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Reply to the Editor:

We thank Chahine and colleagues for their letter in response to our article discussing on-pump and off-pump coronary artery bypass grafting in patients with left main stem disease.¹ We never claimed that off-pump coronary artery bypass surgery is the best strategy for patients with left main disease. Our conclusion was that “off-pump coronary artery surgery in patients with left main stem disease is a safe procedure that will reduce morbidity and mortality and similar long-term survival compared with conventional on-pump revascularization.”

We are aware of the results of the 2 recent randomized studies referred to in the letter. The Coronary Artery Bypass Grafting Off or On Pump Revascularization trial² did not demonstrate any substantial difference between the 2 techniques, and the study concluded that “There was no significant difference between off-pump and on-pump CABG with respect to the 30-day rate of death, myocardial infarction, stroke, or renal failure requiring dialysis.” Those authors go on to say, “The use of off-pump CABG resulted in reduced rates of transfusion, reoperation for perioperative bleeding, respiratory complications, and acute kidney injury but also resulted in an increased risk of early revascularization.”² However, investigators in the Veterans Affairs Randomized On/Off Bypass trial³ concluded that the results of surgeries performed off-pump were inferior to conventional on-pump coronary artery bypass graft surgery. That study, as pointed out in

a recent editorial,⁴ had several major limitations. More than 70% of eligible patients (ie, scheduled for urgent or elective coronary artery bypass grafting) were excluded because of clinical reservations of the surgical team or small target vessels. This suggests inexperience on the part of surgeons in the trial, who were required to have performed just 20 off-pump coronary artery bypass procedures (OPCAB) to participate. Conversion to on-pump coronary artery bypass, which is known to increase morbidity and mortality, occurred in >12% of cases, much greater than the 1% to 3% reported by centers specializing in OPCAB. In the OPCAB group, >50% of patients received red blood cell transfusions, which contrasts with the 30% in previous randomized trials. Finally, only a small minority of the studied population were high-risk patients, a group more likely to benefit from OPCAB.

At the Bristol Heart Institute we have been performing OPCAB surgery for >17 years. We are a high volume center, with OPCAB accounting for 70% of all coronary procedures. We recognize that OPCAB surgery is a technically demanding procedure that should be performed in a high volume center to obtain optimal outcome. We think that OPCAB is a technique for the many and not the few (both surgeons and patients) but only with structured training and supervision in the right environment.⁴

Finally, with regard to the specific question on the incidence of stroke, in our article we reported a similar 0.4% incidence of transient cerebrovascular accident (CVA) in both groups and 0% and 0.9% of permanent CVA in the off-pump and on-pump groups, respectively. With off-pump procedures it is possible to minimize manipulation of the aorta because there is no requirement for cannulation when performing total arterial revascularization. However, in our series a majority of patients also received vein grafts that were anastomosed to the ascending aorta using

a side bite exclusion clamp. The incidence of CVA was low regardless if patients were operated on using the on-pump or off-pump technique. We have no reason to believe that this information is inaccurate given that it was obtained from our institution's prospectively collected database. Permanent CVA is a clearly defined event that is most unlikely to have been missed by our clinicians.

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VARIABLE ON TREATMENT PLATELET REACTIVITY IN CORONARY ARTERY BYPASS GRAFTING PATIENTS SUGGESTS THE NEED FOR PERIOPERATIVE PLATELET FUNCTION TESTING

To the Editor:

With great interest we have read a recent article from Deja and colleagues¹ on preoperative aspirin in an elective coronary artery bypass grafting population. The authors conducted a single-center, double-blind, randomized trial comparing its effects to placebo. The primary endpoints were more than 750 mL of bleeding during the first 12 hours postoperatively and

more than 1000 mL of total discharge from the chest drains. The secondary endpoint was a composite of cardiovascular death, myocardial infarction, and repeat revascularization. All patients discontinued aspirin 7 days before surgery. The night before surgery, they received either 300 mg of aspirin or placebo. Starting 6 hours postoperatively, a daily 300 mg dose of aspirin was continued in all patients. The study results in the aspirin group revealed a significant increase in postoperative bleeding and a long-term hazard decrease of nonfatal coronary events (myocardial infarction and repeat revascularization). We wish to point out a few confounders and current antiplatelet therapy issues that we believe readers should consider when interpreting the study results.

As acknowledged by the authors, the contemporary cardiac surgery practice encourages aspirin administration up until surgery. We noted that one quarter of the patients had undergone percutaneous coronary intervention 4 months (range, 2-10) before surgery. The recommendation guidelines for antiplatelet therapy after percutaneous coronary intervention suggest that most of those patients were receiving dual antiplatelet therapy after undergoing that procedure.² The authors do not mention if the patients were taking thienopyridines before surgery. If they were taking thienopyridines, how many days before surgery were they told to stop taking them? We consider this of great importance for the study end points because thienopyridines have a much greater influence on postoperative bleeding than aspirin.

A major confounder in the present study we consider to be the lack of platelet response to aspirin quantification. Recent evidence has shown significant individual variability in the response to aspirin and its link to outcomes.³ The terms "aspirin resistance" and "high on-treatment residual platelet reactivity" have been introduced. Accordingly, the reported prevalence of "aspirin resistance"

varies widely from less than 1% to 61%.⁴ Platelet function tests, such as whole blood platelet aggregometry and impedance aggregometry, quantify the aspirin response. Just recently, we published a study addressing the prevalence of "aspirin resistance" using a point-of-care platelet function analyzer in a coronary artery bypass grafting population.⁵ According to the platelet function results, individually tailored dose-dependent aspirin therapy could be recommended to reduce adverse effects (eg, bleeding) and preserve the beneficial effects. Continuous aspirin therapy up until surgery could prevent preoperative ischemic events, particularly in the residual platelet reactivity population. Preoperative discontinuation could be advised for those with a pronounced response to aspirin.

Although it is most likely true that patients taking preoperative aspirin bleed more than the patients who discontinued aspirin and that the incidence of the long-term composite of cardiovascular death, myocardial infarction, and repeat revascularization could be reduced, it is important to keep in perspective the limitations of this study. Additional research and implementation of platelet function tests in everyday clinical practice will only improve patient management and, hopefully, reduce morbidity and mortality.

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Reply to the Editor:

We would like to thank Kopjar and colleagues¹ for their interest in our study and comments on our report. Our study definitely shows that preoperative aspirin use increases postoperative bleeding but simultaneously provides some data to support the belief that it might be acceptable because of the improved long-term outcome.²

As rightly raised by Kopjar and colleagues,¹ aspirin resistance constitutes a major issue in modern cardiology and cardiac surgery. Its effect on clinical outcome has been established in many studies.³ The number of aspirin nonresponders and weak responders after coronary artery bypass surgery is estimated to be quite high.⁴ That we did not assess platelet function could, therefore, be considered a major limitation of the study. However, the beauty of a randomized design is that, by definition, it equalizes the confounders in both treatment arms. It is even more so when a study is double blinded and placebo controlled, as ours was. Thus, we believe the results of our study are sound and valid, even if the "aspirin resistance" was not assessed.

In addition, the increased bleeding incidence in patients receiving aspirin preoperatively in our study has