JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 9, NO. 8, 2016

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcin.2016.02.040

EDITORIAL COMMENT

Bleeding Avoidance Strategies, Performance Measures, and the Emperor's New Clothes*

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"The Emperor's New Clothes" is a short fairy tale by Hans Christian Andersen about 2 swindlers posing as weavers who promised a vain emperor the finest, best new suit of clothes from a fabric that was invisible to those who were stupid or incompetent (1). Although the Emperor and his ministers could not see the clothes themselves, they pretended that they could for fear of appearing unfit for their positions. When the Emperor paraded naked before his subjects in his "new clothes," no one dared to say that he didn't see any clothes until a child cried out, "But he has nothing on at all!" So, what does this have to do with percutaneous coronary intervention (PCI) and bleeding avoidance strategies (BAS)?

Interventional cardiology has made dramatic contributions to reducing the ischemic complications of coronary artery disease. More recently, there has been a major focus on periprocedural BAS to decrease bleeding events that have been associated with increased costs, prolonged hospital stays, and increased short- and long-term morbidity and mortality (2,3). The BAS concept was first tested in the National Cardiovascular Data Registry CathPCI Registry by examining the use of bivalirudin anticoagulation in place of unfractionated heparin and vascular closure devices (VCDs) in place of manual femoral artery compression (4). More recent studies have included radial artery access instead of femoral artery access as a third BAS (5).

Bivalirudin was initially unsuccessful in clinical trials (6), but was eventually embraced as a superior anticoagulant for PCI because it reduced bleeding events in subsequent trials with different protocols. It has become less popular recently as acquisition costs have tripled and skeptics have argued that most of the benefit documented in prior clinical trials was due to modifying endpoint definitions and using a comparator that included higher unfractionated heparin doses than are currently needed and a platelet glycoprotein IIb/IIIa receptor inhibitor that usually is not currently needed (7).

VCDs were developed to achieve hemostasis at the femoral artery puncture site. Whereas they provide rapid hemostasis, are more comfortable for the patient than manual compression, and reduce time to ambulation, it is not clear that they reduce access site complications (3,8). Limitations include small risks for misuse, unsuccessful deployment, leg ischemia, and groin infection.

Radial artery access, compared with femoral artery access, decreases access site bleeding complications and has been enthusiastically promoted. Sometimes lost in the debate are the limitations of radial artery access that include increased radiation exposure (in some labs), challenges with arterial loops, catheter entrapment, radial artery occlusion in 5% to 10% of patients (9), and the risk of ostial coronary artery dissection by coronary catheters that need improved designs. When radial artery access fails or cannot support PCI demands, crossover to femoral artery access is required, the patient has 2 arterial punctures, and bleeding risk may be increased if operator skill in femoral artery access

*Editorials published in *JACC: Cardiovascular Interventions* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Interventions* or the American College of Cardiology.

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or laboratory skill in femoral artery sheath removal is not maintained.

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In this issue of *JACC: Cardiovascular Interventions*, Vora et al. (10) present an analysis of the impact of BAS on hospital-level variation in bleeding rates following PCI. Again using the National Cardiovascular Data Registry CathPCI Registry, they evaluated 2,459,686 procedures reported from 1,358 PCI sites between July 2009 and June 2013. Bleeding events occurred in 125,361 (5.1%) patients, with wide variation across hospitals (2.65% in the fifth percentile to 9.36% in the 95th percentile). Unfortunately, no data were presented on bleeding severity, bleeding site, or transfusion rate. BAS was more commonly used in lower risk patients and lower volume hospitals. The analysis showed only a 1.26% reduction in variation in bleeding rates with radial artery access, a 5.85% reduction with bivalirudin anticoagulation, and a 0.88% reduction with VCD deployment. Importantly, patient risk factors accounted for 20% of the hospital variation, whereas more than 70% of the variation in bleeding rates remained unexplained. The authors concluded that BAS resulted in a "modest reduction" in hospital variation in bleeding rates. My conclusion is that 92% of the variation in hospital-level bleeding rates was not due to BAS and requires further explanation. In their Discussion, the authors offer a nice argument on why bleeding rate may not be a suitable quality indicator or performance measure for determining reimbursement rates or institutional financial penalties, a more reasonable conclusion from an analysis that failed to support the hypothesis that BAS would decrease hospital-level variation in bleeding rates. Similar to mortality rates that are too low to discriminate between hospitals, and adjusted 30-day readmission rates that are rarely due to procedural complications, add bleeding rate as another poor candidate for a PCI performance measure.

It was predictable that VCDs would not be associated with a reduction in bleeding rates, as that is consistent with prior literature (3,8); it is not clear why they continue to be included as a BAS. Similarly, the small reduction in bleeding variation with bivalirudin is not surprising, although it could be argued that it was the avoidance of glycoprotein IIb/IIIa inhibitors, rather than the use of bivalirudin, that made the difference (7). The big surprise in this report was that radial artery access had no impact on bleeding variation. In an earlier patient-level analysis from the same registry, a significant absolute reduction (8.0% for women, 4.1% for men) in bleeding risk with radial artery access was demonstrated (5). It is possible that important hospital-level bleeding reduction improvements were lost in the limitations of the database and the complexity of the statistical analysis or that the results might have been different with a higher rate of radial artery access than utilized in this cohort analysis (approximately 12%).

Nevertheless, the authors did not address the failure of radial artery access to impact bleeding rates in their study, perhaps because of the cognitive dissonance associated with their previous ideological position on radial artery access superiority. Further confusing the debate on radial artery access has been the overlap between access site vascular injury events and bleeding events, the difference between access site and non-access site bleeding events, and the conflation of in-hospital events that are PCI complications with post-discharge events that are confounded by other variables including comorbidities and oral antithrombotic medications. In particular, the claim of a late mortality advantage for radial artery access over femoral artery access is difficult to understand without a proven causal biologic mechanism (9,11).

The 2015 European Society of Cardiology Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation (12) gives a Class IA recommendation for radial artery access over femoral artery access, despite referencing no difference in ischemic and bleeding outcomes in 1 randomized trial (13), no difference in patients undergoing PCI in another randomized trial (14), and no difference in major adverse cardiac events in the MATRIX (Minimizing Adverse Haemorrhagic Events by TRansradial Access Site and Systemic Implementation of angioX) Access trial (11). In the MATRIX Access trial, there also were no differences in Thrombolysis In Myocardial Infarction or GUSTO (Global Utilization Of Streptokinase and t-PA For Occluded Arteries) major bleeding, but there were small reductions in major bleeding using the BARC (Bleeding Academic Research Consortium) definition (1.6% vs. 2.3%; $p = 0.013$) and in all-cause mortality (1.6% vs. 2.2%; $p = 0.045$). The conclusion that radial artery access was superior in this trial has been challenged by those who highlight that the benefit was limited to centers that performed >80% of their PCIs with radial artery access and who also had an unexpectedly high number of adverse events in their low volume femoral artery access cohort (15).

U.S. interventionalists have been criticized for being slow to adopt radial artery access (9,11). And yet, the radialists need to avoid hubris and prove to the skeptics that they are not wearing the emperor's new

clothes when they promote the superiority of radial artery access over femoral artery access for all patients. Many low- and medium-volume operators (common in the United States) who document low bleeding rates with femoral artery access remain concerned that inclusion or exclusion criteria or unmeasured patient and investigator characteristics may have exerted an impact in studies favoring radial artery access and they are mindful of the limitations of radial artery access that may balance the small bleeding benefit in their individual practice experiences. Although bleeding events are decreased with radial artery access, there is enough equipoise on major adverse clinical events in the literature to challenge the ESC Class 1A recommendation on radial artery access that appears to be based on 1 meta-analysis (12). Only a properly designed randomized trial with appropriate endpoints that proves a causal relationship between vascular access site complications and mortality can resolve that controversy, as there appears to be no impact on myocardial infarction, stroke, target vessel revascularization, or stent thrombosis (11).

The observation by Vora et al. (10) that 70% of the hospital-level bleeding variation was unexplained may be due to operator techniques and processes of care that were not measured. Operator results should be better with greater experience and higher annual procedure volumes using either access site. Optimizing the femoral artery puncture site is facilitated by fluoroscopic landmark identification and ultrasound guidance and might be safer with micropuncture technique. Choice, dose, and duration of antithrombotic medications should balance efficacy and safety. This is important because non-access site bleeding constitutes two-thirds of all bleeding events with PCI and is associated with twice the mortality risk of access site bleeding (16). Smaller sheath size, shorter dwell times, and dedicated sheath withdrawal personnel are also important in reducing bleeding risk with femoral artery access. An updated definition of BAS might exclude VCDs and include best access site and sheath removal strategies; and adjunctive pharmacotherapy recommendations and doses. Also, transfusion should be limited to patients with compromised hemodynamic status or hemoglobin <7 g/dl. Prospective bleeding risk assessment may help stratify patients and impact strategies and interventions to lower individual patient risk even though the study by Vora et al. did not show a hospital-level benefit (17).

It is not clear to everyone that radial artery access should be the exclusive or default approach for cardiac catheterization (18). The best interventional cardiologists maintain expertise in both radial and femoral artery access and make individual access site decisions based on many clinical variables, especially procedural technical considerations. Despite the results of this study, most of us will agree that radial artery access decreases access site complications in the subgroup of patients at increased risk for femoral artery complications. However, it remains quite possible that operator/laboratory experience and expertise, and patient variables, rather than access site, determine clinical outcomes. Importantly, this study does not support the use of bleeding rate as a hospital-level PCI performance measure.

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KEY WORDS bleeding, percutaneous coronary intervention, radial artery