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Commentary: Enough is enough, but when is enough enough?

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“You never know what is enough unless you know what is more than enough”

—William Blake (1757-1827)

The use of preoperative clopidogrel in patients with acute coronary syndrome (ACS) undergoing coronary artery bypass grafting (CABG) surgery has dogged the lives of cardiac surgeons. There is abundant evidence consistently showing that this strategy is associated with higher rates of bleeding and re-opening, as well as other adverse events.¹⁻³ In this issue of the *Journal*, Qu and colleagues⁴ present a well-executed retrospective study with a large sample size of 5543 patients. The authors used inverse probability weighting, which is a robust statistical analysis method to disconnect confounders and treatment.⁵ To no one's surprise, this study showed a significantly increased risk of the composite of major adverse cardiac and cerebrovascular events, major bleeding, and transfusion in patients with ACS and preoperative exposure of clopidogrel within 5 days of CABG. Most of these findings are not novel because they have been consistently demonstrated by numerous studies in the past, as summarized in Table E1 in this study.⁴

What was compelling for this reader was that the primary outcome of this study was predominantly driven by stroke, with most events presumed to be ischemic because only 2 patients had intracranial hemorrhages. This is counterintuitive because one would expect that the use of preoperative clopidogrel would reduce the risk of ischemic stroke because of its antithrombotic effect. The authors speculated that the increased risk of stroke in these patients could be a sequela of bleeding complications (reoperation and bleeding).

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CENTRAL MESSAGE

It is well established that preoperative clopidogrel use in patients with ACS undergoing CABG is associated with higher rates of complications. We need to move on.

Regardless, the message is the same; clopidogrel should be discontinued preoperatively in patients with ACS undergoing CABG. Why is this not gaining traction? Are the current findings not anticipated or not justified based on what we already know at this time? Are we hoping if we keep repeating this natural experiment, the results might change? What are the factors that are preventing us from dealing with this?

We need to focus our attention and effort in developing individualized care for each patient. For example, development of specific risk-stratification tools and implementation of platelet function testing might help in determining the best timing to discontinue clopidogrel or any other antiplatelet agent in patients with ACS undergoing CABG. The duration of clopidogrel discontinuation should not be a merely arbitrary number that fits all patients. In addition, the role of intravenous antiplatelet agents with a shorter half-life as a means to transition to CABG should be encouraged.

As far as we are concerned, this issue has been answered. We hope the next questions address the mechanisms, not just of the adverse outcomes, but of our health systems that inefficiently repeat history.

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Commentary: Rushing to revascularize may be risky, but one size does not fit all

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Optimal timing of coronary artery bypass grafting (CABG) in the context of acute coronary syndrome (ACS) and dual antiplatelet therapy remains controversial and practice patterns vary. Despite consensus among guidelines that minimum 5-day preoperative clopidogrel cessation is ideal,^{1,2} risk of adverse events during the washout period is dependent on coronary anatomy. Further, baseline bleeding risk varies among patients and the evidence for optimal timing of CABG is mixed.³⁻⁵ Clopidogrel cessation decreases the risk for bleeding and resultant secondary complications, but comes at the cost of a potentially increased risk of recurrent myocardial infarction (MI) or other thrombotic events. We congratulate Qu and colleagues⁶ for addressing this controversy.

Their study is a single-center retrospective observational analysis of 5543 patients undergoing post-ACS CABG.

CENTRAL MESSAGE

Proceeding with CABG before clopidogrel washout is associated with adverse perioperative outcomes. Is this the place for patient-tailored decision making?

Using institutional registry data, the authors compared those receiving clopidogrel within 5 days of CABG (n = 820; 15%) versus those for whom clopidogrel was stopped >5 days in advance (n = 4723; 85%). The primary outcome, a composite of stroke, all-cause mortality, and MI at 30 days, was worse, not better, in the late cessation group (odds ratio, 1.63; 95% confidence interval, 1.16-2.29; $P = .005$). The same pattern was seen in all secondary 30-day outcomes in descending order of effect size, including stroke, transfusion, major bleeding events (defined by validated CABG-specific bleeding criteria⁷), and re-exploration for bleeding. In other words, early cessation of clopidogrel was associated with both a reduction in bleeding and a reduction in thrombotic events. The authors implemented inverse probability treatment weighting to account for baseline differences and sensitivity analysis with propensity score matching reinforce the robustness of the findings. The small number of patients who did not undergo CABG due to cardiovascular events during the preoperative waiting period were also included

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