spective there was no blinding of the nurses or clinicians to clopidogrel and aspirin exposure.

This lack of blinding is crucial to determine whether the main outcomes of the study are credible. The investigators acknowledged that recording of blood loss may be biased, but so could the decision to use blood and blood products (guidelines for the use of blood and blood products were not stated in their report). Also, no data were provided on the use of antifibrinolytic drugs. Use of drugs like aprotinin and tranexamic acid in patients with a high risk of bleeding is now well established, and this data would be relevant, particularly in patients who underwent re-exploration (2–4). Moreover, although the Society of Thoracic Surgeons' guidelines for re-exploration were used, these are open to interpretation, and the decision of a surgeon not blinded to clopidogrel therapy may be biased.

In addition, there was no measure of platelet function to demonstrate the fact that platelet aggregation was different between the two groups preoperatively and that this difference persists postoperatively and therefore directly accounts for the difference in postoperative bleeding and other outcome measures used. This is particularly important because the time from last clopidogrel dose to surgery ranged from 0 to 7 days, and in some patients, particularly those in whom clopidogrel therapy was stopped at least 5 days before surgery, other factors may have caused bleeding. In the Clopidogrel in Unstable Angina to prevent Recurrent Ischaemic Events (CURE) trial, patients in whom clopidogrel therapy was halted less than five days before surgery had a trend toward more major bleeding than those on placebo (9.6% vs. 6.3%, $p = 0.06$), whereas this trend was not seen in patients in whom surgery was performed more than five days after clopidogrel therapy was stopped (5).

In our experience, patients on clopidogrel and aspirin up to the time of surgery can be operated on safely provided a pro-coagulant drug like aprotinin or tranexamic acid is used intraoperatively. As discussed by Hongo et al. (1), antiplatelet therapy that is continued up to the time of surgery may be beneficial; in the case of aspirin it may improve mortality (6), and clopidogrel may reduce platelet activation owing to cardiopulmonary bypass (7,8). Until the question of the role of a pro-coagulant and platelet-protective drug (9) like aprotinin is defined, it is premature to conclude that surgery for patients with a history of clopidogrel exposure within seven days of operation should be delayed.

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REPLY

We are pleased that Dr. Akowuah and colleagues found our study (1) of interest. We acknowledge the inherent limitations of the study design, and we reiterate that further studies are needed to better define the role of clopidogrel before coronary artery bypass grafting (CABG) surgery. We believe it premature, however, to dismiss the credibility of the main outcomes of this study based on the lack of blinding. Chest tube output, the main measure of postoperative bleeding, is a highly objective and straightforward measurement. Because the nurses who recorded the amount of drainage were not aware of the questions being evaluated by the study, we have no reason to believe there was motive for misrepresentation. Reoperation for bleeding, the main clinical outcome, although a more subjective end point, was directed by institutional clinical guidelines. Patients went for reoperation when chest tube outputs either exceeded 300 ml over 2 consecutive h, or 500 ml over 1 h. As seen in Figure 1 of our study (1), patients with clopidogrel exposure who underwent reoperation all had 24-h chest tube outputs in excess of 4,000 ml, notably more than that of other patients.

The concern raised by Dr. Akowuah and colleagues regarding the use of antifibrinolytic agents is an important one. In our study, aprotinin was administered to eight patients (13.6%) exposed to clopidogrel and one patient (0.6%) without exposure. Any hemostatic effect of this agent would be expected to reduce adverse bleeding outcomes in the clopidogrel group, thus diminishing the differences seen between the groups. Ever since the completion of our study, we have started to use aprotinin routinely when immediate surgery is unavoidable in patients with clopidogrel exposure, and we are finding that perioperative bleeding is substantially reduced in most, but not all, cases. We echo the sentiment that the role of preoperative antiplatelet therapy in combination with antifibrinolytic agents is promising, but it is a role that is still undefined. Until further studies establish the efficacy of aggressive preoperative antiplatelet therapy, we maintain that caution should be exercised when patients ex-

posed to a combination of clopidogrel and aspirin present for CABG surgery.

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