Invasive strategy within 24 hours of thrombolysis reduced death, nonfatal reinfarction, and ischemia-induced revascularization in STEMI


**Question**
In patients with thrombolized ST-segment elevated myocardial infarction (STEMI), is a routine invasive strategy (IS) within 24 hours of thrombolysis (TL) better than an ischemia-guided conservative strategy (CS) for reducing clinical outcomes?

**Methods**
Design: Randomized controlled trial (Grupo de Análisis de la Cardiopatía Isquémica Aguda [GRACIA-1]).
Allocation: Concealed.*
Blinding: Blinded (data collectors, outcome assessors, data analysts, and data safety and monitoring committee).*
Follow-up period: 1 year.
Setting: 22 centers in Spain and Portugal.
Patients: 500 patients > 18 years of age (mean age 60 y, 86% men) who met criteria for STEMI and received TL within 12 hours of pain onset. Exclusion criteria included cardiogenic shock (sustained systolic blood pressure [BP] < 90 mm Hg with no response to fluids, or systolic BP < 100 mm Hg with vasopressors); pregnancy; and current use of anticoagulants.
Intervention: 248 patients were allocated to an IS (routine coronary angiography and adequate revascularization [REVASC] if feasible and indicated) within 24 hours after TL. Duration of heparinization was determined based on angiographic findings. The IS group also received oral ticlopidine, 500 mg, or clopidogrel, 300 mg, and had catheterization within 6 to 24 hours of TL. 252 patients were allocated to an ischemia-guided CS (prescience angiography and REVASC done only if spontaneous or stress-provoked ischemia occurred). Heparinization was maintained up to 48 hours after TL. All patients received chewable aspirin, 200 to 500 mg, intravenous TL, β-blockers, and angiotensin-converting enzyme inhibitors, as accepted.

**Outcomes:** Composite of death, nonfatal reinfarction, or ischemia-induced REVASC. Secondary outcomes included frequency of REVASC induced by spontaneous recurrence of ischemia during the index time in hospital, and death.

Patient follow-up: 98% (intention-to-treat analysis).

**Main Results**
Fewer IS-group patients had the composite endpoint than did CS-group patients (Table). Groups did not differ for death or nonfatal reinfarction (Table). More patients who received the CS had REVASC induced by spontaneous recurrence of ischemia (relative risk 4.94, 95% CI 2.09 to 11.66). The IS group had a shorter stay in hospital (mean index hospital duration 7.1 vs 10.5 d, P < 0.001). Groups did not differ for major bleeding or vascular complications.

**Conclusion**
In patients with thrombolized ST-segment elevated myocardial infarction, a routine invasive strategy within 24 hours of thrombolysis was better than an ischemia-guided conservative strategy for reducing death, nonfatal reinfarction, and ischemia-induced revascularization.

**Sources of funding:** Spanish Ministry of Health; Spanish Network for Cardiovascular Research; Spanish Society of Cardiology; Guidant; Lilly.

*See Glossary.

**Routine invasive strategy within 24 hours of thrombolysis vs ischemia-guided conservative strategy for ST-segment elevated myocardial infarction at 1 year†**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Invasive strategy</th>
<th>Conservative strategy</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite endpoint</td>
<td>9%</td>
<td>20%</td>
<td>54% (29 to 71)</td>
<td>9 (6 to 21)</td>
</tr>
<tr>
<td>Death or nonfatal reinfarction</td>
<td>7%</td>
<td>12%</td>
<td>41% (−4 to 66)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

*Composite endpoint = death, nonfatal reinfarction, or revascularization. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

**Commentary**
The efficacy and safety of modern percutaneous coronary intervention (PCI) (including stenting, thienopyridines, and glycoprotein IIb/IIIa–receptor antagonists) is leading to a convergence in management of acute coronary syndromes (ACSs). In STEMI, randomized trials that compare an interventional strategy with TL have shown 30% to 50% reductions in mortality, reinfarction, and recurrent ischemia with PCI (1). The FRISCII, TACTICS, RITA3, and VINO trials have shown that, compared with a CS, a routine IS reduced death and MI from 18% to 72% at 4 to 6 months (2). In the ISAR-COOL study, IS reduced death or large nonfatal MI by 50% at 30 days compared with 3 to 5 days of aggressive medical therapy before angiography in non–ST-elevation ACS (3). The GRACIA-1 study by Fernandez-Avilés and colleagues extends this observation to early-post-TL STEMI patients. Specifically, routine IS with REVASC (when indicated) reduced death, reinfarction, and ischemia-driven REVASC by 54% compared with ischemia-guided CS at 1 year. This finding with current PCI-stent technology contrasts with the lack of benefit or even increased hazard that was observed in older studies that used early routine balloon angioplasty after TL.

Because PCI technology has improved, the benefits now outweigh the procedural hazards in most patients with ACS. Recent and ongoing studies of drug-eluting stents, direct thrombin inhibitors, microvascular protection, and facilitated PCI strategies will yield additional improvements in the outcomes of routine IS. Except for patients at high risk for procedure-related complications and events, routine early angiography and myocardial REVASC should be embraced in the full spectrum of ACS patients.

*See Glossary.

**References**