Low-Molecular-Weight Heparin as an Adjunct to Thrombolysis in ST Elevation Myocardial Infarction

The Enoxaparin and Thrombolysis Reperfusion for Acute Myocardial Infarction Treatment (ExTRACT)–Thrombolysis in Myocardial Infarction (TIMI)-25 study demonstrated that the administration of enoxaparin sodium, 30 mg intravenously, followed by subcutaneous injections of 1 mg/kg twice daily (dose modified in patients 75 years or older), compared with intravenous unfractionated heparin (UFH), 60 U/kg bolus (maximum 4000 U), followed by 12 U/kg/h (initial maximum, 1000 U/h, and subsequently adjusted to maintain an activated partial thromboplastin time of 1.5-2.0 times the control value), reduced the risk of nonfatal reinfarction in patients with ST elevation myocardial infarction (STEMI) treated with thrombolysis. Because the ExTRACT-TIMI 25 study seems likely to be the last large trial evaluating the efficacy and safety of low-molecular-weight heparin (LMWH) in patients with STEMI, we added the results of this pivotal 20 000 patient trial to our meta-analysis published in 2005. Our updated literature search identified 1 additional study by Wang and colleagues published in 2006 involving 186 patients with STEMI who were randomized to receive pantaparinux sodium or UFH; this study was also added to our meta-analysis.

Including the ExTRACT-TIMI 25 study and the study by Wang et al in our meta-analysis substantially increased the number of outcome events (number of reinfarctions increased from 253 events to 1043 events; death, from 412 events to 1911 events; and major bleeding events, from 206 events to 520 events), thereby greatly improving the precision of the estimates of effect size. A reduced risk of reinfarction became evident after the first trial in 2001, when 4078 patients had been randomized and 144 reinfarctions had occurred (Figure). Cumulative data from subsequent trials resulted in a narrowing of the 95% CI, but the point estimates remained similar. A statistically significant increase in the risk of major bleeding with LMWH compared with UFH was not evident until after the publication of the results of the ExTRACT-TIMI 25 study in 2006. There was a nonsignificant 8% lower risk of death observed with LMWH compared with UFH during hospitalization or at days 7 (P=.10) and 30 (P=.08) (Table).

All of the estimates obtained from our updated analysis are similar to our original meta-analysis, approximating a one-half reduction in reinfarction during hospitalization or at day 7 and a one-third reduction in reinfarction through day 30. There was no significant heterogeneity among the trials for any of the outcomes examined, and the data from this meta-analysis represent the best esti-
mates of the efficacy and safety of LMWH compared with UFH in patients with STEMI treated with thrombolysis.

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Patient- and Physician-Oriented Web Sites and Drug Surveillance: Bisphosphonates and Severe Bone, Joint, and Muscle Pain

Postmarketing surveillance and the determination of the real-world safety profile of prescription drugs is arguably flawed. Recent identification of significant adverse effects associated with newly-approved prescription drugs support the sometimes-held view that a new system needs to be introduced. The present voluntary system has not provided a sufficient early warning system, and some have called for active systems that probe for potential adverse effects of approved prescription drugs.1 Patient-oriented Web sites may provide an opportunity to identify potential adverse effects early in a drug’s postmarket history. In 2005, Wysowski and Chang2 published a letter regarding a series of case reports submitted to the Food and Drug Administration (FDA) on severe bone, joint, and muscle pain associated with the use of alendronate so-