

Association Between Use of Bleeding Avoidance Strategies and Risk of Periprocedural Bleeding Among Patients Undergoing Percutaneous Coronary Intervention

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IMPROVING HOSPITAL SAFETY IS A recognized health care priority in the United States.¹ There is an important opportunity to improve the safety of percutaneous coronary intervention (PCI), a treatment performed approximately 1 million times a year in the United States alone.² Periprocedural bleeding is the most common noncardiac complication of PCI and is associated with risk of early mortality^{3,4} as well as higher costs of care.⁵ Moreover, the rate of periprocedural bleeding varies substantially across institutions and is modifiable through the use of bleeding avoidance strategies such as vascular closure devices, bivalirudin, and radial access. Underscoring the importance of bleeding complications and the opportunity for improvement, the Centers for Medi-

See also pp 2148 and 2188.

Context Bleeding complications with percutaneous coronary intervention (PCI) are associated with adverse patient outcomes. The association between the use of bleeding avoidance strategies and post-PCI bleeding as a function of a patient's preprocedural risk of bleeding is unknown.

Objective To describe the use of 2 bleeding avoidance strategies, vascular closure devices and bivalirudin, and associated post-PCI bleeding rates in a nationally representative PCI population.

Design, Setting, and Patients Analysis of data from 1 522 935 patients undergoing PCI procedures performed at 955 US hospitals participating in the National Cardiovascular Data Registry (NCDR) CathPCI Registry from January 1, 2004, through September 30, 2008.

Main Outcome Measure Periprocedural bleeding.

Results Bleeding occurred in 30 654 patients (2%). Manual compression, vascular closure devices, bivalirudin, or vascular closure devices plus bivalirudin were used in 35%, 24%, 23%, and 18% of patients, respectively. Bleeding events were reported in 2.8% of patients who received manual compression, compared with 2.1%, 1.6%, and 0.9% of patients receiving vascular closure devices, bivalirudin, and both strategies, respectively ($P < .001$). Bleeding rates differed by preprocedural risk assessed with the NCDR bleeding risk model (low risk, 0.72%; intermediate risk, 1.73%; high risk, 4.69%). In high-risk patients, use of both strategies was associated with lower bleeding rates (manual compression, 6.1%; vascular closure devices, 4.6%; bivalirudin, 3.8%; vascular closure devices plus bivalirudin, 2.3%; $P < .001$). This association persisted following adjustment using a propensity-matched and site-controlled model. Use of both strategies was used least often in high-risk patients (14.4% vs 21.0% in low-risk patients, $P < .001$).

Conclusions In a large national PCI registry, vascular closure devices and bivalirudin were associated with significantly lower bleeding rates, particularly among patients at greatest risk for bleeding. However, these strategies were less often used among higher-risk patients.

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care & Medicaid Services has identified bleeding and hematoma after cardiovascular procedures to be quality indicators among centers participating in its Acute Care Episode demonstration.⁶

To assist clinicians in identifying patients' risks for periprocedural bleed-

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ing, a risk model was previously developed and validated using the National Cardiovascular Data Registry (NCDR) CathPCI Registry.⁷ This model uses preprocedural variables to predict risk of bleeding events after PCI. To date, however, whether this model is useful in identifying patients with greater potential to benefit from bleeding avoidance strategies is unknown. It is also unknown whether clinicians treat the highest-risk patients preferentially. Failure to treat the highest-risk patients with bleeding avoidance strategies would demonstrate the potential for risk-stratifying patients at the time of PCI to direct therapy.

To address these gaps in knowledge, we described peri-PCI bleeding rates associated with the use of manual compression, vascular closure devices, bivalirudin, or both strategies (vascular closure devices plus bivalirudin) in patients across a spectrum of preprocedural bleeding risk; we also examined current patterns of the use of these strategies as a function of bleeding risk.

METHODS

Data Source and Definitions

The NCDR CathPCI Registry is a voluntary nationwide reporting system for diagnostic cardiac catheterization and PCI procedures jointly sponsored by the American College of Cardiology (ACC) and the Society for Cardiovascular Angiography and Interventions. Descriptions of the NCDR have been published.^{8,9} Demographic, clinical, procedural, and institutional data elements from diagnostic catheterization and PCI procedures are collected at more than 1100 participating centers. Data are entered via either a secure Web-based platform or software provided by ACC-certified vendors into a secure, centralized database (CathPCI version 3.04) stored at the ACC Heart House in Washington, DC. Data quality assurance includes automatic system validation and reporting of data completeness, random on-site auditing of participating centers, and education and training for site data managers.¹⁰ A comprehensive description of

NCDR data elements and definitions is available at <http://www.ncdr.com/WebNCDR/ELEMENTS.ASPX>.

All data elements and definitions were prospectively defined by a committee of the ACC. Race/ethnicity data were reported by patients or family and recorded in the medical record. Trained chart abstractors recorded race/ethnicity on the standard NCDR CathPCI case report form. The options were white, black, Hispanic, Asian, Native American, and other. Glomerular filtration rate was calculated using admission serum creatinine values and the abbreviated Modification of Diet in Renal Disease formula.¹¹

This study was approved by the Saint Luke's Health System institutional review board and was determined to meet the definition of research not requiring informed consent.

Study Patients and Exclusions

Only patients who underwent PCI via the femoral artery approach were included in this analysis. Exclusion criteria consisted of patients with more than 1 PCI procedure during a hospitalization (since bleeding events could not reliably be attributed to a specific procedure), incomplete data for calculation of expected bleeding rates, PCI through access of a nonfemoral artery (ie, radial, brachial), cardiogenic shock, missing device data, death in the catheterization laboratory, or unknown data on bleeding events.

Bleeding Avoidance Strategies and Risk Stratification

Candidate bleeding avoidance strategies consisted of vascular closure devices (Angio-Seal [St Jude Medical, St Paul, Minnesota], Perclose A-T [Abbott Vascular, Abbott Park, Illinois], or other) without bivalirudin; bivalirudin (Angiomax [The Medicines Company, Parsippany, New Jersey]) without vascular closure devices; or both strategies (vascular closure devices plus bivalirudin). Patients receiving manual compression did not receive vascular closure devices or bivalirudin and thus served as the reference group.

Bleeding rates were determined for all patients and within 3 clinically important subgroups, based on patients' pre-PCI bleeding risk scores derived using the NCDR CathPCI bleeding risk model.⁷ Risk scores were generated for each patient in this study based on the inverse logarithmic sum of the β coefficients for each of the following pre-PCI variables: ST-segment elevation myocardial infarction (MI), non-ST-segment elevation MI, female sex, previous congestive heart failure, no previous PCI, New York Heart Association/Canadian Cardiovascular Society Class IV heart failure, peripheral vascular disease, age, and estimated glomerular filtration rate.

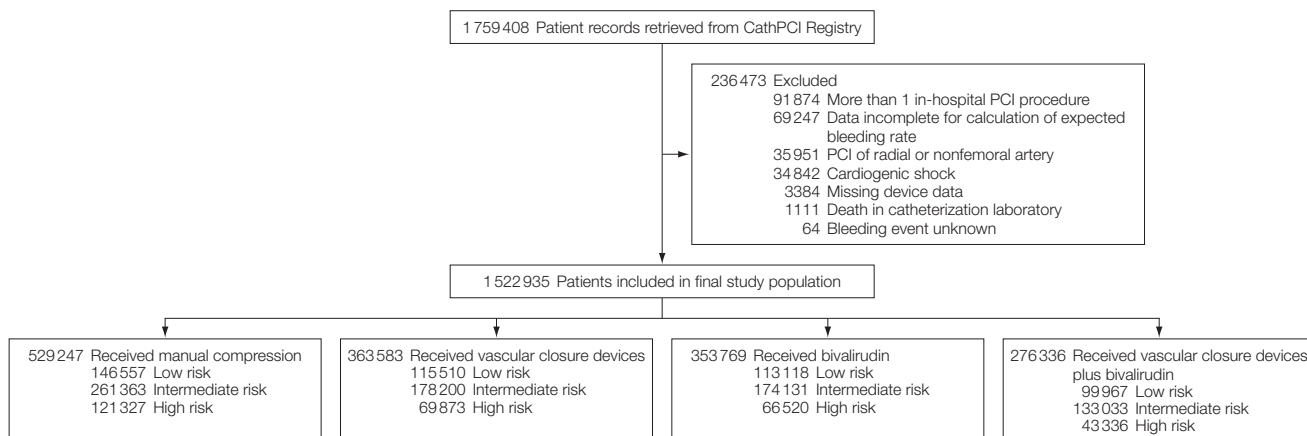
Study Outcomes

In-hospital bleeding complications following PCI were ascertained and voluntarily reported by centers. The primary outcome for this study was periprocedural bleeding, which, as defined by the NCDR CathPCI data definition, required a blood transfusion or a prolonged hospital stay for management or was associated with a decrease (>3 g/dL) in hemoglobin level.

Statistical Analysis

Demographic data were described across treatment groups as mean (SD) for continuous variables and number (%) for categorical variables. Patients with attempted use of vascular closure devices were included with the vascular closure devices group. Based on individual risk scores calculated using the NCDR CathPCI bleeding risk model,⁷ patients were categorized into 3 groups of risk for post-PCI bleeding events occurring during hospitalization: low ($<1\%$), intermediate ($1\%-3\%$), and high ($>3\%$).

To minimize confounding, a propensity score match analysis was implemented. Scores for each bleeding avoidance strategy (manual compression, vascular closure devices, bivalirudin, or vascular closure devices plus bivalirudin) were derived using a multinomial regression model.¹²⁻¹⁶ Variables used to derive these propensity scores

Figure. Selection of Study Population by Bleeding Avoidance Strategies

Records retrieved from National Cardiovascular Data Registry CathPCI version 3.04. PCI indicates percutaneous coronary intervention.

were demographics (age, sex, race/ethnicity); clinical characteristics (body mass index, New York Heart Association heart failure classification); coronary artery disease risk factors (diabetes, hypertension, dyslipidemia, smoking, family history of coronary artery disease); coronary artery disease history (PCI, coronary artery bypass graft surgery, MI); other cardiovascular disease history (congestive heart failure, cerebrovascular disease, peripheral vascular disease, valve surgery, cardiac transplantation); other disease history (chronic obstructive pulmonary disease, renal failure); and presenting syndrome (no symptoms, atypical chest pain, stable angina, unstable angina, ST-segment elevation MI, and non-ST-segment elevation MI).

Matching was performed simultaneously on all strategy propensity scores within the bleeding risk groups using nearest-neighbor matching without replacement, with a caliper width of 0.5%.¹² Absolute standardized differences were computed to evaluate matching effectiveness and displayed graphically¹⁷⁻¹⁹; values less than 10% and closer to zero demonstrate a more balanced cohort.¹⁷ Hierarchical modeling was then performed on the matched cohort to account for hospital characteristics. From this model, odds ratios were obtained to estimate

the number of patients needed to treat to prevent 1 bleeding event for each strategy compared with manual compression.²⁰⁻²²

Statistical significance was defined as $P < .05$. All statistical analyses were performed by the Saint Luke's Mid America Heart Institute Department of Biostatistics using SAS version 9.2 (SAS Institute, Cary, North Carolina).

RESULTS

Population Characteristics

From January 1, 2004, to September 30, 2008, 1 759 408 patients underwent PCI. After exclusions (FIGURE), there were 1 522 935 eligible patients at 955 centers. Patient demographics, clinical characteristics, risk factors, disease history, admission presentation, and selected hospital characteristics for the entire population and for subgroups according to bleeding avoidance strategy are shown in TABLE 1 and TABLE 2.

Overall, bleeding occurred in 30 429 patients (2%). Bleeding rates by candidate strategy for the overall study population are shown in TABLE 3 and eFigure 1 (available at <http://www.jama.com>). Manual compression was used in 35% of patients, vascular closure devices in 24%, bivalirudin in 23%, and vascular closure devices plus bivalirudin in 18%. Bleeding events were re-

ported in 2.8% of patients who received manual compression, compared with 2.1% receiving vascular closure devices, 1.6% receiving bivalirudin, and 0.9% receiving both strategies ($P < .001$) (Table 3 and eFigure 1).

According to the NCDR CathPCI bleeding risk model, bleeding risk was classified as low (<1%) in 475 152 patients (31%), intermediate (1%-3%) in 746 727 (49%), and high (>3%) in 301 056 (20%). Observed rates of bleeding in these categories were 0.72%, 1.73%, and 4.69%, respectively. Bleeding rates associated with candidate strategies stratified by preprocedural risk category are shown in Table 3 and eFigure 1. In the low-risk group, manual compression was associated with a bleeding rate of 0.9%, vascular closure devices with a rate of 0.9%, bivalirudin with a rate of 0.6%, and vascular closure devices plus bivalirudin with a rate of 0.4% ($P < .001$). As preprocedural risk of bleeding increased, differences in actual bleeding rates between strategies became more pronounced. In the intermediate-risk group, manual compression was associated with a bleeding rate of 2.3%, vascular closure devices with a rate of 1.9%, bivalirudin with a rate of 1.4%, and vascular closure devices plus bivalirudin with a rate of 0.8% ($P < .001$); in the high-risk group, the corresponding

rates were 6.1%, 4.6%, 3.8%, and 2.3%, respectively ($P < .001$).

Propensity-Matched and Site-Adjusted Analysis

In the overall group, 508 455 of 529 247 eligible patients receiving manual compression (96%) were propensity matched using multinomial regres-

sion modeling to patients who received bleeding avoidance strategies. Corresponding values were 144 594 of 146 557 (99%) in the low-risk group, 252 898 of 261 363 (97%) in the intermediate-risk group, and 110 963 of 121 327 (91%) in the high-risk group. The effectiveness of propensity matching in the total cohort is demonstrated

in eFigure 2, which is a standardized difference plot for variables used in the propensity model. After matching, the absolute standardized difference between patients who received bleeding avoidance strategies and controls for each covariable was 0% to 1%.

TABLE 4 shows in-hospital bleeding events, odds ratios, the estimated num-

Table 1. Patient and Clinical Characteristics by Treatment Type^a

Characteristic	No. (%)				
	Total (N = 1 522 935)	Manual Compression (n = 529 247)	Vascular Closure Devices (n = 363 583)	Bivalirudin (n = 353 769)	Vascular Closure Devices + Bivalirudin (n = 276 336)
Demographics					
Age, mean (SD), y	64.3 (12.1)	63.87 (12.33)	63.34 (12.26)	65.43 (11.86)	64.77 (11.80)
Men	1 011 992 (66.5)	350 424 (66.21)	250 753 (68.97)	225 235 (63.67)	185 580 (67.16)
White	1 289 673 (84.8)	449 617 (85.05)	301 908 (83.18)	303 317 (85.82)	234 831 (85.11)
Clinical characteristics					
Height, mean (SD), cm	171.30 (10.84)	171.22 (10.89)	171.73 (10.77)	170.81 (10.90)	171.50 (10.73)
Weight, mean (SD), kg	87.71 (20.45)	87.25 (20.42)	88.22 (20.28)	87.29 (20.71)	88.47 (20.40)
Body mass index, mean (SD) ^b	29.8 (6.3)	29.7 (6.3)	29.8 (6.2)	29.8 (6.4)	30.0 (6.3)
Obesity ^c	643 500 (42.25)	219 470 (41.47)	153 233 (42.15)	150 813 (42.63)	119 984 (43.42)
Current CHF	136 489 (8.96)	48 658 (9.19)	30 799 (8.47)	33 173 (9.38)	23 859 (8.63)
NYHA class					
I	480 785 (31.57)	160 016 (30.24)	125 209 (34.44)	107 678 (30.44)	87 882 (31.81)
II	355 937 (23.37)	107 093 (20.24)	79 475 (21.86)	90 682 (25.64)	78 687 (28.48)
III	415 651 (27.30)	146 439 (27.67)	87 352 (24.03)	107 952 (30.52)	73 908 (26.75)
IV	270 376 (17.76)	115 629 (21.85)	71 508 (19.67)	47 412 (13.40)	35 827 (12.97)
Coronary artery disease risk factors					
Diabetes	509 455 (33.45)	173 024 (32.69)	113 130 (31.12)	129 335 (36.56)	93 966 (34.00)
Hypertension	1 190 098 (78.15)	405 122 (76.55)	272 906 (75.06)	290 085 (82.00)	221 985 (80.33)
Dyslipidemia	1 167 108 (76.64)	392 248 (74.12)	269 478 (74.12)	283 174 (80.05)	222 208 (80.42)
Smoking					
Never	600 315 (38.87)	196 423 (37.12)	143 554 (39.49)	138 026 (39.02)	114 318 (41.37)
Past	543 091 (35.17)	178 466 (33.72)	121 980 (33.55)	132 027 (37.32)	102 545 (37.11)
Current	400 845 (25.96)	154 297 (29.16)	97 995 (26.96)	83 681 (23.66)	59 439 (21.51)
Estimated GFR, mean (SD)	73.77 (29.62)	73.60 (29.88)	75.02 (30.48)	72.46 (29.06)	74.09 (28.61)
Family history of coronary artery disease ^d	392 815 (25.80)	135 320 (25.57)	100 704 (27.70)	86 660 (24.50)	70 131 (25.38)
Coronary artery disease history					
PCI	576 207 (37.84)	182 518 (34.49)	125 649 (34.56)	151 835 (42.92)	116 205 (42.05)
CABG	291 773 (19.16)	98 038 (18.52)	59 980 (16.50)	79 189 (22.39)	54 566 (19.75)
Myocardial infarction	427 655 (28.08)	144 381 (27.28)	96 191 (26.46)	106 403 (30.08)	80 690 (29.20)
Other cardiovascular disease history					
CHF	136 483 (8.96)	54 661 (10.33)	32 255 (8.87)	43 082 (12.18)	28 751 (10.40)
Cerebrovascular disease	174 811 (11.48)	60 260 (11.39)	34 638 (9.53)	48 214 (13.63)	31 699 (11.47)
Peripheral vascular disease	181 787 (11.74)	65 568 (12.39)	33 064 (9.09)	50 678 (14.33)	29 477 (10.67)
Previous valve surgery	17 267 (1.13)	5929 (1.12)	3672 (1.01)	4505 (1.27)	3161 (1.14)
Previous cardiac transplant	3463 (0.23)	1257 (0.24)	732 (0.20)	899 (0.25)	575 (0.21)
Other disease history					
Chronic lung disease	248 918 (16.35)	86 586 (16.36)	52 995 (14.58)	65 139 (18.41)	44 198 (15.99)
Renal failure	83 029 (5.45)	30 004 (5.67)	18 028 (4.96)	21 369 (6.04)	13 628 (4.93)

Abbreviations: CABG, coronary artery bypass graft surgery; CHF, congestive heart failure; GFR, glomerular filtration rate; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

^a $P < .001$ for all comparisons within bleeding avoidance strategy groups.

^bCalculated as weight in kilograms divided by height in meters squared.

^cBody mass index of 30 or greater.

^dIn relative(s) younger than 55 years.

ber needed to treat to prevent 1 bleeding event, and the estimated reduction in bleeding events per 1000 patients treated with each strategy relative to manual compression in the matched, site-adjusted cohort. Data are displayed for the overall population and by preprocedural bleeding risk group.

Independent of preprocedural risk, the use of vascular closure devices, bivalirudin, and vascular closure devices plus bivalirudin were associated with fewer bleeding events per 1000 patients treated (6.7 [95% confidence interval {CI}, 5.7-7.7], 8.5 [95% CI, 7.6-9.3], and 14.2 [95% CI, 13.5-14.8] events,

respectively). In patients receiving both strategies, the high-risk group had fewer bleeding events per 1000 patients treated compared with the intermediate- and low-risk groups (30.5 [95% CI, 27.9-32.8] vs 12.5 [95% CI, 11.6-13.3] and 5.3 [95% CI, 4.5-6.0] events, respectively).

Table 2. Admission Presentation and Hospital Characteristics by Treatment Type^a

Characteristic	No. (%)				
	Total (n = 1 522 935)	Manual Compression (n = 529 247)	Vascular Closure Devices (n = 363 583)	Bivalirudin (n = 353 769)	Vascular Closure Devices + Bivalirudin (n = 276 336)
Admission presentation					
No symptoms	196 190 (12.88)	55 961 (10.57)	42 224 (11.61)	54 346 (15.36)	43 659 (15.80)
Atypical chest pain	113 339 (7.44)	32 570 (6.15)	27 031 (7.44)	27 758 (7.85)	25 980 (9.40)
Stable angina	260 582 (17.11)	73 109 (13.81)	57 179 (15.73)	69 093 (19.53)	61 201 (22.15)
Unstable angina	527 624 (34.65)	168 813 (31.90)	113 413 (31.19)	142 473 (40.27)	102 925 (37.25)
NSTEMI	238 305 (15.65)	98 866 (18.68)	64 921 (17.86)	43 239 (12.22)	31 279 (11.32)
STEMI	186 810 (12.27)	99 900 (18.88)	58 796 (16.17)	16 843 (4.76)	11 271 (4.08)
PCI type					
Elective	758 110 (49.79)	220 576 (41.68)	157 348 (43.28)	212 562 (60.09)	167 624 (60.67)
Urgent	553 524 (36.35)	196 634 (37.16)	140 023 (38.52)	121 995 (34.49)	94 872 (34.34)
Emergency	209 465 (13.76)	110 990 (20.97)	65 758 (18.09)	19 011 (5.37)	13 706 (4.96)
Salvage	1662 (0.11)	968 (0.18)	422 (0.12)	172 (0.05)	100 (0.04)
Hospital characteristics					
Region					
West	244 853 (16.11)	71 085 (13.47)	73 065 (20.15)	41 801 (11.83)	58 902 (21.36)
Northeast	177 930 (11.71)	56 353 (10.68)	60 120 (16.58)	28 392 (8.04)	33 065 (11.99)
Midwest	505 125 (33.24)	198 609 (37.63)	119 220 (32.88)	104 043 (29.45)	83 253 (30.19)
South	591 568 (38.93)	201 679 (38.22)	110 237 (30.40)	179 071 (50.68)	100 581 (36.47)
Community type					
Rural	177 441 (15.92)	59 727 (15.44)	54 008 (21.02)	31 542 (11.48)	32 164 (16.38)
Urban	937 476 (84.08)	327 222 (84.56)	202 931 (78.98)	243 165 (88.52)	164 158 (83.62)
Profit type					
Government	23 838 (1.57)	7895 (1.49)	4948 (1.36)	5988 (1.69)	5007 (1.81)
Private/community	1 356 756 (89.09)	465 238 (87.91)	319 915 (87.99)	318 550 (90.04)	253 053 (91.57)
University	142 341 (9.35)	56 114 (10.60)	38 720 (10.65)	29 231 (8.26)	18 276 (6.61)
Annual PCI volume, mean (SD)	1095.81 (735.18)	1058.04 (704.88)	981.16 (732.27)	1303.62 (782.65)	1052.94 (678.44)

Abbreviations: NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

^a*P* < .001 for all comparisons within bleeding avoidance strategy groups.

Table 3. Bleeding Rates by Pre-Percutaneous Coronary Intervention Risk of Bleeding and Use of Bleeding Avoidance Strategies^a

Risk Category ^b	No. (%)			
	Manual Compression (n = 529 247)	Vascular Closure Devices (n = 363 583)	Bivalirudin (n = 353 769)	Vascular Closure Devices + Bivalirudin (n = 276 336)
Overall	14 742 (2.8)	7642 (2.1)	5547 (1.6)	2498 (0.9)
Low (<1%) ^c	1349 (0.9)	1063 (0.9)	637 (0.6)	368 (0.4)
Intermediate (1%-3%) ^d	5996 (2.3)	3377 (1.9)	2413 (1.4)	1121 (0.8)
High (>3%) ^e	7397 (6.1)	3202 (4.6)	2497 (3.8)	1009 (2.3)

^a*P* < .001 for all comparisons within bleeding avoidance strategy groups.

^bSee "Methods" for details of risk categories.

^cData available for 475 152 patients.

^dData available for 746 727 patients.

^eData available for 301 056 patients.

Table 4. Estimated Reductions in Bleeding Events Relative to Manual Compression Following Site-Adjusted Propensity Matching

Risk Category ^a	Treatment, No. ^b	In-hospital Bleeding Events, No. (%) ^{c,d}	OR (95% CI)	NNT (95% CI) ^d	Reduction in Bleeding Events per 1000 Patients Treated (95% CI)
All patients					
Manual compression	508 455	13 597 (2.7)	1 [Reference]		
Vascular closure devices	205 606	5050 (2.5)	0.77 (0.73-0.80)	148 (130-175)	6.7 (5.7-7.7)
Bivalirudin	172 471	3224 (1.9)	0.67 (0.63-0.70)	118 (107-132)	8.5 (7.6-9.3)
Vascular closure devices + bivalirudin	130 378	1361 (1.0)	0.38 (0.35-0.42)	70 (68-74)	14.2 (13.5-14.8)
Total	1 016 910	23 232 (2.3)			
Low (<1%)					
Manual compression	144 594	1320 (0.9)	1 [Reference]		
Vascular closure devices	54 217	532 (1.0)	1.07 (0.93-1.22)	NS	NS
Bivalirudin	48 378	296 (0.6)	0.65 (0.56-0.77)	315 (247-470)	3.2 (2.1-4.0)
Vascular closure devices + bivalirudin	41 999	166 (0.4)	0.42 (0.34-0.51)	188 (167-222)	5.3 (4.5-6.0)
Total	289 188	2314 (0.8)			
Intermediate (1%-3%)					
Manual compression	252 898	5722 (2.3)	1 [Reference]		
Vascular closure devices	103 095	2077 (2.0)	0.76 (0.71-0.81)	169 (141-217)	5.9 (4.6-7.1)
Bivalirudin	85 800	1311 (1.5)	0.69 (0.63-0.74)	153 (131-187)	6.5 (5.3-7.6)
Vascular closure devices + bivalirudin	64 003	573 (0.9)	0.39 (0.35-0.44)	80 (75-86)	12.5 (11.6-13.3)
Total	505 796	9683 (1.9)			
High (>3%)					
Manual compression	110 963	6555 (5.9)	1 [Reference]		
Vascular closure devices	48 294	2441 (5.1)	0.79 (0.75-0.82)	81 (66-109)	12.3 (9.2-15.3)
Bivalirudin	38 293	1617 (4.2)	0.67 (0.62-0.73)	56 (49-66)	17.9 (15.1-20.6)
Vascular closure devices + bivalirudin	24 376	622 (2.6)	0.42 (0.38-0.47)	33 (31-36)	30.5 (27.9-32.8)
Total	221 926	11 235 (5.1)			

Abbreviations: CI, confidence interval; OR, odds ratio; NNT, number needed to treat; NS, not significant.

^aSee "Methods" for details of risk categories.

^bPatients in treatment group matched 1:1 to controls (manual compression); total sample population is 2 times the number treated.

^cPropensity-matched cohort; data not adjusted for site.

^dNumber of patients needed to treat to prevent 1 bleeding event (compared with manual compression).

Use of Strategies by Strata of Bleeding Risk

The frequency of use of bleeding avoidance strategies according to estimated pre-PCI risk of bleeding is shown in TABLE 5. Manual compression was used most often in the highest-risk patients and least often in the intermediate- and lowest-risk cohorts (40.3% vs 35.0% and 30.8%, respectively; $P < .001$), while the use of vascular closure devices plus bivalirudin was highest in low-risk patients (21.0%) and lower in intermediate-risk (17.8%) and high-risk (14.4%) patients ($P < .001$).

COMMENT

Using data from more than 1.5 million patients in the NCDR CathPCI Registry, we compared bleeding rates among patients undergoing PCI and receiving strategies to mitigate bleeding across a spectrum of preprocedural risk

Table 5. Use of Bleeding Avoidance Strategies by Estimated Pre-Percutaneous Coronary Intervention Risk of Bleeding^a

Strategy	Risk Category, No. (%) ^b		
	Low (n = 475 152)	Intermediate (n = 746 727)	High (n = 301 056)
Manual compression	146 557 (30.8)	261 363 (35.0)	121 327 (40.3)
Vascular closure devices	115 510 (24.3)	178 200 (23.9)	69 873 (23.2)
Bivalirudin	113 118 (23.8)	174 131 (23.3)	66 520 (22.1)
Vascular closure devices + bivalirudin	99 967 (21.0)	133 033 (17.8)	43 336 (14.4)

^a $P < .001$ for all comparisons within bleeding avoidance strategy groups.

^bSee "Methods" for details of risk categories.

for bleeding. Among high-risk patients, the use of vascular closure devices plus bivalirudin was associated with an absolute 3.8% lower bleeding rate, which translates into an estimated number needed to treat of 33 to prevent 1 bleeding event as compared with manual compression. Lower rates of bleeding associated with this treat-

ment strategy were proportionately less in intermediate- and low-risk patients. Despite the association between the use of vascular closure devices plus bivalirudin and lower bleeding rates among the highest-risk patients, these patients were the least likely to receive both strategies and most likely to receive manual compres-

sion. This apparent risk-treatment paradox highlights an opportunity for routine preprocedural risk stratification as a means to identify patients ideally suited for individualized bleeding avoidance strategies with the goal of increasing the safety of PCI.

Targeting bleeding complications as a quality-improvement goal holds great potential for improving the safety and cost-effectiveness of PCI. Among the more than 1 million PCIs performed annually in US hospitals, bleeding is a morbid and costly complication, occurring in 2% to 6% of patients,²³⁻²⁷ with wide variability across institutions. Major bleeding events result in an average 4- to 6-day increase in length of stay^{28,29} and, on average, increase hospital costs by \$6000 to \$8000.⁵ In addition to its association with nonfatal MI^{28,30} and stroke,³⁰ periprocedural bleeding is also strongly associated with early^{3,4} and late³ mortality. Bleeding also exposes many patients to the added risk of blood transfusions.²³ According to the Healthcare Cost and Utilization Project, 50% of patients experiencing bleeding following PCI receive a blood transfusion, which is associated with greater median length of stay (2 vs 6 days) and greater mean hospital charges (\$48 000 vs \$85 000).³¹

The current study found that higher-risk patients—those with the greatest potential to benefit from bleeding avoidance strategies—were the least likely to be treated with such strategies in contemporary clinical practice. Conversely, the lowest-risk patients were the most likely to receive bleeding avoidance strategies, supporting the presence of a risk-treatment paradox.³²⁻³⁵ This phenomenon has been demonstrated in a variety of medical treatment scenarios, including lower rates of angiotensin-converting enzyme inhibitor or β -blocker use in patients with severe heart failure,³² lower use of angiography after acute MI,³⁶⁻³⁸ and lower use of statins in higher-risk patients with angiographically confirmed coronary disease.³⁹

Several factors may contribute to the higher use of bleeding avoidance strat-

egies in lower-risk patients found in this study. First, assessing the risk for bleeding in clinical practice is neither inherently intuitive nor commonly used. Second, physicians have more experience using bivalirudin in lower-risk patients, since it was first studied in patients undergoing elective PCI and only recently in higher-risk patients (ie, those with ST-segment elevation MI).⁴⁰ Lastly, the prior published data for bleeding mitigation with vascular closure devices has been limited.⁴¹⁻⁴³

The results of this study suggest the need for additional research to better understand why higher-risk patients are least likely to receive bleeding avoidance strategies but also suggest the need to test interventions to overcome the risk-treatment paradox, such as enabling physicians to purposefully direct bleeding avoidance strategies to patients by providing preprocedural estimates of post-PCI bleeding. Translation of the findings in this study into clinical practice to optimally guide the use of such strategies will be challenging. Incorporating risk models into everyday care, which requires capturing risk factors, estimating individual risk, and presenting information in a clear and understandable manner at the point of care for physicians, is currently not feasible for many clinical environments. However, with the current national investment in health information technology, increasing literature on clinical decision support, increasing focus by regulatory and other agencies on the documentation of patient risk to guide care, and the development of quality-of-care tools by entities such as the ACC and the Society for Cardiovascular Angiography and Interventions, the health care environment is increasingly capable of supporting the implementation of point-of-care interventions to help guide effective and safe care.

It should be noted that there are more supporting data on the efficacy of bivalirudin than on that of vascular closure devices with regard to bleeding avoidance. In randomized trials including patients with broad indications for PCI (elective or acute coronary syn-

dromes), bivalirudin has been demonstrated to reduce major bleeding following PCI to an extent comparable with the findings in this observational study.^{24,44-46} Randomized controlled trials demonstrating reductions in bleeding associated with the use of vascular closure devices were designed to assess ambulation time rather than bleeding. A meta-analysis of 30 clinical studies, including 4000 patients, showed a trend for reduced vascular complications associated with the Angio-Seal device (odds ratio, 0.46; 95% CI, 0.20-1.04; $P = .06$).⁴² A recent analysis from the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial also suggests that a significant reduction in major bleeding is associated not only with the use of bivalirudin but also with vascular closure devices in patients undergoing PCI in the setting of unstable angina or non-ST-segment elevation MI.⁴³ Similar to our study, the greatest reduction in bleeding was seen in patients receiving both a vascular closure device and bivalirudin.

Given the findings of our observational study and that previous data linking vascular closure devices to bleeding are both limited and from non-randomized studies, an adequately powered randomized trial of vascular closure devices evaluating post-PCI bleeding end points is needed. It is also important to note that data on vascular closure devices and bivalirudin were published during a period overlapping with data collection in the present study, and bivalirudin was not included in PCI guidelines⁴⁷ until 2006. Thus, there may be important temporal trends for rates of strategies not investigated in this study.

Several aspects of this work should be considered when interpreting our results and in translating these findings to clinical practice. First, this was not a randomized trial; thus, a causal relationship between bleeding avoidance and evaluated strategies cannot be concluded. Second, potential unmeasured confounding is a limitation of all observational studies. We sought to

minimize confounding through the use of a center-adjusted, multinomial propensity-matched analysis, which successfully balanced the observable patient and treatment characteristics; nevertheless, some unmeasured confounding may have been present. The NCDR CathPCI Registry also does not currently collect data on complications related to vascular closure devices. However, the reported frequency of such complications is low.⁴⁸

Third, activated clotting time is not available in the NCDR CathPCI Registry, which limited our ability to assess the relationship between heparin dosing, level of anticoagulation, and bleeding, which could have further informed the observed variability in bleeding among the cohort receiving manual compression.

Fourth, some patients are not suited to receive bleeding avoidance strategies. For example, bivalirudin is not recommended in the setting of therapeutic anticoagulation with prior agents, including unfractionated or low-molecular-weight heparin with or without a glycoprotein IIb/IIIa agent. Bivalirudin is also not currently recommended in patients undergoing PCI for a chronic total occlusion.⁴⁹ Furthermore, mitigation of bleeding risk may be neutralized with the concomitant use of glycoprotein IIb/IIIa inhibitors and in the setting of renal failure. Vascular closure devices are also not recommended for use given several anatomical limitations, such as puncture at the site of an anatomical arterial bifurcation, presence of severe calcification, or presence of severe obstructive peripheral artery disease; the reasons for not using a vascular closure device for a given patient are not collected in the CathPCI Registry. To the extent that some of these examples cluster more frequently in patients at intermediate or high risk for bleeding, there will be a reduction in potential to offset the apparent risk-treatment paradox observed in this study.

CONCLUSIONS

In a large, national PCI registry, the use of vascular closure devices and bivali-

rudin was associated with significantly lower rates of periprocedural bleeding. However, there was an apparent risk-treatment paradox, whereby patients at greatest risk of bleeding were least likely to receive a bleeding avoidance strategy. These findings emphasize the opportunity to improve the safety of PCI and to further explore cost efficacy by directing such strategies to those patients most likely to benefit from them.

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Study concept and design: Marso, House, Kennedy, Spertus, Rumsfeld.

Acquisition of data: House.

Analysis and interpretation of data: Marso, Amin, House, Kennedy, Spertus, Rao, Cohen, Messenger, Rumsfeld.

Drafting of the manuscript: Marso, House, Spertus, Rumsfeld.

Critical revision of the manuscript for important intellectual content: Marso, Amin, House, Kennedy, Spertus, Rao, Cohen, Messenger, Rumsfeld.

Statistical analysis: Marso, Amin, House, Kennedy, Rao.

Administrative, technical, or material support: Marso, House, Spertus, Messenger, Rumsfeld.

Study supervision: Marso, Rumsfeld.

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