Make It Simple: From the Nordic Bifurcation I, II, and III Trials

Assoc. Prof. Andrejs Erglis
Latvian Centre of Cardiology
Paula Stradins Clinical University Hospital
Riga, LATVIA
NORDIC I

Nordic Bifurcation Study (NORDIC I): the randomized study on simple versus complex stenting of coronary artery bifurcation lesions /completed/

413 patients randomized

207 patients
Stenting MV

206 patients
Stenting MV+SB

Clinical follow-up after 1, 6, 14, 24 and 36 months

MV (n=207)

MV+SB (n=206)

True bifurcations 71%
(DS>50% in MV and SB)

Both stenting strategies has a high and similar procedural success, but simple stenting strategy is associated with reduced procedure and fluroscopy times (Nordic I)

<table>
<thead>
<tr>
<th>Procedural Characteristics</th>
<th>MV n=207</th>
<th>MV+SB n=206</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MV stented</td>
<td>206 (99.5)</td>
<td>203 (98.5)</td>
<td>0.31</td>
</tr>
<tr>
<td>SB stented</td>
<td>9 (4.3)</td>
<td>196 (95.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>No. of stents</td>
<td>1.3±0.6</td>
<td>2.2±0.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Final kissing balloon</td>
<td>65 (32)</td>
<td>152 (74)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Procedural success</td>
<td>200 (97)</td>
<td>194 (94)</td>
<td>0.35</td>
</tr>
<tr>
<td>Procedure time, min</td>
<td>62±51</td>
<td>76 ±40</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fluoroscopy time, min</td>
<td>15±9</td>
<td>21±10</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Contrast volume, mL</td>
<td>233±93</td>
<td>283±117</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values are mean ±SD n (%)
A significantly lower incidence of increased levels of biomarkers was seen in the simple stenting group.

<table>
<thead>
<tr>
<th></th>
<th>MV n=153</th>
<th>MV + SB n=126</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3 elevation (%)</td>
<td>8</td>
<td>18</td>
<td>0.011</td>
</tr>
<tr>
<td>&gt;5 elevation (%)</td>
<td>4</td>
<td>13</td>
<td>0.008</td>
</tr>
<tr>
<td>&gt;10 elevation (%)</td>
<td>3</td>
<td>5</td>
<td>NS</td>
</tr>
</tbody>
</table>
Nordic Bifurcation Study: Major Adverse Cardiac Events

MACE rates are low with both the provisional stenting and elective 2-stent technique

<table>
<thead>
<tr>
<th>Individual Endpoints</th>
<th>MV n=207</th>
<th>MV + SB n=206</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6 months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac death, n(%)</td>
<td>2 (1.0)</td>
<td>2 (1.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Total death, n(%)</td>
<td>2 (1.0)</td>
<td>3 (1.5)</td>
<td>0.61</td>
</tr>
<tr>
<td>MI, n(%)</td>
<td>0 (0.0)</td>
<td>1 (0.5)</td>
<td>0.31</td>
</tr>
<tr>
<td>TVR, n(%)</td>
<td>4 (1.9)</td>
<td>4 (1.9)</td>
<td>0.99</td>
</tr>
<tr>
<td>Stent thrombosis, n(%)</td>
<td>1 (0.5)</td>
<td>0 (0.0)</td>
<td>0.31</td>
</tr>
<tr>
<td>TLR, n(%)</td>
<td>4 (1.9)</td>
<td>2 (1.0)</td>
<td>0.36</td>
</tr>
<tr>
<td><strong>36 months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total death (%)</td>
<td>2.9</td>
<td>5.8</td>
<td>0.15</td>
</tr>
<tr>
<td>Cardiac death (%)</td>
<td>1.4</td>
<td>1.5</td>
<td>1.00</td>
</tr>
<tr>
<td>MI (%)</td>
<td>3.0</td>
<td>3.6</td>
<td>0.78</td>
</tr>
<tr>
<td>TLR (%)</td>
<td>8.0</td>
<td>9.7</td>
<td>0.60</td>
</tr>
<tr>
<td>TVR (%)</td>
<td>9.5</td>
<td>11.7</td>
<td>0.52</td>
</tr>
<tr>
<td>Stent thrombosis (%)</td>
<td>2.5</td>
<td>1.0</td>
<td>0.45</td>
</tr>
</tbody>
</table>

*MACE: cardiac death, index lesion MI, TVR, stent thrombosis

Iwar Sjögren EuroPCR 2009
Nordic Bifurcation Study: Stent Thrombosis

Stent thrombosis rate at 36 months without differences between the stenting strategies

Iwar Sjögren EuroPCR 2009
Mortality remained low at 14 months without differences between the stenting strategies.
Nordic Bifurcation Study:
QCA results

QCA results showed no significant differences between two stenting strategies at 8 months (Nordic I)

Nordic Bifurcation Study: IVUS results

*IVUS results showed no differences between two stenting strategies at 8 months (Nordic I)*

One centre results: \( n=27 \) MV, \( n=35 \) MV+SB

\( \% \text{NIV} = \frac{\text{Neointimal Volume}}{\text{Stent Volume}} \times 100 \)

### Minimum Lumen Area (mm²)

- **Main Branch**
  - MV: 5.4
  - MV+SB: 5.5
  - \( P=0.720 \)

### Minimum Stent Area (mm²)

- **Main Branch**
  - MV: 5.5
  - MV+SB: 5.7
  - \( P=0.504 \)

Andrejs Erglis TCT 2008
Plaque Modification Before Stenting

**Hypothesis:** Plaque modification before stent deployment may minimize arterial injury and subsequent neointimal proliferation and may prevent restenosis formation:

- it minimizes plaque shifting between main branch and side branch and thus helps avoiding side branch stenting
- it gives perfect stent apposition with reduced inflation pressure even if very long stents are deployed
- *in the future when bioabsorbable stents will be available it can be an essential tool to perform complete “vessel repair procedures”*
Acting mechanisms of Regular and Cutting balloons

**Regular balloon**
- Entire balloon surface contact the vessel wall – arterial wall damage
- Multiple rips and tears in media
- Endothelium is completely disrupted, large hematoma has formed due to trauma

**Cutting balloon**
- Injury localized to the scoring sites - reduced trauma
- Media with no visible disruption
- Endothelial layer remains intact
**CB substudy**

- Single centre substudy (Nordic I, II+ Riga bifurcation registry) to compare the safety and efficacy of plaque modification with cutting balloon (CB) before main vessel stenting and/or side branch treatment in bifurcation lesion.

<table>
<thead>
<tr>
<th>8 Months Outcomes</th>
<th>CB n= 209</th>
<th>Non-CB n= 347</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, n (%)</td>
<td>7 (3.3)</td>
<td>10 (2.9)</td>
<td>0.802</td>
</tr>
<tr>
<td>MI, n (%)</td>
<td>7 (3.3)</td>
<td>9 (2.6)</td>
<td>0.609</td>
</tr>
<tr>
<td>Non Q MI, n (%)</td>
<td>6 (12)</td>
<td>4 (8)</td>
<td>0.518</td>
</tr>
<tr>
<td>ST, n (%)</td>
<td>5 (2.4)</td>
<td>10 (2.6)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>TLR, n (%)</td>
<td>11 (5.3)</td>
<td>38 (11.0)</td>
<td>0.021</td>
</tr>
<tr>
<td>TVR, n (%)</td>
<td>17 (8.1)</td>
<td>48 (13.8)</td>
<td>0.056</td>
</tr>
</tbody>
</table>
NORDIC III

Nordic-Baltic Bifurcation Study III: A prospective randomized trial of side branch dilatation strategies in patients with coronary bifurcation lesions undergoing treatment with a single stent /active, not recruiting/

Bifurcation patients with successful MV stenting n=477

No Kissing balloon n=239

Kissing balloon n=238

Clinical follow-up after 1 and 6 months n=477 (100%)

No kissing (n=239) Kissing (n=238)

True bifurcations: 51.8% Kissing vs. 54.6% No kissing, p=ns
Medina classification 1,1,1 - 1,0,1 - 0,1,1

Matti Niemela TCT 2009
Nordic III: Major Adverse Cardiac Events

Primary end point
MACE (cardiac death, index lesion MI, TLR, stent thrombosis) after 6 months

Event Free Survival

P=ns

Matti Niemela TCT 2009
NORDIC II

Nordic Stent Technique Study (NORDIC II): the first randomized clinical and angiographic comparison of the crush and the culotte bifurcation stent techniques /active, not recruiting/

425 patients randomized

209 patients CRUSH-stenting
215 patients CULOTTE-stenting

Clinical follow-up after 1, 6 and 14 months

Crush (n=209) and Culotte (n=215) patient distribution

True bifurcations: 73.3% Crush vs. 82.3% Culotte, p=0.03 (Medina classification 1,1,1 - 1,0,1 - 0,1,1)

Nordic II: Major Adverse Cardiac Events

Primary Endpoint
Cardiac death, MI, TVR and stent thrombosis

P=NS

Nordic II: QCA results

There is a trend towards less restenosis of the entire bifurcation lesion because of significantly reduced SB in-stent restenosis in patients treated with the CULOTTE technique (Nordic II)

Keep It Simple!

- The technique of stenting of main vessel and optional stenting of side branch can be recommended as the routine bifurcation stenting technique.
- A strategy of routine kissing balloon dilatation of side branch through the MV stent did not improve the 6-month clinical outcome as compared to a strategy of no kissing balloon dilatation.
- Plaque modification with CB may give positive impact on TLR after 8 months.
- If using two stent strategy – preference should be given to Culotte stenting, associated with lower restenosis rate than Crush.