Authors' Reply

To the Editor:

We appreciate the insightful comments by Petricevic et al, and the opportunity to respond to their letter. Regarding the effect aspirin had on outcomes in our study, in a second arm of our study not yet published, we conducted aspirin responsiveness testing using the VerifyNow Aspirin Assay (Accumetrics, San Diego, CA). Our results were presented at the 2013 American Heart Association Scientific Sessions,[1] and reveal that aspirin responsiveness units (ARU) were significantly lower in patients whose last dose of aspirin was <24 hours prior to coronary artery bypass grafting (CABG) vs ≥ 24 hours prior to CABG (443 ± 65 vs 526 ± 98 ARU; $P < 0.004$). Additionally, higher ARU was associated with less perioperative bleeding, and patients below the ARU 412 cut point (defined as the lowest ARU tertile) were more like to have at least 1 platelet transfusion (54% vs 9%, $P = 0.005$) or major bleeding (25% vs 0%, $P = 0.026$) within 24 hours of surgery. These results are consistent with other studies of perioperative bleeding and aspirin responsiveness testing prior to CABG.[2] Thus, the importance of aspirin responsiveness has not been overlooked by our group and is being further investigated.

As we acknowledged in our article, we were unable to perform multivariable adjustment for potential confounders given the small sample size inherent to this pilot study. Although this does limit our availability to draw definitive conclusions from our results, baseline characteristics, procedural characteristics, and periprocedural medication use were fairly consistent across P2Y12 reaction unit (PRU) subgroups, adding some validity to our findings. Our results set the stage for a larger study, in which multivariable adjustment could be performed. In such a study, a combined PRU and ARU analysis would be especially interesting, as it would help elucidate the independent (or perhaps combined) effects of $P2Y_{12}$ receptor inhibition and aspirin responsiveness on perioperative bleeding events during surgery.

We agree that moving forward, studies in this area should utilize a uniform definition of perioperative bleeding, as heterogeneity in end-point definitions will limit the ability to pool results between studies.[3,4] Further, we generally agree with the thoughtful considerations for future studies outlined by Petricevic et al, especially the need for larger studies to better define a "therapeutic window" of platelet function that minimizes ischemic risk and potential harm from major bleeding in patients exposed to antiplatelet agents prior to surgery. We believe our study moves the

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field forward in this direction, as it is one of the first to use a point-of-care assay to define a specific threshold of $P2Y_{12}$ reactivity at which serious perioperative bleeding events can be minimized.

Our research highlights that there is an unmet need to personalize surgical delay in patients exposed to antiplatelet agents prior to surgery. A large, prospective, strategy-based study is needed to determine if selecting patients for surgery based on a PRU threshold could be noninferior or even reduce bleeding events compared to a uniform 5- to 7-day waiting period prior to CABG. It is our hope that such a study could allow the field to embrace an individualized waiting period prior to surgery based on platelet function testing rather than a one-size-fits-all approach. Such an approach holds the potential to improve patient outcomes by minimizing surgical delay, reducing surgical blood loss and blood product transfusion, and possibly reducing healthcare expenditures in the process.

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