Rethinking Loading Dose Clopidogrel in Light of Increased Bleeding Complications in Bypass Patients

The recent paper by Berger et al. (1) brings to light an important point that we think affects a majority of cardiologists and cardiac surgeons alike. The use of clopidogrel is now widespread, and the American College of Cardiology/American Heart Association (ACC/AHA) guidelines (2) highlight the indications for its use. However, more often we anecdotally observe indiscriminate use of loading dose clopidogrel, especially by emergency room physicians and internists, leading to delays in emergent or urgent coronary artery bypass grafting (CABG) and/or increased bleeding complications.

The guidelines (2) list a Class I indication for choosing between clopidogrel or a glycoprotein IIb/IIIa inhibitor when an early invasive strategy is chosen in patients with unstable angina/non–ST-segment elevation myocardial infarction. The guidelines do not specify the timing of its use, and herein is where the problem lies. It is reasonable to deduce from the current published data that (3) clopidogrel could be given during catheterization after coronary anatomy is determined, especially in patients going to catheterization within 6 h and particularly in those patients that might need bypass. These patients might be better served with more aggressive use of other anticoagulants and glycoprotein IIb/IIIa inhibitors that are easily reversible, thereby circumventing having to wait 5 days after loading dose clopidogrel.

A large study by Mehta et al. (4) showed that almost one-third of patients needed CABG within 5 days of clopidogrel use. These had increased need for red cell transfusions.

Studies are lacking on how to discriminate who might need CABG. Sadanandan et al. (5) did show that a validated risk scoring system might be applied to discriminate patients who might have a higher chance of needing CABG and thus holding clopidogrel use until coronary anatomy is defined.

The authors feel that more widespread use of risk scoring systems might improve patient outcomes for CABG and better discriminate the need for loading dose clopidogrel, especially because effective and quickly reversible anticoagulant agents have been safely used and widely studied (e.g., glycoprotein IIb/IIIa inhibitors).

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REFERENCES

Reply

We thank Drs. Patel and Mascarenhas for their insightful comments. Indeed, the management algorithm for patients with unstable angina/non–ST-segment elevation myocardial infarction does provide Class I options for platelet-directed pharmacotherapy on a background of aspirin, particularly among those in whom an early invasive strategy is selected according to validated risk scores (1). An ability to discriminate with a high degree of accuracy among patients likely to require surgical revascularization would undoubtedly facilitate a more targeted approach to pharmacotherapy, thereby avoiding delays, concomitant risks for recurring events (2), and perioperative hemorrhagic complications (3). Clearly the impact of treatment decisions is far-reaching, and might well become an even greater challenge with the introduction of increasingly robust platelet antagonists and their accompanying prolonged biological half-lives.

The preemptive identification of patients with surgical anatomy at the time of presentation is not a simple task, with existing models providing modest predictive accuracy and calibration (4,5). In addition, the ultimate decision to perform surgical over percutaneous revascularization is influenced by many factors—patient, family, physician, hospital, and healthcare system–specific considerations each apply. The risk of hemorrhage is also influenced by numerous variables not restricted to antithrombotic therapy (6).

The concomitant development and carefully designed investigation of short-acting or readily reversible antithrombotic agents, point-of-care measurement devices that permit a clear assessment of perioperative perturbation of hemostatic potential, and high-throughput platforms for advanced biomarkers to better predict patient-specific risk of bleeding (7) will collectively enrich and