Fondaparinux reduced death or reinfarction in acute ST-segment elevation myocardial infarction


**Clinical impact ratings:** Emergency Med ★★★★★☆, Hospitalists ★★★★★☆, Cardiology ★★★★★★☆, Hematol/Thrombo ★★★★★✩

**Question**
In patients with acute ST-segment elevation myocardial infarction (STEMI), is fondaparinux better than usual care for reducing death or reinfarction?

**Methods**
Design: Randomized placebo-controlled trial (Organization for the Assessment of Strategies for Ischemic Syndromes [OASIS-6]).
Allocation: Unclear allocation concealment.*
Blinding: Blinded (clinicians and patients).*
Follow-up period: 3 to 6 months.
Setting: 447 centers in 41 countries.
Patients: 12 092 patients (mean age 62 y, 72% men) who presented with STEMI within 24 hours of pain onset (shortened to < 12 h after about 4300 patients had been enrolled). Exclusion criteria were contraindication to anticoagulants, receipt of oral anticoagulants, or creatinine levels > 265.2 mg/dL (3.0 mmol/L).
Intervention: Patients were stratified by no indication for use of unfractionated heparin (UFH) or indication for UFH. Patients with no indication for UFH received fondaparinux, 2.5 mg subcutaneously (n = 2823), or placebo (n = 2835) for up to 8 days or hospital discharge. Patients for whom UFH was indicated received fondaparinux, 2.5 mg subcutaneously, plus UFH placebo (n = 3213) or fondaparinux placebo plus a bolus injection of UFH, 60 IU/kg, followed by an infusion of 12 IU/kg per hour for 24 to 48 hours (n = 3221).

**Outcomes:**
- A composite endpoint of death or reinfarction at 30 days. Secondary outcomes were the composite endpoint assessed at 9 days and at study end (3 to 6 mo) and bleeding.
- Patient follow-up: 99.7% (intention-to-treat analysis).

**Main results**
Patients who received fondaparinux had a lower incidence of the composite endpoint at 30 days than did patients who received placebo or UFH (Table). The reduction was also seen at 9 days and persisted to study end (Table). Groups did not differ for major bleeding using TIMI and OASIS-5 definitions (Table). The effect of fondaparinux was not heterogeneous between the 2 strata at 9 or 30 days, and effect sizes were almost identical by study end. In stratum 2 patients, no benefit of fondaparinux over UFH was seen in those having percutaneous coronary intervention (PCI).

**Conclusion**
In patients with acute ST-segment elevation myocardial infarction, fondaparinux reduced death or reinfarction better than usual care without increasing bleeding.

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*See Glossary.

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<th>Fondaparinux vs placebo or unfractionated heparin (UFH) for ST-segment elevation myocardial infarction†</th>
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<td><strong>Outcomes</strong></td>
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<td>Composite endpoint‡</td>
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<td>Severe hemorrhage (TIMI)</td>
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<td>Major bleeding (OASIS-5)</td>
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†TIMI = Thrombolysis in Myocardial Infarction; OASIS = Organization for the Assessment of Strategies for Ischemic Syndromes. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from hazard ratios and control event rates in article.

*Death or reinfarction.

**Commentary**
The OASIS-5 (1) and OASIS-6 studies legitimize fondaparinux, a synthetic factor Xa inhibitor, as a treatment option to UFH or low-molecular-weight heparin (LMWH) in acute coronary syndromes. In OASIS-6, fondaparinux was superior to placebo in reducing death or MI in STEMI, and inexplicably did so with lower bleeding rates. These results support the use of anticoagulant therapy in patients with STEMI not receiving reperfusion therapy, as recently shown with enoxaparin therapy in the ExTRACT-TIMI 25 study (3), where all patients received lytic therapy. Furthermore, the 8-day duration of fondaparinux therapy, instead of 2 days of heparin therapy, may explain its superiority. Both OASIS-6 and ExTRACT-TIMI-25 (3) suggest that anticoagulant therapy in STEMI should be continued for longer than the currently recommended 48 hours of UFH.

One might think that a less expensive, safer, and more effective drug would simplify management of patients with STEMI and become dominant or universal. But concerns about the use of fondaparinux in the cardiac catheterization laboratory may limit its use in North America. One might think that a less expensive, safer, and more effective drug would simplify management of patients with STEMI and become dominant or universal. But concerns about the use of fondaparinux in the cardiac catheterization laboratory may limit its use in North America.

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**References**