

Enoxaparin was more effective than unfractionated heparin in STEMI, regardless of type of fibrinolytic agent used

Giraldez RR, Nicolau JC, Corbalan R, et al. Enoxaparin is superior to unfractionated heparin in patients with ST elevation myocardial infarction undergoing fibrinolysis regardless of the choice of lytic: an ExTRACT-TIMI 25 analysis. *Eur Heart J*. 2007;28:1566-73.

Clinical impact ratings: Emergency Med ★★★★★☆ Hospitalists ★★★★★☆ Cardiology ★★★★★☆

QUESTION

In patients with ST-elevation myocardial infarction (STEMI), how effective and safe is enoxaparin compared with unfractionated heparin (UFH) when combined with fibrinolysis using either fibrin-specific agents or streptokinase (SK)?

METHODS

Design: Prespecified subgroup analysis of a randomized controlled trial (Enoxaparin and Thrombolysis Reperfusion for Acute MI Treatment—Thrombolysis in MI [ExTRACT-TIMI] Study 25).

Allocation: {Concealed}†.*

Blinding: Blinded (clinicians, patients, {data collectors, and outcome assessors}‡).*

Follow-up period: 30 days.

Setting: {674 centers in 48 countries}†.

Patients: 20 479 patients ≥ 18 years of age (median age 60 y, 77% men) who presented within 6 hours of the onset of STEMI symptoms and were scheduled to have fibrinolysis.

Intervention: Enoxaparin to hospital discharge (maximum 8 d) {*n* = 10 256}† or UFH for ≥ 48 hours {*n* = 10 223}†. 16 283 patients received a fibrin-specific lytic agent (69% alteplase, 25% tenecteplase, and 7% reteplase), and 4139 received SK (at the discretion of the treating physician).

Outcomes: Composite endpoint (death or MI), secondary composite endpoint (death, MI, or recurrent myocardial ischemia leading

to urgent revascularization), major bleeding, and net clinical benefit composite endpoint (death, MI, or major bleeding).

Patient follow-up: 99.7% (intention-to-treat analysis).

MAIN RESULTS

Enoxaparin reduced risks for the 3 composite endpoints, but increased risk for major bleeding, regardless of type of fibrinolytic agent used (although some outcomes did not reach statistical significance in the SK cohort) (Table). Tests for interaction between antithrombin group and type of fibrinolytic agent were statistically nonsignificant for all outcomes.

CONCLUSION

In patients with ST-elevation myocardial infarction, enoxaparin reduced risk for death or nonfatal myocardial infarction but increased risk for major bleeding more than unfractionated heparin regardless of type of fibrinolytic agent used.

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*See Glossary.

†Antman EM, Morrow DA, McCabe CH, et al. *N Engl J Med*. 2006;354:1477-88.

‡Information provided by author.

Enoxaparin vs unfractionated heparin (UFH) in patients undergoing fibrinolysis for ST-elevation myocardial infarction (MI) at 30 days[§]

Outcomes	Type of fibrinolytic	Enoxaparin	UFH	RRR (95% CI)	NNT (CI)
Death or MI	Fibrin-specific	10%	12%	20% (12 to 27)	42 (31 to 72)
	Streptokinase	10%	12%	15% (-4 to 31)	Not significant
Death, MI, or urgent revascularization	Fibrin-specific	12%	14%	21% (14 to 28)	33 (25 to 50)
	Streptokinase	12%	15%	20% (5 to 33)	34 (21 to 134)
Death, MI, or major bleeding	Fibrin-specific	11%	13%	16% (8 to 23)	49 (34 to 100)
	Streptokinase	12%	13%	10% (-9 to 25)	Not significant
				RRI (CI)	NNH (CI)
Major bleeding	Fibrin-specific	2.0%	1.2%	87% (42 to 147)	96 (57 to 198)
	Streptokinase	2.4%	2.0%	37% (-12 to 112)	Not significant

[§]Abbreviations defined in Glossary. RRR, RRI, NNT, NNH, and CI calculated from odds ratios in article, adjusted for geographic region; age; weight; location of the MI; history of angina, hypertension, or diabetes; time to fibrinolysis; and systolic blood pressure, heart rate, and Killip class at hospital admission.

COMMENTARY

Intravenous UFH is administered with alteplase, reteplase, and tenecteplase to prevent reocclusion of an infarcted artery after successful reperfusion for STEMI. For years, UFH was not routinely recommended in patients treated with SK because of the latter's long duration of action and anticoagulant properties. The trial by Giraldez and colleagues supports recent data on SK, suggesting that patients treated with any fibrinolytic agent should receive anticoagulation until hospital discharge.

The benefit of enoxaparin over UFH may have resulted from the longer duration of therapy (7 vs 2 d), rather than pharmacologic superiority. Subcutaneous administration twice daily and reliable anticoagulation, which eliminates the need for therapeutic monitoring, make enoxaparin easier to administer than intravenous UFH.

Bleeding rates were increased with enoxaparin, although dose adjustments in older patients reduced this risk compared with the higher rates seen in previous trials. However, additional dosing guidelines need to be developed for patients with decreased renal function (creatinine clearances of 30 to 60 mL/min) to achieve bleeding rates similar to UFH. A strategy of early cardiac catheterization, percutaneous coro-

nary intervention, and cessation of anticoagulation after the procedure would decrease the bleeding risk associated with longer duration of anticoagulation, make choice of agent less important, and facilitate early hospital discharge.

Fondaparinux is another anticoagulant awaiting regulatory approval for this indication. Advantages include once-daily subcutaneous dosing and lower cost than enoxaparin. In the OASIS-6 study (1), fondaparinux was similar to UFH in efficacy and bleeding risk. Although enoxaparin can be used to support percutaneous coronary intervention after fibrinolysis, an additional anticoagulant with anti-factor IIa activity (e.g., UFH, enoxaparin, or bivalirudin) is required with fondaparinux because of the risk for catheter thrombosis. Both agents are contraindicated in patients with severe renal impairment (creatinine clearance < 30 mL/min).

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Reference

1. Yusuf S, Mehta SR, Chrolavicius S, et al. *JAMA*. 2006;295:1519-30.