ORIGINAL RESEARCH

Reversing the "Risk-Treatment Paradox" of Bleeding in Patients Undergoing Percutaneous Coronary Intervention: Risk-Concordant Use of Bleeding Avoidance Strategies Is Associated With Reduced Bleeding and Lower Costs

Amit P. Amin, MD, MSc; Samantha Miller, RN; Brandon Rahn, MHA; Mary Caruso, RN; Andrew Pierce, MHA; Katrine Sorensen, MS; Howard Kurz, MD; Alan Zajarias, MD; Richard Bach, MD; Jasvindar Singh, MD; John M. Lasala, MD, PhD; Hemant Kulkarni, MD; Patricia Crimmins-Reda, RN

***Background*—**Bleeding is a common, morbid, and costly complication of percutaneous coronary intervention. While bleeding avoidance strategies (BAS) are effective, they are used paradoxically less in patients at high risk of bleeding. Whether a patient-centered approach to specifically increase the risk-concordant use of BAS and, thus, reverse the risk-treatment paradox is associated with reduced bleeding and costs is unknown.

***Methods and Results*—**We implemented an intervention to reverse the bleeding risk-treatment paradox at Barnes-Jewish Hospital, St. Louis, MO, and examined: (1) the temporal trends in BAS use and (2) the association of risk-concordant BAS use with bleeding and hospital costs of percutaneous coronary intervention. Among 3519 percutaneous coronary interventions, there was a significantly increasing trend (P=0.002) in risk-concordant use of BAS. The bleeding incidence was 2% in the risk-concordant group versus 9% in the risk-discordant group (absolute risk difference, 7%; number needed to treat, 14). Risk-concordant BAS use was associated with a 67% (95% confidence interval, 52–78%; P<0.001) reduction in the risk of bleeding and a $4738 (95% confidence interval, 3353–6122; P<0.001) reduction in per-patient percutaneous coronary intervention hospitalization costs (21.6% cost-savings).

***Conclusions*—**In this study, patient-centered care directly aimed to make treatment-related decisions based on predicted risk of bleeding, led to more risk-concordant use of BAS and reversal of the risk-treatment paradox. This, in turn, was associated with a reduction in bleeding and hospitalization costs. Larger multicentered studies are needed to corroborate these results. As clinical medicine moves toward personalization, both patients and hospitals can benefit from a simple practice change that encourages objectivity and mitigates variability in care. **(*J Am Heart Assoc*. 2018;7:e008551. DOI: 10.1161/JAHA.118.008551.)**

Key Words: anticoagulant • bleeding • cost • percutaneous coronary intervention • radial artery catheter

Bleeding is the most common complication of the percutaneous coronary intervention (PCI) procedure.[1–4] Bleeding is life-threatening, morbid, and painful and increases patients' risks of short- and long-term mortality.[2,5,6] Bleeding occurs in 2% to >10% of the more than 600 000 patients who undergo PCI each year.[2,3,5,6] Bleeding costs $12 000 per episode; therefore, there are significant health and economic burdens for patients and for society at large.[7–14] Although many hospitals have high rates of bleeding, few hospitals have systematically attempted to reduce bleeding to make PCI safer and more inexpensive.

Bleeding after PCI is predictable and modifiable, and validated risk-prediction models can accurately quantify a patient's risk before bleeding occurs.[4,15,16] If bleeding risk is known, a patient-centered approach that targets patients at risk with effective bleeding avoidance strategies (BAS) can be used, such as bivalirudin,[17,18] radial access,[1,19] and vascular closure devices (VCDs).[3] Frequently, patients at risk of bleeding also have renal disease and calcified vessels and are perceived to have difficulties with BAS use. Therefore, BAS are currently used inconsistently, particularly among patients with the highest risk of bleeding, hence called the bleeding *risk-treatment paradox*.[3] A prior analysis by our group from

From the Cardiovascular Division (A.P.A., K.S., A.Z., R.B., H. Kurz, J.S., J.M.L.) and Center for Value and Innovation (A.P.A., S.M., B.R., M.C., P.C.-R.), Washington University School of Medicine, St. Louis, MO; Barnes-Jewish Hospital, St. Louis, MO (A.P.A., S.M., B.R., M.C., A.P., A.Z., R.B., H. Kurz, J.S., J.M.L., P.C.-R.); M&H Research, LLC, San Antonio, TX (H. Kulkarni).

Correspondence to: Amit P. Amin, MD, MSc, Cardiology Division, Washington University School of Medicine, Campus Box 8086, 660 South Euclid Avenue, St. Louis, MO 63110. E-mail: aamin@wustl.edu

Received January 4, 2018; accepted August 16, 2018.

Clinical Perspective

What Is New?

- In patients undergoing percutaneous coronary intervention, bleeding avoidance strategies are used paradoxically less in patients at high risk of bleeding (the bleeding risk-treatment paradox), but few studies have directly attempted to reverse the bleeding risk-treatment paradox.
- We prospectively implemented a patient-centered approach directly aimed to encourage risk-concordant use of bleeding avoidance strategies to reverse the bleeding risk-treatment paradox, which was associated with a 67% reduction in bleeding with an absolute risk difference of 7%, a number needed to treat of 14, and a $4738 per-patient reduction in percutaneous coronary intervention hospitalization costs.

What Are the Clinical Implications?

- The bleeding risk-treatment paradox in patients undergoing percutaneous coronary intervention is pervasive in the United States. Our study demonstrates the feasibility and need of reversing it to reduce bleeding nationally.
- By focusing on bleeding risk at the point-of-care, it was feasible to impact the risk-treatment paradox and achieve risk-concordant use of bleeding avoidance strategies, which, in turn, was associated with large reductions in bleeding and costs.

national data for 1.5 million PCI procedures revealed a clear risk-treatment paradox.[3]

There have been few efforts[20,21] to reverse the bleeding risk-treatment paradox. In spite of the observation over the past few years that the use of transradial access demonstrates an increasing trend,[22] systematic risk-based use of BAS is far from established and, in fact, demonstrates a large risk-treatment paradox.[23] Conceptually, a patient-centered approach to specifically increase the risk-concordant use of BAS and reverse the risk-treatment paradox to reduce bleeding has not been examined. Furthermore, the impact of such risk-concordant BAS use on hospital costs has not been examined. We, therefore, implemented a specific intervention to reverse the risk-treatment paradox at Barnes-Jewish Hospital (BJH) in St. Louis, MO, and examined: (1) the temporal trends in BAS use and (2) the association of risk-concordant BAS use with bleeding outcomes and hospital costs of PCI.

Methods

Patient-Centered Intervention

We implemented a patient-centered approach via a nurse-led health information technology solution[24,25] to translate a bleeding risk-prediction model,[4] to predict individualized bleeding risk in the cardiac catheterization laboratory, to explicitly bring bleeding risk to the physician's attention via a decision aid, and to encourage risk-concordant use of BAS for patients at risk. Before the decision on choice of access and anticoagulant use was made, the intraprocedural nurse performed a mandatory "time-out" to include the predicted bleeding risk from the decision aid, with a hard stop to not proceed unless the bleeding risk was acknowledged by the attending physician. Thus, the treatment decisions for BAS made by the physician were based fully on the predicted risks of bleeding.

Study Design and Implementation

This study was designed as a patient-centered, pre-post quasi-experimental design to investigate PCI bleeding outcomes and BAS use from the years preceding the implementation compared with those after the implementation. We implemented the patient-centered approach by a nurse-led, health information technology solution, ePRISM, to translate NCDR (National Cardiovascular Data Registry) CathPCI bleeding risk-prediction model[4] to generate personalized estimates of bleeding risk, which were displayed as a decision aid in the catheterization laboratory to inform physicians of each patient's personalized bleeding risk before PCI (Figure 1). The decision aid encouraged physicians to use risk-concordant BAS, aligned with each patient's personalized bleeding risk (Figure 1). We also performed monthly audits and feedback for peer-to-peer comparisons of physicians' bleeding rates and risk-concordant use of BAS, to align use of BAS with patients' bleeding risk.

Study Population

This study included 3519 PCIs (conducted in 3366 patients) at BJH in St. Louis, MO, from July 2012 to September 2015. We used BJH data from the NCDR CathPCI Registry. The CathPCI Registry itself is cosponsored by the American College of Cardiology and the Society for Cardiovascular Angiography and Interventions, and has been used extensively in the past.[26] This registry evaluates characteristics, treatments, and outcomes of patients undergoing PCI and/or diagnostic catheterization.[26] Complete definitions for all predefined variables are available at the American College of Cardiology's NCDR website (http://cvquality.acc.org/en/NCDR-Home/Registries/Hospital-Registries.aspx). The CathPCI Registry is available for numerous hospitals, but this study was solely limited to BJH, where we implemented the patient-centered approach. The aforementioned, patient-centered approach was instituted in May 2013. However, a period of ≈6 months was required for training and routine use of this intervention. Therefore, our study tenure could be

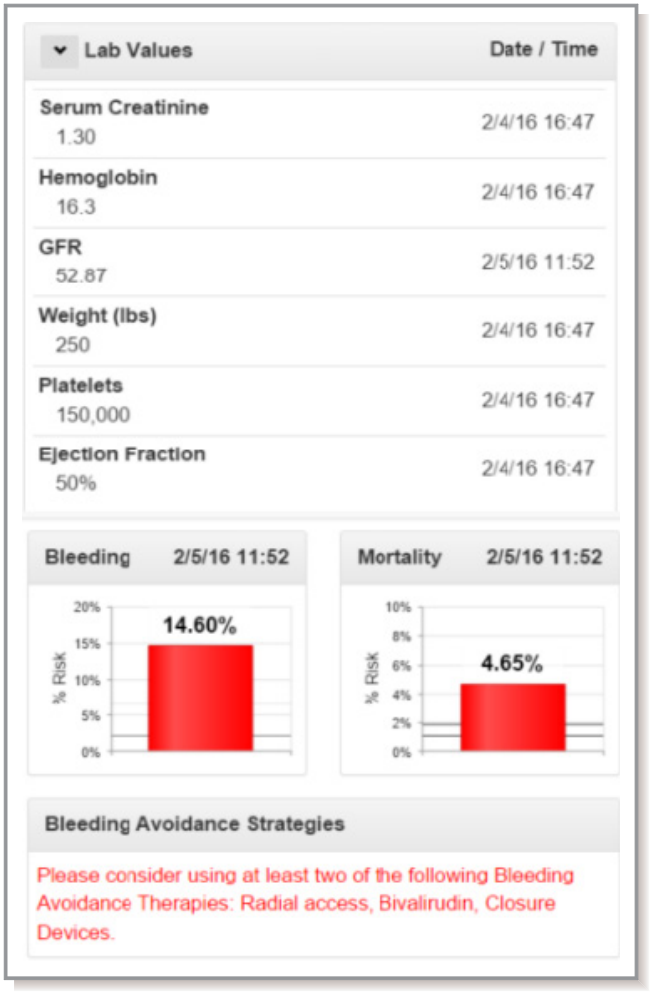

Figure 1. Decision aid used for encouraging risk-concordant use of bleeding avoidance strategies. GFR indicates glomerular filtration rate.

conceptually divided into 2 phases: the years 2012–2013 represent the baseline scenario, while the years 2014–2015 represent the changes after the implementation was fully in place. However, the adoption of this patient-centered intervention was gradual and represented a continuum of change in clinical practice over the study period. The study was approved by Washington University's institutional review board, and no informed consent was required.

Predictors and Outcomes

BAS included procedural access through the radial artery, bivalirudin administration, and use of VCDs. The preprocedural, predicted bleeding risk for each PCI was classified into 1 of 3 strata: low (<0.02), moderate (0.02–0.065), or high (≥0.065). These thresholds corresponded to the categorization used by the NCDR CathPCI bleeding risk model.[4] A risk-concordant approach to BAS use was defined as no BAS use for low predicted bleeding risk, but at least 1 BAS for the moderate predicted bleeding risk, and 2 BAS for high predicted bleeding risk.

The primary outcome of interest was post-PCI bleeding defined by NCDR CathPCI criteria as any of the following: (1) bleeding event within 72 hours; (2) hemorrhagic stroke; (3) tamponade; (4) post-PCI transfusion for patients with a nonmissing preprocedure hemoglobin level of <8 g/dL; and (5) absolute hemoglobin decrease from pre- to post-PCI of ≥3 g/dL with a nonmissing preprocedure hemoglobin of ≤16 g/dL.[26] A secondary outcome of interest was total operating costs from the hospital's perspective. The total operating costs for a case were directly available (except for the last quarter) from the finance department of BJH, which included direct and indirect and fixed and variable costs. Costs were inflation-adjusted to the 2016 US dollar using the medical consumer pricing index (https://www.bls.gov/cpi/). Since the outcomes of bleeding and costs relate to the index PCI procedure, the unit of all analyses is the PCI procedure and not the individual patient.

Considering the observational nature of this work, adoption of the patient-centered approach to encourage risk-concordant use of BAS yielded 2 post-facto comparative groups—a group of patients in whom the BAS choices made were concordant with the bleeding risk estimates as described above (the risk-concordant group), and the remaining patients were categorized as the risk-discordant group, reflecting a risk-treatment paradox.[3] This study is observational and compares the outcomes and costs in the risk-concordant and risk-discordant groups.

Statistical Analysis

Continuous variables were described as means and SDs and categorical variables were described as proportions. Comparison of continuous variables across categories of a dichotomous variable was performed using Student *t* test. Clinical benefit of the use of risk-concordant BAS was estimated as absolute risk reduction, number needed to treat (defined as inverse of absolute risk reduction), and odds ratio. Independent association of risk concordance with outcomes was determined using logistic regression model adjusting for the predicted bleeding risk (obtained from several clinical variables from the CathPCI bleeding risk model[4]) and predicted risk of mortality (obtained from several clinical variables from the CathPCI mortality risk model[27]). Improvements in costs were measured using cost differences between the risk-concordant and risk-discordant groups indexed to the risk-discordant group and converted to a percent as follows: $100\times(C_C-C_D)/C_D$, where C_C and C_D represent the average per-patient costs in the risk-concordant and risk-discordant groups, respectively. Temporal trends were assessed using calendar year as a predictor in logistic or linear regression

models for categorical or continuous dependent variables, respectively. The influence of the patient-centered approach on study outcomes was examined by comparing the risk-concordant BAS use, hospitalization costs, and bleeding rates before and after the implementation using chi-square test for categorical variables and Mann–Whitney test for continuous variables. Statistical significance was estimated at a type I error rate of 0.05. All analyses were conducted using Stata 12.0 statistical package (StataCorp). The analytic methods and study materials will be made available to other researchers upon request for purposes of reproducing the results or replicating the procedure. The data will not be made publicly available as they belong to BJH.

Results

Study Participants

Data for this study came from 3366 patients, of whom 145 (4.3%) underwent 2 PCIs and 8 (0.2%) underwent 3 PCIs during the study period. Among the patients undergoing PCIs (n=3519), the average age was 64 years, with 1116 (32%) individuals in the octogenarian age group. Obesity (body mass index >30 kg/m^2, 43%), diabetes mellitus (44%), dyslipidemia (88%), and hypertension (92%) were common and frequently coexisted. There was a high proportion of chronic renal (30%) and lung (22%) disease. The average left ventricular ejection fraction was 52.1%, and 20% to 55% individuals had a significant history of heart failure, coronary artery disease, myocardial infarction, peripheral artery disease, or previous cardiac interventions. Furthermore, coronary disease of 2 of 3 major coronary vessels that often required 2 stents, with an average 1.4 number of lesions, was common. Overall, ≈80% of the PCIs used at least 1 BAS—the most common being the use of a closure device with femoral access (65%) and bivalirudin (41%) and the least common being radial access (12%).

Presence of Risk-Treatment Paradox

Comparison of the patient characteristics across the risk-concordant and risk-discordant groups is provided in Table 1. The risk-treatment paradox was observed: risk-concordant BAS use was lower in the patients with higher bleeding risk in general. For example, in patients with diabetes mellitus, chronic kidney disease, current dialysis, and history of heart failure, myocardial infarction or peripheral arterial disease, which all contributed to a higher bleeding risk, there was a lower likelihood of risk-concordant BAS use. Of the 478 patients classified preprocedurally as having a low risk of bleeding, 414 (86.6%) received at least 1 BAS, but a smaller proportion of patients with moderate and high bleeding risk (82.8% and 72.3%, respectively) received at least 1 BAS. These findings underscore a risk-treatment paradox in BAS use and emphasize the need for greater risk-concordant use of BAS.

Influence of Risk-Concordant BAS Use on Outcomes and Cost of PCI

We found that the incidence of bleeding events was 2% in the risk-concordant versus 9% in the risk-discordant group, which yielded an absolute 7% higher risk difference and a number needed to treat of 14 (Table 2). In the univariable logistic regression model, risk-concordant BAS use was associated with bleeding events with an odds ratio of 0.20 (95% confidence interval [CI], 0.14–0.29; $P<0.001$). When adjusted for the risk of bleeding and the risk of mortality, risk-concordant BAS use was associated with bleeding events with an odds ratio of 0.33 (95% CI, 0.22–0.48, $P<0.001$), implying a 67% relative risk reduction (95% CI, 52–78%) when BAS were aligned with risk of bleeding (model 3, Table 2). This full model predicted a bleeding event with an accuracy of 82%. These findings indicate a strong and independent association of risk-concordant BAS use with the outcomes of PCI.

Similarly, when we compared the total operating per-patient costs from a hospital perspective, we observed that the risk-concordant use of BAS was associated with a $4738 (95% CI, $3353–$6122; $P<0.001$) reduction in hospital costs that translated to a cost-savings of 21.6% (Table 2). Thus, risk-concordant use of BAS was strongly and independently associated with improvements in both costs and bleeding outcomes.

We then examined whether the increased costs associated with the use of bivalirudin and VCDs among femoral cases and bivalirudin alone among radial cases was offset by the costs-savings. The cost benefit associated with specific combinations of the BAS is presented in Table 3. We found that in patients with moderate and high predicted risk of bleeding, all BAS—singly or in combination—offered significant cost-savings.

Temporal Trends in BAS Use

After we implemented the patient-centered approach for risk-concordant use of BAS, there was a gradual increase in the risk-aligned use of BAS. We tested the hypothesis that the increasing acceptance of risk-concordant BAS use over time is directly proportional to an improvement in bleeding event rates and total operating costs. We observed that the proportion of patients who received risk-concordant BAS use increased over time (Figure 2A). It was 49% in the calendar year 2012, 46% in the year 2013, 53% in the year 2014, and 56% in the calendar year 2015 (P value for trend <0.001). Concomitantly, the bleeding incidence rate

Table 1. Patient and Procedural Characteristics

Characteristic	Risk-Concordant BAS (n=1866)	Risk-Discordant BAS (n=1653)	*P* Value
Patient characteristics			
Age, mean±SD, y	64.3±12.0	64.6±12.6	0.459
Women, No. (%)	563 (30.2)	572 (34.6)	0.005
Body mass index, mean±SD	30.5±6.51	29.8±7.62	0.002
Diabetes mellitus, No. (%)	794 (42.6)	752 (45.5)	0.079
Dyslipidemia, No. (%)	1654 (88.6)	1440 (87.1)	0.166
Hypertension, No. (%)	1707 (91.5)	1511 (91.4)	0.941
Chronic lung disease, No. (%)	396 (21.2)	374 (22.6)	0.315
Chronic kidney disease (GFR ≤60) (N=3506), No. (%)	369 (19.8)	577 (35.1)	<0.001
Current dialysis, No. (%)	29 (1.6)	120 (7.3)	<0.001
Pre-PCI ejection fraction, mean±SD (N=2375)	53.6±13.5	50.3±15.0	<0.001
Prior coronary artery bypass graft surgery, No. (%)	519 (27.8)	420 (25.4)	0.107
Prior cerebrovascular disease, No. (%)	375 (20.1)	362 (21.9)	0.190
Prior heart failure, No. (%)	699 (37.5)	692 (41.9)	0.008
Prior myocardial infarction, No. (%)	923 (49.5)	887 (53.6)	0.013
Prior peripheral arterial disease, No. (%)	314 (16.8)	397 (24.0)	<0.001
Prior PCI, No. (%)	1024 (54.9)	915 (55.4)	0.776
Procedural characteristics			
No. of lesions, mean±SD	1.38±0.66	1.45±0.74	0.002
Total lesion length, mean±SD	37.7±25.8	39.7±26.4	0.023
No. of diseased vessels, mean±SD	1.79±0.83	1.82±0.83	0.319
No. of stents, mean±SD	1.80±1.05	1.97±1.16	<0.001
BAS*			
No. of BAS used by bleeding risk categories			
Low risk (n=478), mean±SD (No.†)	0.0±0.0 (64)	1.43±0.49 (414)	
Moderate risk (n=1815), mean±SD (No.†)	1.37±0.48 (1503)	0.0±0.0 (312)	
High risk (n=1226), mean±SD (No.)†	2.00±0.0 (299)	0.63±0.48 (927)	
Radial access, No. (%)	310 (16.6)	98 (5.93)	
Bivalirudin, No. (%)	1066 (57.1)	353 (21.4)	
Closure devices, No. (%)‡	1285 (82.6)	726 (46.7)	
At least 1 BAS, No. (%)	1802 (96.6)	1001 (60.6)	

*Since the definition of risk concordance directly uses information from bleeding avoidance strategies (BAS) use, no statistical hypotheses were tested for the variables in this group.
†SD of 0 indicates that all values were identical for that category.
‡Closure is only assessed for percutaneous coronary interventions (PCIs) with femoral access (n=3111).

decreased from 9.8% in the calendar year 2012, 6.5% in the year 2013, 5.3% in the year 2014, and 3.8% in the calendar year 2015 (*P* value for trend <0.001). Furthermore, the costs of PCI were $19 666 in 2012, $20 348 in 2013, $19 320 in 2014, and $17 836 in 2015 (*P* value for trend <0.001).

We also compared the proportion of patients who received risk-aligned use of BAS in 2012–2013 (before the implementation fully began) with that in 2014–2015 (during or after the implementation). We observed a 6% increase in the use of BAS (from ≈50% in 2012–2013 to ≈56% in 2014–2015, *P*=0.0004) (Figure 2B). This increase was consistently associated with a 1.4% reduction in the incidence of bleeding (from 4.4% to 2012–2013 to 3.0% in 2014–2015, *P*=0.0279) and a decrease in hospitalization costs by $1429 per-patient (from $15 610 in 2012–2013 to $14 181 in 2014–2015, *P*<0.0001) (Figure 2B).

Together, these results suggest that an increasing proportion of risk-concordant BAS use may translate to improved

Table 2. Association of Risk-Concordant BAS Use With Occurrence of Bleeding

Analysis	Result
Bleeding events in the risk-concordant BAS group, No. (%)	38 (2.0)
Bleeding events in the risk-discordant BAS group, No. (%)	156 (9.4)
P value	<0.001
Absolute risk reduction, %	7.4
No. needed to treat	14
Relative risk (95% CI, *P* value)*	
Model 1: univariable	0.20 (0.14–0.29, <0.001)
Model 2: adjusted for predicted bleeding risk	0.33 (0.22–0.48, <0.001)
Model 3: adjusted for predicted bleeding and mortality risk	0.33 (0.22–0.48, <0.001)
Area under the ROC curve for model 3 (95% CI)†	0.82 (0.79–0.85)
Total operating costs (2016 US$)	
Risk-concordant BAS, mean (95% CI)	17 219 (16 375–18 064)
Risk-discordant BAS, mean (95% CI)	21 957 (20 837–23 077)
Cost-savings (average per-patient cost reduction attributable to risk concordance) (95% CI), 2016 US$	$4738 ($3353–$6122)
Cost-savings (95% CI), %	21.6 (15.8–26.9)

BAS indicates bleeding avoidance strategies; CI, confidence interval; ROC, receiver operating characteristic.
*Relative risk of bleeding in the risk-concordant group as compared with the risk-discordant group.
†Predictive accuracy of the model.

costs and bleeding outcomes of PCI. Indeed, our results project that if *all* the patients from BJH from 2012 through 2015 included in this study were to receive risk-concordant use of BAS then the overall bleeding rates could have decreased from the overall 5.5% to 2.1% and the per-patient total operating costs could have decreased from the overall $19 449 to $17 219, representing an annual $2.41 million in potential savings. In actuality, the average costs of PCI in the earlier part of the implementation from June 2012 to December 2013 were $20 114 per PCI for 1574 cases, while the average costs of PCI in the later part of the implementation from January 2014 to September 2015 were $18 797 per PCI for 1604 cases, translating to $2.11 million in actual accrued savings.

Discussion

This is the first prospective observational study to directly address reversal of the bleeding risk-treatment paradox via a focused patient-centered intervention. Our study found that the risk-treatment paradox was commonly observed. By focusing on risk of bleeding at the point of care, it was feasible to impact but also difficult to fully reverse the risk-treatment paradox. Nonetheless, even partial reductions in the risk-treatment paradox, achieved by the risk-concordant use of BAS, were associated with substantial reductions in the incidence of bleeding and hospital costs. The association of risk-concordant use of BAS, with reductions in the incidence of bleeding and hospital costs was independent of bleeding risk and mortality risk. Furthermore, an increasing trend in risk-concordant use of BAS was associated with concomitant reducing trends in the incidence of bleeding and hospital costs.

The Institute of Medicine defines patient-centered care as "care that is respectful of and responsive to individual patient preferences, needs, and values," ensuring that patient needs and values guide all clinical decisions.[28–31] The Institute of Medicine has recognized patient-centered care as 1 of 6 major domains of healthcare quality.[28–31] While the healthcare community widely recognizes the potential of health information technology in enabling patient-centered care, we have yet to see patient-centered care being used to improve PCI outcomes in the catheterization laboratory—an area of critical need, and a very large service area, where >600 000

Table 3. Cost-Savings Associated With Combinations of BAS

BAS Used					
Radial	Bivalirudin	VCDs	No.	%	Cost-Savings (2016 US$)
No	No	No	652	21.44	Reference
No	No	Yes	1004	33.02	−5108.15 (−7301.25 to −2915.04)
No	Yes	No	344	11.31	−1390.74 (−4235.47 to 1454.00)
No	Yes	Yes	676	22.23	−5896.44 (−8272.16 to −3520.73)
Yes	No	No	182	5.98	−4934.37 (−8672.03 to −1196.71)
Yes	Yes	No	183	6.02	−5074.00 (−8821.30 to −1326.70)

BAS indicates bleeding avoidance strategies; VCDs, vascular closure devices.

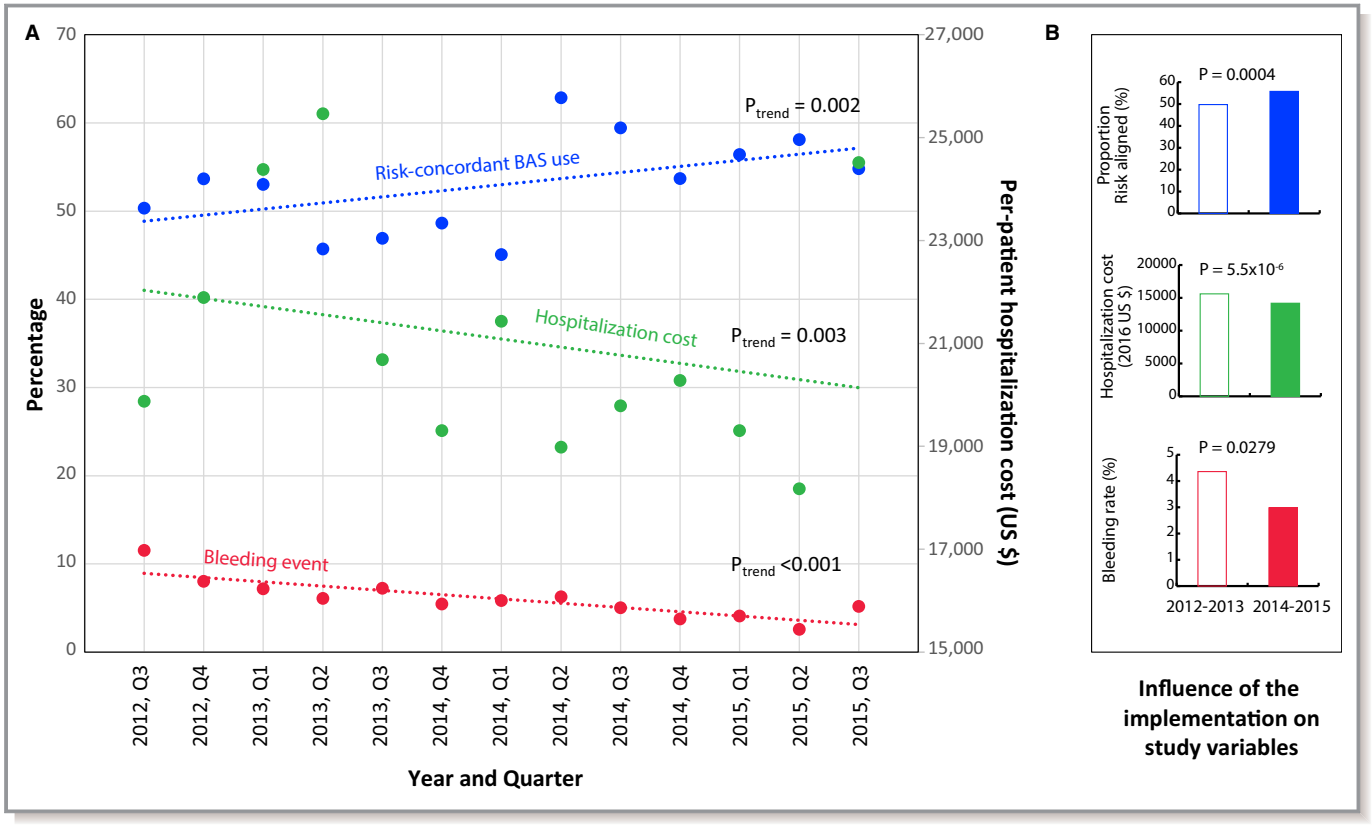

Figure 2. Trends in risk-concordant use of bleeding avoidance strategies (BAS), bleeding rates, and hospitalization costs. **A**, Quarterly estimates of risk-concordant BAS use, bleeding rates, and hospitalization costs. Dashed, color-coded lines represent the least squares regression lines. **B**, Comparison of risk-concordant BAS use, bleeding rate, and hospitalization costs before (hollow bars) and after (solid bars) implementation of the patient-centered approach. *P*, significance values estimated using chi-square test for risk-concordant BAS use and bleeding rates and using Mann–Whitney *U* test for hospitalization costs. Costs are shown as inflation-adjusted 2016 US$. The corresponding regression equations are as follows: logit (proportion risk-concordant)=0.0275×quarter−0.0727; logit (bleeding rate)=−0.0698×quarter−2.8242; hospitalization cost=−250.23×quarter+21 088.68. Q indicates quarter.

PCI procedures are performed annually in the United States alone.

The presence of a risk-treatment paradox implies that care in the catheterization laboratory is not aligned to the predicted risk of bleeding. Frequently, BAS are used the least for patients with the highest risk of bleeding, which we observed in our hospital as well. A challenge to reversing the risk-treatment paradox is that physician behavior may be influenced by clinical notions rather than evidence-based facts.[32] For example, bleeding is considered an unpredictable and unavoidable event and, hence, to date, there have been no systematic or sustained efforts to reduce PCI-related bleeding. Directly contradicting this notion is the fact that the risk of bleeding is both predictable[4] and modifiable[2,3] and our study demonstrates that bleeding is preventable by explicitly accounting for the bleeding risk in decision-making and reversing the risk treatment paradox.

It is important to note that our study is consistent with prior studies demonstrating that it is difficult to change physician behavior.[33] Physicians in the United States have autonomy in decisions about care for patients, and thus their decisions are significant drivers of healthcare cost and outcomes. In the era of alternate payment models, targeting providers and physicians to improve the value of care is anticipated. However, physician behavior is difficult to change.[33] Despite explicitly targeting bleeding risk before a case, the risk-concordant use of BAS was seen in only 57% of patients in the year 2015—2 years after introducing it in 2013. Nonetheless, even this modest degree of change in physician practice was associated with a marked reduction in bleeding outcomes and cost. It is therefore both important and required to use results from studies such as this to highlight and encourage the use of evidence-based, objective methods of bleeding management in PCI.

While bleeding is known to increase costs of care, this is the first report to show that a reduction in bleeding event rates is also associated with a parallel reduction in costs. A bleeding event costs $8000 to $12 000. By using BAS in a risk-concordant manner, we observed a $4738 (95% CI, 3353–6122; *P*<0.001) reduction in per-patient PCI costs

translating to a 21.6% cost-savings. It is also noteworthy that even though closure devices and bivalirudin are considered to be relatively expensive options, these BAS continue to be associated with significant cost-savings (as shown in Table 3) when used in a risk-concordant fashion.

Study Limitations

This study must be interpreted in light of some limitations. First, our study is from a single hospital, which may limit its generalizability. Nevertheless, it demonstrates an important proof-of-concept that even a modest improvement in patient-centered care results in substantial improvements in outcomes and costs. Since the risk-treatment paradox is pervasive in the United States, our study demonstrates the feasibility and need of reversing it to reduce bleeding. Second, our study is observational in nature and the reduction in bleeding and costs observed with patient-centered care should be interpreted as an association and not causal in nature. For example, changes in catheterization laboratory physician staffing can also influence the practice of BAS use and, hence, outcomes. However, during this study period, there were no changes in physician staffing of our catheterization laboratories. Another change that could potentially explain an increasing trend in bivalirudin use is the availability of generic bivalirudin. However, generic bivalirudin was approved by the Food and Drug Administration in July 2015, which marked the end of our study period and is unlikely to have impacted our results. Still, the presence of other unknown confounders related to the catheterization laboratory operation cannot be ruled out. Third, while we studied a large number of PCIs, the rarity of the bleeding event can influence the statistical power. We thus derived post hoc power estimates and found that the large bleeding incidence differential and cost differential provided a statistical power in excess of 99% for our study. Fourth, we used VCDs and bivalirudin as BAS and this is a controversial issue. While VCDs have shown an association with reduced bleeding using the NCDR CathPCI bleeding definition,[3] other studies have shown only modest benefit, selective benefit in high-risk cases, or no benefit at all.[34,35] Last, the unit of analysis was PCI and not patients. While some residual correlation in the <5% patients who underwent >1 PCI can theoretically influence the results, we believe that such an influence would be minimal given that 91.4% of the PCIs in our sample were contributed to by unique patients.

Conclusions

Patient-centered care that directly aims to make treatment-related decisions based on predicted probability of bleeding is urgently required. Larger and multicentered studies are also needed to corroborate and generalize these results. As clinical medicine inches toward personalization of care, both the patient (through reduced rates of adverse outcomes) and the hospitals (via substantial reduction in per-patient costs) are likely to benefit by a simple change of practice that encourages objectivity and mitigates variability in care.

Data Access and Responsibility

Drs Amin, Sorensen, and Kulkarni had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Acknowledgments

No sponsor participated in the design and conduct of the study, collection, analysis, or interpretation of the data, nor in the preparation, review, or approval of the article.

Disclosures

Dr Amin is funded by a comparative effectiveness research KM1 career development award from the Clinical and Translational Science Award program of the National Center for Advancing Translational Sciences of the National Institutes of Health (grant numbers UL1TR000448, KL2TR000450, and TL1TR000449) and the National Cancer Institute of the National Institutes of Health (grant number 1KM1CA156708-01) and an AHRQ R18 grant award (grant number R18HS0224181-01A1), and is a consultant to Terumo. The remaining authors have no disclosures to report.

References

1. Baklanov DV, Kim S, Marso SP, Subherwal S, Rao SV. Comparison of bivalirudin and radial access across a spectrum of preprocedural risk of bleeding in percutaneous coronary intervention: analysis from the National Cardiovascular Data Registry. *Circ Cardiovasc Interv*. 2013;6:347–353.
2. Chhatriwalla AK, Amin AP, Kennedy KF, House JA, Cohen DJ, Rao SV, Messenger JC, Marso SP; National Cardiovascular Data Registry. Association between bleeding events and in-hospital mortality after percutaneous coronary intervention. *JAMA*. 2013;309:1022–1029.
3. Marso SP, Amin AP, House JA, Kennedy KF, Spertus JA, Rao SV, Cohen DJ, Messenger JC, Rumsfeld JS; National Cardiovascular Data Registry. Association between use of bleeding avoidance strategies and risk of periprocedural bleeding among patients undergoing percutaneous coronary intervention. *JAMA*. 2010;303:2156–2164.
4. Rao SV, McCoy LA, Spertus JA, Krone RJ, Singh M, Fitzgerald S, Peterson ED. An updated bleeding model to predict the risk of post-procedure bleeding among patients undergoing percutaneous coronary intervention: a report using an expanded bleeding definition from the National Cardiovascular Data Registry CathPCI Registry. *JACC Cardiovasc Interv*. 2013;6:897–904.
5. Genereux P, Giustino G, Witzenbichler B, Weisz G, Stuckey TD, Rinaldi MJ, Neumann FJ, Metzger DC, Henry TD, Cox DA, Duffy PL, Mazzaferri E, Yadav M, Francese DP, Palmerini T, Kirtane AJ, Litherland C, Mehran R, Stone GW. Incidence, predictors, and impact of post-discharge bleeding after percutaneous coronary intervention. *J Am Coll Cardiol*. 2015;66:1036–1045.
6. Kwok CS, Rao SV, Myint PK, Keavney B, Nolan J, Ludman PF, de Belder MA, Loke YK, Mamas MA. Major bleeding after percutaneous coronary intervention and risk of subsequent mortality: a systematic review and meta-analysis. *Open Heart*. 2014;1:e000021.

7. Lindsey JB, Cohen DJ, Stolker JM, Meht SK, Mahoney E, Robertus K, House JA, Kennedy K, Riggs L, Rao SV, Marso SP. The impact of bivalirudin on percutaneous coronary intervention-related bleeding. *EuroIntervention*. 2010;6:206–213.
8. Milkovich G, Gibson G. Economic impact of bleeding complications and the role of antithrombotic therapies in percutaneous coronary intervention. *Am J Health Syst Pharm*. 2003;60:S15–S21.
9. Pinto DS, Stone GW, Shi C, Dunn ES, Reynolds MR, York M, Walczak J, Berezin RH, Mehran R, McLaurin BT, Cox DA, Ohman EM, Lincoff AM, Cohen DJ; ACUITY (Acute Catheterization and Urgent Intervention Triage Strategy) Investigators. Economic evaluation of bivalirudin with or without glycoprotein IIb/IIIa inhibition versus heparin with routine glycoprotein IIb/IIIa inhibition for early invasive management of acute coronary syndromes. *J Am Coll Cardiol*. 2008;52:1758–1768.
10. Cohen DJ, Lincoff AM, Lavelle TA, Chen HL, Bakhai A, Berezin RH, Jackman D, Sarembock IJ, Topol EJ. Economic evaluation of bivalirudin with provisional glycoprotein IIB/IIIA inhibition versus heparin with routine glycoprotein IIB/IIIA inhibition for percutaneous coronary intervention: results from the REPLACE-2 trial. *J Am Coll Cardiol*. 2004;44:1792–1800.
11. Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, Bravata DM, Dai S, Ford ES, Fox CS, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Soliman EZ, Sorlie PD, Sotoodehnia N, Turan TN, Virani SS, Wong ND, Woo D, Turner MB; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2012 update: a report from the American Heart Association. *Circulation*. 2012;125:e2–e220.
12. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, Carnethon MR, Dai S, de Simone G, Ford ES, Fox CS, Fullerton HJ, Gillespie C, Greenlund KJ, Hailpern SM, Heit JA, Ho PM, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, McDermott MM, Meigs JB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Rosamond WD, Sorlie PD, Stafford RS, Turan TN, Turner MB, Wong ND, Wylie-Rosett J; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2011 update: a report from the American Heart Association. *Circulation*. 2011;123:e18–e209.
13. Bakhai A, Cohen DJ. Economic implications of bivalirudin in the cardiac catheterization laboratory. *Rev Cardiovasc Med*. 2006;7(suppl 3):S35–S42.
14. Amin AP, Marso SP, Rao SV, Messenger J, Chan PS, House J, Kennedy K, Robertus K, Cohen DJ, Mahoney EM. Cost-effectiveness of targeting patients undergoing percutaneous coronary intervention for therapy with bivalirudin versus heparin monotherapy according to predicted risk of bleeding. *Circ Cardiovasc Qual Outcomes*. 2010;3:358–365.
15. Mehran R, Pocock SJ, Nikolsky E, Clayton T, Dangas GD, Kirtane AJ, Parise H, Fahy M, Manoukian SV, Feit F, Ohman ME, Witzenbichler B, Guagliumi G, Lansky AJ, Stone GW. A risk score to predict bleeding in patients with acute coronary syndromes. *J Am Coll Cardiol*. 2010;55:2556–2566.
16. Mehta SK, Frutkin AD, Lindsey JB, House JA, Spertus JA, Rao SV, Ou FS, Roe MT, Peterson ED, Marso SP; National Cardiovascular Data Registry. Bleeding in patients undergoing percutaneous coronary intervention: the development of a clinical risk algorithm from the National Cardiovascular Data Registry. *Circ Cardiovasc Interv*. 2009;2:222–229.
17. Barria Perez AE, Rao SV, Jolly SJ, Pancholy SB, Plourde G, Rimac G, Poirier Y, Costerousse O, Bertrand OF. Meta-analysis of effects of bivalirudin versus heparin on myocardial ischemic and bleeding outcomes after percutaneous coronary intervention. *Am J Cardiol*. 2016;117:1256–1266.
18. Shah R, Rogers KC, Matin K, Askari R, Rao SV. An updated comprehensive meta-analysis of bivalirudin vs heparin use in primary percutaneous coronary intervention. *Am Heart J*. 2016;171:14–24.
19. Rao SV, Cohen MG, Kandzari DE, Bertrand OF, Gilchrist IC. The transradial approach to percutaneous coronary intervention: historical perspective, current concepts, and future directions. *J Am Coll Cardiol*. 2010;55:2187–2195.
20. Spertus JA, Decker C, Gialde E, Jones PG, McNulty EJ, Bach R, Chhatriwalla AK. Precision medicine to improve use of bleeding avoidance strategies and reduce bleeding in patients undergoing percutaneous coronary intervention: prospective cohort study before and after implementation of personalized bleeding risks. *BMJ*. 2015;350:h1302.
21. Rao SC, Chhatriwalla AK, Kennedy KF, Decker CJ, Gialde E, Spertus JA, Marso SP. Pre-procedural estimate of individualized bleeding risk impacts physicians' utilization of bivalirudin during percutaneous coronary intervention. *J Am Coll Cardiol*. 2013;61:1847–1852.
22. Hannan EL, Farrell LS, Walford G, Berger PB, Stamato NJ, Venditti FJ, Jacobs AK, Holmes DR Jr, Sharma S, King SB III. Utilization of radial artery access for percutaneous coronary intervention for ST-segment elevation myocardial infarction in New York. *JACC Cardiovasc Interv*. 2014;7:276–283.
23. Wimmer NJ, Resnic FS, Mauri L, Matheny ME, Piemonte TC, Pomerantsev E, Ho KK, Robbins SL, Waldman HM, Yeh RW. Risk-treatment paradox in the selection of transradial access for percutaneous coronary intervention. *J Am Heart Assoc*. 2013;2:e000174. DOI: 10.1161/JAHA.113.000174
24. Arnold SV, Decker C, Ahmad H, Olabiyi O, Mundluru S, Reid KJ, Soto GE, Gansert S, Spertus JA. Converting the informed consent from a perfunctory process to an evidence-based foundation for patient decision making. *Circ Cardiovasc Qual Outcomes*. 2008;1:21–28.
25. Spertus JA, Bach R, Bethea C, Chhatriwalla A, Curtis JP, Gialde E, Guerrero M, Gosch K, Jones PG, Kugelmass A, Leonard BM, McNulty EJ, Shelton M, Ting HH, Decker C. Improving the process of informed consent for percutaneous coronary intervention: patient outcomes from the Patient Risk Information Services Manager (ePRISM) study. *Am Heart J*. 2015;169:234–241.
26. Moussa I, Hermann A, Messenger JC, Dehmer GJ, Weaver WD, Rumsfeld JS, Masoudi FA. The NCDR CathPCI Registry: a US national perspective on care and outcomes for percutaneous coronary intervention. *Heart*. 2013;99:297–303.
27. Peterson ED, Dai D, DeLong ER, Brennan JM, Singh M, Rao SV, Shaw RE, Roe MT, Ho KK, Klein LW, Krone RJ, Weintraub WS, Brindis RG, Rumsfeld JS, Spertus JA; NCDR Registry Participants. Contemporary mortality risk prediction for percutaneous coronary intervention: results from 588,398 procedures in the National Cardiovascular Data Registry. *J Am Coll Cardiol*. 2010;55:1923–1932.
28. Tzelepis F, Sanson-Fisher RW, Zucca AC, Fradgley EA. Measuring the quality of patient-centered care: why patient-reported measures are critical to reliable assessment. *Patient Prefer Adherence*. 2015;9:831–835.
29. Tzelepis F, Rose SK, Sanson-Fisher RW, Clinton-McHarg T, Carey ML, Paul CL. Are we missing the Institute of Medicine's mark? A systematic review of patient-reported outcome measures assessing quality of patient-centred cancer care. *BMC Cancer*. 2014;14:41.
30. Stewart M, Brown JB, Donner A, McWhinney IR, Oates J, Weston WW, Jordan J. The impact of patient-centered care on outcomes. *J Fam Pract*. 2000;49:796–804.
31. Mitchell PH. Patient-centered care—a new focus on a time-honored concept. *Nurs Outlook*. 2008;56:197–198.
32. Decker C, Garavalia L, Garavalia B, Gialde E, Yeh RW, Spertus J, Chhatriwalla AK. Understanding physician-level barriers to the use of individualized risk estimates in percutaneous coronary intervention. *Am Heart J*. 2016;178:190–197.
33. Wilensky G. Changing physician behavior is harder than we thought. *JAMA*. 2016;316:21–22.
34. Cox T, Blair L, Huntington C, Lincourt A, Sing R, Heniford BT. Systematic review of randomized controlled trials comparing manual compression to vascular closure devices for diagnostic and therapeutic arterial procedures. *Surg Technol Int*. 2015;27:32–44.
35. Jiang J, Zou J, Ma H, Jiao Y, Yang H, Zhang X, Miao Y. Network meta-analysis of randomized trials on the safety of vascular closure devices for femoral arterial puncture site haemostasis. *Sci Rep*. 2015;5:13761.