

# Continued Antiplatelet Therapy and Risk of Bleeding in Gastrointestinal Procedures: A Systematic Review

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- BACKGROUND:** Management of perioperative antiplatelet medications in gastrointestinal (GI) surgery is challenging. The risk of intraoperative and postoperative bleeding is associated with perioperative use of antiplatelet medication. However, cessation of these drugs may be unsafe for patients who are required to maintain antiplatelet use due to cardiovascular conditions. The objective of this systematic review was to compare the risk of intraoperative or postoperative bleeding among patients who had GI surgery while on continuous antiplatelet therapy (aspirin, clopidogrel, or dual therapy) with the risk among those not taking continuous antiplatelet medication.
- STUDY DESIGN:** We reviewed articles published between January 2000 and July 2015 from the Medline Ovid and Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases. Studies involving any GI procedures were included if the articles met our inclusion criteria (listed in Methods). The following key words were used for the search: *clopidogrel*, *Plavix*, *aspirin*, *antiplatelet*, *bleeding*, *hemorrhage*, and *digestive system surgical procedures*. Quality of the studies was assessed, depending on their study design, using the Newcastle-Ottawa score or the Cochrane Collaboration's tool for assessing risk of bias.
- RESULTS:** Twenty-two studies were eligible for inclusion in the systematic review. Five showed that the risk of intraoperative bleeding or postoperative bleeding among patients who had GI surgery while on continuous antiplatelet therapy was higher compared that for those not on continuous therapy. The remaining 17 studies reported that there was no statistically significant difference in the risks of bleeding between the continuous antiplatelet therapy group and the group without continuous antiplatelet therapy.
- CONCLUSIONS:** The risk of bleeding associated with GI procedures in patients receiving antiplatelet therapy was not significantly higher than in patients with no antiplatelet or interrupted antiplatelet therapy. (J Am Coll Surg 2016;222:890–905. © 2016 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

According to the CDC and Prevention, heart disease is the leading cause of death in the United States. About 610,000 people die of heart disease every year, accounting for

almost 1 in every 4 deaths.<sup>1</sup> The estimated cost of heart disease in the US is as much as \$170 billion annually, this cost having been attributed in large part to evidence-based medical treatments. Platelet-directed pharmacotherapies (also referred to as antiplatelet therapy)<sup>2</sup> cost about \$7.8 billion nationwide in 2011.<sup>3</sup> Antiplatelet therapies include aspirin, clopidogrel, and other thienopyridine-class drugs. Concomitant treatment with aspirin and clopidogrel is referred to as dual antiplatelet therapy. Indications for the use of antiplatelet drugs include a variety of cardiovascular diseases, but they are most often used for the prevention of cardiac events after acute coronary syndromes, especially after stroke, myocardial infarction, or placement of coronary artery stents.<sup>4-9</sup> Generally, antiplatelet therapy is prescribed for 12 months, but may also be used for

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### Abbreviations and Acronyms

ASGE	= American Society for Gastrointestinal Endoscopy
ASA	= American Society of Anesthesiologists
EBL	= estimated blood loss
ESD	= endoscopic submucosal dissection
EUS-FNA	= endoscopic ultrasonography-fine needle aspiration
GI	= gastrointestinal
OR	= odds ratio
PEG	= percutaneous endoscopic gastrostomy
POB	= postoperative bleeding
TCB	= Trucut biopsy

longer periods in patients with drug-eluting coronary artery stents.<sup>10</sup>

While on antiplatelet therapy, some patients may require noncardiac surgery. Management of perioperative medication can be challenging for surgeons. On one hand, the risk of intraoperative and postoperative bleeding in gastrointestinal (GI) surgery has been significantly associated with perioperative use of antiplatelet therapy.<sup>11-13</sup> On the other hand, cessation of these drugs may be unsafe for patients who are required to maintain antiplatelet therapy due to their cardiovascular conditions.<sup>14,15</sup> So, according to 2009 American College of Cardiology Foundation/American Heart Association (ACCF/AHA) guidelines, procedures that will cause significant postoperative bleeding risk should be deferred until patients have completed an appropriate course of antiplatelet therapy (12 months after drug-eluting stent implantation if they are not at high risk of bleeding, and a minimum of 1 month for bare-metal stent implantation).<sup>16</sup>

Based on the CDC/National Center of Health Statistics National Hospital Discharge Survey in 2010, the rate of operation on the GI system was 195.8 per 10,000, which makes GI surgery the fourth most common of all inpatient procedures.<sup>17</sup> The definition of GI surgery here includes operation on the esophagus, International Classification of Diseases, Ninth Revision, Clinical Modification procedure codes 42, stomach 43–44, intestine 45–46, appendix 47, rectum and anus 48–49, liver 50, gallbladder and pancreas 51–52, hernia repair 53, and others 54, 17.1–17.3, and 17.63. Previous systematic review studies have focused on specific surgery types, such as endoscopic procedures or colonoscopy.<sup>11,18-20</sup> The primary objective of this systematic review was to compare the risk of intraoperative or postoperative bleeding among patients who had any type of GI surgery while on continuous antiplatelet therapy (aspirin, clopidogrel, or dual therapy) with the risk among those not on therapy. As far as we are aware,

this is the first systematic review that assesses the risk of bleeding after GI procedures in general, rather than focusing on specific subtypes of GI surgery.

## METHODS

### Search strategy

Articles published between January 2000 and July 2015 were collected from the Medline Ovid and Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases. Searches were conducted independently by one of the authors (XF) with the help of a professional librarian. The following key words were used for the search: *clopidogrel*, *Plavix*, *aspirin*, *antiplatelet*, *bleeding*, *hemorrhage*, and *digestive system surgical procedures*. The detailed search strategy for Medline Ovid and CINAHL is presented in [Appendix Table 1](#).

Studies were included if they were original research published in a peer-reviewed journal; reported data from a primary study (ie were not a review, systematic review, letter, guideline, case report, case series, or editorial); were a retrospective or prospective cohort study, case-control study, or randomized clinical trial; contained both an antiplatelet group and a non-antiplatelet group; did not include animals; included participants aged 18 years and older; and were written in English.

Articles were screened in 3 steps: removing duplicates, by abstract, and by full text. After removing duplicates, articles were excluded systematically in each step based on the inclusion criteria listed above. Screening was conducted initially by XF, and verified by DJ. In the case of disagreement, final decisions were made after discussion between these 2 reviewers. The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement<sup>21</sup> is shown in [Figure 1](#).

To aid in applying the inclusion and exclusion criteria, and to record data for the review, a data extraction form was completed for every study. The complete extraction table can be found in [Appendix Table 2](#). A short version is included in the manuscript ([Table 1](#)). Complete data extracted from each article include author, year, study design, study setting, drug/s used, study sample sizes, strategy for cohort selection (eg cases, controls), surgery type, bleeding risk of studied procedure per *Management of Antithrombotic Agents for Endoscopic Procedures*,<sup>44</sup> baseline cohort characteristics recorded, outcome (with definition, if available), association measure (odds ratio [OR], difference in blood loss, etc), and study results.

### Quality assessment

Quality of the studies was assessed depending on study design. For case-control studies and cohort studies, the

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