Preoperative antiplatelet use does not increase incidence of bleeding after major operations

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Background. *This study examined the outcomes of patients holding or continuing clopidogrel during the preoperative period.*

Methods. *We reviewed all patients taking clopidogrel who underwent one of 72 different Current Procedural Terminology code procedures, representing major emergency and elective general thoracic and vascular operations from 2009–2012 at a single institution. Demographics, comorbidities, aspirin use, details of coronary stents, and perioperative events were collected.*

Results. *A total of 2,154 major operative procedures were performed on 1,851 patients during the study period. A total of 213 patients (11.5%) were taking clopidogrel at the time of their last office visit or hospital admission and were then instructed to hold or continue the drug prior to an operation. A total of 205 procedures in 200 patients comprised the final study population. Clopidogrel was held in 116 procedures for ≥5 days prior to operative intervention (56.6%, Group A), and clopidogrel was administered within 5 days of an operation in 89 procedures (43.4%, Group B). There were no differences between the 2 groups regarding estimated blood loss, units transfused, myocardial infarction, stroke, acute visceral or peripheral ischemia, or death within 30 days.*

Conclusion. *We did not identify significantly increased adverse patient outcomes in those patients who received preoperative clopidogrel within this population. We assert that it appears to be reasonable and safe to continue antiplatelet therapy with clopidogrel in this population in elective situations and that preoperative clopidogrel use does not increase the risk of bleeding in emergency circumstances. (Surgery 2016;160:968-76.)*

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Dual antiplatelet therapy with acetylsalicylic acid (ASA) and clopidogrel (Plavix; Bristol-Myers Squibb, New York, NY) in the early postintervention period after placement of a percutaneous coronary artery is considered the standard of care to prevent in-stent thrombosis.[1] Antiplatelet agents are also employed frequently in patients at high risk for sequelae of coronary, cerebrovascular, and peripheral arterial disease.

Antiplatelet drug management in patients with pre-existing coronary artery diseases remains an important consideration when these patients require an emergency or major elective operative procedure. Surgeons often face the dilemma of temporarily stopping antiplatelet therapy and risking adverse cardiac outcomes, specifically coronary stent thrombosis, or continuing treatment risking increased operative or postoperative bleeding and its associated consequences.[2,3] Because the lifespan of a platelet is 8–9 days, the current standard of care includes stopping antiplatelet therapy for 5–7 days before an elective operative procedure or administering platelet transfusions in patients requiring an emergency operation when indicated. ASA acts by inhibiting irreversibly platelet production, whereas clopidogrel inhibits platelet activation and aggregation. The prescribing information from Bristol-Myers Squibb recommends holding clopidogrel for 5 days prior to major elective operations to decrease the risk of bleeding[4]; recommendations may vary in patients with bare stents during the first year after implantation.

Several studies have investigated the use of antiplatelet drugs and adverse effects in cardiac surgery; however, few studies have examined the perioperative management of patients undergoing

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general surgery, thoracic surgery, and vascular surgery.[3] Previous studies have reported that preoperative clopidogrel use should not delay an operation in spite of the risk of bleeding.[5,6] We designed a retrospective review to evaluate whether use of perioperative antiplatelet drugs, specifically clopidogrel, increased the rate of adverse operative outcomes during or after major emergency or elective general, thoracic, and vascular operations. We hypothesized that use of preoperative antiplatelet drugs would increase the rates of operative and postoperative bleeding as well as morbidity and mortality.

METHODS

Approval by our Institutional Review Board was obtained. We identified 72 different Current Procedural Terminology codes to represent major emergency and elective general, thoracic, and vascular operations. Codes were chosen based on the complexity of the procedure, high likelihood for operative blood loss, and likelihood of being performed in an emergency situation.

The institutional database repository was queried for all patients who underwent one of the selected procedures at our large, academic medical center from January 1, 2009, to December 31, 2012. Patients taking clopidogrel at the time of their latest office visit or hospital admission just prior to an operation were included for study. All patients had a history and physical examination within 30 days as required by our institutional policy. We determined if the drug had been stopped or continued by reviewing the surgeon's note and the medication reconciliation record at the time of hospital admission. If a patient underwent multiple procedures, only the first procedure per hospitalization was included for study. Patients were excluded if it could not be deciphered from the electronic medical record whether clopidogrel was held or administered preoperatively.

Demographics, comorbidities, aspirin use (any dose), details of any indwelling coronary artery stents, and perioperative events were collected. A comorbid diagnosis was considered when it was stated clearly by the physician or surgeon in the preoperative history and physical examination. Statistical significance was determined using the Fisher exact test for discrete data and the Student *t* test for continuous data.

RESULTS

A total of 72 different Current Procedural Terminology codes included 8 thoracic, 36 vascular, and 28 general operative codes associated with 550, 651, and 953 procedures, respectively. In total, 2,154 major operations were performed on 1,851 patients during the study period across all hospitalizations. Of these, 213 patients (11.5%) were taking clopidogrel at the time of their last office visit or hospital admission just prior to an operation. Thirteen patients were excluded, because it was unclear from the medical record if clopidogrel was discontinued preoperatively. Five patients underwent 2 of the defined procedures during separate hospitalizations, with a total of 205 procedures in 200 patients to comprise the study population (Table I). Clopidogrel was stopped preoperatively in 116 procedures in 112 patients for ≥5 days prior to operative intervention (56.6%, Group A), and clopidogrel was administered within 5 days of an operation for 89 procedures in 88 patients (43.4%, Group B; Fig).

Patients in Group A were more likely to have aspirin of any dose withheld prior to an operation ($P < .001$). Group A also had a greater rate of chronic obstructive pulmonary disease (35.3% vs 14.6%, $P < .01$) and malignancy (40.5% vs 15.7%, $P < .01$), as well as a lesser prevalence of peripheral arterial disease (62.1% vs 86.5%, $P < .01$) and presence of a peripheral vascular stent (19.8% vs 39.3%, $P < .01$; Table II).

No patients in Group A received preoperative platelets compared to 2 patients in Group B (2.1%) who received an average of 1.5 units of pooled platelets (P = not significant). Three patients in Group A suffered an acute perioperative myocardial infarction compared to one patient in Group B (2.6% vs 1.1%, $P > .6$). In Group A, 29.3% of patients required immediate transfusion (within 48 hours of an operation) or delayed transfusion (48 hours from operation to discharge) compared to 38.2% of Group B patients ($P = .23$).

Additionally, there were no significant differences between Group A and Group B regarding intraoperative estimated blood loss (390 mL vs 300 mL, $P = .19$), number of units transfused (2.7 vs 2.5, $P = .81$), cerebrovascular accident (0.9% vs 2.2%, $P = .58$), acute visceral or peripheral ischemia (2.6% vs 3.4%, $P = 1.00$), or death within 30 days (2.6% vs 3.4%, $P = 1.00$; Table III). When patients who received preoperative platelets were excluded, there was no statistical difference in perioperative transfusion, estimated blood loss, myocardial infarction, cerebrovascular accident, acute visceral or peripheral ischemia, or death within 30 days ($P \geq .22$ each).

Three patients who had clopidogrel withheld suffered a perioperative acute myocardial infarction; one of these patients suffered cardiac arrest