THE CCU CORNER

Optimal Use of GPIIb/IIIa Inhibitors in High-Risk ACS

BY GEORGE PHILIPPIDES, M.D., AND ERIC H. AWTRY, M.D.

The Problem

The use of intravenous glycoprotein IIb/IIIa inhibitors has become an integral part of treating patients with acute coronary syndromes as part of an "invasive approach" consisting of early coronary angiography with an eye toward percutaneous or surgical revascularization. These potent antiplatelet agents have been evaluated in numerous large, randomized, placebo-controlled trials that included over 30,000 subjects with ACS.

But one important clinical question remains unanswered: Is the reduction in ischemic events by upstream use of GPIIb/IIIa inhibitors powerful enough to warrant the potential increased risk of hemorrhagic complications of prolonged therapy, or is it better to administer the agents just before stent deployment? Should the cardiologist on call treat appropriate high-risk ACS patients with GPIIb/IIIa inhibitors as soon as they are admitted to the CCU or telemetry floor, or should therapy be deferred until the interventional cardiologist identifies a culprit vessel for PCI?

The Evidence

The Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) Timing trial sought to answer this question by following 9,207 patients with moderate- and high-risk ACS features who were undergoing an invasive treatment strategy. They were randomized to routine upstream or deferred GPIIb/IIIa inhibitor therapy. Deferred use was associated with a statistically nonsignificant 12% increase in ischemic events, mostly unplanned revascularizations, and did not meet the predefined statistical criterion for noninferiority. However, the deferred strategy offered a significantly lower rate of major bleeding, so overall, there was no difference in the net clinical outcome (composite of death, MI, unplanned revascularization, and major bleeding) at 30 days.

Patients in the ACUITY Timing trial underwent PCI at a median of about 4 hours from randomization, so the duration of GPIIb/IIIa therapy in the "upstream" group was significantly shorter than what is generally seen in routine clinical practice in the United States. This abbreviated period of upstream therapy was probably too short to adequately assess the different strategies, and this trial should probably not change the use of GPIIb-IIIa inhibitors in most practices. The ongoing Early Glycoprotein IIb/IIIa Inhibition in Non-ST-Segment Elevation Acute Coronary Syndrome (EARLY ACS) trial is evaluating the efficacy of "upstream" versus "deferred" therapy in ACS patients who are scheduled to undergo "next day" cardiac cath, a setting more commonly seen in contemporary practice.

Several trials, including the ACUITY Strategy trial, have suggested that use of the direct thrombin inhibitor bivalirudin alone reduces ischemic complications to a similar extent as heparin plus GPIIb/IIIa inhibitors, while lowering the risk of major bleeding complications.

Clinical Experience

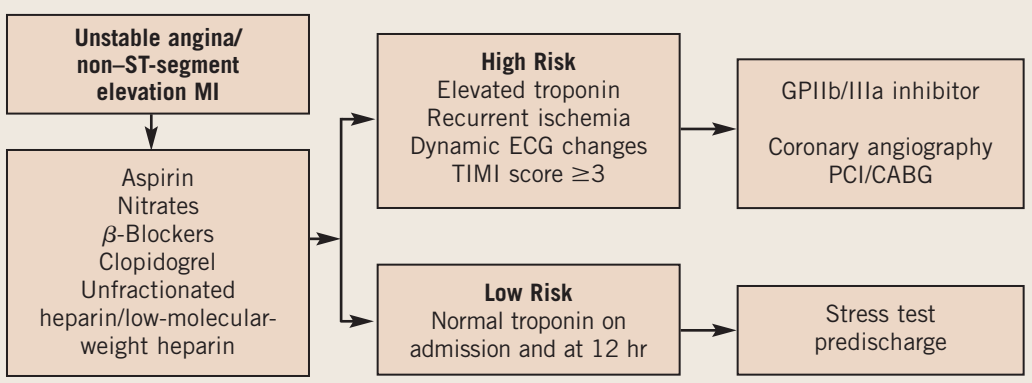
Based on the bulk of clinical data available to date, we recommend initially treating all ACS patients with aspirin (with or without clopidogrel), β-blockers, nitrates, and a heparin as per established American Heart Association/American College of Cardiology guidelines. Patients with high-risk features (including ischemic ECG changes, elevated serum troponin levels, recurrent/refractory ischemia) and patients with a history of coronary artery bypass graft surgery or PCI within 6 months are scheduled for early coronary angiography, within 24 hours when possible, with an eye toward revascularization.

In our hospital, GPIIb/IIIa inhibitors are started after the patient is admitted to the CCU or cardiology service or after the patient is seen by the cardiology consultant. We prefer that GPIIb/IIIa inhibitor therapy be started only after the cardiology service is contacted to assure proper use of these powerful and expensive agents and to help the noncardiology clinical teams arrange a timely cardiac catheterization. Electronic prompts accompany all elevated troponin values in the computer, which remind the clinician to contact the cardiology service if clinically indicated.

We prefer an upstream strategy of GPIIb/IIIa use, consisting of IV eptifibatide when coronary angiography/PCI cannot be performed within a 12- to 24-hour period.

We defer GPIIb/IIIa therapy until PCI is about to be performed in patients who are scheduled for "same day" catheterization or have a high risk for bleeding complications. ■

Recommended Strategy in ACS: Boston Medical Center Guidelines



Source: Dr. Philippedes and Dr. Awtry

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Myocardial Infarctions Rising in Nonagenarians as Ranks Swell

BY BRUCE JANCIN
Denver Bureau

NEW ORLEANS — The number of acute myocardial infarctions in 90- to 99-year-olds is rising sharply in tandem with rapid growth in the nonagenarian population, Dr. William J. Kostis reported at the annual meeting of the American College of Cardiology.

Percutaneous or surgical revascularization is performed much less frequently in nonagenarians with a first myocardial infarction than in younger myocardial infarction patients but is associated with a 66% reduction in 1-year all-cause mortality, compared with that in nonagenarians who don't get revascularized, added Dr. Kostis of the Robert Wood Johnson Medical School, New Brunswick, N.J.

He presented a study of all 10,213 nonagenarians hospitalized with a first myocardial infarction in New Jersey in 1986-2002. The data came from the Myocardial Infarction Data Acquisition System (MIDAS), a unique registry that captures all admissions for myocardial infarction statewide.

The annual number of nonagenarians with a first MI nearly doubled from 828 women and 426 men in 1986 to 1,598 women and 840 men in 2002. The incidence was relatively stable, however: 1.4% in 1986 and 1.5% in 2002 for women, and 1.8% in 1986 and 1.9% in 2002 for men.

In-hospital mortality following both Q wave and non–Q wave MI remained stable at about 35% and 15%, respectively, during 1986-2002. Yet overall in-hospital mortality in nonagenarian MI patients dropped over time, largely because the proportion of less deadly non–Q wave MIs rose. Dr. Kostis cited two possible explanations for this trend in an interview: increased use of sensitive serum markers of myocardial infarction such as troponin I allows earlier identification of infarcts before Q waves develop, and public education efforts aimed at getting patients to present to the hospital sooner after symptom onset.

Overall 1-year mortality was 52% in both men and women. This rate dropped by two-thirds in those who underwent coronary revascularization.

But while utilization of revascularization in nonagenarians increased over the study years, rates remained far lower than in younger MI patients.

For example, percutaneous revascularization was performed in about 5% of nonagenarian MI patients in 2002, compared with 30% of younger patients statewide. Dr. Kostis speculated that the low rates might be due to physician reluctance to intervene in the very elderly because of extensive comorbidities, or perhaps to less willingness of nonagenarians to provide informed consent, although there are no data addressing these possibilities. ■