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# Bridging to Surgery With Intravenous Platelet Inhibitors: Are We Treating the Patient or Ourselves?

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Dual antiplatelet therapy (DAPT) remains a cornerstone of medical therapy to minimize major adverse cardiovascular events (MACE), including stent thrombosis, after percutaneous coronary intervention (PCI). As interruption or early discontinuation of DAPT after PCI significantly increases the risk of MACE [1], the decision to discontinue DAPT in the perioperative setting for either cardiac or non-cardiac surgery remains a clinical dilemma. In an effort to mitigate the increased risk of early discontinuation of DAPT before surgery, clinicians have adopted a "bridging" strategy in which 1) thienopyridines such as clopidogrel and prasugrel, along with the oral P2Y12 inhibitor ticagrelor, are held before surgery; 2) short-acting intravenous platelet inhibitors are initiated with either glycoprotein IIb/IIIa inhibitors such as eptifibatide and tirofiban or the P2Y12 inhibitor cangrelor; and 3) the intravenous platelet inhibitor is discontinued shortly before surgery, with reinitiation of oral antiplatelet therapy shortly after surgery. This strategy was assessed in the BRIDGE trial, in which patients with acute coronary syndrome treated with PCI and stent placement discontinued oral thienopyridines before cardiac surgery and were randomized to either placebo or cangrelor [2]. Cangrelor did not increase the risk of periprocedural bleeding while it maintained adequate platelet inhibition prior to surgery [2]. However, this strategy is costly not only given the increased cost associated with the prolonged infusion of intravenous platelet inhibitors but also because of the prolonged hospitalization before surgery, as the infusion is administered in the inpatient setting. Furthermore, there is a paucity of data regarding whether this bridging strategy decreases perioperative MACE in prospective randomized controlled trials. In fact, while oral antiplatelet therapy was shown to increase the risk of surgical bleeding, there was no evidence that continuation of oral antiplatelet therapy in the perioperative setting had any impact on reducing myocardial infarction, stroke, or mortality [3]. Additionally, the incidence of thrombotic MACE in the setting of antiplatelet therapy interruption for surgery within 2 years of PCI is quite low, at 1% [4].

In this issue of the journal, Dargham and colleagues present an observational study of 60 patients who underwent bridging with intravenous antiplatelet therapy with cangrelor (n=8), tirofiban (n=4), and eptifibatide (n=46) before undergoing either cardiac (n=15) or non-cardiac surgery (n=45) [5]. The patients in this study are representative of the complex patients we see in the everyday clinical setting and have significant comorbidities. In fact, the majority of patients in this study were undergoing bridging for elective surgery and underwent bridging with intravenous antiplatelet therapy more than 6 months after their index PCI, suggesting that the reason for bridging included prior complex PCI or other clinically pertinent indications. The study demonstrated that intravenous platelet inhibition prior to surgery did not mitigate the risk of perioperative thrombotic events, as there were at least 5 patients who experienced myocardial infarction within 30 days. Furthermore, a large number of individuals developed significant bleeding in the surgical setting. These data appear consistent with a prior meta-analysis that suggested that bridging with glycoprotein IIb/IIIa inhibitors did not abolish the risk of thrombotic MACE but was associated with increased risk of bleeding [6]. The authors provide an excellent commentary on the struggle physicians face with balancing the risk of bleeding and prevention of thrombotic events while also highlighting the issue of cost, which should definitely be considered given the importance of resource utilization [5].

Although a bridging strategy has its limitations, it is important to consider alternative strategies to minimize the risk of perioperative thrombotic events and bleeding. The ability to reverse the antiplatelet effects of ticagrelor may potentially obviate the need to discontinue ticagrelor several days before surgery. A novel ticagrelor reversal agent, PB2452, resulted in immediate and sustained reversal of the antiplatelet effects of ticagrelor within 5 minutes after administration of the bolus, and the reversal of platelet inhibition was maintained during the duration of infusion [7]. The reversal agent was tested in healthy volunteers, and thus, the actual safety of ticagrelor reversal in the perioperative setting remains to be studied. While the manuscript by

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Dargham and colleagues [5] continues to fill in our clinical experience in "real world" patients receiving intravenous platelet inhibition for bridging to surgery, these data highlight the need for well-conducted randomized controlled trials comparing a bridging strategy to cessation of DAPT and continuation of aspirin monotherapy. I think it is useful to keep these data in mind when formulating therapeutic care plans for patients awaiting surgery, as bridging with intravenous platelet inhibitors may increase bleeding risk without mitigating the risk of stent thrombosis. We must ask ourselves whether we are really treating the patient or simply our fear of stent thrombosis.

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