Recent guidelines published by American College of Cardiology/American Heart Association Task Forces on the care of patients with acute coronary syndromes (ACS) include Level I recommendations for the use of antithrombin therapy. The antithrombin therapies used most often in ACS are unfractionated heparin (UFH) and low-molecular-weight heparins (LMWHs); the most commonly used LMWH is enoxaparin. For the physician caring for a patient with suspected or confirmed ACS in the Emergency Department (ED), initiation of antithrombotic therapy has traditionally been viewed as a very basic intervention. The choice between UFH and LWMH for the patient needing anticoagulation, however, often seems increasingly complicated. Despite the publication of many studies addressing this choice--more in the non-ST-segment-elevation (NSTEMI) ACS patient population than in those with ST-segment elevation (STEMI)--there remains much debate over the optimal agent for each management (interventional and medical) strategy.

STE ACS Patients The 2004 Guidelines recommend the use of UFH in STEMI patients, regardless of revascularization strategy, with a I-C rating. A small mortality benefit attributable to UFH use in patients managed with lytic agents has been demonstrated. Specifically, a bolus of 60U/kg (maximum 4000U) UFH followed by an infusion of 12U/kg/hr (maximum 1000U/hr) is recommended in STEMI patients receiving alteplase, reteplase, or tenecteplase (I-C). The activated partial thromboplastin time (aPTT) in these patients should be maintained at 1.5-2 times control (50-70 sec). Further, UFH should be given to patients receiving nonselective fibrinolytic agents (streptokinase, anistreplase, urokinase) if they are at high risk for systemic emboli (I-B), or to patients receiving streptokinase regardless (IIb-B). The different levels of support for UFH derive from the recognition that the nonspecific lytic agents produce a systemic coagulopathy and are themselves anticoagulants, while streptokinase and the more fibrin-specific agents are either procoagulants or induce little systemic anticoagulation.
In patients managed with primary PCI, weight-adjusted boluses of UFH 70-100U/kg are recommended by the Task Force, with the goal of maintaining an activated clotting time (ACT) in the catheterization lab of 250-350 seconds. The initial bolus-infusion regimen described above is appropriate for ED anticoagulation of the STEMI patient prior to PCI.

Cardiologists may choose to reduce heparin doses if platelet glycoprotein IIb/IIIa receptor (GP-IIb/IIIa) antagonists are being used. A baseline platelet count should be obtained in the ED before UFH is administered, to assist in subsequent monitoring for heparin-induced thrombocytopenia.

LMWHs receive less specific support in the 2004 STEMI Guidelines. There is a IIb-B recommendation in favor of a LMWH in patients younger than 75, with normal renal function (serum creatinine less than 2.5mg/dL in men or 2.0mg/dL in women), who are receiving lytic therapy.1 Enoxaparin (30mg IV bolus, then 1mg/kg subcutaneously every 12 hours), used with full dose tenecteplase, is the best-studied regimen in this regard; in ASSENT-3, patients under 75 years of age who received this combination had lower rates of 30-day mortality, inhospital reinfarction, and inhospital recurrent ischemia than did patients who received UFH and tenecteplase. This difference was not maintained at one-year follow-up. There are two Class III recommendations regarding LMWHs in STEMI: they should not be administered to patients over the age of 75 if receiving lytics (weight of evidence, B), and they should not be given to patients with significant renal dysfunction regardless of age (B).

The direct antithrombin agent bivalirudin is recommended in the 2004 STEMI Guidelines only as alternative to UFH in patients receiving streptokinase who are known to have a history of heparin-induced thrombocytopenia.

NSTE ACS Patients A number of important studies have addressed the choice between LMWH (namely, enoxaparin) and UFH in managing patients with unstable angina and NSTE myocardial infarction. There is a clear advantage (superior efficacy and equivalent safety) to enoxaparin in conservatively treated NSTE ACS patients; this is reflected by a I-A recommendation for enoxaparin as first-line therapy in the European Society of Cardiology guidelines. The preferred management of high-risk patients with NSTE ACS in the United States, however, is interventional. The most aggressive studies of interventional care of NSTE ACS--A to Z and SYN-ERGY--failed to conclusively demonstrate a clinically significant difference between the two anticoagulation options. Unlike earlier studies, however, these two studies may have confounded the impact of antithrombin therapy with early invasive management, improved stent technology, and adjunctive potent antiplatelet therapy.

The issue of performing PCI in patients anticoagulated with LMWH and therefore whose aPTT or activated clotting time (ACT) do not accurately reflect the extent of anticoagulation, was addressed by Collet et al, who showed in a study of 293 UA/NSTEMI patients that PCI can be performed safely with the usual dose of enoxaparin. Because the anticoagulant effect of UFH can be more readily reversed than that of LMWH, UFH is preferred in patients likely to undergo CABG within 24 hours, although the need for CABG cannot reliably be predicted in the ED.

The advantages of LMWH preparations vis-à-vis the ease of subcutaneous administration and the absence of a need for monitoring are particularly appealing in the ED. Furthermore, the LMWHs stimulate platelets less than UFH and are less frequently associated with heparin-induced thrombocytopenia. Finally, the response to enoxaparin may be magnified in patients who present at higher risk, and it appears from...
multiple studies\textsuperscript{12-15} that LMWH therapy can be safely combined with advanced antiplatelet therapy in patients with NSTE ACS. The usual dose of enoxaparin in NSTE ACS is 1mg/kg subcutaneously every 12 hours, but various IV doses have also been explored.\textsuperscript{11,15}

A systematic overview of 21,946 patients involved in the six major studies comparing enoxaparin and UFH in NSTE ACS, shows a composite superiority of enoxaparin in the prevention of the composite endpoint of death + MI at 30 days, with no significant differences in major bleeding or need for transfusion.\textsuperscript{19} There was no difference in mortality. This meta-analysis was complicated by frequent off-protocol crossover of patients’ antithrombin therapy, usually from enoxaparin to UFH at the time of intervention. Patients from these trials who received solely enoxaparin, when compared to those who received solely UFH, gained a statistically significant 14.6% relative risk reduction for 30-day death + MI, a nonsignificant trend towards mortality reduction, and no difference in rates of transfusion (Figures 1 and 2).\textsuperscript{19}

**SUMMARY**

In a majority of ACS patients encountered in EDs in the United States in 2004—conservatively managed NSTE ACS patients plus those STEMI patients who receive lytic therapy—there appears to be a consistent efficacy advantage to the use of enoxaparin over UFH, with equivalent bleeding risk between the two options. In patients with ACS managed...
interventionally, the data are not as clear, and it is appropriate for emergency physicians and interventional cardiologists to work together to develop institution-specific protocols, starting in the ED, that reflect the latest data and minimize the likelihood of antithrombin cross-over after ED management. The ease of use, convenience, and medical error reduction accompanying LMWH use in the ED are arguments in favor of that approach, regardless of subsequent strategy.

REFERENCES


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