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CORRESPONDENCE

Anti-platelet therapy and the anaesthesiologist: controversies and unresolved clinical dilemmas continue

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Editor - Reducing platelet function with antiplatelet agents is one of the most important factors in the prevention and treatment of thrombotic vascular events in patients affected by atherosclerosis. Aspirin is the primary medication used for this indication, however many patients require dual antiplatelet therapy (DAPT) consisting of aspirin and a $P2Y_{12}$ receptor inhibitor. Patients receiving DAPT are more and more frequently presenting for non-cardiac surgery (NCS) and perioperative management.

Anaesthesiologists are repeatedly faced with the dilemma of what to do with DAPT in the perioperative period. It is a tricky decision whether to continue DAPT in order to protect against thrombo-embolic events or to stop DAPT before surgery to reduce the risk of significant perioperative bleeding, especially since there is limited evidence. Recent studies provides some evidence describing outcomes in patients treated with aspirin or DAPT. Results of the POISE-2 trial clearly indicate that continuing low-dose aspirin caused an increase in major bleeding during the perioperative period.[1] A Canadian study analysing 201 patients who underwent NCS after prior percutaneous coronary intervention (PCI) showed that incidence of major adverse cardiac events (MACE) was high (20%), despite adequate antiplatelet therapy, and there was no association between preoperative platelet inhibition and incidence of MACE.[2] A recently published European study (OBTAIN) analysing a larger cohort of post-PCI patients suggested lack of protection by perioperative DAPT, while risk of bleeding was increased.[3] In contrast to the Canadian study, the OBTAIN trial did not standardize monitoring for MACE so may have underestimated the rates of MACE.

This issue of *British Journal of Anaesthesia* contains another paper contributing to the important discussion of perioperative DAPT management.[4] The authors of this paper clearly and concisely described the perioperative management of these high-risk patients, and analysed the perioperative course in seven patients receiving DAPT who required surgical intervention after recent intracranial stenting of an aneurysm. In preparation for their surgical procedure, oral therapy was interrupted and bridged with an intravenous $P2Y_{12}$ receptor inhibitor (cangrelor). Platelet inhibition was measured with the point of care device VerifyNow™ (company, location). None of the patients experienced bleeding or thrombo-embolic complications; one patient suffered from rupture of a giant aneurysm, an event most likely unrelated to the study protocol. This is the first description of patients with recent intracranial stenting who were successfully managed with bridging without increasing the risk of bleeding. We look forward to confirmation of these promising results on a larger patient cohort.

As clinical anaesthesiologists we are not fully satisfied with current guidelines for managing DAPT.[5] We know that keeping patients on DAPT post-PCI is not protecting patients from the high incidence of MACE or bleeding perioperatively. Perhaps using bridging with short acting antiplatelet agents is the solution to minimise bleeding risk while maintaining antithrombotic protection throughout the perioperative period? Hopefully, future, larger studies on patients receiving DAPT after intracranial stenting and undergoing NCS will provide high-quality evidence capable of informing future updated guidelines.

Declaration of interest

The authors declare that they have no conflicts of interest.

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Bridging antiplatelet therapy with cangrelor in patients with recent intracranial stenting undergoing invasive procedures: a prospective case series

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Editor-Dual antiplatelet therapy (DAPT) with aspirin and an oral $P2Y_{12}$ receptor antagonist is the standard of care to prevent thromboembolic events for patients undergoing intracranial artery stenting for aneurysm treatment.[1,2] The risk of stent thrombosis is particularly high during the first weeks, especially when antiplatelet therapy is prematurely discontinued. Therefore, DAPT is prescribed for 3-12 months followed by aspirin alone for several months.

Some patients require unplanned invasive procedures early after stent implantation. For moderate and high bleeding risk procedures, discontinuation of $P2Y_{12}$ antagonists is needed to restore platelet function,[3] but exposes patients to an increased risk of thromboembolic events. To reduce this risk, bridging with cangrelor might be proposed by analogy to patients at very high risk of coronary stent thrombosis for whom cardiologists recommend a bridging strategy based on i.v. antiplatelet agents including cangrelor.[4,5] Cangrelor is an i.v. $P2Y_{12}$ antagonist, characterised by potent, predictable, and reversible platelet inhibition, with a quick onset and offset of action. The BRIDGE trial demonstrated that cangrelor could be safely used in patients with coronary disease to maintain platelet inhibition, despite discontinuation of oral $P2Y_{12}$ antagonists before cardiac surgery.[6]

We report the first experience of bridging antiplatelet therapy with cangrelor in patients with recent intracranial stenting who were undergoing an invasive procedure requiring $P2Y_{12}$ antagonist discontinuation. We aimed to assess the efficacy of cangrelor infusion in maintaining platelet inhibition during discontinuation of the $P2Y_{12}$ antagonist according to a standardised cangrelor bridging protocol directly adapted from the BRIDGE trial.[6] This prospective, observational study was conducted from July 2017 to July 2018 in two centres in France, after institutional review board approval Fondation Rothschild, Paris, France (CE_20171208_2_AGR). All patients provided written informed consent.

Consecutive patients managed with the standardised cangrelor bridging protocol were included. This protocol was dedicated to patients receiving DAPT (aspirin associated with clopidogrel, prasugrel, or ticagrelor) for intracranial stenting with high thromboembolic risk and undergoing any unplanned invasive procedure requiring $P2Y_{12}$ antagonist discontinuation (i.e. moderate and high bleeding risk procedures).[7] High thromboembolic risk was defined as an intracranial stent implantation within 1 month, or within 3 months if other risk factors were associated.[8]

The protocol included platelet function testing at 12 predefined time points (Fig. 1), using, as in the BRIDGE trial, the validated point-of-care VerifyNow $P2Y_{12}$ Assay (Werfen, Le Pré-Saint-Gervais, France)[6,11,12] that measures platelet aggregation to assess platelet reactivity to $P2Y_{12}$ antagonists, quantified as $P2Y_{12}$ reaction units (PRU). Patients with PRU value below 240 were considered as responders to $P2Y_{12}$ antagonists, either cangrelor or oral $P2Y_{12}$ antagonist. Collected data included patient characteristics, stents and DAPT, antiplatelet agent management, and platelet function testing. Clinical thromboembolic or bleeding complications, cerebral CT scan results, and cangrelor-related side-effects (dyspnoea, thrombocytopenia) were recorded from protocol initiation to 7 days after surgery. Descriptive statistics used median (minimum-maximum) for quantitative variables and numbers (%) for qualitative ones.

The standardised protocol was applied seven times for five high bleeding risk procedures and two moderate bleeding risk