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Patterns of Use and Comparative Effectiveness of Bleeding Avoidance Strategies in Men and Women Following Percutaneous Coronary Interventions

An Observational Study From the National Cardiovascular Data Registry

Stacie L. Daugherty, MD, MSPH,* Lauren E. Thompson, MD,† Sunghee Kim, PhD,‡ Sunil V. Rao, MD,‡§ Sumeet Subherwal, MD, MBA,‡§ Thomas T. Tsai, MD, MSc,*‖ John C. Messenger, MD,* Frederick A. Masoudi, MD, MSPH*

Aurora and Denver, Colorado; and Durham, North Carolina

Objectives This study sought to compared the use and effectiveness of bleeding avoidance strategies (BAS) by sex.

Background Women have higher rates of bleeding following percutaneous coronary intervention (PCI).

Methods Among 570,777 men (67.5%) and women (32.5%) who underwent PCI in the National Cardiovascular Data Registry's CathPCI Registry between July 1, 2009 and March 31, 2011, in-hospital bleeding rates and the use of BAS (vascular closure devices, bivalirudin, radial approach, and their combinations) were assessed. The relative risk of bleeding for each BAS compared with no BAS was determined in women and men using multivariable logistic regressions adjusted for clinical characteristics and the propensity for receiving BAS. Finally, the absolute risk differences in bleeding associated with BAS were compared.

Results Overall, the use of any BAS differed slightly between women and men (75.4% vs. 75.7%, $p = 0.01$). When BAS was not used, women had significantly higher rates of bleeding than men (12.5% vs. 6.2%, $p < 0.01$). Both sexes had similar adjusted risk reductions of bleeding when any BAS was used (women, odds ratio: 0.60, 95% confidence interval [CI]: 0.57 to 0.63; men, odds ratio: 0.62, 95% CI: 0.59 to 0.65). Women and men had lower absolute bleeding risks with BAS; however, these absolute risk differences were greater in women (6.3% vs. 3.2%, $p < 0.01$).

Conclusions Women continue to have almost twice the rate of bleeding following PCI. The use of any BAS was associated with a similarly lower risk of bleeding for men and women; however, the absolute risk differences were substantially higher in women. These data underscore the importance of applying effective strategies to limit post-PCI bleeding, especially in women. (J Am Coll Cardiol 2013;61:2070–8) © 2013 by the American College of Cardiology Foundation

Peri-procedural bleeding is the most common noncardiac complication following percutaneous coronary intervention (PCI) and is associated with high morbidity and mortality (1–3). Historically, women have been at higher risk for peri-procedural bleeding following PCI compared with men (4–10). Bleeding avoidance strategies (BAS), including vascular closure devices (VCDs), bivalirudin, and radial access, are increasingly used and have been associated with decreased rates of bleeding following PCI (8,9,11–13). In practice, however, those at the highest predicted risk for bleeding are often the least likely to receive BAS at the time of PCI, suggesting a "risk-treatment paradox" (11). Whether

From the *Department of Medicine and the Division of Cardiology, University of Colorado School of Medicine, Aurora, Colorado; †Department of Medicine, University of Colorado School of Medicine, Aurora, Colorado; ‡Duke Clinical Research Institute, Durham, North Carolina; §Department of Medicine, Division of Cardiology, Duke University, Durham, North Carolina; and the ‖Cardiology Section, Veterans Administration Eastern Colorado Health Care System, Denver, Colorado. This research was supported by the American College of Cardiology Foundation's National Cardiovascular Data Registry (NCDR). Dr. Daugherty is supported by the National Heart, Lung, and Blood Institute (Award Number K08HL103776). The views expressed in this paper represent those of the authors, and do not necessarily represent the official views of the NCDR, its associated professional societies identified at www.ncdr.com, or the National Heart, Lung, and Blood Institute. Dr. Rao is a consultant for and receives consulting honoraria from The Medicines Company and Terumo. Dr. Masoudi is the Senior Medical Officer for the NCDR; and has received research grant support from the American College of Cardiology Foundation, and the Oklahoma Foundation for Medical Quality. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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women, who are known to be at high risk for bleeding, receive BAS during PCI as frequently as men in contemporary practice has not been determined. Furthermore, whether BAS are associated with similar reductions in peri-procedural bleeding in women compared with men is not known.

To address these gaps in knowledge, we compared the use of BAS (VCDs, bivalirudin, radial access, or their combinations) by sex and conducted an observational comparative effectiveness study of BAS to determine whether the lower risk of bleeding associated with BAS use was similar between women and men. This study was designed to provide a contemporary assessment of the use of BAS and the extent to which BAS may reduce the risk of this common adverse consequence in women undergoing PCI.

Methods

Data source. Data were obtained from the National Cardiovascular Data Registry's (NCDR) CathPCI Registry, which is an initiative of the American College of Cardiology (ACC) Foundation and the Society for Cardiovascular Angiography and Interventions. A detailed description of the registry has been published previously (14). Demographic, clinical, procedural, and institutional data elements for PCI procedures are collected at more than 1,400 participating centers throughout the United States (~80% of hospitals with invasive catheterization laboratories). Data are entered via a secure Web-based platform or via software provided by ACC certified vendors. Data quality assurance measures include automatic system validation and reporting of data completeness, random on-site auditing of participating centers, and education and training of site data managers (15).

Study population. All patients within the CathPCI Registry discharged after PCI between July 1, 2009 and March 31, 2011 were candidates for inclusion (n = 606,382 patients at 1,232 sites). Patients whose PCI did not use either a radial or femoral approach (n = 1,997) and those who underwent more than 1 PCI procedure during their hospital stay (n = 12,488) were excluded. Patients were also excluded if they had cardiogenic shock (n = 12,746), died the same day as the procedure (n = 568), or if they were missing data to determine a bleeding event (n = 165). Patients were also excluded if they received manual compression and a closure device (n = 7,382) because it was felt these cases might reflect failed deployment of the closure device. In addition, patients who had radial access and received a closure device (n = 106) or bivalirudin, radial access, and a closure device (n = 153) were excluded because this combination of treatments was felt to reflect procedures with combined femoral and radial access that might inherently pose a higher risk for peri-procedural bleeding irrespective of the BAS strategy used. After applying exclusions (total of 5.9% excluded), 570,777 patients at 1,230 sites remained. Among the final study cohort, 385,103 (67.5%) were men and 185,674 (32.5%) were women (Fig. 1).

Study outcomes. In-hospital bleeding complications following PCI were ascertained and reported by participating centers. Peri-procedural bleeding was defined according to the CathPCI V4 data definitions and included: 1) any documented bleeding event that occurred within 72 h after PCI regardless of site (including access site bleeding, access site hematoma, retroperitoneal bleeding, gastrointestinal bleeding, genital-urinary bleeding, intracerebral hemorrhage); 2) pericardial tamponade; 3) any transfusion following PCI (except among patients with pre-procedure hemoglobin ≤8 g/dl or those who underwent coronary artery bypass grafting during their hospital stay); or 4) any absolute decline of ≥3 g/dl in hemoglobin level (except for patients with pre-procedure hemoglobin >16 g/dl) (16).

Abbreviations and Acronyms

ACC = American College of Cardiology
BAS = bleeding avoidance strategy
CI = confidence interval
NCDR = National Cardiovascular Data Registry
NSTEMI = non–ST-elevation myocardial infarction
NYHA = New York Heart Association
OR = odds ratio
PCI = percutaneous coronary intervention
STEMI = ST-elevation myocardial infarction
VCD = vascular closure device

Bleeding avoidance strategies. BAS studied included: 1) VCDs alone (see Online Table 1 for list of specific devices included); 2) bivalirudin alone (Angiomax, The Medicines Company, Parsippany, New Jersey); 3) bivalirudin with VCD; 4) radial access alone; and 5) radial access with bivalirudin. Patients receiving manual compression who did not receive VCD, bivalirudin, or radial access served as the referent group for effectiveness comparisons.

Pre-procedural bleeding risk estimation. Estimated bleeding risk scores based upon pre-procedural patient characteristics were derived using the CathPCI bleeding risk model, version 4 (17). Risk scores were generated for each patient based on the inverse logarithmic sum of the beta coefficients for each of the following pre-PCI variables: sex, age, body mass index, previous cerebrovascular disease, chronic lung disease, previous PCI, peripheral vascular disease, diabetes mellitus, left ventricular ejection fraction, chronic kidney disease, PCI status (defined as elective, urgent, emergent, or salvage), ST-segment elevation myocardial infarction (STEMI), non–ST-segment elevation myocardial infarction (NSTEMI), cardiac arrest within 24 h, pre-procedure New York Heart Association (NYHA) class IV heart failure, estimated glomerular filtration rate, pre-procedure hemoglobin, pre-procedure Thrombolysis In Myocardial Infarction flow, number of diseased vessels, use of fibrinolytics before PCI, subacute stent thrombosis, Society for Cardiovascular Angiography and Intervention lesion class, and lesion location (proximal left anterior descending or left main vs. other).

Statistical analysis. Baseline demographic, clinical, procedural, and hospital characteristics were compared between