Revascularisation or medical therapy in elderly patients with aCute anginAL syndromes

The (RINCAL) trial

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☑ I do not have any potential conflict of interest to declare
Why this study?

- Octogenarians with nSTEACS are an increasingly common clinical presentation
- Current guidelines advocate an early (24-72 hours) invasive strategy for patients with intermediate- or high-risk nSTE-ACS
- The very elderly (≥80 years) are under-represented in nSTE-ACS trials
- Frailty, truncated life expectancy, impaired cognition, therapeutic adherence, co-morbidity are all relevant factors in this cohort

Managing NSTEMI in elderly patients: ESC recommendations 2011.

Hamm C et al, EurHeartJ 2011;32:2999-
What did we study?

• Hypothesis: An early invasive strategy + OMT would be superior to OMT alone for the management of nSTE-ACS in the very elderly

• All-comer investigator-initiated multicentre open-label randomised controlled trial

• 750 patients were needed (randomisation 1:1) to achieve 80% power (2-sided $\alpha=0.05$) to detect a 10% difference in outcomes
How was the study executed?

**Inclusion criteria**
- ≥80 years old
- NSTE-ACS
  - ischaemic ECG changes
  - and elevated Troponin T or I
- suitable for either angiography ± revascularisation or OMT only

**Exclusion criteria**
- STEMI
- cardiogenic shock
- unsuitable for revascularisation
- life expectancy <1 year
- recent major bleeding

**Primary endpoint**
- composite of all-cause mortality and non-fatal reinfarction at 1 year post randomisation

**Secondary endpoints**
- unplanned revascularisation
- stroke
- major bleeding
- in-hospital acute kidney injury
- angina burden at 3 months and 1 year
- stent thrombosis
- hospital readmission for NSTE-ACS
- in-hospital major complication
What are the essential results?

### Assessed for eligibility
- **n=541**

### Randomisation 1:1
- **Invasive strategy + optimal medical therapy (n=137) (
  Angiogram performed r=115
  Angiogram not done r=22**
- **Optimal medical therapy only (n=136)
  (n=136)

### Lost to follow-up r=1
- Discontinued Intervention r=0
- Withdrew consent r=1

### Excluded (n=20)
- Not meeting inclusion criteria r=129
- Declined to participate r=1
- Other reasons r=17

### Mean age (range)
- Intervention (n=124): 84.8 (80 to 95)
- Optimal medical therapy (n=126): 85.2 (80 to 95)

### Female
- Intervention: 60/124 (48.4%)
- Optimal medical therapy: 58/126 (46.0%)

### Previous MI
- Intervention: 33/123 (26.8%)
- Optimal medical therapy: 35/123 (28.5%)

### Previous PCI
- Intervention: 21/122 (17.2%)
- Optimal medical therapy: 16/124 (12.9%)

### Previous CABG surgery
- Intervention: 12/124 (9.7%)
- Optimal medical therapy: 10/123 (8.1%)

### Hypertension
- Intervention: 87/124 (70.2%)
- Optimal medical therapy: 82/124 (66.1%)

### Type 2 diabetes mellitus
- Intervention: 33/124 (26.6%)
- Optimal medical therapy: 19/125 (15.2%)

### COPD
- Intervention: 10/124 (15.3%)
- Optimal medical therapy: 12/123 (9.8%)

### Previous CVA
- Intervention: 25/124 (20.2%)
- Optimal medical therapy: 26/124 (21.0%)

### Peripheral vascular disease
- Intervention: 5/124 (4.1%)
- Optimal medical therapy: 3/124 (2.4%)

### Aortic aneurysm
- Intervention: 0/124 (0%)
- Optimal medical therapy: 1/122 (0.8%)

### Current smoker
- Intervention: 10/124 (8.1%)
- Optimal medical therapy: 4/122 (3.3%)

### Killip Class I
- Intervention: 99/120 (82.5%)
- Optimal medical therapy: 93/117 (79.5%)

### Killip Class II
- Intervention: 14/120 (11.7%)
- Optimal medical therapy: 22/117 (18.8%)

### ECG - AF
- Intervention: 24/123 (19.5%)
- Optimal medical therapy: 24/120 (20.0%)

### ECG - Q waves
- Intervention: 0/122 (0%)
- Optimal medical therapy: 7/119 (5.9%)

### ECG - ST depression
- Intervention: 32/122 (26.2%)
- Optimal medical therapy: 29/119 (24.4%)

### ECG - T wave inversion
- Intervention: 50/122 (41.0%)
- Optimal medical therapy: 45/119 (37.8%)

### ECG - LBBB
- Intervention: 0/122 (0%)
- Optimal medical therapy: 0/119 (0%)

### Troponin ≤200
- Intervention: 40/124 (32.3%)
- Optimal medical therapy: 44/125 (35.2%)

### Troponin >200
- Intervention: 84/124 (67.7%)
- Optimal medical therapy: 81/125 (64.8%)

### GRACE <170
- Intervention: 73/118 (61.9%)
- Optimal medical therapy: 63/111 (56.8%)

### GRACE 170-200
- Intervention: 27/118 (22.9%)
- Optimal medical therapy: 32/111 (28.8%)

### GRACE >200
- Intervention: 18/118 (15.2%)
- Optimal medical therapy: 16/111 (14.4%)

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**p-value**
- 0.37
- 0.80
- 0.89
- 0.38
- 0.82
- 0.59
- 0.030
- 0.25
- 1.00
- 0.50
- 0.50
- 0.17
- 0.62
- 0.15
- 1.00
- 0.007
- 0.77
- 0.69
- 1.00
- 0.69
- 0.69
- 0.50
- 0.37
- 1.00
What are the essential results?

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n=124)</th>
<th>OMT (n=126)</th>
<th>HR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined primary endpoint</td>
<td>23/124 (18.5%)</td>
<td>28/126 (22.2%)</td>
<td>0.79</td>
<td>0.45 – 1.36</td>
<td>0.39</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>13/124 (10.5%)</td>
<td>14/126 (11.1%)</td>
<td>0.94</td>
<td>0.44 – 1.99</td>
<td>0.86</td>
</tr>
<tr>
<td>Non-fatal reinfarction</td>
<td>12/124 (9.7%)</td>
<td>18/126 (14.3%)</td>
<td>0.64</td>
<td>0.31 – 1.32</td>
<td>0.23</td>
</tr>
</tbody>
</table>

Kaplan-Meier plot for primary endpoint

<table>
<thead>
<tr>
<th>Secondary endpoints</th>
<th>Intervention (n=124)</th>
<th>Optimal medical therapy (n=126)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unplanned revascularisation</td>
<td>2/124 (1.6%)</td>
<td>8/126 (6.4%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Permanent stroke</td>
<td>3/124 (2.4%)</td>
<td>3/126 (2.4%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>7/124 (5.6%)</td>
<td>3/126 (2.4%)</td>
<td>0.21</td>
</tr>
<tr>
<td>Canadian Cardiovascular Society angina class at 1 year</td>
<td>No angina 78/100 (78.0%)</td>
<td>No angina 72/101 (71.3%)</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td>Class 1 15/100 (15.0%)</td>
<td>Class 1 17/101 (16.8%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Class 2 5/100 (5.0%)</td>
<td>Class 2 10/101 (9.9%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Class 3 2/100 (2.0%)</td>
<td>Class 3 2/101 (2.0%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Class 4 0/100 (0%)</td>
<td>Class 4 0/101 (0.9%)</td>
<td></td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>0/124 (0%)</td>
<td>0/126 (0%)</td>
<td>1.00</td>
</tr>
<tr>
<td>In-hospital major complications</td>
<td>4/124 (3.2%)</td>
<td>2/126 (1.6%)</td>
<td>0.45</td>
</tr>
</tbody>
</table>
Why is this important?

• There was no significant difference between an early intervention versus OMT strategy in elderly high-risk NSTE-ACS patients for the combined primary endpoint of nonfatal MI and all-cause mortality at 1 year.

• There was a non-significant increase in non-fatal MI and unplanned revascularisation among patients treated with optimal medical therapy.

• In the invasively managed arm patients underwent angiography and revascularisation successfully with little morbidity.

• Patients who underwent revascularisation were more likely to be free of angina at 3 months, although angina burden was similar at 1 year.

• Major limitations
  • trial stopped early for slow recruitment
  • underpowered to adequately test the primary hypothesis.
The essentials to remember

- Why?
  - optimal management of NSTE-ACS in very elderly (≥80 years) patients is poorly defined

- What?
  - to determine whether an intervention-guided strategy + OMT was superior to OMT alone for the primary combined endpoint of all-cause mortality and non-fatal reinfarction at 1 year in very elderly NSTE-ACS patients

- How?
  - all-comer investigator-initiated multicentre open-label randomised controlled trial conducted in the United Kingdom

- What are the results?
  - there was no significant difference in the primary combined endpoint at 1 year between either strategy

- Why is this important?
  - highlights the importance of ensuring patients receive guideline-mandated medical therapy irrespective of age. Conservative management, as oppose to invasive guided strategies, of elderly high-risk NSTE-ACS patients does not appear to influence mortality at 1 year, but does increase the risk of further myocardial infarction and unplanned revascularisation.