BJA

British Journal of Anaesthesia, 116 (4): 493–500 (2016)

doi: 10.1093/bja/aev556
Advance Access Publication Date: 16 February 2016
Cardiovascular

Effectiveness of platelet inhibition on major adverse cardiac events in non-cardiac surgery after percutaneous coronary intervention: a prospective cohort study

M. Wąsowicz[1,2,3], S. Syed[4], D. N. Wijeysundera[1,3,5,6], Ł. Starzyk[1], D. Grewal[1], T. Ragoonanan[1], P. Harsha[4], G. Travis[4], J. Carroll[1], K. Karkouti[1,2,3,6] and W. S. Beattie[1,2,3,*]

[1]Department of Anesthesia and Pain Management, Toronto General Hospital/University Health Network, 200 Elizabeth Street, Toronto, ON, Canada M5G 2C4, [2]The Peter Munk Cardiac Centre, Toronto General Hospital, 200 Elizabeth Street, Toronto, ON, Canada M5G 2C4, [3]Department of Anesthesia, University of Toronto, 12 Floor, 123 Edward Street, Toronto, ON Canada M5G 1E2, [4]Department of Anesthesia Hamilton Health Sciences Corporation, McMaster University, 237 Barton Street East, Hamilton, ON, Canada L8L 2X2, [5]Li Ka Shing Knowledge Institute of St Michael's Hospital, 209 Victoria Street, Toronto, ON, Canada M5B 1T8, and [6]Institute of Health Policy Management and Evaluation, 155 College Street, Toronto, ON, Canada M5T 3M6

*Corresponding author. E-mail: scott.beattie@uhn.ca

Abstract

Background: Platelet inhibition is mandatory therapy after percutaneous coronary intervention (PCI). Withdrawal of oral antiplatelet agents has been linked to increased incidence of postoperative adverse cardiac events in post-PCI patients having non-cardiac surgery (NCS). There is limited knowledge of temporal changes in platelet inhibition in this high-risk surgical population. We therefore performed a multicentre prospective cohort study evaluating perioperative platelet function and its association with postoperative major adverse cardiac events (MACE).

Methods: In 201 post-PCI patients having NCS, we assessed the association between platelet function and postoperative MACE. We performed perioperative platelet function testing using a platelet mapping assay (PMA). Troponin-I was measured every 8 h for 2 days, then daily until day 5. Myocardial infarction was assessed using the third universal definition. We used multivariable logistic regression to assess the association between platelet inhibition and MACE.

Results: Major adverse cardiac events occurred in 40 patients within 30 days of surgery. Thirty-two of these events were non-ST-elevation myocardial infarction, four ST-elevation myocardial infarction, and four exacerbation of congestive heart failure. We were unable to show an association between platelet inhibition and MACE. The PMA showed declining levels of platelet inhibition the longer the antiplatelet therapy was withheld before surgery. Logistic regression did not show an association between preoperative platelet function or the type of stent and MACE. We found an increased cardiac risk of MACE after surgery within 6 weeks of PCI.

Conclusions: The incidence of MACE in patients undergoing NCS after previous PCI is high in spite of adequate perioperative antiplatelet therapy.

Accepted: December 4, 2015

Clinical trial registration: NCT 01707459 (registered at http://www.clinicaltrials.gov).

Key words: major adverse cardiac events; non-cardiac surgery; percutaneous coronary intervention; platelet inhibition

Editor's key points

- Discontinuation of antiplatelet therapy after percutaneous coronary intervention (PCI) has been implicated in major adverse cardiac events (MACE).
- The association between platelet function and MACE was assessed in a prospective cohort study of 201 post-PCI subjects undergoing non-cardiac surgery.
- There was no association between preoperative platelet inhibition and the high incidence of MACE following PCI, with no evidence of in-stent thrombosis.

Approximately 2 million individuals undergo percutaneous coronary intervention (PCI) each year in Europe and North America.[1 2] A significant proportion of post-PCI patients (5–20%) present for non-cardiac surgery within a year.[3] Numerous retrospective observational studies have drawn attention to the increased risk of major adverse cardiac events (MACE) in this patient population[4–7] that has been linked to the preoperative cessation of antiplatelet therapy.[4]

The optimal antiplatelet regimen for these high-risk patients, one that balances the risk between perioperative bleeding and stent thrombosis, is currently unknown. Literature on prospective studies investigating the problem is limited.[8–10]

The past and present American College of Cardiology/American Heart Association (ACC/AHA) guidelines for management of cardiac patients undergoing non-cardiac surgery propose an algorithm to manage post-PCI patients.[11 12] These recommendations suggest that the management of elective surgery should be based on the following factors: the interval from stent implantation, the type of stent, and antiplatelet therapy. Recommendations include postponing elective non-cardiac surgery for 30 days after bare metal stents (BMS) and 12 months after drug-eluting stents (DES; III class of recommendation, level of evidence B), and that a consensus decision regarding the relative risks of continuing antiplatelet therapy can be useful (IIa, level C). Additionally, we could find no compelling evidence for a routine antithrombotic bridging strategy upon preoperative discontinuation of oral antiplatelet agents.

It is well recognized that non-cardiac surgery in patients with previous PCI is associated with excessive cardiac events. We therefore undertook this prospective, multicentre cohort study to evaluate the elements of the ACC/AHA guidelines (platelet inhibition, timing, type of stent, and patient characteristics) on the incidence of MACE. The primary objective of this study was to test the hypothesis that adequate platelet inhibition is associated with reduced incidence of MACE.

Methods

The investigation was registered at http//www.clinicaltrials.gov (NCT 01707459) and conducted according to the established guidelines of proper conduct of medical research involving human subjects. The study protocol was reviewed and approved by the local Research Ethics Boards of each participating hospital (University Health Network, one hospital; Hamilton Health Sciences Corporation, two hospitals). Patients were recruited to participate in the study during their visit in the pre-anaesthesia consultation clinics (same-day admission patients) or in the hospital (inpatients). Written informed consent was obtained from all subjects participating in the study. All aspects of patient privacy and confidentiality were preserved.

Inclusion and exclusion criteria are presented in Supplementary data, Table 1. Briefly, we recruited subjects who received BMS within 2 yr of scheduled surgery or DES within any time frame.[13 14] All subjects were instructed to continue their antiplatelet agents until the date of surgery. If the subjects presented a high risk of intraoperative bleeding as judged by the surgeon, the surgeon had an option to discontinue dual antiplatelet therapy or to maintain aspirin until the day of surgery.

Outcomes

The primary outcome of interest was MACE, which was defined as any of the following events: (i) myocardial infarction (MI) as defined by the third universal definition;[15] (ii) exacerbation of congestive heart failure; (iii) stent thrombosis; (iv) need for revascularization; and (v) death within 30 days of surgery. Full definitions of the end points are presented in Supplementary data, Table 2. Troponin measurements (Dade Behring Dimensions Assay, Munich, Germany) were performed every 8 h (the allowed deviation from time of sample collection was 1 h) for the first 48 h after surgery, then routinely once a day until the fifth postoperative day or until hospital discharge if planned earlier. Likewise, ECG was performed routinely every day for 5 days after surgery or until discharge. Any subject with ischaemic symptoms causing haemodynamic instability had transthoracic or transoesophageal echocardiography performed to assess for new regional wall motion abnormalities. Subjects were monitored daily by study personnel for signs or symptoms of MACE, need for transfusions, or presence of bleeding complications. Severe postoperative anaemia was defined as postoperative haemoglobin <90 g litre^{-1}.[16 17] Clinically important major bleeding was defined as the need for transfusion of >2 units of red blood cells or blood loss >1000 ml.[17 18] These criteria are similar to those defined by the International Society on Thrombosis and Haemostasis for major bleeding in a clinical trial[18]. None of the surgeries involved 'closed spaces', such as neurosurgery or eye surgery, in our cohort.

The diagnosis of MI was made using the third universal definition by independent analysis, with blinding of the results of platelet function tests. This involves using elevation of biomarkers (troponin), clinical symptoms, ECG changes pathognomonic for ischaemia, and imaging results.

The effect of aspirin, clopidogrel, or both on platelet function (percentage inhibition) was assessed using the platelet mapping assay (PMA; Haemonetics, Braintree, MA, USA), a modification of thromboelastography. The PMA is a point-of-care tool, with high sensitivity to platelet inhibition by aspirin, clopidogrel, or both. Platelet inhibition is expressed as a percentage of total function. It has been previously validated against light transmission aggregometry[19 20] and used in a variety of clinical situations as described.[21 22]

Platelet mapping assay measurements were made on the morning of surgery (before the start of anaesthesia), after surgery (in the postanaesthesia care unit), and on the first postoperative day (within four hours of scheduled time of sample collection).