The NOTION trial

Ten-year follow-up after transcatheter or surgical aortic valve implantation in severe aortic valve stenosis

Clinical outcomes and aortic bioprosthetic durability

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On behalf of the NOTION investigators

28/08/2023
Declaration of interest

- I have nothing to declare
Surgical risk

Extreme
High
Intermediate
Low

STS-score (%)

PARTNER 1B
CoreValve ER
PARTNER 1A
CoreValve HR
PARTNER 2
SURTAVI
NOTION
PARTNER 3
Evolut LR
Surgical risk

Extreme  High  Intermediate  Low

PARTNER 1B  CoreValve ER  PARTNER 1A  CoreValve HR  PARTNER 2  SURTAVI  NOTION  PARTNER 3  Evolut LR

STS-score (%)

Age (years)
<table>
<thead>
<tr>
<th><strong>Objective:</strong></th>
<th>To compare TAVI vs. SAVR in lower risk patients ≥70 years eligible for surgery (all-comers population)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome:</strong></td>
<td>Composite rate of all-cause mortality, stroke or myocardial infarction at 1 year (VARC II-defined)</td>
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<tr>
<td><strong>Design:</strong></td>
<td>Prospective, multi-centre, non-blinded, randomised</td>
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<tr>
<td><strong>Enrollment period:</strong></td>
<td>December 2009 - April 2013</td>
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</tbody>
</table>
| **Treatment:** | TAVI with self-expanding CoreValve  
SAVR with any bioprosthesis |
Flowchart

All Enrolled (N = 280)

Intention-to-treat TAVI (N = 145)
- Died prior to procedure (n = 3)
  - TAVI (N = 141)

As-treated TAVI (N = 142)
- Crossover TAVI to SAVR (n = 1)

As-implanted TAVI (N = 139)
- Crossover TAVI to SAVR (n = 3)

Crossover SAVR to TAVI (n = 1)

Intention-to-treat SAVR (N = 135)
- Died prior to procedure (n = 1)
  - SAVR (N = 133)

As-treated SAVR (N = 134)
- Not implanted (n = 2)
  - As-implanted SAVR (N = 135)
## Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>TAVI (N = 145)</th>
<th>SAVR (N = 135)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Years</td>
<td>79.2 (4.9)</td>
<td>79.0 (4.7)</td>
</tr>
<tr>
<td>Male</td>
<td>78 (53.8%)</td>
<td>71 (52.6%)</td>
</tr>
<tr>
<td>STS-score</td>
<td>2.9% (1.6)</td>
<td>3.1% (1.7)</td>
</tr>
<tr>
<td>STS-score &lt; 4%</td>
<td>121 (83.4)</td>
<td>108 (80.0)</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>26 (17.9%)</td>
<td>28 (20.7%)</td>
</tr>
<tr>
<td>Peripheral Vascular Disease</td>
<td>6 (4.1%)</td>
<td>9 (6.7%)</td>
</tr>
<tr>
<td>Pre-existing pacemaker</td>
<td>5 (3.4%)</td>
<td>6 (4.4%)</td>
</tr>
<tr>
<td>Prior Myocardial infarction</td>
<td>8 (5.5%)</td>
<td>6 (4.4%)</td>
</tr>
<tr>
<td>Known atrial fibrillation</td>
<td>40/144 (27.8%)</td>
<td>34/133 (25.6%)</td>
</tr>
<tr>
<td>NYHA III or IV</td>
<td>70 (48.6)</td>
<td>61 (45.5)</td>
</tr>
</tbody>
</table>

All p-values > 0.05
All-cause mortality

P = 0.84
HR 0.97; 95% CI: 0.72 - 1.30

TAVI vs SAVR:
- TAVI: 64.0%
- SAVR: 62.7%

Follow-up (Years):
- SAVR: 135, 123, 120, 112, 102, 95, 83, 75, 64, 56, 48
All-cause mortality, Stroke, Myocardial infarction

p = 0.93
HR 0.99; 95% CI: 0.74 - 1.32

Follow-up (Years)

0 1 2 3 4 5 6 7 8 9 10

All-cause mortality, Stroke or Myocardial Infarction (%)

TAVI 145 133 128 116 110 93 81 73 65 56 49
SAVR 135 122 118 110 99 92 80 71 60 52 46
### Complications at 10 years

<table>
<thead>
<tr>
<th></th>
<th>TAVI (N = 145)</th>
<th>SAVR (N = 135)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>62.7</td>
<td>64.0</td>
<td>0.84</td>
</tr>
<tr>
<td>Cardiovascular death</td>
<td>49.5</td>
<td>51.2</td>
<td>0.65</td>
</tr>
<tr>
<td>Stroke</td>
<td>9.7</td>
<td>16.4</td>
<td>0.11</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>9.7</td>
<td>6.7</td>
<td>0.34</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>11.0</td>
<td>8.2</td>
<td>0.43</td>
</tr>
<tr>
<td>New-onset atrial fibrillation</td>
<td>52.0</td>
<td>74.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>New permanent pacemaker</td>
<td>44.7</td>
<td>14.0</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Bioprosthetic Valve Dysfunction (BVD)

Structural Valve Deterioration:
- Intrinsic permanent changes of the prosthetic valve (i.e., calcification, leaflet fibrosis, tear or flail) leading to degeneration and/or haemodynamic dysfunction

Nonstructural Valve Deterioration:
- Any abnormality not intrinsic to the prosthetic valve itself (i.e., intra- or para-prosthetic regurgitation, prosthesis malposition, patient-prosthesis mismatch, late embolization) leading to degeneration and/or dysfunction

Thrombosis:
- Thrombus development on any structure of the prosthetic valve, leading to dysfunction with or without thromboembolism

Endocarditis:
- Infection involving any structure of the prosthetic valve, leading to perivalvular abscess, dehiscence, pseudoaneurysms, fistulae, vegetations, cusp rupture or perforation

Capodanno et al. Eur Heart J. 2017; 38:3382-90
Structural Valve Deterioration

**Moderate or severe haemodynamic structural valve deterioration**

- Mean gradient $\geq 20$ mmHg **OR**
- Mean gradient $\geq 10$ mmHg change from 3 months **OR**
- Moderate/severe intra-prosthetic aortic regurgitation (*new or worsening from discharge*)

Capodanno et al. Eur Heart J. 2017; 38:3382-90
Structural Valve Deterioration (SVD)

- Structural valve deterioration
  - TAVI (n = 130): 20.2%
  - SAVR (n = 120): 37.7%
  - p-value: 0.0008

- Moderate structural valve deterioration
  - Mean gradient 20 - 40 mmHg
    - TAVI: 14.3%
    - SAVR: 34.0%
    - p-value: <0.0001
  - Mean gradient 10 - 20 mmHg from 3 months
    - TAVI: 13.3%
    - SAVR: 18.5%
    - p-value: 0.21
  - Moderate intraprostatic AR
    - TAVI: 4.5%
    - SAVR: 0%
    - p-value: 0.018

- Severe structural valve deterioration
  - Mean gradient ≥40 mmHg
    - TAVI: 0.8%
    - SAVR: 5.7%
    - p-value: 0.024
  - Mean gradient ≥20 mmHg from 3 months
    - TAVI: 2.3%
    - SAVR: 10.9%
    - p-value: 0.006
  - Severe intraprostatic AR
    - TAVI: 0%
    - SAVR: 0%
    - p-value: -
Modified Structural Valve Deterioration

Modified SVD criteria

Mean gradient $\geq 20$ mmHg \textbf{AND}

Mean gradient $\geq 10$ mmHg change from 3 months \textbf{OR}

Moderate/severe intra-prosthetic aortic regurgitation (new or worsening from discharge)
### Modified Structural Valve Deterioration (SVD)

**Graph:**
- **TAVI** line: Red
- **SAVR** line: Blue

<table>
<thead>
<tr>
<th>Follow-up (Years)</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TAVI</strong></td>
<td>133</td>
<td>131</td>
<td>128</td>
<td>117</td>
<td>109</td>
<td>96</td>
<td>82</td>
<td>71</td>
<td>56</td>
<td>45</td>
<td>32</td>
</tr>
<tr>
<td><strong>SAVR</strong></td>
<td>123</td>
<td>122</td>
<td>116</td>
<td>107</td>
<td>96</td>
<td>85</td>
<td>70</td>
<td>61</td>
<td>48</td>
<td>40</td>
<td>33</td>
</tr>
</tbody>
</table>

**HR 0.71; 95% CI: 0.39 - 1.27**

**p = 0.25**

**Table:**

<table>
<thead>
<tr>
<th></th>
<th>TAVI (n = 133)</th>
<th>SAVR (n = 123)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified structural valve deterioration</td>
<td>15.3</td>
<td>21.6</td>
<td>0.25</td>
</tr>
<tr>
<td>Modified moderate structural valve deterioration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Mean gradient 20 - 40 mmHg and mean gradient 10 – 20 mmHg from 3 months</td>
<td>12.2</td>
<td>19.9</td>
<td>0.07</td>
</tr>
<tr>
<td>- Moderate intraprosthetic AR</td>
<td>4.5</td>
<td>0</td>
<td>0.018</td>
</tr>
<tr>
<td>Modified severe structural valve deterioration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Mean gradient ≥40 mmHg and mean gradient ≥20 mmHg from 3 months</td>
<td>0</td>
<td>5.0</td>
<td>0.01</td>
</tr>
<tr>
<td>- Severe intranprosthetic AR</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Condition</td>
<td>TAVI (n = 130)</td>
<td>SAVR (n = 121)</td>
<td>p-value</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>---------------</td>
<td>----------------</td>
<td>---------</td>
</tr>
<tr>
<td>Bioprosthetic valve dysfunction</td>
<td>67.8</td>
<td>81.2</td>
<td>0.007</td>
</tr>
<tr>
<td>Structural valve deterioration</td>
<td>20.2</td>
<td>37.7</td>
<td>0.0008</td>
</tr>
<tr>
<td>Non-structural valve deterioration</td>
<td>59.2</td>
<td>70.6</td>
<td>0.030</td>
</tr>
<tr>
<td>- Paravalvular leakage</td>
<td>25.4</td>
<td>2.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>- Patient-Prosthesis mismatch</td>
<td>48.9</td>
<td>69.8</td>
<td>0.0008</td>
</tr>
<tr>
<td>Clinical valve thrombosis</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>7.2</td>
<td>7.4</td>
<td>0.95</td>
</tr>
</tbody>
</table>
Bioprosthetic Valve Failure

Valve-related death
Death caused by BVD or sudden unexplained death following diagnosis of BVD

Aortic valve re-intervention
TAVI or SAVR following diagnosis of BVD

Severe hemodynamic structural valve deterioration
Mean gradient $\geq$ 40 mmHg OR
Mean gradient $\geq$ 20 mmHg change from 3 months OR
Severe AR (new or worsening from discharge)
Bioprosthetic Valve Failure

<table>
<thead>
<tr>
<th>Event</th>
<th>TAVI (n = 130)</th>
<th>SAVR (n = 120)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioprosthetic valve failure</td>
<td>10.8</td>
<td>15.1</td>
<td>0.32</td>
</tr>
<tr>
<td>Valve-related death</td>
<td>5.0</td>
<td>3.7</td>
<td>0.60</td>
</tr>
<tr>
<td>Severe structural valve deterioration</td>
<td>3.1</td>
<td>11.0</td>
<td>0.014</td>
</tr>
<tr>
<td>Aortic valve re-intervention</td>
<td>4.3</td>
<td>2.2</td>
<td>0.33</td>
</tr>
</tbody>
</table>

HR 0.72, 95% CI: 0.36 - 1.45

p = 0.32
Limitations

Limited population size

Exploratory analyses

No use of echocardiographical CoreLab

Only transthoracic echocardiography for trial screening and transcatheter heart valve sizing

Only use of self-expanding 1st generation CoreValve for TAVI
Gratitude

Thanks to The Danish heart foundation and Medtronic inc. for economical support

Thanks to all the investigators and study nurses for continued support
Ten years of Follow-up for lower surgical risk patients randomised to TAVI vs SAVR

**Similar** risk of all-cause mortality, Stroke and Myocardial infarction

**Higher** risk of severe structural valve deterioration after SAVR

**Similar** risk of Bioprosthetic valve failure
Aortic bioprosthesis performance

* $p < 0.05$ - TAVI vs SAVR

$^\#$ $p < 0.05$ - intragroup comparison with 3 months

<table>
<thead>
<tr>
<th>Follow-up (Years)</th>
<th>TAVI - Gradient</th>
<th>SAVR - Gradient</th>
<th>TAVI - EOA</th>
<th>SAVR - EOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>124</td>
<td>117</td>
<td>125</td>
<td>118</td>
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<tr>
<td>0.5</td>
<td>126</td>
<td>117</td>
<td>126</td>
<td>116</td>
</tr>
<tr>
<td>1</td>
<td>122</td>
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<td>10</td>
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<tr>
<td>40</td>
<td>36</td>
<td>38</td>
<td>36</td>
<td>36</td>
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</tbody>
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Effective Orifice Area

0.0 0.2 0.4 0.6 0.8 1.0 1.2 1.4 1.6 1.8

Means 50

25 30 35 40 45 50

TAVI SAVR

TAVI - Gradient  SAVR - Gradient  TAVI - EOA  SAVR - EOA

ESC Congress 2023
Amsterdam & Online
*p < 0.05 - TAVI vs SAVR