CORONARY ARTERY DISEASE AND TAVI:
PCI BEFORE, DURING OR NEVER

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POTENTIAL CONFLICTS OF INTEREST

Speaker’s name:  **PETER WENAWESER, MD**

- I have the following potential conflicts of interest to report:
  - Research contracts
  - Lecture and procotring fees from Medtronic, Edwards Lifesciences, Boston Scientific
  - Employment in industry
  - Stockholder of a healthcare company
  - Owner of a healthcare company
  - Other(s)
Case 1 Presentation

- 88 yr old male
  - NYHA III
- Severe low-flow, low-gradient AS
  - AVA 0.74 cm²
  - Mean gradient 24 mmHg
  - LVEF 35%
- Risk Scores
  - EuroSCORE II: 39.59%
  - Logistic EuroSCORE: 64.49%
  - STS Score: 13.18%

- Medical history
  - Previous CABG 1998
    - LIMA – LAD
    - Vein - LCX
  - Type 2 DM
    - Insulin dependent
  - Permanent atrial fibrillation
    - OAC
  - Permanent Pacemaker for AVIII block
  - Previous stroke
  - Frail (MMSE 19/27)
CORONARY ANGIOGRAM

LAD

LIMA - LAD
CORONARY ANGIOGRAM

Vein - LCX

RCA
CASE 1 PRESENTATION

What would you do?

– TAVI
– TAVI plus PCI in one procedure
– TAVI plus staged PCI
– PCI plus staged TAVI
– Medical treatment
CASE 2 PRESENTATION

• 82 y/o female
  – NYHA IV, ACS

• Severe low-flow, low-gradient AS
  – AVA 0.7 cm$^2$
  – Mean gradient 31 mmHg
  – LVEF 40%

• Risk Scores
  – Logistic EuroSCORE: 33.7
  – Standard ES: 13

• Medical history
  – NSTEMI and STEMI ant. 2013/14
  – 3V CAD:
    • LM 90%, prox. LAD 90%, mid LAD 50%
    • RCA 75%
  – Chron. kidney disease (eGFR43)
  – Hypothyreosis
  – Infrarenal aortic aneurysm
    • Operation 5 years ago
TAVI and CAD
MECHANISMS OF DISEASE
CORONARY ARTERY DISEASE


LDL INFILTRATION
MACROPHAGE ACTIVATION
INFLAMMATION
END-STAGE DISEASE
MECHANISMS OF DISEASE
AORTIC STENOSIS


Initiating factors:
- Bicuspid valve
- Genetic factors
- Shear stress

Early Lesion
- T cell
- LDL
- Monocyte
- Oxidized LDL
- Macrophage
- Ang II

Disease Progression:
- Age and sex
- Increased serum lipids
- Increased blood pressure
- Diabetes and metabolic syndrome
- Smoking

End-Stage Disease
- Wnt3, Lrp5, and β-catenin
- Calcification
  - Increased alkaline phosphatase
  - Increased BMP-2
  - Increased osteocalcin

Phenotypic transformation
- Fibroblast
- Osteoblast
- Osteopontin

LDL Infiltration
- Macrophage Activation
- Inflammation
- End-Stage Disease
GENOMEWIDE ASSOCIATION OF CORONARY ARTERY DISEASE & AORTIC VALVE CALCIFICATION

CORONARY ARTERY DISEASE

SNP rs1333049 ON CHROMOSOME 9

OR 2.05 (1.63-2.57) FOR AORTIC VALVE CALCIFICATION

SNP rs10455872 ON CHROMOSOME 6

CORONARY ARTERY DISEASE

SAMANI NJ ET AL N ENGL J MED 2007;357:443-53

N=1,926 PATIENTS WITH CAD
N=2,938 CONTROL PATIENTS

AORTIC VALVE CALCIFICATION

THANASSOULIS G ET AL N ENGL J MED 2013;368:503-12

N=6,942 PATIENTS WITH AORTIC VALVE CALCIFICATION
Risk Factors

- Age
- Family History
- Diabetes
- Gender
- Smoking
- Hypertension
- Hypercholesterolemia

Coronary Artery Disease
PREVALENCE OF VALVULAR HEART DISEASE BY AGE

AORTIC STENOSIS AND AGE

OR 2.51, 95%-CI 2.02–3.12
PER 10YR INCREASE

MORE PREVALENT IN MEN
OR 1.52, 95%CI 1.02–2.26

NKOMO VT ET AL LANCET 2006;386:1005-11
CORONARY ARTERY DISEASE-RISK CONTINUUM

Aortic Stenosis - Risk Continuum

- **Normal**
- **Aortic sclerosis**
- **Mild-to-moderate aortic stenosis**
- **Severe aortic stenosis**

**Non-Invasive Tests:**
- Echocardiography
- Tread-Mill Test

**Invasive Tests:**
- Cardiac Catheterization

- **Echocardiography**
  - Diastolic Dysfunction
  - LV Hypertrophy

**Relative Mortality (%)**

- **Clinically silent**
- **Clinically apparent**

**Questions:**
- Acute Aortic Syndrome?
- Global Myocardial Ischemia
- Sudden Cardiac Death
CAD & TAVI: PREVALENCE - 2

% 60 – 50 – 40 – 30 – 20 – 10 – 0 –

CAD & TAVI: PREVALENCE - 3

% with CAD at Baseline

- CoreValve US Pivotal Trial ER (n=489): 81.8%
- CoreValve US Pivotal Trial HR TAVR: 75.4%
- PARTNER A TAVR (n=348): 74.9%
- PARTNER B TAVR (n=179): 67.6%
- PARTNER Sapien (n=276): 67.4%
- PARTNER Sapien XT (n=284): 65.5%
- ADVANCE (n=1015): 57.6%
- Italian Registry (n=663): 48.3%
- FRANCE 2 (n=3195): 47.9%
- UK Registry (n=870): 47.6%
- SOURCE XT (n=2688): 44.3%
**IMPACT OF CAD ON TAVI 30-DAY MORTALITY**

<table>
<thead>
<tr>
<th>Study</th>
<th>CAD</th>
<th>No CAD</th>
</tr>
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<tbody>
<tr>
<td>Dewey et al</td>
<td>13.1</td>
<td>1.2</td>
</tr>
<tr>
<td>Masson et al</td>
<td>11.5</td>
<td>6.3</td>
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<tr>
<td>Gautier et al</td>
<td>10</td>
<td>3.8</td>
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<tr>
<td>Khawaja et al</td>
<td>16.7</td>
<td>7</td>
</tr>
<tr>
<td>Stefanini et al</td>
<td>7</td>
<td>5.1</td>
</tr>
<tr>
<td>Ussia et al</td>
<td>6</td>
<td>5.9</td>
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</tbody>
</table>

*p=0.009, p=ns, p=0.005*
**IMPACT OF CAD ON TAVI**

**1-YEAR MORTALITY**

<table>
<thead>
<tr>
<th>Study</th>
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<tbody>
<tr>
<td>Dewey et al</td>
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<tr>
<td>Ussia et al</td>
<td>14.5</td>
<td>15.9</td>
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</tbody>
</table>

*p* = 0.006

** ns**
Prognostic Value of Coronary Artery Disease Among Patients Undergoing TAVI

N=2,472
Prevalence of CAD 52% (42-65)

Median follow-up 452 days (357-585)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Weight</th>
<th>IV, Random, 95% CI</th>
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</thead>
<tbody>
<tr>
<td>Dewey, 10</td>
<td>1.3</td>
<td>2.8</td>
<td>0.5%</td>
<td>3.67 [0.02, 887.05]</td>
</tr>
<tr>
<td>Gasparetto, 11</td>
<td>0.08</td>
<td>0.79</td>
<td>6.8%</td>
<td>1.08 [0.23, 5.10]</td>
</tr>
<tr>
<td>Moat, 11</td>
<td>0.09</td>
<td>0.37</td>
<td>31.0%</td>
<td>1.09 [0.53, 2.26]</td>
</tr>
<tr>
<td>Presbitero, 12</td>
<td>0.08</td>
<td>0.88</td>
<td>5.5%</td>
<td>1.08 [0.19, 6.08]</td>
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<tr>
<td>Schnabel, 12</td>
<td>-0.02</td>
<td>0.53</td>
<td>15.1%</td>
<td>0.98 [0.35, 2.77]</td>
</tr>
<tr>
<td>Torino, 12</td>
<td>0.08</td>
<td>0.97</td>
<td>4.5%</td>
<td>1.08 [0.16, 7.25]</td>
</tr>
<tr>
<td>Ussia, 12</td>
<td>-0.11</td>
<td>0.34</td>
<td>36.7%</td>
<td>0.90 [0.46, 1.74]</td>
</tr>
</tbody>
</table>

Total (95% CI) 100.0% 1.00 [0.67, 1.50]

Heterogeneity: Tau²= 0.00; Chi²= 0.41, df = 6 (P = 1.00); I²= 0%
Test for overall effect: Z = 0.02 (P = 0.98)

D'Ascenzo F et al Int J Cardiol 2013;168:2528-2532
### Management of Coronary Artery Disease in Patients with Valvular Heart Disease

Vahanian et al. ESC Guidelines on Valvular Heart Disease 2012

<table>
<thead>
<tr>
<th></th>
<th>Class</th>
<th>Level</th>
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</table>
| Coronary angiography is recommended before valve surgery in patients with severe valvular heart disease and any of the following:  
- history of coronary artery disease  
- suspected myocardial ischaemia  
- left ventricular systolic dysfunction  
- in men aged over 40 years and postmenopausal women  
- ≥1 cardiovascular risk factor. | I | C |
| Coronary angiography is recommended in the evaluation of secondary mitral regurgitation. | I | C |
| CABG is recommended in patients with a primary indication for aortic/mitral valve surgery and coronary artery diameter stenosis ≥70%. | I | C |
| CABG should be considered in patients with a primary indication for aortic/mitral valve surgery and coronary artery diameter stenosis 50–70%. | IIa | C |

**Prior to Valve Surgery**

**Preoperative coronary angiography**

**Concomitant Revascularization**

In case of significant coronary artery stenosis
TAVI, PCI AND IMPACT OF COMPLETE REVASCULARIZATION

Wenaweser P et al EuroIntervention 2011;7:541-548
**Primary endpoint:**
Cardiac death, stroke, MI

**N=445, MEAN AGE 82.5±5.8**

**BASELINE CORONARY ARTERY DISEASE SEVERITY**
BASELINE SYNTAX SCORE 16.5±12.5

**High SS vs. No CAD: HR 2.24 (95% CI 1.18-4.23)**

**Low SS vs. No CAD: HR 1.23 (95% CI 0.68-2.21)**

High rSS tertile (> 14) was associated with higher rates of the primary endpoint at 1 year (no CAD:12.5%, low rSS: 16.5%, high rSS: 26.3%, P = 0.043).
## TIMING OF PCI

<table>
<thead>
<tr>
<th>PCI Prior to TAVI</th>
<th>PCI Combined with TAVI</th>
<th>PCI After TAVI</th>
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<tbody>
<tr>
<td>Pro</td>
<td>Pro</td>
<td>Pro</td>
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<tr>
<td>Con</td>
<td>Con</td>
<td>Con</td>
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</table>

- **PCI Prior to TAVI**
  - Simplified coronary access with no prosthetic valve in place
  - DAPT required after PCI may impact post-TAVI bleeding
- **PCI Combined with TAVI**
  - Decreases the risk of mortality while waiting for TAVR
  - Increased dye load (contrast nephropathy), longer procedure time
- **PCI After TAVI**
  - Treating severe AS first may improve myocardial perfusion, decreasing need for PCI
  - Potential access issues, valve struts interfering with coronary cannulation

- **Less risk of hemodynamic instability and ischemia during TAVI**
- **Risks of performing PCI in the presence of severe AS**
- **Reduction of vascular complications by needing one access site**
- **Catheter manipulation could move the valve**

- **Minimize contrast load by giving it at 2 separate times**
- **Less risk of hemodynamic instability and ischemia during TAVI**
- **Higher risk of hemodynamic instability and ischemia during TAVI**
Treatment Algorithm for Elective Cases

Patients with severe AS+CAD

Heart team evaluation

TAVI

Obstructive CAD*

Yes

Complex multivessel CAD (SYNTAX Score >22)

Yes

Staged PCI

TAVI

No

Severe renal impairment†

No

**Concomitant PCI + TAVI

SAVR

Obstructive CAD*

Yes

SAVR + CABG

SAVR + hybrid PCI

No

Isolated TAVI

Isolated SAVR

2014 ESC/EACTS Guidelines:

SAVR + CABG

>70% coronary artery diameter stenosis in a major epicardial vessel (Class I, level of evidence C)

50-70% coronary artery diameter stenosis in a major epicardial vessel (Class IIa, level of evidence C)

TAVI + PCI

>70% coronary diameter stenosis in proximal segments (Class IIa, level of evidence C)

†Severe renal impairment = eGFR <30 mL/min/1.73m²
Management of patients with CAD and TAVI: Risk-based Algorithm

CAD

- ACS
- Left main
- Ischemia > 10%
- Single vessel
- Severe 0.7-1 cm²
- Critical < 0.5 cm²

AS

- CAD
- AS
- Two staged procedure
  1. PCI
  2. TAVR

- CAD
- AS
- One staged procedure
  Consider circulatory support
  1. PCI
  2. BAV

- AS
- CAD
- Two staged procedure
  1. TAVR
  2. Re-evaluation CAD

Nickenig et al 2015
CASE 1 PRESENTATION

What would you do?

- TAVI
- TAVI plus PCI in one procedure
- TAVI plus staged PCI
- PCI followed by TAVI staged
- Medical treatment
Case 2: TAVI and PCI Left Main in one Procedure
CONCLUSIONS

• CAD is frequently associated with aortic stenosis in patients undergoing TAVI
• CAD and AS share similar pathophysiology
• Presence of CAD per se does not appear to lead to adverse clinical outcomes following TAVI
• Rather, severity of CAD appears to be more important
• More data required on impact of complete vs incomplete revascularization on clinical outcomes after TAVI
• Concomitant PCI of proximal lesions is feasible and should be considered after careful risk evaluation
CORONARY ARTERY DISEASE AND TAVI: PCI BEFORE, DURING OR NEVER

THANK YOU

peter.wenaweser@bluewin.ch
<table>
<thead>
<tr>
<th>Time</th>
<th>Session Title</th>
<th>Organizer/Presenter</th>
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<tbody>
<tr>
<td>16:45 - 18:15</td>
<td>Workshop 3</td>
<td>Panoramasaal</td>
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<td>Open issues related to TAVI</td>
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<td>Vorsitz/Modération: Ch. Huber (Bern, CH); F. Nietlispach (Zürich, CH)</td>
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<td>TAVI plus severe mitral insufficiency: How to address multiple valvular problems?</td>
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<td>F. Maisano (Zürich, CH)</td>
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<td>Utility vs futility: Any benefit of TAVI in severe LV dysfunction or severe COPD?</td>
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<td>D. Tüller (Zürich, CH)</td>
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<td>TAVI for bicuspid aortic stenosis and aortic regurgitations</td>
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<td>R. Jeger (Basel, CH)</td>
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<td>TAVI plus CAD: PCI before, during or never?</td>
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<td>P. Wenaweser (Bern, CH)</td>
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<td>TAVI and renal insufficiency: The scope of the problem</td>
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<td>E. Eeckhout (Lausanne, CH)</td>
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<td>Final discussion and wrap up</td>
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<td>M. Roffi (Genève, CH)</td>
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