Danish registry of ACS
DANAMI Studies

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Death from IHD 2005-2008

- signifikant øget dødelighedsindeks
- > 5% øget dødelighedsindeks, ikke signifikant
- dødelighedsindeks mellem + og - 5% af landsgennemsnittet
- > 5% mindsket dødelighedsindeks, ikke signifikant
- signifikant mindsket dødelighedsindeks
Danish registries

- The register of causes of death
- The civil register → vital status
- The national patient register
- The register of causes of death

Birth
010111-xxxx
**AMI and Triple Therapy**  

**Inclusion and endpoints**

Admitted with first-time MI between 2000-2005  
Age $\geq 30$ years

Claimed at least one prescription within 90 days of
- aspirin
- clopidogrel
- vitamin K antagonists

N=40,812

<table>
<thead>
<tr>
<th>Therapy Type</th>
<th>Prescriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monotherapy</td>
<td>aspirin, clopidogrel, vitamin K antagonists</td>
</tr>
<tr>
<td>Dual therapy</td>
<td>aspirin+clopidogrel, Vitamin K antagonists+ aspirin</td>
</tr>
<tr>
<td>Triple therapy</td>
<td>all three drugs</td>
</tr>
</tbody>
</table>

Non-fatal + fatal bleeding after 18 months
Results

Non-fatal and fatal bleeding

Bleeding
- Increased age
- Male sex
- Malignant disease
- Previous bleeding

Treatment
- Cardiac heart failure
- Diabetes
- NSAIDs
- PPIs
Results

Figure 2A: Adjusted risk of non-fatal and fatal bleedings

- **aspirin monotherapy**: HR = 1.00 (reference)
- **clopidogrel monotherapy**: HR = 1.33, 95% CI: 1.11-1.59
- **VKA monotherapy**: HR = 1.23, 95% CI: 0.94-1.61
- **aspirin+clopidogrel**: HR = 1.47, 95% CI: 1.28-1.69
- **VKA+aspirin**: HR = 1.84, 95% CI: 1.51-2.23
- **VKA+clopidogrel**: HR = 3.52, 95% CI: 2.42-5.11
- **triple therapy**: HR = 4.05, 95% CI: 3.08-5.33
Results

- **Numbers needed to harm**

- **If experiencing a bleeding:**
  Risk of re-MI and death x 3

<table>
<thead>
<tr>
<th>Treatment</th>
<th>NNH, adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monotherapy</strong></td>
<td></td>
</tr>
<tr>
<td>aspirin alone</td>
<td>Reference</td>
</tr>
<tr>
<td>clopidogrel alone</td>
<td>115·7</td>
</tr>
<tr>
<td>VKA alone</td>
<td>165·9</td>
</tr>
<tr>
<td><strong>Dual therapy</strong></td>
<td></td>
</tr>
<tr>
<td>aspirin+clopidogrel</td>
<td>81·2</td>
</tr>
<tr>
<td>aspirin+VKA</td>
<td>45·4</td>
</tr>
<tr>
<td>VKA+clopidogrel</td>
<td>15·2</td>
</tr>
<tr>
<td><strong>Triple therapy</strong></td>
<td></td>
</tr>
<tr>
<td>triple treatment</td>
<td>12·5</td>
</tr>
</tbody>
</table>
Atrial Fibrillation Patients with MI or PCI
n= 16.879

Atrial fibrillation subjects eligible for inclusion with admission for either MI (n=13,970) or PCI (n=2,909) with no PCI/MI events one year prior from January 1, 2001 to December 31, 2009 (total n=16,879)

Excluded (n=4,714)
- Fatal or non-fatal bleeding during quarantine period (224)
- Fatal or non-fatal stroke/TCL arterial embolism/pulmonary embolism during quarantine period (394)
- Coronary death or non-fatal MI during quarantine period (2,465)
- Death from other causes (414)
- Not receiving antithrombotic therapy at inclusion (1,216)
- Age below 30 years (1)

Fulfilling inclusion criteria after seven day quarantine period after discharge and included in the study (n=12,165)

Aspirin (n=3,277) or clopidogrel (n=689) or OAC (n=711)
Aspirin + clopidogrel (n=3,590)
OAC + aspirin (n=1,504)
OAC + clopidogrel (n=548)
OAC + aspirin + clopidogrel (n=1,896)

Lamberts M........Gislason G et al. JACC 2013
Initial antithrombotic treatment and crude rates of ischemic stroke and bleeding according to predicted risk

Lamberts M........Gislason G et al. JACC 2013
Benefit and safety with triple therapy versus dual therapies

Lamberts M……….Gislason G et al. JACC 2013
Cause of death according to antithrombotic treatment at time of death

Lamberts M........Gislason G et al. JACC 2013
DANAMI Studies

Copenhagen University
Department of Cardiology
Rigshospitalet
Copenhagen
DANAMI 3

Rationale and setup
Randomisering
Postconditionering
Deferred stenting
PRIMULTI (Flerkarsyge)
Flowchart
Brugernavn: aal-danami3
Adgangskode: danami3
Skriv patientens CPR nummer

Herefter

Bekræft med OK
Udfyld TIMI-flow

Stillingtagen til om pt. kan randomiseres
Hvis patienten **ikke** kan randomiseres

Anfør hvorfor. Alle felter skal udfylDES med ja eller nej
1. Randomisation

DANAMI-3

STEMI

CAG

TIMI 0-1

TIMI 2-3

wire / thrombect / balloon dil

TIMI 2-3

Postcon

Conv

Defer

MVD

IRA only

Complete

2. Randomisation (PRIMULTI)
Cardioprotective strategies

1. Conventional PPCI
2. Deferred strategy
3. Remote conditioning
4. Pharmacological conditioning
5. Mechanical postconditioning

Occluded coronary artery → Reperfusion → Myocardial injury
Angiographic picture – no flow
In-hospital mortality and TIMI flow

\[ p = 0.003 \]

- **CTFC < 14 TIMI 4 flow**: 0.0% (n=41)
- **14 ≤ CTFC ≤ 40 TIMI 3 flow**: 2.8% (n=18/640)
- **CTFC > 40 TIMI 0–2 flow**: 6.2% (n=35/563)

Gibson. Circulation 1999
Treatment of acute myocardial infarction

- Myocardial infarction without reperfusion
- Myocardial infarction with reperfusion
- Myocardial infarction with reperfusion and cardioprotection

ischemic preconditioning

% Infarction of the Ischemic Zone

Shows that infarct size can be modified

Murry et al, Circulation 1986;74:1124-1136
Postconditioning – rabbit study

Mechanical postconditioning

- Occluded coronary artery
- Reperfusion

Conventional treatment

- 30 sec
- Reperfusion injury

Mechanical postconditioning

- Balloon inflations – deflations
- 30 sec
Method – salvage index

Salvage index: \( \frac{\text{Area at risk} - \text{infarct}}{\text{Area at risk}} \)
POSTCON – Magnetic resonance scan (MRI)

N=118

- LVEF: Postconditioning 53%, Conventional treatment 53% (p=0.987)
- Infarct size/LV mass: Postconditioning 14%, Conventional treatment 17% (p=0.037)
- Infarct size/area at risk: Postconditioning 51%, Conventional treatment 63% (p=0.007)
- Salvage ratio: Postconditioning 49%, Conventional treatment 37% (p=0.007)

Δ 32%

Lønborg et al. Circ Cardiovasc Interv 2010
The thrombus revisited
Deferred stent strategy

Acute
Deferred stenting

- Occluded coronary artery
- Reperfusion

Conventional PPCI

Deferred strategy

Reperfusion injury

Stent
STEMI

CAG

TIMI 0-1

TIMI 2-3

wire / thrombect / balloon dil

TIMI 2-3

Postcon

Conv

Defer

MVD

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Complete

DANAMI-3

1. Randomisation

2. Randomisation (PRIMULTI)
TIMI 0-1 TIMI 2-3
Postcon
wire / thrombect / balloon dil
TIMI 2-3
MVD
Defer Conv
IRA only
Complete
STEMI
CAG
1. Randomisation
DANAMI-3
2. Randomisation
(PRIMULTI)

Myocardial salvage
Endpoints

Primary

Cardiac death, re-admission heart failure (postcon vs. control)

Cardiac death, re-infarction, re-admission heart failure (Defer vs. Control)

Secondary

MRI measures
Deferred stenting in STEMI – a pilot

3 mo control angio

*Excluded

124 STEMI

77 TIMI <3

110 Thrombectomy/ balloon dilatation

11* TIMI <3

47 TIMI 3

14 No thrombectomy/ balloon dilatation

113 DEFER

4 CABG

43 No stent

66 Stent

1. Procedure

Inclusion

2. Procedure

>35% stenosis

Eurointervention 2013;8:1126-1133
## Deferred stenting in STEMI – a pilot

<table>
<thead>
<tr>
<th></th>
<th>N=32</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final infarct size, g</td>
<td>11.2 (10.2)</td>
</tr>
<tr>
<td>Area at risk, g</td>
<td>48.8 (22.2)</td>
</tr>
<tr>
<td>LV mass, g</td>
<td>170.0 (40.8)</td>
</tr>
<tr>
<td>LVEF baseline, %</td>
<td>54.2 (9.4)</td>
</tr>
<tr>
<td>LVEF 3 months, %</td>
<td>64.9 (7.7)*</td>
</tr>
<tr>
<td>Final infarct size / area at risk, %</td>
<td>20.9 (16.6)</td>
</tr>
<tr>
<td>Final infarct size / LV mass, %</td>
<td>6.3 (5.2)</td>
</tr>
<tr>
<td>Myocardial salvage index</td>
<td>0.79 (0.17)</td>
</tr>
</tbody>
</table>

Mean values (SD); LV: left ventricular; EF: ejection fraction; *p <0.05 compared with LVEF baseline
Deferred stenting in STEMI – a pilot

<table>
<thead>
<tr>
<th></th>
<th>Overall study population</th>
<th>Anterior infarct location</th>
<th>Non-anterior infarct location</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$n$</td>
<td>Exenatide</td>
<td>$n$</td>
</tr>
<tr>
<td>Salvage index$^a$</td>
<td>54</td>
<td>0.71 ± 0.13</td>
<td>51</td>
</tr>
<tr>
<td>Infarct size (g)/area at risk (g)</td>
<td>54</td>
<td>0.30 ± 0.15</td>
<td>51</td>
</tr>
<tr>
<td>Area at risk (g)</td>
<td>54</td>
<td>42 ± 21</td>
<td>51</td>
</tr>
<tr>
<td>Final infarct size (g)</td>
<td>60</td>
<td>13 ± 9</td>
<td>57</td>
</tr>
<tr>
<td>Final infarct size (%LV)</td>
<td>60</td>
<td>11 ± 7</td>
<td>57</td>
</tr>
<tr>
<td>LVEF 3 months (%)</td>
<td>60</td>
<td>55 ± 9</td>
<td>57</td>
</tr>
<tr>
<td>Salvage index$^b$</td>
<td>20</td>
<td>0.74 ± 0.11</td>
<td>21</td>
</tr>
<tr>
<td>Infarct size (g)/area at risk (g)</td>
<td>20</td>
<td>0.27 ± 0.12</td>
<td>21</td>
</tr>
<tr>
<td>Area at risk (g)</td>
<td>20</td>
<td>53 ± 24</td>
<td>21</td>
</tr>
<tr>
<td>Final infarct size (g)</td>
<td>23</td>
<td>17 ± 11</td>
<td>25</td>
</tr>
<tr>
<td>Final infarct size (%LV)</td>
<td>23</td>
<td>13 ± 9</td>
<td>25</td>
</tr>
<tr>
<td>LVEF 3 months (%)</td>
<td>23</td>
<td>55 ± 11</td>
<td>25</td>
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$Lønborg$ et al. $EHJ$ 2012;33:1491-1499
Included patients May 2013

Total 1715
"DANAMI-4"

- Remote conditioning
- "KONDI 2"
CONCLUSIONS

- Recent studies from Danish registries confirm the risks associated with triple therapy in patients after MI as well as in patients with chronic atrial fibrillation who suffers MI or undergo PCI.
- These results confirm the findings from the “small” randomised WOEST Trial.
CONCLUSIONS

• No re-flow is associated with a poor clinical outcome

• Mechanical conditioning and deferred stent strategy are promising concepts in reducing myocardial injury in acute infarction

• Clinical studies are needed to see whether surrogate markers can be translated into clinical endpoints
Thank you for your attention
Benefit and safety with triple therapy versus dual therapies according to baseline antithrombotic treatment regimen

Triple therapy is used as reference (hazard ratio=1.00).
1. Reach a clinical endpoint with respect to mechanical postconditioning

2. Test deferred stent strategy

3. Randomise MVD