Published in final edited form as:

Cardiology. 2015 ; 132(3): 159–162. doi:10.1159/000434641.

Temporal Trends in Bleeding among ACS Patients: Is it going up or down? Does it matter?

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Abstract

Bleeding is one of the most common complications among patients presenting with acute coronary syndrome (ACS) and is often precipitated by therapeutic intervention with potent antithrombotic medications and invasive procedures to restore perfusion to ischemic myocardium. Major bleeding is associated with short- and long-term morbidity and mortality, and percutaneous coronary intervention (PCI) related bleeding is now tracked as a hospital quality indicator in the United States. As antithrombotic therapy has become more potent, there may be concern that with contemporary ACS management, the risk of bleeding is even higher now than it has been in the past.

In this issue of *Cardiology*, Sabbag and colleagues [1] utilize a large Israeli registry of patients presenting with acute coronary syndrome (ACS) from 2004–2010 to describe temporal trends of major bleeding and associated outcomes. Among the 11,538 patients enrolled in the study, 142 (1.2%) had a major bleeding event (MBE), defined as one of the following: a decrease in hemoglobin of 5mg/dL or a hematocrit drop of >15%, intracranial hemorrhage, or retroperitoneal bleeding. Bleeding events were then further divided into access site and non-access site bleeding. Despite a modest decrease in bleeding events from 2000–2004, rates of bleeding increased markedly over the study period, with the highest rates of reported bleeding in 2010, the last year of collected data. This is in the setting of increasing use of primary PCI and decreasing use for fibrinolytic therapy in patients presenting with ST-segment elevation MI (STEMI). Although rates of major adverse and cerebrovascular events (MACCE) were lower in all patients during this time period, patients experiencing a MBE had worse short- and long-term outcomes compared with patients who did not have a bleeding episode.

Although the overall rate of bleeding is low and likely reflects the specific bleeding definition utilized, the increasing rate of major bleeding over time described in this analysis is concerning and stands in stark contrast to prior studies in large registries, none of which have shown significant increase in bleeding rates over time despite the use of more robust antithrombotic strategies. Utilizing data from more than 1.7 million patients in the National Cardiovascular Data Registry's CathPCI Registry, Subherwal and colleagues described a 20% reduction in major bleeding events following PCI from 2005–2009. In that analysis, rates of bleeding reduction were similar among patients presenting with unstable angina/

hematoma (8%), both of which could be significantly reduced with radial artery access, which was almost never used among patients in this study. Multiple prior studies have demonstrated the benefit of transradial access with respect to access site complications and bleeding reduction. Among patients presenting with STEMI, the RIFLE-STEACS Trial showed reduced rates of the primary outcome of death/MI/stroke/target vessel revascularization among patients undergoing transradial PCI (13.6% vs. 21.0%) along with significant mortality (5.2% vs. 9.2%, $p=0.02$) and bleeding (7.8% vs. 12.2%, $p=0.026$) reductions. More recently, the MATRIX Trial highlighted the superiority of radial approach in patients presenting with ACS with reductions in BARC bleeding and all-cause mortality among patients undergoing transradial access [6]. Previous trials, including the ACUITY [7], HORIZONS-AMI [8], and EUROMAX [9] trials have demonstrated reduced rates of major bleeding with bivalirudin among patients presenting with ACS undergoing PCI, and bivalirudin use has been implemented as a bleeding avoidance strategy. However, more recent data from the HEAT-PPCI [10] have suggested that a periprocedural regimen of heparin only in the setting of increased transradial use and more potent antiplatelet therapies may have similar efficacy and bleeding. Although this is currently a topic of major debate, bivalirudin may play a role in bleeding reduction in high-risk patients, particularly those undergoing transfemoral PCI like those in the study by Sabbag. Finally, it should be noted that the data for bleeding reduction with vascular closure devices is mixed and may not support a significant role as part of a comprehensive bleeding reduction strategy.

The authors are to be commended for drawing attention to this concerning trend among patients in this registry. The most recent results demonstrating continued increase in major bleeding events in Israel should serve as a focal point to develop a comprehensive strategy for bleeding reduction incorporating procedural innovations as well as appropriate administration and dosing of anticoagulant and antiplatelet agents among ACS patients. Encouraging is the fact that major bleeding has decreased markedly worldwide from the earlier era of ACS management, suggesting that increasing focus and attention to bleeding and the implementation of evidence-based bleeding avoidance strategies should reverse the trend of increased bleeding and worse short-and long-term outcomes observed in this study.

Acknowledgments

Author Disclosures

AN Vora: Dr. Vora was funded by NIH T-32 training grant T32 HL069749 and L30 HL124592. However, no relationships exist related to the analysis presented.

SV Rao: Dr. Rao reports research funding from Bellerophon; consulting for Terumo Medical, The Medicines Company, Medtronic, Astra Zeneca, and ZOLL.

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Table**Strategies to Reduce Bleeding Among Acute Coronary Syndrome Patients**

Pharmacologic	Procedural	Other
Consider lower aspirin maintenance dose (100mg)	“Radial first” approach	Risk stratification using bleeding risk tool
Appropriate dosing of anticoagulant therapies	Ultrasound-guided femoral access	Routine and rigorous quality improvement initiative to track risk-adjusted bleeding rates
Bivalirudin in high risk subgroups if femoral approach is used	Consideration of vascular closure device (more evidence needed)	
Avoidance of prasugrel in patients with history of stroke/TIA, weight < 60kg, age ≥ 75 years		
Selective use of glycoprotein IIb/IIIa inhibitors		
Gastrointestinal prophylaxis with proton pump inhibitor		