Coronary artery bypass grafting (CABG) aims to reduce immediate and longer-term risks of myocardial infarction and death in patients with coronary artery disease. CABG is, however, associated with its own thrombotic risks of perioperative myocardial infarction, stroke, pulmonary embolism, and bowel infarction. These risks are of major concern to the patient and referring cardiologist. Although antiplatelet drugs such as aspirin and clopidogrel can reduce thrombotic events, they might add to a competing risk of excessive bleeding during and after surgery. Excessive bleeding leads to intraoperative and postoperative hypovolemia and hypotension, delayed completion of surgery, and higher rates of blood transfusion, postoperative tamponade, and reoperation for bleeding. The bleeding risks most often trouble the cardiac surgeon, and the traditional practice has been to stop aspirin before elective cardiac surgery.

How can we resolve the competing risks of bleeding complications (not uncommon, but sometimes serious and life threatening) versus thrombotic complications in the immediate preoperative and early postoperative period (far less common, but usually serious)? Is it true that efforts to minimize perioperative thrombotic risk will invariably increase bleeding complications? Cardiologists and surgeons have different perspectives and may weigh these issues differently, and it remains unclear as to how most CABG patients would perceive these risks and what their preferences may be. Cardiologists in particular will be familiar with this issue in the nonsurgical setting. The decision to commence anticoagulation for chronic atrial fibrillation must consider the likelihood of embolic stroke versus the possibility of serious bleeding complications, such as intracerebral hemorrhage. The latter situation is guided by numerous large-scale clinical trials. This is not the case in the CABG setting.

Aspirin is associated with bleeding in both cardiac and noncardiac surgery, although the absolute detrimental effects seem to be modest. Béilisle and Hardy reviewed >50 studies that included >10,000 patients as well as their own data from 5426 patients operated on at the Montreal Heart Institute. They concluded that, although aspirin therapy increased postoperative blood loss, it was <300 mL—this should not increase use of blood products if a strict transfusion protocol were followed. Others have found a small increase in transfusion requirements with aspirin in CABG, 23% versus 19%, but more importantly, a significant increase in the rate of reoperation, 3.7% versus 2%; P < 0.05. In addition, there is a consistent link between both blood transfusion requirements and surgical reoperation and poor outcomes and decreased survival after cardiac surgery. Therefore, although bleeding complications may appear to be short lived, there may be ongoing adverse effects on immune function, graft patency, and other as yet undefined processes that follow CABG.

On the other hand, acute withdrawal of chronic aspirin therapy results in a prothrombotic state, potentially placing the perioperative patient at excess risk. This is clearly the case for those with recently implanted coronary stents, for which perioperative maintenance of dual antiplatelet therapy is recommended, the only exceptions being intracranial neurosurgery and perhaps prostatic surgery because of the much higher bleeding risks.

Should aspirin be stopped before CABG, and if so, when? Professional organizations differ in their recommendations, with some recommending stopping 3 to 5 days before surgery and others recommending 7 to 10 days. The present report by Jacob and colleagues indicate that late (within 5 days of CABG) discontinuation of aspirin is not associated with any measurable differences in thrombotic complications after CABG when compared with early (at least 6 days before CABG) discontinuation. Rates of a composite outcome that included in-hospital myocardial infarction, stroke, and mortality were comparable between groups: 1.7% versus 1.8%; P = 0.8. They did, however, identify a significant increase in transfusion requirements with late discontinuation, and it was suggested that there is an increased risk of reoperation of around 40% (3.4% versus 2.4%), although this was not statistically significant (P = 0.1) in their adjusted analysis.

The study of Jacob et al has several strengths. This was a large dataset from a respected institution. Although nonrandomized and retrospective, the authors adjusted for known confounders using propensity matching. But the study was not powered to identify clinically important outcomes such as reoperation, late myocardial infarction, or mortality. The authors chose to dichotomize their groups into early and late discontinuation using a cut-off value of 5 days. This is a rational choice in view of the discrepant guidelines from major professional bodies. However, it is widely ac-
knowledge that the effects and duration of aspirin, like clopidogrel, are variable and can be modified by genetic and other factors. There is some evidence demonstrating that platelet inhibition is minimal 4 days after stopping aspirin, so it is likely that some patients in the “late” discontinuation group had minimal platelet inhibition and therefore had reduced antithrombotic protection and bleeding risk. Conversely, some in the “early” discontinuation group may have had persistent platelet inhibition. This overlap of aspirin-platelet responsiveness will dilute the intergroup comparisons and reduce the capacity to characterize the true beneficial and adverse effects of aspirin in CABG. It does, however, represent real-world practice. Because of all the patients in this study received antifibrinolytic therapy with aminocaproic acid, this also may limit any bleeding risk with late discontinuation of aspirin. This was not a randomized trial. It is likely that the reasons for continuing or late stopping of aspirin are varied and may bias the results. These include oversight or confusion regarding date of CABG (a random effect?), a perception of low bleeding risk (biased in favor of late discontinuation of aspirin in the safety-bleeding analyses), or high thrombotic risk (biased against late discontinuation of aspirin in the efficacy analysis). The latter 2 issues are unlikely to be adequately adjusted for in the analysis.

Current high-level evidence regarding the best management of aspirin before elective CABG is limited to observational studies, with few randomized trials. In fact, a recent overview could only identify 10 relevant studies involving 1748 patients. The pooled results showed a significant increase in blood loss and transfusion requirements in the aspirin-treated patients, but no significant difference in reoperation rates. Perhaps the most important finding from the study was that the included studies were heterogeneous and of low methodological quality, with the authors concluding that high-quality prospective trials are needed to assess the effect of aspirin on important postoperative outcomes. A later overview that included 8 randomized trials but only 805 participants found that preoperative aspirin increased postoperative bleeding by 105 mL (95% CI: 19 to 191); \( P = 0.016 \), and reoperation (odds ratio 2.52 [95% confidence interval: 1.18 to 5.38]); \( P = 0.017 \). Once again, the authors called for a large randomized trial to determine the safety and efficacy of preoperative aspirin in cardiac surgery.

Current perioperative practice in CABG and noncardiac surgical practice is variable. Many cardiac surgeons and cardiac surgical institutions are happy for patients to continue their aspirin therapy up to the day of CABG; others strictly reinforce a discontinuation policy. The Society of Thoracic Surgeons have a Class IIa recommendation to stop aspirin 3 to 5 days before elective CABG in order to reduce transfusion-related complications, but for high-risk CABG they recommend continuation of aspirin. For those not on aspirin, they recommend commencing aspirin before elective or urgent/emergent CABG (Class IIa). In contrast, the American Society of Chest Physicians recommends continuing aspirin up to and beyond the time of CABG surgery (Grade 1C). The American College of Cardiology and American Heart Association guideline recommends that aspirin should be stopped 7 to 10 days before CABG. The underlying cause for such disparate guidelines is, of course, a lack of clear and compelling randomized trial data. One recent small trial suggests that aspirin may be beneficial and safe in the noncardiac surgical setting, and a large trial, POISE-2 (www.clinicaltrials.gov, ref NCT01082874), is underway to definitively test this hypothesis.

But what should we do in CABG? The study by Jacob et al provides some reassurance as to the comparable postoperative cardiovascular complications after CABG for both early and late discontinuation of aspirin. But the bigger question is whether or not we should be stopping aspirin at all, and whether or not antifibrinolytic therapy can help prevent any bleeding complications of aspirin while at the same time continuing its antithrombotic benefit. These are the aims of the in-progress ATACAS trial. If aspirin used on the day of CABG leads to a reduction in thrombotic complications, without major bleeding complications, then there will be no need to stop aspirin before elective CABG.

Disclosures
Dr Myles is a principal investigator for the Australian National Health and Medical Research Council-funded ATACAS trial, an investigator-initiated factorial trial investigating the safety and effectiveness of aspirin and tranexamic acid in coronary artery surgery.

References

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Stopping Aspirin Before Coronary Artery Surgery: Between the Devil and the Deep Blue Sea
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