2012 Update to The Society of Thoracic Surgeons Guideline on Use of Antiplatelet Drugs in Patients Having Cardiac and Noncardiac Operations*

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Introduction and Rationale for Revision

The Society of Thoracic Surgeons (STS) Workforce on Evidence Based Surgery provides recommendations for practicing thoracic surgeons based on available medical evidence. Part of the responsibility of the Evidence Based Workforce is to continually monitor published literature and to periodically update recommendations when new information becomes available. In 2005, STS Workforce efforts included publication of recommendations regarding the use of antiplatelet agents during cardiac operations [1]. Since then, new antiplatelet agents appeared on the market and significant new information appeared in the literature, such that revision of the 2005 guidelines is justified. This document represents synthesis of new information regarding the use of antiplatelet agents in the perioperative period. Additional features of this publication include broader discussion of point-of-care testing to monitor platelet function and wider exploration of treatment options of patients exposed to antiplatelet drugs who need urgent operation.

*The Society of Thoracic Surgeons Clinical Practice Guidelines are intended to assist physicians and other health care providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis, management, or prevention of specific diseases or conditions. These guidelines should not be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the same results. Moreover, these guidelines are subject to change over time, without notice. The ultimate judgment regarding the care of a particular patient must be made by the physician in light of the individual circumstances presented by the patient.

For the full text of this and other STS Practice Guidelines, visit http://www.sts.org/resources-publications, at the official STS Web site (www.sts.org).

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A. Search Methods

The search methods used to survey the published literature changed in the current guideline version compared with the previously published guideline [1]. In the interest of transparency, literature searches were conducted using standardized Medical Subject Heading (MeSH) terms from the National Library of Medicine PUBMED database list of search terms. The following terms comprised the standard baseline search terms for all topics and were connected with the logical "OR" connector: extracorporeal circulation (MeSH number E04.292 includes extracorporeal membrane oxygenation, left heart bypass, hemofiltration, hemoperfusion and cardiopulmonary bypass); cardiovascular surgical procedures (MeSH number E04.100 includes off-pump coronary artery bypass graft surgery [CABG], CABG, myocardial revascularization, all valve operations, and all other operations on the heart); vascular diseases (MeSH number C14.907 includes dissections, aneurysms of all types including left ventricular aneurysms, and all vascular diseases); and pharmacologic actions (MeSH number D27.505 includes molecular mechanisms, physiologic effects, and therapeutic use of drugs).

Use of these broad search terms allowed specific topics to be added to the search with the logical "AND" connector. This search methodology provided a broad list of generated references specific for the search topic. Individual members of the writing group read the retrieved references for their assigned topics and formulated recommendations based on assessment of the relevant literature. Only English language articles contributed to the final recommendations. For almost all topics reviewed,

Appendices for this article are available in the Auxiliary Annals section of the STS website http://www.sts.org/annals-thoracic-surgery/auxiliary-annals.

REPORT

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Abbreviations and Acronyms

ACC = American College of Cardiology
ACS = acute coronary syndrome
ADP = adenosine diphosphate
AHA = American Heart Association
CABG = coronary artery bypass graft surgery
COX = cyclooxygenase
CYP = cytochrome P450
GP = glycoprotein
ICU = intensive care unit
MeSH = Medical Subject Heading
MI = myocardial infarction
PCI = percutaneous coronary intervention
PDE = phosphodiesterase
STS = The Society of Thoracic Surgeons

only evidence relating to adult patients were entered into the final recommendations, primarily because of limited availability of high-quality evidence relating to pediatric patients having cardiac procedures.

B. Duties of the Writing Group

Members of the writing group, assigned to a specific topic made recommendations about use of antiplatelet agents in the perioperative period based on review of important articles obtained using the search technique described above. The quality of information for a given recommendation allowed assessment of the level of evidence as recommended by the American Heart Association (AHA)/American College of Cardiology Foundation (ACCF) Task Force on Practice Guidelines (available at: http://www.americanheart.org/downloadable/heart/12604770597301209methodology_manual_for_acc_aha_writing_committees.pdf). Writers assigned to the various antiplatelet drug topics wrote and developed new or amended recommendations, but each final recommendation that appears in this revision was approved by at least a two-thirds majority favorable vote from all members of the writing group. Table 1 and Appendix 1 (see Appendix in Auxiliary Annals section of the STS website http://www.sts.org/auxiliaryannals/Ferraris-2012-94-5-1761-Appendices1-2.pdf) contain summaries of recommendations and the results of the voting for each recommendation, and explain any major individual dissensions. Appendix 2 (see Appendix in Auxiliary Annals section of the STS website http://www.sts.org/auxiliaryannals/Ferraris-2012-94-5-1761-Appendices1-2.pdf) documents the authors' potential conflicts of interest and industry disclosures.

C. Types of Antiplatelet Drugs and Their Mechanisms of Action

1) Nonsteroidal Antiinflammatory Agents

Aspirin (acetylsalicylic acid) and other nonsteroidal antiinflammatory agents inhibit platelets by blocking the formation of thromboxane A2, a potent platelet activator (Table 2). The extent of platelet inhibition for each nonsteroidal antiinflammatory agent depends on the ratio of cyclooxygenase (COX)-1 to COX-2 activity, half-life, and reversibility. Although several nonsteroidal antiinflammatory agents possess antiplatelet activity, discussion is frequently limited to aspirin as it is frequently prescribed for the prevention of cardiovascular events and irreversibly inhibits platelet function for the life of the platelet.

The natural precursors to aspirin—including willow bark—have been exploited for centuries to alleviate pain [2]. It was not until the 1950s that Dr Lawrence Craven hypothesized that a small daily dose of aspirin could prevent coronary thrombosis, and this finding went largely unnoticed for some time [3]. Now, several therapeutic mechanisms for aspirin exist, including a rapid and direct antiplatelet effect. Aspirin irreversibly inhibits COX-1 in platelets by acetylating a serine residue, thereby preventing arachidonic acid binding to the active site of the enzyme [4]. In platelets, low doses of aspirin are effective because platelets do not have a nucleus and, consequently, have minimal capability to synthesize new COX-1 enzyme. Combined with this fact, the irreversible effect of aspirin implies that production and release of new platelets from the bone marrow is required to restore platelet function. There is no direct antidote available to reverse the antiplatelet effects of aspirin on circulating platelets. Platelet transfusion can indirectly reverse the effects of aspirin by increasing the total circulating pool of platelets while agents like recombinant factor VIIa can overcome the aspirin effect by stimulating other platelet receptors (eg, thrombin receptors) that are more potent platelet-activating agents.

There is strong clinical evidence to support the value of aspirin for reducing death, myocardial infarction, and stroke in patients at risk for thrombotic events; however, this benefit is accompanied by a higher risk of bleeding [5]. In general, smaller doses of aspirin (75 mg to 100 mg daily) are considered equally effective as higher doses (300 mg to 325 mg daily) and demonstrate the lowest level of bleeding risk [6]. In patients undergoing cardiac operations, the risk to benefit ratio for preoperative aspirin is dependent on the urgency of operation, cardiovascular risk of the patient, concomitant antithrombotic medications, and risk for bleeding [1].

There is documented variability in response to aspirin, and all antiplatelet drugs for that matter, as some patients have excessive platelet inhibition and may be at increased risk for bleeding whereas another volunteer has reduced inhibition and may demonstrate higher thrombotic risk [7]. Much less studied is the incidence of increased or accentuated response to antiplatelet agents. Consideration of simple population variation suggests that response to drugs is distributed normally with equal numbers of patients having accentuated response or lack of response to orally administered drugs. A simple example of this variation is shown in Figure 1. In the study depicted in Figure 1, aspirin administration to 7 normal volunteers resulted in 1 volunteer having a bleeding time in excess of 14 minutes whereas another volunteer had