???

Time to Permanent Pacemaker Implantation

Peak PR
Peak QRS

Self-expanding Balloon - expanded

Recovery of AVB: 50%

Post-Procedure Day

Percent

Tamim Nazif et al. JACC Cardiovascular intervention 2015

Monitoring duration: based on ECG

- 1,064 pts undergoing TAVR in 3 Switzerland centers
- Electrocardiograms (ECGs) at baseline and post-TAVR were analyzed
- MDT CV (45%) - E SAPIEN (55%)

Incidence of PPI after TAVI

Proportion of delayed PPI according to PRE-operative ECG

Toggweiler S. The Electrocardiogram After Transcatheter Aortic Valve Replacement Determines the Risk for Post-Procedural High-Degree AV Block and the Need for Telemetry Monitoring. JACC interv 2016
Predictors of AVB after TAVI: ECG

→ No WQRS or prolonged PR: no risk of AVB!
→ Other pts: At risk for delayed high-degree AVB. RBBB (risk 20%-35%), LBBB (risk 7%-16%).
→ LBBB should be monitored until stable ECG for >48h.
→ “Very long PR (???) and RBBB should be implanted temporarily or definitely”.

Toggweiler S. The Electrocardiogram After Transcatheter Aortic Valve Replacement Determines the Risk for Post-Procedural High-Degree AV Block and the Need for Telemetry Monitoring. JACC interv 2016
## Role of EPS

<table>
<thead>
<tr>
<th>STUDY</th>
<th>Methods - Pts</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rubin</td>
<td>HV monitoring during TAVR 18 pts MDT CV</td>
<td>Observational 1 late AVB (HV 76ms)</td>
</tr>
<tr>
<td>Akin</td>
<td>HV (day +7), PPI (HV &gt;75ms) 45 pts MDT CV</td>
<td>LBBB was predictive of delayed AVB (HV&lt;75ms) - HV values not predictive</td>
</tr>
<tr>
<td>Eksik</td>
<td>EP study immediate pre- and post-TAVR 18 pts ES</td>
<td>HV prolonged &gt; 70ms in only 4 pts. 1 late AVB after 6m</td>
</tr>
<tr>
<td>J. Invasive Cardiol. 2013</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lopez-Aguilera</td>
<td>EP study immediate pre- and post-TAVR 137 pts MDT CV</td>
<td>HV not predictive of late AVB</td>
</tr>
<tr>
<td>Kostopoulou</td>
<td>EP study 30 pts MDT CV</td>
<td>Pre-operative HV &gt; 52ms predict AVB during TVAR</td>
</tr>
<tr>
<td>Europace 2016</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Predictors of AVB after TAVI: EPS?

- **84** patients (33% CV and **67% ES**).
- **Serial HV intervals** measured 15 ' before and after TAVR and lately (D +2 ES/ D +5 CV)
- → **NOP-LBBB**: 20%
- → **Late AVB**: 12%

- The presence of post-operative AVB (persistent or transient) was the only predictive factor for the presence of high degree AVB in multivariate analysis (OR 139.2; [14.89–1301.28])

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Predictors of AVB after TAVI: EPS?

✓ 75 pts (86% CV and 14% ES) were studied before and 4-5 days post TVAR

✓ → NOP-LBBB: 27%
✓ → Late AVB: 13% (all MDT CV)

✓ Delta-HV interval of ≥13 ms predicted AV block (100.0% sens. / 84.4% spec.)

✓ In NOP-LBBB, HV interval of ≥65 ms predicted AV block (83.3% sens. and 81.6% spec). Hazard ratio 1.073 per ms (95% confidence interval 1.029–1.119; P = .001) for AV block and all cause mortality.
Predictors of AVB after TAVI?

Pre-procedure:

- Gender (male)
- Pre-existing long PR
- Pre-existing WQRS
  - RBBB (RR x7!!!)
  - LAD
- Cusp Ca$^{2+}$ volume
  - LCC > 14mm$^3$
  - RCC > 5mm$^3$
  - Mitral annulus
- Narrow LVOT

Per-procedure:

- Valve type
  - MDT CV: 25%
  - MDT CV Evolutr: 16%
  - MDT CV Evolut pro: 10%
  - E. Sapiens 3: 12.5%
  - E Sapiens XT: 12.6%
  - Lotus: 26.6%
  - Lotus EXT: 16%
  - Lotus Edge: 9.5%
- Oversizing...
  (LVOT/prosthesis size)
- Implantation depth
- Transient AVB

Post-procedure:

- Persistent LBBB (>160ms)
- HV interval (> ???)

Siontis G. JACC 2014
Van der Boon R. Catheter Cardiovasc interv. 2015
Nazif T. JACC 2015
Boerlage-Van Dijk K. PACE 2014
Bax J. European Heart j
...
Conclusions

*High-degree atrioventricular block* is most commonly observed in the immediate periprocedural period but will persist beyond 48 hours in 2% to 20% of patients.

Specific *timing of pacemaker implant* has not been formally studied and will always depend on the individual clinical situation.

Patients with *new bundle branch block* after TAVR may be at risk for syncope and development of atrioventricular block.

*LBBB* post TVAR are at risk of progressing to AVB.

Due to its pathophysiological mechanism, the progression to AVB is very *difficult to predict* and can occur very lately after TVAR.
2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients With Bradycardia and Cardiac Conduction Delay

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>B-NR</td>
<td>1. In patients who have new atrioventricular block after transcatheter aortic valve replacement associated with symptoms or hemodynamic instability that does not resolve, permanent pacing is recommended before discharge (S8.1.2.4-1–S8.1.2.4-4).</td>
</tr>
<tr>
<td>IIA</td>
<td>B-NR</td>
<td>2. In patients with new persistent bundle branch block after transcatheter aortic valve replacement, careful surveillance for bradycardia is reasonable (S8.1.2.4-5, S8.1.2.4-6).</td>
</tr>
<tr>
<td>IIb</td>
<td>B-NR</td>
<td>3. In patients with new persistent LBBB after transcatheter aortic valve replacement, implantation of a PPM may be considered (S8.1.2.4-4, S8.1.2.4-7–S8.1.2.4-10).</td>
</tr>
</tbody>
</table>

Referenced studies that support recommendations are summarized in Online Data Supplement 49.
