JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
© 2015 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER INC.

VOL. 65, NO. 20, 2015
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2015.03.567

THE PRESENT AND FUTURE

STATE-OF-THE-ART REVIEW

Bleeding Avoidance Strategies During Percutaneous Coronary Interventions

Mandeep Singh, MD, MPH

ABSTRACT

Bleeding avoidance strategies for percutaneous coronary interventions continue to evolve with the availability of newer antiplatelet and anticoagulation therapies. Advances in interventional practices have altered the balance between ischemic and bleeding complications. With the availability of rapidly-acting platelet adenosine diphosphate–receptor antagonists, the need for routine glycoprotein IIb/IIIa inhibitors has diminished. Recent meta-analyses and trials have advanced our knowledge of vascular access and different anticoagulation regimens. Vascular closure devices have long been used for early ambulation; however, more recent results demonstrating lower bleeding complications from observational registries are encouraging. This review synthesizes this information, taking into account changes in the landscape of interventional practice with respect to current bleeding avoidance strategies. (J Am Coll Cardiol 2015;65:2225–38) © 2015 by the American College of Cardiology Foundation.

Bleeding and vascular complications in patients undergoing percutaneous coronary interventions (PCIs) are associated with significant costs, prolonged hospital stays, and increased short- and long-term morbidity and mortality (1–5). The risk of bleeding is modifiable, and improving bleeding and vascular complication rates provides an opportunity to improve the health care and safety of PCI. In that regard, the Centers for Medicare and Medicaid Services (6) have identified bleeding and hematoma following cardiovascular procedures as quality indicators (7).

Marso et al. (8) used the term "bleeding avoidance strategies" to highlight the importance of bivalirudin and vascular closure devices (VCDs) in reducing bleeding, using data on more than 1.5 million patients undergoing PCI at hospitals participating in the National Cardiovascular Data Registry (NCDR) (8). In high-risk patients, the use of both bivalirudin and VCD was associated with significantly lower bleeding rates. Since the publication of this study, pharmacotherapy and technological advances have shed new light on factors that can further mitigate bleeding risk in patients undergoing PCI.

With this backdrop, this review will report recent advances associated with meaningful reduction in bleeding complications following PCI. It will also review the current data on the status of bivalirudin and VCD. Last, this review will provide the reader with a practical strategy to help individualize a patient's bleeding risk and deploy interventions to reduce bleeding in high-risk patients.

DEFINITION OF BLEEDING

Bleeding complications have been identified as a crucial endpoint to test the safety and efficacy of new antithrombotic drugs, cardiac devices, or PCI. Reduction in bleeding events is associated with improved survival, and prevention of major bleeding may represent an important step in improving outcomes by balancing the safety and efficacy of pharmacotherapy and devices used during PCI (9).

From the Division of Cardiovascular Diseases, Department of Internal Medicine, Mayo Clinic, Rochester, Minnesota. Dr. Singh has reported that he has no relationships relevant to the contents of this paper to disclose.
Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.
You can also listen to this issue's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

Manuscript received November 19, 2014; revised manuscript received March 31, 2015, accepted March 31, 2015.

ABBREVIATIONS AND ACRONYMS

ACS = acute coronary syndrome(s)

ACT = activated clotting time

BARC = Bleeding Academic Research Consortium

CABG = coronary artery bypass graft

GP = glycoprotein

NCDR = National Cardiovascular Data Registry

PCI = percutaneous coronary intervention

VCD = vascular closure device

Lack of unanimity in defining bleeding has led to variation in the incidence of bleeding across institutions performing PCI (1). The definition of bleeding continues to evolve, and 4 such definitions are highlighted in **Figure 1**. One definition, coined by the Bleeding Academic Research Consortium (BARC), classifies bleeding into 5 clinically-meaningful categories (10). This definition not only captures the cause (procedural or nonprocedural) of bleeding, but also reflects on the severity, site, and prognostic implications (6). BARC also gives due consideration to coronary artery bypass graft (CABG)-related bleeding, as up to 12% of patients presenting with acute coronary syndromes (ACS) may undergo CABG during index hospitalization. The key determinants of CABG-related bleeding include: duration (24 h for chest tube and 48 h for intracranial bleed and transfusions); site (intracranial); and need for reoperation. The second definition proposed by the NCDR is being used to calculate the bleeding risk score (11). This definition encompasses a broader range of access and nonaccess bleeding and accounts for pre-procedure hemoglobin. Previously, bleeding was largely defined by variables included in the TIMI (Thrombolysis In Myocardial Infarction) and GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) trials (12,13). **Figure 1** highlights the significant heterogeneity in definitions of bleeding. Such variations make the adjudication of endpoints, intertrial comparisons, and care process improvements difficult, if not impossible.

There are still some unresolved issues. First, clinicians still must use the NCDR definition to calculate the bleeding risk from PCI, and BARC or other definitions need to be utilized to judge severity. Second, the NCDR definition is for bleeding within 72 h of PCI and is mainly geared to capture PCI-related complications, whereas the BARC definition may need to be used to calculate the short- and long-term bleeding risk. Third, at present, access and nonaccess bleeding are not well-differentiated. Nonaccess-site bleeds are more common in patients who present with ACS, have an adverse prognostic

FIGURE 1 Outline of Bleeding Definitions From Different Studies

BARC	NCDR	TIMI	GUSTO
Type 0: No bleeding Type 1: Bleeding is not actionable Type 2: Any overt, actionable sign of hemorrhage Type 3: Type 3a: Overt bleeding plus hemoglobin drop 3 to <5 g/dl and any transfusion with overt bleeding Type 3b: Overt bleeding plus hemoglobin drop ≥5 g/dl.Includes cardiac tamponade and bleeding requiring surgical intervention or vasoactive agents Type 3c: Intracranial or intraocular bleed compromising vision Type 4: CABG-related bleeding Perioperative intracranial bleeding within 48 h Reoperation after closure of sternotomy for the purpose of controlling bleeding Transfusion of ≥5 U whole blood or packed red blood cells within 48 h Chest tube output ≥2L within 24 h Type 5: Fatal bleeding 5a: Probable 5b: Definite	# Arterial access site bleeding: •External •Hematoma >10 cm for femoral >5 cm for brachial >2 cm for radial # Retroperitoneal, gastrointestinal, or genitourinary bleeding; intracranial hemorrhage; cardiac tamponade # Post-procedure hemoglobin decrease of 3 g/dl. In patients with a pre-procedure hemoglobin level ≤16 g/dl or post-procedure non-bypass surgery-related blood transfusion for patients with a pre-procedure hemoglobin level ≥8gm/dl	Minimal: Overt hemorrhage associated with a fall in hemoglobin <3 g/dl (hematocrit of <9%) Minor: any clinically overt sign of hemorrhage associated with a fall in hemoglobin of 3 to ≤5 g/dl (or hematocrit 9 to ≤5%) Major: (1) Intracranial or (2) clinically significant overt signs of hemorrhage associated with a drop in hemoglobin of >5 g/dl (hematocrit of >15%)	Mild Bleeding that does not meet criteria for either severe or moderate bleeding Moderate Bleeding that requires blood transfusion but does not result in hemodynamic compromise Severe or life-threatening either intracranial hemorrhage or bleeding that causes hemodynamic compromise and requires intervention

BARC = Bleeding Academic Research Consortium; CABG = coronary artery bypass graft; GUSTO = Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries; NCDR = National Cardiovascular Data Registry; TIMI = Thrombolysis In Myocardial Infarction.