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# Impact of Bleeding on Quality of Life in Patients on DAPT

## Insights From TRANSLATE-ACS

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**ABSTRACT**

**BACKGROUND** Prolonged dual antiplatelet therapy (DAPT) is recommended after an acute myocardial infarction (AMI) to reduce ischemic events but is associated with increased rates of major and minor bleeding.

**OBJECTIVES** This study sought to determine the incidence of post-percutaneous coronary intervention (PCI) bleeding that occurs on contemporary DAPT and its impact on quality of life (QOL).

**METHODS** We studied 9,290 AMI patients treated with PCI and discharged alive between April 2010 and September 2012. Post-discharge bleeding was categorized according to the Bleeding Academic Research Consortium (BARC) definition. The primary outcome was the 6-month Euro QOL-5 Dimension (EQ-5D) index score (a measure of health utility); a secondary outcome was the EQ-5D visual analog scale (VAS) at 6 months.

**RESULTS** Of the 9,290 patients with AMI, bleeding events occurred as follows: any BARC bleeding: 24.2%; BARC 1: 9.1%; BARC 2: 13.8%; BARC 3: 1.1%; BARC 4: 0.03%; and BARC 5: 0%. Those who experienced any BARC bleeding had lower scores across all 5 EQ-5D domains (mobility, self-care, usual activities, pain, and anxiety), as well as lower EQ-5D VAS and EQ-5D index scores. After clinical risk adjustment, any BARC bleeding was independently associated with 6-month EQ-5D index score ($p < 0.0001$) and lower QOL ($p < 0.001$). Both the EQ-5D index and the VAS score declined in a stepwise fashion with increasing BARC severity.

**CONCLUSIONS** Among patients undergoing PCI for AMI, bleeding during follow-up was associated with worse 6-month utility and QOL. Although even minor bleeding was associated with impaired health status and QOL, the degree of impairment increased in a stepwise fashion with bleeding severity. (J Am Coll Cardiol 2016;67:59–65)


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**ABBREVIATIONS AND ACRONYMS**

**ADP** = adenosine diphosphate

**AMI** = acute myocardial infarction

**BARC** = Bleeding Academic Research Consortium

**DAPT** = dual antiplatelet therapy

**DCRI** = Duke Clinical Research Institute

**EQ-5D** = Euro QOL-5 Dimension

**PCI** = percutaneous coronary intervention

**QOL** = quality of life

**STEMI** = ST-segment elevation myocardial infarction

**VAS** = visual analog scale

The incidence and prognostic significance of bleeding occurring during hospitalization for an acute myocardial infarction (AMI) or following percutaneous coronary intervention (PCI) is well recognized (1–5). However, little is known about the risk of post-discharge bleeding in patients on dual antiplatelet therapy (DAPT) after AMI or PCI. The prognostic significance of post-discharge bleeding of patients on DAPT was recently underscored using the Bleeding Academic Research Consortium (BARC) consensus definitions, which were developed to standardize the reporting of bleeding in clinical trials and practice. Several studies and trials have now validated these definitions (6–10) and their value in outpatient assessment of bleeding via a telephone interview. It is now possible to identify very minor BARC type 1 bleeding, defined as "bleeding that does not cause the patient to seek medical care or hospitalization, and is not actionable" but may still be significant from the patient's perspective (8).

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The incidence and impact of post-PCI bleeding on patient quality of life (QOL) after AMI have not been well studied, particularly in the context of a greater uptake of the more potent $P2Y_{12}$ inhibitors in routine contemporary practice. Additionally, the health-state "disutility" of bleeding events according to increasing severity of the BARC bleeding definition has never been quantified. Therefore, we examined data from the large prospective, multicenter TRANSLATE-ACS (Treatment With Adenosine Diphosphate [ADP] Receptor Inhibitors: Longitudinal Assessment of Treatment Patterns and Events After Acute Coronary Syndrome) study (NCT01088503) study (11) that collected both patient self-reported and hospitalized bleeding events to: 1) investigate the incidence of bleeding after PCI for an AMI; and 2) examine the impact of bleeding events on health-related QOL and health-state utilities.

## METHODS

The TRANSLATE-ACS study is a prospective observational longitudinal registry led by the Duke Clinical Research Institute (DCRI) and conducted at 233 hospitals in the United States from April 2010 to October 2012 (11). The TRANSLATE-ACS study enrolled 12,365 patients with either ST-segment elevation myocardial infarction (STEMI) or non-STEMI who underwent PCI and were treated with an ADP receptor inhibitor during the index hospitalization. Patients were excluded from the TRANSLATE-ACS study if informed consent for longitudinal follow-up could not be obtained or if the patient was participating in a clinical trial specifying ADP receptor inhibitor use during the first year post-AMI.

For this analysis, we started with 11,649 patients and excluded those who died in hospital (n = 13) or by 6 months (n = 106), those with missing baseline (n = 76) or 6-month Euro QOL-5 Dimension (EQ-5D) data (n = 1,928), and those with incomplete medical records or whose hospitalization events could not be validated (n = 236), resulting in a final population of 9,290 subjects.

**DATA DEFINITIONS.** Patient-reported bleeding was assessed via centralized telephone interviews conducted by the DCRI at 6 weeks and 6 months post-AMI. Post-discharge bleeding was defined as any bleeding or severe bruising event that was patient-reported, associated with an antiplatelet medication change, or an independently adjudicated bleeding rehospitalization based on medical record review. Each bleeding event was classified according to the BARC definitions (8). BARC type 1 bleeding represented bleeding that was not actionable and did not cause the patient to seek unscheduled studies or treatment and was ascertained by patient report. BARC type 2 reflected overt actionable bleeding not fitting criteria for the other bleeding types. For patients with multiple bleeding events, the most severe BARC bleeding type was assigned (12).

The EQ-5D index score collected at the 6-month patient interview was the primary outcome of interest. This score is an indirect measure of utility for health, measuring health status in 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. It generates an index-based summary score based upon societal preference weights (13–15) using a unique scoring algorithm (13). Utility scores enable comparisons of burden of disease across conditions and the calculation of quality-adjusted life-years, an outcome used frequently to evaluate the cost-effectiveness of health care programs and strategies. We

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calculated the EQ-5D index score from the EQ-5D domains both at baseline and at 6 months. Of note, the EQ-5D has previously been validated for ACS patients (14).

Six-month health-related QOL assessed via the EQ-5D visual analog scale (VAS) score was the secondary outcome of interest. For this endpoint, patients estimate their overall health status on a 20-cm VAS with the endpoints being "Best imaginable health state" (score = 100) and "Worst imaginable health state" (score = 0) (14,15).

**STATISTICAL ANALYSIS.** Baseline patient demographic and clinical characteristics were compared by post-discharge BARC bleeding status (any BARC bleeding vs. none) using the chi-square test for categorical variables and the Wilcoxon rank sum test for continuous variables. To estimate the independent association between post-discharge BARC bleeding and 6-month EQ-5D index, we developed a mixed-effects linear regression model with 6-month EQ-5D index as the dependent variable, adjusting for baseline EQ-5D index as a covariate and with site as random effect (16) (hierarchical model). The model adjusted for other demographic and disease severity characteristics, as well as potential confounders of the relationship between bleeding and health status: age, sex, race, insurance status, body mass index, diabetes, hypertension, smoking, prior PCI, prior MI, prior coronary artery bypass graft surgery, peripheral vascular disease, stroke, dialysis, lung disease, congestive heart failure within the prior 2 weeks, cardiogenic shock within 24 h, atrial fibrillation, multivessel disease, ejection fraction, MI type (STEMI vs. non-STEMI), heart rate, blood pressure, baseline laboratory values of creatinine and hemoglobin, second-generation ADP receptor inhibitor use at discharge, warfarin or other anticoagulant agent use at discharge, Patient Health Questionnaire-2 depression score, marital status, and employment status. A similar approach was used to analyze the secondary outcome of EQ-5D VAS.

In order to place these results into a clinical context, we also estimated the magnitude of the difference in QOL by using Cohen's d, which is a dimensionless index that measures the magnitude of a treatment effect (17,18). Cohen's d is the standardized difference between 2 means and is given by:

$$\theta = \frac{\mu_1 - \mu_2}{\sigma}$$

where $\mu_1$ is the mean for one population, $\mu_2$ is the mean for the other population, and $\sigma$ is the population SD (17,18). An effect size of 0.2 is considered small, 0.5 moderate, and 0.8 large (18). Finally, we compared the disutility of minor bleeding (BARC type 1) with more severe bleeding (BARC types 2 to 5 or BARC types 3 to 5) using the same modeling approach detailed in the preceding text. All analyses were conducted using SAS version 9.2 (SAS Institute, Cary, North Carolina) by an independent statistician at the DCRI.

## RESULTS

Among the 9,290 AMI patients in the TRANSLATE-ACS study who underwent PCI and were discharged on DAPT, 51% presented with STEMI, 10% underwent PCI via radial access, 10% underwent multivessel PCI, and drug-eluting stents were used in 72%. In-hospital major bleeding occurred in 3%, and DAPT at discharge included clopidogrel in 68%, prasugrel in 29%, and ticagrelor in 2%.

**INCIDENCE OF BLEEDING DURING FOLLOW-UP.** Over the 6-month follow-up period, any BARC bleeding occurred in 2,246 (24.2%) of the 9,290 AMI patients. BARC type I bleeding occurred in 849 (9.1%) patients. The incidence of more severe bleeding was as follows: BARC type 2 (13.8%), BARC type 3a (0.5%), BARC type 3b (0.6%), and BARC type 4 (0.03%). There were no patients with fatal (BARC type 5) bleeding. According to the clinical characteristics of patients with any BARC bleeding versus those who did not bleed (**Table 1**), patients with any BARC bleeding post-discharge were more likely to be female, have a lower body weight, have a slightly lower hemoglobin and creatinine clearance, and less likely to be of black race or have diabetes or a prior PCI. They were also more likely to experience an overt bleeding episode during their index ACS hospitalization. Patients with post-discharge bleeding were more likely to have been discharged on a higher-potency ADP receptor inhibitor such as prasugrel or ticagrelor and were more likely to have been receiving an oral anticoagulant agent at discharge (**Table 1**).

**ASSOCIATION OF BARC BLEEDING WITH HEALTH-STATE UTILITY AND QOL.** Patients who developed any BARC bleeding had lower baseline responses across the EQ-5D domains of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression compared with those without subsequent bleeding (Online Table 1, Online Figure 1). The baseline EQ-5D index health-state utility scores were 0.83 ± 0.19 versus 0.86 ± 0.17 (mean difference 0.03; $p < 0.0001$) for patients with bleeding versus no bleeding. At 6-month follow-up, these values were 0.82 ± 0.19 versus 0.86 ± 0.17 (mean difference 0.04; $p < 0.0001$). Similarly, baseline EQ-5D VAS scores were also lower for patients with bleeding versus no bleeding

**TABLE 1 Baseline Demographics and Clinical Characteristics**

| | Overall (N = 9,290) | BARC Bleed (n = 2,246) | No BARC Bleed (n = 7,044) | p Value |
|---|---|---|---|---|
| Demographics | | | | |
| Age, yrs | 60.6 ± 11.4 | 60.9 ± 11.3 | 60.6 ± 11.4 | 0.3293 |
| Male | 6,763 (72.8) | 1,441 (64.2) | 5,322 (75.6) | <0.0001 |
| White | 8,320 (89.6) | 2,036 (90.7) | 6,284 (89.2) | 0.0604 |
| Private health insurance | 6,083 (65.5) | 1,498 (66.7) | 4,585 (65.1) | 0.2276 |
| Medicare insurance | 3,205 (34.5) | 817 (36.4) | 2,388 (33.9) | 0.0374 |
| Past medical history | | | | |
| Diabetes | 2,350 (25.3) | 513 (22.8) | 1,837 (26.1) | 0.0021 |
| Hypertension | 6,217 (66.9) | 1,461 (65.1) | 4,756 (67.5) | 0.0360 |
| Dyslipidemia | 6,184 (66.6) | 1,468 (65.4) | 4,716 (67.0) | 0.1867 |
| Current/recent smoker | 3,370 (36.3) | 805 (35.8) | 2,565 (36.4) | 0.6444 |
| Prior MI | 1,731 (18.6) | 372 (16.6) | 1,359 (19.3) | 0.0037 |
| Prior PCI | 1,932 (20.8) | 416 (18.5) | 1,516 (21.5) | 0.0022 |
| Prior CABG | 855 (9.2) | 185 (8.2) | 670 (9.5) | 0.0681 |
| Prior stroke or TIA | 483 (5.0) | 113 (5.0) | 370 (5.3) | 0.6777 |
| Peripheral artery disease | 577 (6.2) | 137 (6.1) | 440 (6.3) | 0.8050 |
| Prior heart failure | 497 (5.4) | 105 (4.7) | 392 (5.6) | 0.1025 |
| Atrial fibrillation/flutter | 423 (4.6) | 105 (4.7) | 318 (4.5) | 0.7514 |
| Dialysis | 89 (1.0) | 20 (0.9) | 69 (1.0) | 0.7036 |
| Chronic lung disease | 867 (9.3) | 241 (10.7) | 626 (8.9) | 0.0088 |
| GI/GU bleeding within past 6 months | 93 (1.0) | 27 (1.2) | 66 (0.9) | 0.2727 |
| In-hospital medications | | | | |
| Aspirin | 9,137 (98.4) | 2,202 (98.0) | 6,935 (98.5) | 0.2870 |
| Clopidogrel | 7,042 (75.8) | 1,591 (70.8) | 5,451 (77.4) | <0.0001 |
| Prasugrel | 2,818 (30.3) | 794 (35.4) | 2,024 (28.7) | <0.0001 |
| Ticagrelor | 237 (2.6) | 59 (2.6) | 178 (2.5) | 0.7031 |
| UFH | 6,958 (74.9) | 1,650 (73.5) | 5,308 (75.4) | 0.1524 |
| LMWH | 1,812 (19.5) | 442 (19.7) | 1,370 (19.5) | 0.8288 |
| Fondaparinux | 32 (0.34) | 5 (0.22) | 27 (0.38) | 0.3829 |
| Bivalirudin | 4,506 (48.5) | 1,053 (46.9) | 3,453 (49.0) | 0.0828 |
| Fibrinolytic agents | 379 (7.9) | 74 (6.4) | 305 (8.3) | 0.0682 |
| Glycoprotein IIb/IIIa inhibitors | 4,159 (44.8) | 1,013 (45.1) | 3,146 (44.7) | 0.5759 |
| In-hospital laboratory values | | | | |
| Pre-procedure CK-MB, ng/ml | 36.0 ± 74.0 | 35.3 ± 90.2 | 36.2 ± 68.4 | 0.0618 |
| Pre-procedure troponin I, ng/ml | 6.7 ± 25.0 | 6.1 ± 19.9 | 6.9 ± 26.4 | 0.0184 |
| Pre-procedure hemoglobin, g/dl | 14.2 ± 1.9 | 14.1 ± 2.0 | 14.2 ± 1.8 | 0.0001 |
| Pre-procedure creatinine, mg/dl | 1.1 ± 0.7 | 1.1 ± 0.6 | 1.1 ± 0.7 | |

*Continued on the next page*

(69.8 ± 19.7 vs. 71.6 ± 19.0; mean difference 1.8; p = 0.0002) and at 6-month follow-up (72.8 ± 18.5 vs. 75.7 ± 17.1; mean difference 2.9; p < 0.0001) (Online Table 1).

After adjustment for baseline health status and clinical factors, any BARC bleeding by 6 months was independently associated with a decrement in health-state utility and QOL at 6 months (**Central Illustration**, **Table 2**). For the EQ-5D index, bleeding was associated with a change of −0.033 (95% confidence interval: −0.041 to −0.026; p < 0.0001; Cohen's d: 0.24). For the EQ-5D VAS, any BARC bleeding was associated with a 6-month difference of −2.5 (95% confidence interval: −3.3 to −1.8; p < 0.0001; Cohen's d: 0.17). As expected, more severe bleeding categories were associated with a greater decrement in utility and health status as assessed by the EQ-5D index and the EQ-5D VAS, respectively. However, even minor (i.e., BARC type 1) bleeding was associated with significant decreases in adjusted QOL by both measures (**Central Illustration**, **Table 2**).

## DISCUSSION

Using contemporary, nationally representative data from the TRANSLATE-ACS study, we were able to quantify the disutility and QOL associated with post-AMI bleeding occurring in the context of clopidogrel and higher-potency ADP receptor inhibitor use. We found that any BARC bleeding occurred in nearly 1 in 4 patients during the first 6 months after AMI among patients receiving DAPT. After adjusting for baseline EQ-5D, as well as other patient and treatment characteristics, post-discharge bleeding was associated with significant decrements in both health-state utility value and QOL as measured by the EQ-5D index and EQ-5D VAS scores, respectively. Although more severe types of bleeding (BARC types 3 or 4) were associated with larger decrements in utility and health status, even the most minor bleeding episodes (BARC type 1) were associated with a measurable decline in these metrics.

One important question that arises from these results: are the observed decrements in QOL associated with bleeding clinically meaningful? With the EQ-5D index-based scores, the minimum clinically important differences have been estimated for some disease conditions (21–23), but empirical work has not been performed for bleeding. Our study showed a 0.033 decrement in utility and Cohen's d of 0.24 associated with any BARC bleeding. In comparison, lung cancer and limb reconstruction surgery are both associated with reductions in the EQ-5D index-based scores of 0.05 (22,23). Walters et al. (23) observed that for most disease conditions, the "effect sizes" for EQ-5D index scores were in the "small-to-moderate" range of 0.20 to 0.50 using Cohen's criteria. For example, all cancers are associated with minimally important differences in the range of 0.07 to 0.09 (22). In this context, our study findings suggest that bleeding has a clinically meaningful impact on patients' QOL, comparable to the effect sizes observed for other serious disease conditions.

This study builds upon the findings of prior literature showing that BARC type 1 nuisance bleeding while on clopidogrel therapy is associated with a decrement in patient QOL (24). The present study includes a larger study population of patients treated

with clopidogrel, as well as higher-potency antiplatelet agents and thus is very representative of contemporary clinical practice patterns in the United States. We also have quantified the decrement in utility and QOL of all types of BARC bleeding in addition to BARC type 1 nuisance bleeding. Of note, the decrement in QOL scores with BARC type 1 bleeding was almost identical in magnitude to that observed in our prior study from the TRIUMPH (Translational Research Investigating Underlying Disparities in Acute Myocardial Infarction Patients' Health Status) registry (25).

Bleeding on DAPT occurs commonly. In the present study, nearly 1 in 4 patients had some form of bleeding on DAPT during a 6-month follow-up period. Therefore, this study has important implications for clinical practice, as well as for future clinical trials. It identifies that post-AMI bleeding occurring on DAPT is an outcome of direct clinical consequence to patients, irrespective of the severity of the bleeding event. Even the most trivial form of bleeding—the BARC type 1 "nuisance" bleeding events—were associated with significantly reduced utility and QOL. The more severe bleeding events were associated with even greater reductions in utility and QOL. In a prior study from TRANSLATE-ACS, we observed that bleeding is underreported to treating clinicians (12). As antiplatelet and anticoagulant regimens continue to evolve and are applied in routine clinical practice, our study establishes the critical need for more proactive assessment of bleeding, including minor bleeding events, during treatment. When DAPT is clearly necessary for prevention of stent thrombosis and other adverse cardiovascular events after AMI or PCI, patients should be counseled on what to expect to prevent interruptions in treatment. The very high rate of bleeding seen in the first 6 months on DAPT also challenges clinicians to reassess the feasibility of shorter DAPT durations especially in light of newer stent platforms and other innovations (26–31).

Quantifying the utility decrement associated with the BARC bleeding definition has important implications for the conduct of clinical trials. Until recently, patient-reported, less severe forms of bleeding have not been collected or adjudicated in trials. By quantifying the utility decrement associated with the spectrum of bleeding severity, this study places BARC bleeding in context for future clinical trials involving QOL and/or other patient-reported outcomes. These patient-reported outcomes may be especially important for future trials evaluating antiplatelet regimen durations or novel agents associated with a risk of bleeding complications.

**TABLE 1 Continued**

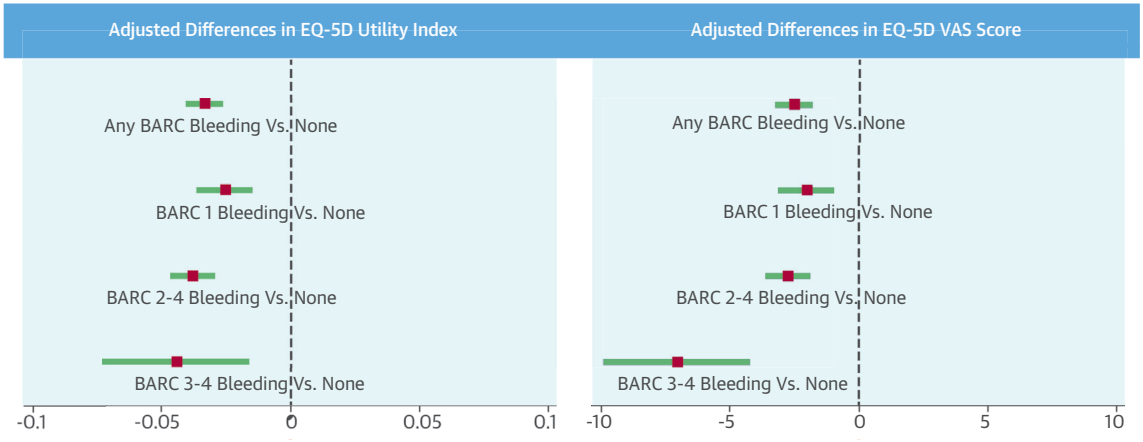
| | Overall (N = 9,290) | BARC Bleed (n = 2,246) | No BARC Bleed (n = 7,044) | p Value |
|---|---|---|---|---|
| Bleeding/transfusion | | | | |
| In-hospital major bleeding event | 290 (3.1) | 86 (3.8) | 204 (2.9) | 0.0268 |
| RBC/whole blood transfusion | 178 (1.9) | 51 (2.3) | 127 (1.8) | 0.1613 |
| In-hospital events | | | | |
| CABG | 29 (0.3) | 1 (0.0) | 28 (0.4) | 0.0090 |
| Myocardial infarction | 48 (0.5) | 15 (0.7) | 33 (0.5) | 0.2512 |
| Cardiogenic shock | 110 (1.2) | 27 (1.2) | 83 (1.2) | 0.9319 |
| Heart failure | 139 (1.5) | 41 (1.8) | 98 (1.4) | 0.1422 |
| CVA/stroke | 8 (0.1) | 1 (0.0) | 7 (0.1) | 0.4403 |
| Length of stay, days | 3.1 ± 2.1 | 3.1 ± 2.3 | 3.0 ± 2.1 | 0.6715 |
| Discharge medications | | | | |
| Clopidogrel | 6,346 (68.3) | 1,385 (61.7) | 4,961 (70.4) | <0.0001 |
| Prasugrel | 2,696 (29.0) | 798 (35.6) | 1,898 (27.0) | <0.0001 |
| Ticagrelor | 197 (2.1) | 47 (2.1) | 150 (2.1) | 0.9195 |
| Any second-generation ADP $P2Y_{12}$ receptor inhibitor | 2,893 (31.2) | 845 (37.7) | 2,048 (29.1) | <0.0001 |
| Aspirin | 9,145 (98.8) | 2,208 (98.8) | 6,937 (98.9) | 0.9703 |
| Anticoagulant agents | 481 (5.2) | 146 (6.5) | 335 (4.8) | 0.0012 |
| PCI data | | | | |
| PCI indication | | | | 0.3889 |
| Immediate PCI for STEMI | 4,134 (44.5) | 1,023 (45.6) | 3,111 (44.2) | |
| PCI for high-risk non-STEMI or unstable angina | 4,308 (46.4) | 1,044 (46.5) | 3,264 (46.3) | |
| Any DES used | 6,671 (71.8) | 1,648 (73.4) | 5,023 (71.3) | 0.0581 |
| Procedure successful | 8,605 (92.6) | 2,089 (93.0) | 6,516 (92.5) | 0.5305 |
| ACTION risk scores | | | | |
| ACTION mortality risk score (19) | 30.1 ± 7.7 | 30.0 ± 7.6 | 30.2 ± 7.7 | 0.6029 |
| ACTION bleeding risk score (20) | 25.4 ± 6.8 | 25.8 ± 6.6 | 25.2 ± 6.8 | <0.0001 |

Values are mean ± SD or n (%).

ACTION = Acute Coronary Treatment and Intervention Outcomes Network Registry; ADP = adenosine diphosphate; BARC = Bleeding Academic Research Consortium; CABG = coronary artery bypass graft surgery; CK-MB = creatine kinase MB isoenzyme; CVA = cerebrovascular accident; DES = drug-eluting stent; GI = gastrointestinal; GU = genitourinary; LMWH = low-molecular-weight heparin; MI = myocardial infarction; PCI = percutaneous coronary intervention; RBC = red blood cell; STEMI = ST-segment elevation myocardial infarction; TIA = transient ischemic attack; UFH = unfractionated heparin.

**STUDY LIMITATIONS.** First, in the TRANSLATE-ACS study, BARC type 1 bleeding was based only on patient self-reporting and may have been subject to recall bias. However, this self-reported method of evaluating BARC type 1 bleeding was specifically intended when the BARC definitions were developed. Second, despite rigorous multivariable adjustment, there remains the possibility of unmeasured confounding in this observational study. Third, the possibility of selection bias due to the exclusion of patients with missing data regarding 6-month health status (n = 1,928; 16.5%) may limit the precision and generalizability of our estimates. Finally, despite observing a statistically significant association between bleeding and a decrement in QOL, the causal nature of this association cannot be inferred given our observational study design.

**CENTRAL ILLUSTRATION** **QOL and Disutility Associated With Bleeding After AMI**

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The stepwise relationship of quality of life (QOL) and utility decrement associated with increasing severity of bleeding. The EQ-5D Utility Index is based on U.S. weights on a −0.11 to 1.00 scale (where 1.00 is best). EQ-5D VAS is on a 1 to 100 scale (where 100 is best). BARC = Bleeding Academic Research Consortium; EQ-5D = Euro QOL-5 Dimension; VAS = visual analog scale. AMI = acute myocardial infarction.

## CONCLUSIONS

We found a very high incidence of BARC bleeding during the first 6 months after AMI among patients discharged on DAPT. Bleeding was associated with worse health-state utility and patient-reported QOL, an association that persisted for even minor BARC type 1 bleeding events. These findings reinforce the need to proactively assess and address patient-reported bleeding concerns while on DAPT. By quantifying the utility decrement associated with the standardized BARC bleeding definition, this study facilitates application and interpretation of bleeding endpoints in future trials of antithrombotic treatment regimens.

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**TABLE 2** **QOL and Utility Decrement Associated With Increasing Severity of Bleeding**

| Model | Effect Estimate | 95% CI | p Value | Cohen's d |
|---|---|---|---|---|
| EQ-5D Utility Index* | | | | |
| Any BARC bleeding vs. none | −0.0334 | −0.0407 to −0.0261 | <0.0001 | 0.24 |
| BARC 1 bleeding vs. none | −0.0257 | −0.0365 to −0.0148 | <0.0001 | |
| BARC 2-4 bleeding vs. none | −0.0381 | −0.047 to −0.0293 | <0.0001 | |
| BARC 3-4 bleeding vs. none | −0.0445 | −0.073 to −0.016 | 0.0022 | |
| EQ-5D VAS† | | | | |
| Any BARC bleeding vs. none | −2.5023 | −3.2525 to −1.752 | <0.0001 | 0.17 |
| BARC 1 bleeding vs. none | −2.0385 | −3.1504 to −0.9266 | 0.0003 | |
| BARC 2-4 bleeding vs. none | −2.7898 | −3.6964 to −1.8831 | <0.0001 | |
| BARC 3-4 bleeding vs. none | −7.0974 | −10.037 to −4.1575 | <0.0001 | |

*Based on U.S. weights; −0.11 to 1.00 scale (where 1.00 is best). †1 to 100 scale (where 100 is best).
CI = confidence interval; EQ-5D = Euro QOL–5 Dimension; QOL = quality of life; VAS = visual analog scale; other abbreviations as in Table 1.

## PERSPECTIVES

**COMPETENCY IN MEDICAL KNOWLEDGE:** Prolonged DAPT is recommended to prevent recurrent ischemic events after AMI and PCI but is associated with increased bleeding. Patients who develop bleeding during DAPT exhibit worse health status and quality of life after 6 months proportionate to the severity of bleeding.

**TRANSLATIONAL OUTLOOK:** Further investigation is needed to elucidate the causes of the adverse long-term effects of bleeding on DAPT and to develop strategies that ameliorate risk.

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**KEY WORDS** antiplatelet therapy, bleeding, percutaneous coronary intervention, quality of life

**APPENDIX** For a supplemental figure and table, please see the online version of this article.