16-year follow-up of the DANish Acute Myocardial Infarction 2 (DANAMI-2) trial

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Declaration of interest

- I have nothing to declare
Background

- The 1990’s landmark trials (Zwolle, PAMI) showed that pPCI treatment was superior to fibrinolysis in patients admitted to invasive centres

- The DANAMI-2 trial (NEJM 2003) is the largest RCT to show that inter-hospital transport for pPCI is superior to fibrinolysis at 30 days of follow-up

- These results were confirmed in the PRAGUE-2 trial
Objective

• To examine the 16-year outcomes of the DANAMI-2 trial

• To provide a very long-term perspective on death and cardiovascular events when comparing pPCI with fibrinolysis in STEMI patients
Included
1,572 STEMI patients

Invasive centres
n=443

Referral hospitals
n=1,129
Included
1,572 STEMI patients

Invasive centres
n=443

- pPCI
  n=223
- Fibrinolysis
  n=220

Referral hospitals
n=1,129

- pPCI
  n=567
- Fibrinolysis
  n=562

Primary endpoint: Composite of death, reinfarction, or disabling stroke at 30 days

Andersen HR et al, NEJM 2003
Included
1,572 STEMI patients

Invasive centres
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Primary endpoint: Composite of death, reinfarction, or disabling stroke at 30 days

Andersen HR et al, NEJM 2003
Patient selection

**Inclusion criteria**
- ST-elevation ≥2 mm in ≥2 contiguous leads
- Age ≥18 years
- Chest discomfort ≥30 mins and ≤12 hours

**Exclusion criteria**
- LBBB
- Contraindication to fibrinolysis
- MI or fibrinolysis within the last 30 days
- Metformin-treated diabetes
Endpoints

Main endpoint:
Composite of death or reinfarction

Additional endpoints:
Death
Reinfarction
Cardiac and non-cardiac death
Endpoints

0-3 years: Clinical follow-up
Endpoint committee adjudication

4-16 years: Registry-based follow-up
Danish Civil Registration System
Danish National Patient Registry
Danish Cause of Death Registry
Statistics

Kaplan-Meier curves and Cox proportional hazards model:
- Composite endpoint and all-cause death

Competing Risk Model:
- Reinfarction, cardiac and non-cardiac death

Restricted mean model*:
- Difference in time to first event

*Kim DH et al, JAMA 2017
## Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Fibrinolysis (n=782)</th>
<th>Primary PCI (n=790)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (IQR)</td>
<td>63 (54-73)</td>
<td>63 (54-72)</td>
<td>0.32</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>73.4</td>
<td>73.5</td>
<td>0.95</td>
</tr>
<tr>
<td>Previous MI (%)</td>
<td>11.8</td>
<td>11.0</td>
<td>0.61</td>
</tr>
<tr>
<td>Anterior index MI (%)</td>
<td>52.6</td>
<td>53.2</td>
<td>0.81</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>7.1</td>
<td>7.4</td>
<td>0.80</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>58.6</td>
<td>58.1</td>
<td>0.85</td>
</tr>
<tr>
<td>Time from symptom onset to randomization (min), median (IQR)</td>
<td>140 (85-235)</td>
<td>135 (85-225)</td>
<td>0.23</td>
</tr>
</tbody>
</table>
16-year follow-up

• 60% of the patients reached the composite endpoint
• 51% died during follow-up
• High data completeness
  – Vital status known for 99.7% of patients
  – Cause of death known for 97.7% of all deaths
Composite endpoint

62.3%  
58.7%

Absolute difference  
3.6%

Hazard ratio (95% CI)  
0.86 (0.76-0.98)

Thrane et al, EHJ 2019
Composite endpoint

62.3%

58.7%

Absolute difference

3.6%

Hazard ratio (95% CI)

0.86 (0.76-0.98)

Mean gain in time to first event (95% CI)

12.3 months (5.0-19.5)

Thrane et al, EHJ 2019
Reinfarction

Absolute difference
24.5% - 19.0% = 5.5%

Hazard ratio (95% CI)
0.75 (0.60-0.93)
Reinfarction

Absolute difference
24.5%
19.0%

Hazard ratio (95% CI)
0.75 (0.60-0.93)

Mean gain in time
11.5 months
(4.8–18.3)
All-cause death

Absolute difference
51.3% - 50.5% = 0.8%

Hazard ratio (95% CI)
0.95 (0.83-1.09)
Cardiac death

Absolute difference
4.4%

22.7% Hazard ratio (95% CI)
18.3% 0.78 (0.63-0.98)
Referral hospitals

n = 1129

Hazard ratio (95% CI)

Composite endpoint: 0.82 (0.71-0.96)
Reinfarction: 0.77 (0.60-0.98)
Death: 0.91 (0.77-1.07)
Cardiac death: 0.79 (0.61-1.01)

Favours pPCI  Favours fibrinolysis
Limitations

• Changes in management and treatment
  • Prehospital triage
  • Anti-thrombotic treatment
  • Optimization of PCI devices and techniques

• Conservative use of rescue PCI after fibrinolysis
Conclusions: 16-year follow-up

Composite endpoint
  • Absolute reduction of 3.6% favouring pPCI
  • >1 year gain in time to first main event with pPCI

Reinfarction
  • Absolute reduction of 5.5% favouring pPCI

Cardiac death
  • Absolute reduction of 4.4% favouring pPCI
Thank you for your attention