An early invasive strategy reduced death, myocardial infarction, and hospital readmissions at 2 years in unstable CAD


**QUESTION**
In patients with unstable coronary artery disease (CAD), how does an early invasive strategy compare with a noninvasive strategy for long-term effectiveness in reducing death, myocardial infarction (MI), hospital readmissions, and late revascularization?

**INTERVENTION**
Patients were allocated to invasive therapy (coronary angiography, revascularization within 7 d of hospital admission, percutaneous coronary intervention for 1 or 2 lesions, and coronary bypass graft surgery for 3-vessel or left main CAD) or noninvasive therapy (coronary angiography for refractory or recurrent symptoms despite maximal medical treatment or severe ischemia on a predischarge symptom-limited exercise test). Exclusion criteria included thrombolysis in the previous 24 hours, previous open heart surgery, angioplasty within the past 6 months, known CAD, ischemic electrocardiographic changes, or elevated biochemical myocardial markers.

**DESIGN**
Randomized (allocation concealed), blinded (outcome assessors), controlled trial with 24-month follow-up (The Fragmin and Fast Revascularization during Instability in Coronary artery disease [FRISC-II]) study.

**SETTING**
58 hospitals in Sweden, Denmark, and Norway.

**PATIENTS**
2457 patients (median age 65 y, 70% men) with symptoms of unstable CAD, most recent episode of chest pain ≤ 48 hours before the start of dalteparin or regular heparin, and signs of myocardial ischemia (ST-segment depression, T-wave inversion, or raised biochemical myocardial markers). Exclusion criteria included thrombolysis in the previous 24 hours, angioplasty within the past 6 months, previous open heart surgery, and age ≥ 75 years. All patients received aspirin and open-label dalteparin for ≥ 5 days. Follow-up was 99%.

**MAIN OUTCOME MEASURES**
Composite endpoint of death or MI. Secondary outcomes were death, MI, late revascularizations, and repeated admissions to the hospital.

**MAIN RESULTS**
Analysis was by intention to treat. Fewer patients in the invasive group had an MI, died, or both, and there were fewer repeated hospital admissions than in the non-invasive group (Table). Although more patients were revascularized at 24 months in the invasive group than the noninvasive group (78% vs 45%, *P* < 0.001), no additional patients were revascularized in the second year of the study. MI, death or MI, and repeated hospital admissions in the invasive group continued to decline during the second year.

**CONCLUSION**
In patients with unstable coronary artery disease, an early invasive strategy reduced death, myocardial infarction, and hospital readmissions over 2 years.

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*See Glossary.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Invasive</th>
<th>Noninvasive</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or MI</td>
<td>12%</td>
<td>16%</td>
<td>26% (10 to 39)</td>
<td>24 (14 to 68)</td>
</tr>
<tr>
<td>Death</td>
<td>4%</td>
<td>5%</td>
<td>32% (2 to 53)</td>
<td>58 (29 to 1061)</td>
</tr>
<tr>
<td>MI</td>
<td>9%</td>
<td>13%</td>
<td>28% (9 to 23)</td>
<td>29 (17 to 94)</td>
</tr>
<tr>
<td>Hospital readmission</td>
<td>45%</td>
<td>64%</td>
<td>31% (25 to 34)</td>
<td>6 (4 to 6)</td>
</tr>
</tbody>
</table>

†MI = myocardial infarction. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

**COMMENTARY**
The 2-year data from the FRISC-II study by Lagerqvist and colleagues provide convincing evidence that an early invasive approach provides superior outcomes for patients with unstable CAD. At 6 months, the FRISC-II data showed a reduction in the composite endpoint of death and MI in the invasive group. The event curves revealed that this benefit persisted at 1 year, with substantial reductions in death and MI. At 2 years, FRISC-II showed a sustained reduction in the individual endpoints of death, MI, and repeated hospitalization.

The TACTICS-TIMI-18 and RITA-3 studies confirmed the 6-month findings of FRISC-II, that an early invasive strategy reduces the combined endpoint of death, MI, and repeated hospitalization (1, 2). All 3 studies enrolled patients in the glycoprotein IIb/IIIa inhibitor and stent era. Furthermore, results from the TIMI-CONDOR trial suggest that a period of pharmacologic “cooling off,” as used in FRISC-II before proceeding with an early invasive strategy, is generally unnecessary (3).