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The Risk of Adverse Cardiac and Bleeding Events Following Noncardiac Surgery Relative to Antiplatelet Therapy in Patients With Prior Percutaneous Coronary Intervention

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Noncardiac surgery (NCS) may be required within the first year after percutaneous coronary intervention (PCI) in approximately 4% of patients and is the second most common reason for premature discontinuation of antiplatelet therapy (APT),which may, in turn, increase the risk of perioperative ischemic events, particularly stent thrombosis. Its continuation may increase the risk of perioperative bleeding. We review current information on the incidence of these events, particularly related to APT, describe potentially useful strategies to minimize the risks of adverse outcomes, and provide recommendations on APT use. (J Am Coll Cardiol 2012;60: 2005–16) © 2012 by the American College of Cardiology Foundation

Percutaneous coronary intervention (PCI) is the most common strategy for myocardial revascularization, with more than a million procedures performed annually in the United States alone (1). Enthusiasm has been tempered by the potentially lethal complication of stent thrombosis (ST) (2). The most important ST predictor is premature discontinuation of dual antiplatelet therapy (DAPT) (3,4). Apart from noncompliance, the second most common reason for early discontinuation of either DAPT or single antiplatelet therapy (APT) is the need for noncardiac surgery (NCS), accounting for one-third of cases (4).

In both retrospective (5) and prospective (6) studies, approximately 4% of patients undergo NCS within the first year after index PCI (approximately 40,000 patients in the United States by current PCI usage). This large cohort presents a challenge for the treating surgeon, anesthesiologist, and cardiologist in managing APT in the perioperative period. On the basis of current American College of Cardiology/American Heart Association guidelines, approximately two-thirds of all NCS procedures in the first year after index PCI are classified as moderate to high risk for major adverse cardiac events (MACE) (5–7). Surgical stress creates a prothrombotic state due to increased platelet activation and decreased fibrinolysis, explaining in part the well-described MACE increase in the perioperative period (8–10).

The small, but persistent, ST risk long after PCI raises the important issue of perioperative management. On the one hand, MACE, particularly ST, is a concern after APT discontinuation; with its continuation, bleeding looms as a persistent danger. In this paper, we review studies of NCS outcomes following PCI with either bare-metal stents (BMS) or drug-eluting stents (DES), particularly in relation to APT, and potential strategies to decrease these risks.

Methods

We performed a PubMed search for full-length articles published within the last 10 years in the English language (abstracts were excluded) with the following key terms: "noncardiac surgery, coronary stent" and "noncardiac surgery, percutaneous coronary intervention." We identified 6 studies with BMS (11–16), 13 with DES (6,17–28), and 6 with both BMS and DES (5,29–33). In 1 study of 103 patients (34), stent type (BMS vs. DES) was unavailable in 75% of patients; we excluded this study except to discuss it relative to anticoagulation strategies. Another paper was excluded because the myocardial infarction (MI) endpoint, although well defined, was not clearly presented (23). We reviewed each study for definitions and incidence of MACE and bleeding, APT status, and factors associated with adverse outcomes. We also performed an extensive English literature search for strategies to prevent MACE. In this presentation, the ischemic risk of surgery was defined as "low,"

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Abbreviations and Acronyms

APT = antiplatelet therapy
ASA = aspirin
BA = balloon angioplasty
BMS = bare-metal stent(s)
DAPT = dual antiplatelet therapy
DES = drug-eluting stent(s)
LMWH = low-molecular-weight heparin
MACE = major adverse cardiac event(s)
MI = myocardial infarction
NCS = noncardiac surgery
PCI = percutaneous coronary intervention
ST = stent thrombosis

"intermediate," or "high," using the American College of Cardiology/American Heart Association guidelines (7).

Current guidelines for management of patients undergoing NCS after PCI. The 2009 American College of Cardiology/American Heart Association and 2010 European Society of Cardiology/European Association of Cardio-Thoracic Surgery guidelines provide a framework for APT management in the perioperative period following PCI (7,35). Given the lack of prospective randomized clinical trials, recommendations are based primarily on expert opinion and relatively small, and mostly retrospective, studies.

Four important variables cited in decision making regarding APT use in the perioperative period include urgency of surgery, PCI type (balloon angioplasty [BA] vs. stenting), stent type (DES vs. BMS), and the duration between PCI and NCS.

Guidelines recommend that elective surgery be postponed for at least 2 weeks after BA, 1 month after BMS, and 1 year after DES. The rationale relates to the time frame for vascular healing and re-endothelialization in animal studies (36). Current guidelines recommend that aspirin (ASA) (81 to 325 mg/day) be continued through the perioperative period if the risk of surgical bleeding is not prohibitive. The decision regarding APT continuation with urgent or emergent surgery is governed by the relative risks of bleeding versus ST in an individual patient. This consideration is reflected in the 2010 European Society of Cardiology/European Association of Cardio-Thoracic Surgery guidelines, where a "case by case" approach is suggested (35).

Limitations of current guidelines and studies. Most published studies are retrospective, single center, and/or with small sample size, limiting generalizability of the results (Table 1). In addition, definition of adverse events, both cardiac and bleeding, details of perioperative APT, and duration of post-operative monitoring vary, making comparisons among studies difficult. Thus, the reader must take these caveats into consideration in drawing conclusions about the risks and efficacy of APT in PCI patients undergoing NCS. In addition, current guidelines provide APT recommendations for only the first year after PCI. The small, but persistent, MACE risk including ST beyond the first year is not addressed. Finally, it should be mentioned that MACE definitions vary in each study; thus, the reader should refer to Tables 2 to 4 to determine what constitutes MACE in each study.

Table 1 Limitations of Current Studies

First Author (Ref. #)	Year	Small Sample Size (N < 100)	Retrospective	APT Status Not Well Defined	MACE Not Well Defined	Bleeding Endpoints Not Well Defined	Single Center	Questionnaire-Based Study
Kaluza et al. (11)	2000	+	+	+			+	
Wilson et al. (12)	2003		+				+	
Sharma et al. (13)	2004	+	+	+			+	
Reddy et al. (14)	2005	+	+	+			+	
Brichon et al. (15)	2006	+	+					
Kim et al. (29)	2008		+	+		+	+	
Nuttal et al. (16)	2008		+	+			+	
Compton et al. (17)	2006	+	+	+			+	
Brotman et al. (18)	2006		+				+	
Conroy et al. (19)	2007	+	+	+	+	+	+	
Schouten et al. (30)	2007	+	+	+		+	+	
Rhee et al. (20)	2008		+			+	+	
Godet et al. (21)	2008	+		+		+	+	
Rabbitts et al. (22)	2008		+	+			+	
Anwaruddin et al. (25)	2009		+			+	+	
Assali et al. (26)	2009	+	+				+	
Van Kuijk et al. (31)	2009		+	+				
Choi et al. (23)	2010	+	+		+		+	
Chia et al. (24)	2010		+			+		+
Berger et al. (6)	2010			+		+		
Gandhi et al. (27)	2010		+	+			+	
Cruden et al. (5)	2010		+	+		+		
Brilakis et al. (28)	2011		+	+		+		
Albaladejo et al. (32)	2011			+				
Brancati et al. (33)	2011		+				+	

+ = limitation present; APT = antiplatelet therapy; MACE = major adverse cardiac event(s); pts= patients.