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Percutaneous Coronary Intervention in Patients With a History of Gastrointestinal Bleeding (From the Blue Cross Blue Shield of Michigan Cardiovascular Consortium)

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Potent antithrombotic agents are routinely prescribed after percutaneous coronary intervention (PCI) to reduce ischemic complications. However, in patients who are at an increased bleeding risk, this may pose significant risks. We sought to evaluate the association between a history of gastrointestinal bleeding (GIB) and outcomes after PCI. We linked clinical registry data from PCIs performed at 48 Michigan hospitals between 1/2013 and 3/2018 to Medicare claims. We used 1:5 propensity score matching to adjust for patient characteristics. In-hospital outcomes included bleeding, transfusion, stroke or death. Post-discharge outcomes included 90-day all-cause readmission and long-term mortality. Of 30,206 patients, 1.1% had a history of GIB. Patients with a history of GIB were more likely to be older, female, and have more cardiovascular comorbidities. After matching, those with a history of GIB (n = 312) had increased post-procedural transfusions (15.7% vs 8.4%; p < 0.001), bleeding (11.9% vs 5.2%; p < 0.001), and major bleeding (2.8% vs 0.6%; p = 0.004). Ninety-day readmission rates were similar among those with and without a history of GIB (34.3% vs 31.3%; p = 0.318). There was no significant difference in post-discharge survival (1 year: 78% vs 80%; p = 0.217; 5 years: 54% vs 51%; p = 0.189). In conclusion, after adjusting for baseline characteristics, patients with a history of GIB had increased risk of post-PCI in-hospital bleeding complications. However, a history of GIB was not significantly associated with 90-day readmission or long-term survival. Published by Elsevier Inc. (Am J Cardiol 2021;155:9−15)

Percutaneous coronary intervention (PCI) is one of the most common cardiovascular procedures performed in the United States with over 480,000 performed annually.[1] Dual antiplatelet therapy with aspirin and a P2Y12 inhibitor is recommended after PCI to prevent ischemic complications.[2,3] Although Dual antiplatelet therapy is used to prevent ischemic complications after PCI, these medications also increase the risk of bleeding complications.[4,5] The gastrointestinal tract is one of the most common sources of bleeding after PCI with reported event rates ranging from 1% to 2.3% .[6−9] Moreover, prior research has demonstrated that post-PCI gastrointestinal bleeding (GIB) is independently associated with major adverse cardiovascular events and death.[10−13] However, whether a patient's history of GIB prior to PCI impacts post-PCI complications remains unclear. Previous research has demonstrated that baseline gastrointestinal comorbidities increase the risk of post-procedural GIB.[7] In this context, we sought to evaluate the association between a patient's history of GIB and post-PCI in-hospital and post-discharge outcomes.

Methods

We performed a retrospective analysis using data collected by the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2), a quality improvement consortium that maintains a registry of all patients undergoing PCI at 48 nonfederal hospitals in Michigan.[14,15] Briefly, BMC2 collects data from all nonfederal hospitals in Michigan using the National Cardiovascular Data Registry Cath-PCI data collection form. The registry is further enhanced by the inclusion of novel variables and rigorous auditing practices.

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See page 14 for disclosure information.

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To evaluate the association between a history of GIB on post-discharge outcomes, we linked BMC2 clinical PCI registry data to Medicare fee-for-service 90-day episodes of care created and maintained by the Michigan Value Collaborative (MVC). MVC is a statewide collaborative focusing on improving the value of health care in the state of Michigan by maintaining and analyzing a claims-based registry of 90-day episodes of care. The MVC dataset and our linkage process have been described previously.[16,17] Briefly, we included MVC episodes for acute myocardial infarction and PCI − the two MVC episode types where PCI may have occurred. Next, the BMC2 clinical registry data were linked to MVC Medicare fee-for-service episodes of care using iterative deterministic matching on hospital national provider identifier, patient date of birth, patient gender, and dates of admission/discharge.

We evaluated consecutive patients who underwent PCI between January 1, 2013 to March 31, 2018. Per our registry definition, we defined GIB as "any occurrence of melena or hematemesis in the last 30 days or any history of GIB including peptic ulcer disease that may influence clinical management during this hospitalization." The University of Michigan Institutional Review Board approved the study and determined that it met the definition of research not requiring informed consent.

In-hospital outcomes included stroke, transfusion, bleeding, major bleeding, and death from any cause. Stroke was defined as a loss of neurological function caused by an ischemic or hemorrhagic event with residual symptoms lasting at least 24 hours after onset or leading to death. Transfusion was defined as transfusion of whole or packed red blood cells from the start of the procedure to the time of discharge. Per the National Cardiovascular Data Registry definition, bleeding was defined as any event that was suspected or confirmed within 72 hours of PCI that was associated with any of the following: (1) drop in serum hemoglobin of ≥3 g/dL, (2) transfusion of whole or packed red blood cells, or (3) procedural intervention/surgery at the bleeding site to stop/reverse or correct the bleeding.[18] Major bleeding was defined as a drop in baseline hemoglobin of >5 g/dL. Among patients with post-procedural bleeding, when data was available, we evaluated the site of bleeding which included the vascular access site, retroperitoneal, gastrointestinal, genitourinary, and other.

Post-discharge outcomes included long-term mortality and 90-day all-cause readmission. All-cause readmission was defined as admission to an acute care hospital for any reason within 90-days after discharge from the incident hospitalization or index PCI procedure. Readmission for GIB was defined using ICD9/ICD10 diagnosis codes in any position on the readmission claim (Supplemental Table 1). Post-discharge mortality was obtained from the Medicare beneficiary file, which includes the date of death for deceased beneficiaries.

Baseline characteristics were compared between patients with and without a history of GIB using Pearson χ^2 or Fisher exact test for categorical variables and Student t tests for continuous variables. We used propensity matching to account for baseline differences between patients with and without a history of GIB. Propensity scores were estimated using logistic regression models adjusting for baseline demographic and clinical variables (Supplemental Table 2).

Patients with a history of GIB were matched in a 1:5 fashion to similar patients without a history of GIB with scores within a caliber of 0.25 standard deviations of the propensity score using a greedy algorithm.[19] We required matching within 4 standard deviations of baseline pre-procedure hemoglobin. We also required exact matching on PCI indication (i.e. immediate PCI for ST-segment elevation myocardial infarction [STEMI], PCI for STEMI in stable patients after successful full-dose thrombolysis, PCI for STEMI in stable patients >12 hours after symptom onset, PCI for STEMI in unstable patients >12 hours after symptom onset, rescue PCI for STEMI after failed thrombolysis, PCI for high-risk non-ST-segment elevation myocardial infarction or unstable angina, and staged PCI).[20]

Logistic regression and Cox proportional hazards models adjusting for all variables used in matching as predictors were used to evaluate the outcomes of 90-day readmission and long-term mortality, respectively[18] (Supplemental Table 2). In the presence of crossing Kaplan−Meier survival curves potentially indicating a violation of the proportional hazard assumption, Kaplan Meier survival function estimates and their standard errors were utilized to display and assess differences in cumulative mortality between the 2 groups of patients at 1 and 2 years post discharge. A p value <0.05 was considered to be statistically significant. All analyses were performed using R, version 3.2.1.[21]

Results

A total of 30,206 patients who underwent PCI at 48 non-federal hospitals in Michigan between January 2013 to March 2018 were linked between the BMC2 clinical registry and the MVC claims-based registry. Of the 30,206 patients who underwent PCI, 342 (1.1%) patients had a history of GIB (Figure 1). Baseline characteristics of the study population are presented in Table 1.

In the unmatched cohort, a history of GIB was significantly associated with increased rates of in-hospital death (5% vs 1.4%; $p < 0.001$), stroke (1.2% vs 0.3%; $p = 0.033$), transfusion (17.3% vs 2.1%; $p < 0.001$), bleeding (12.6% vs 3.2%; $p < 0.001$) and major bleeding (2.6. vs 0.9%; $p = 0.007$) compared with patients without a history of GIB (Supplemental Figure 1).

After propensity score matching, there were 312 patients with a history of GIB matched to 1,560 patients without a history of GIB. The absolute standardized differences were <10% on all matched variables, indicating acceptable covariate balance between the two groups (Supplemental Figure 2). Compared with patients without a history of GIB, those with had a significantly higher rate of post-PCI bleeding (11.9% vs 5.2%; $p < 0.0001$), major bleeding (2.8% vs 0.6%; $p = 0.0037$), and transfusion (15.7% vs 8.4%; $p = 0.0002$) (Figure 2A). Among the patients with post-PCI bleeding the most common sites of bleeding in those with and without a history of GIB were gastrointestinal bleeding and bleeding at the access site (Figure 2B). A history of GIB was not significantly associated with the risk of in-hospital stroke or mortality.

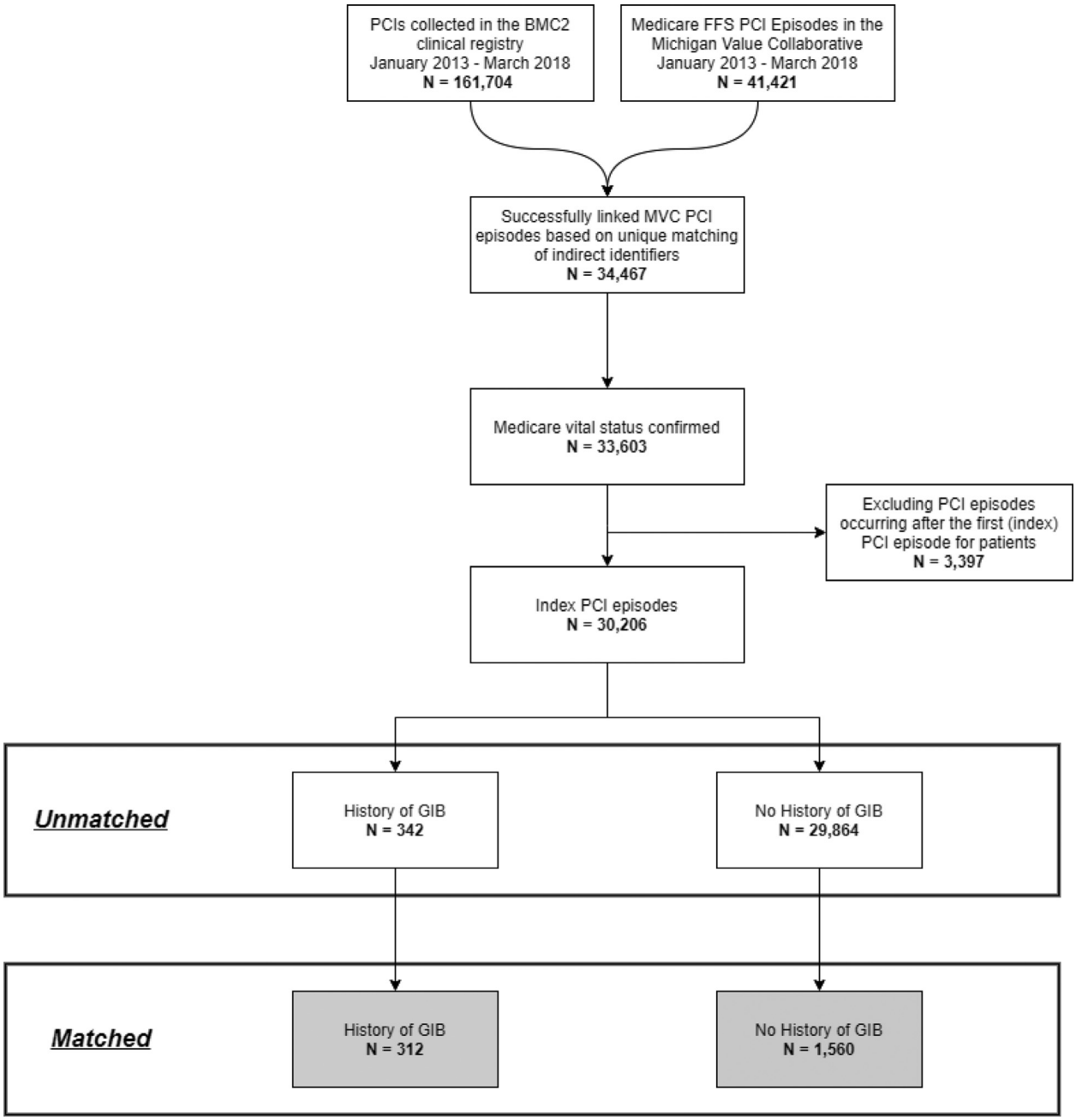

Figure 1. Study flow diagram. BMC2, Blue Cross Blue Shield of Michigan Cardiovascular Consortium; FFS, Fee-for-service; GIB, Gastrointestinal bleed; MVC, Michigan Value Collaborative; PCI, Percutaneous coronary intervention.

In the matched cohort, patients with a history of GIB were less frequently prescribed aspirin at time of discharge compared with patients without a history of GIB. Additionally, patients with a history of GIB were more frequently prescribed clopidogrel and less frequently prescribed more potent P2Y12 inhibitors like ticagrelor and prasugrel (Supplemental Table 3).

Prior to matching, patients with a history of GIB were more likely to be readmitted within 90 days of discharge (33.3% vs 18.9%; $p < 0.001$). However, after matching there was no significant difference in 90-day readmission rates (34.3% vs 31.3%; $p = 0.318$) (Figure 3). Prior to matching, the rate of 90-day readmission for a diagnosis of GIB was 3.22% among those with a history of GIB compared with 0.77% among those without a history of GIB ($p < 0.001$). After matching, there was no significant difference in the rate of 90-day readmission for GIB among those with and without a history of GIB (3.21% vs 1.8%, respectively; $p = 0.122$).

Prior to matching, patients with a history of GIB had a significantly lower rate of survival with a Kaplan-Meier survival rate of 52% at 5 years compared with 71% in those without a history of GIB (Figure 4A), demonstrating the overall poor prognosis of patients with a history of GIB.

Table 1
Baseline characteristics in the unmatched cohort and matched cohort.

Variables	Unmatched			Matched		
	History of GIB (n = 342)	No history GIB (n = 29864)	p value	History of GIB (n = 312)	No history of GIB (n = 1560)	p value
Age (mean ± standard deviation)	73.6 ± 9.75	71.9 ± 9.54	0.001	73.38 ± 9.84	73.8 ± 10.01	0.489
Women	160 (47%)	11944 (40%)	0.013	149 (48%)	804 (52%)	0.247
Body mass index (kg/m^2)	29.5 ± 7.6	30.6 ± 7.4	<0.001	29.7 ± 6.9	29.6 ± 6.6	0.695
Black	47 (14%)	2988 (10%)	0.028	45 (14%)	251 (16%)	0.515
Current/recent smoker within 1 year	70 (21%)	6075 (20%)	0.989	64 (21%)	274 (18%)	0.248
Dyslipidemia	282 (83%)	24721 (83%)	0.910	258 (83%)	1295 (83%)	0.956
Diabetes mellitus	158 (46%)	12388 (42%)	0.089	144 (46%)	795 (51%)	0.137
Hypertension	319 (93%)	26633 (89%)	0.019	293 (94%)	1470 (94%)	0.930
Currently on dialysis	35 (10%)	680 (2.3%)	<0.001	28 (9%)	185 (12%)	0.172
Pre-procedure hemoglobin (mean ± standard deviation)	11.29 ± 2.25	13.24 ± 1.87	<0.001	11.34 ± 2.27	11.42 ± 2.18	0.535
Prior myocardial infarction	145 (42%)	9076 (30%)	<0.001	126 (40%)	643 (41%)	0.834
Prior percutaneous coronary intervention	145 (43%)	12361 (41%)	0.718	132 (42%)	696 (45%)	0.486
Prior coronary artery bypass graft	71 (21%)	5647 (19%)	0.425	66 (21%)	351 (23%)	0.655
Prior heart failure	127 (37%)	5501 (18%)	<0.001	113 (36%)	607 (39%)	0.407
Prior valve surgery/procedure	11 (3%)	664 (2.2%)	0.294	10 (3.2%)	51 (3.3%)	1.000
Cerebrovascular disease	91 (27%)	5614 (19%)	<0.001	83 (27%)	426 (27%)	0.853
Peripheral arterial disease	88 (26%)	5379 (18%)	<0.001	80 (26%)	388 (25%)	0.830
Cardiomyopathy or left ventricle systolic dysfunction	64 (19%)	3147 (11%)	<0.001	55 (18%)	274 (18%)	1.000
Primary access site:			0.044			0.572
Radial access	97 (28%)	10426 (35%)		95 (30%)	426 (27%)	
Femoral access	243 (71%)	19340 (65%)		215 (69%)	1124 (72%)	
Intra-aortic balloon pump	12 (3.5%)	365 (1.2%)	<0.001	7 (2.2%)	41 (2.6%)	0.844
Stable angina pectoris	14 (4.1%)	2970 (9.9%)	<0.001	13 (4.2%)	77 (4.9%)	0.982
Unstable angina pectoris	118 (35%)	13400 (45%)	<0.001	112 (36%)	536 (34%)	0.982
Non-ST-segment elevation myocardial infarction	131 (38%)	7263 (24%)	<0.001	128 (41%)	646 (41%)	0.982
ST-segment elevation myocardial infarction	61 (18%)	4416 (15%)	<0.001	43 (14%)	211 (14%)	0.982

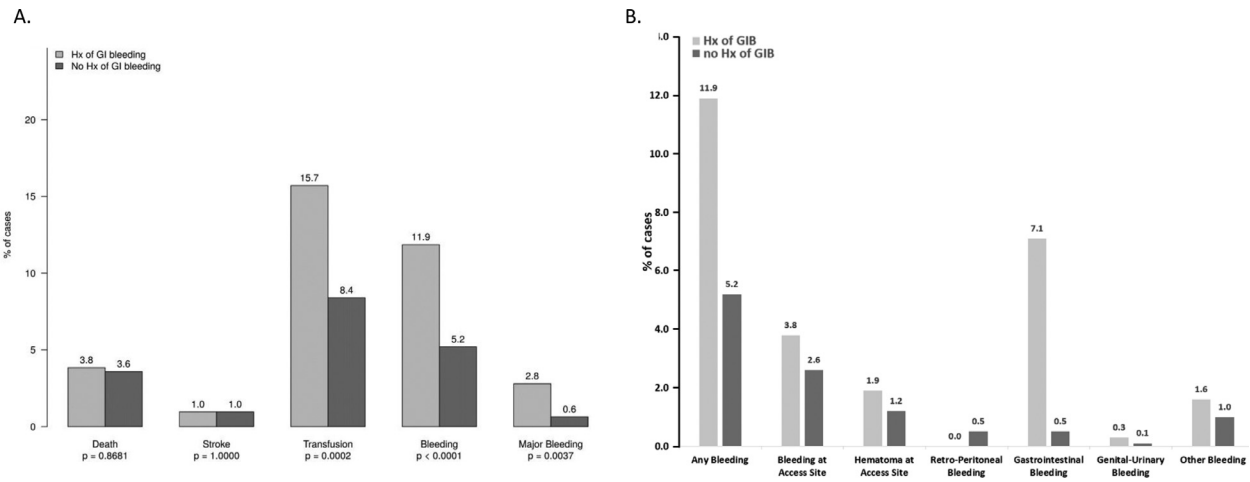

Figure 2. In-hospital outcomes in the matched cohort. A. Bar graph of primary in-hospital outcomes of patients with (light gray) and without (dark gray) a history of GIB after matching. Outcome rates and P values are noted above and below each bar respectively. GIB, gastrointestinal bleed; Hx, history. B. Bar graph of sources of in-hospital post-PCI bleeding among patients with (light gray) and without (dark gray) a history of GIB after matching. Outcome rates noted above each bar. GIB, gastrointestinal bleed; Hx, history.

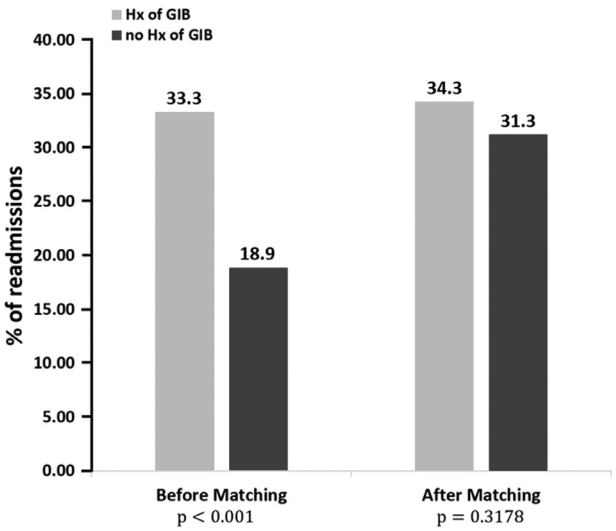

Figure 3. Readmission rates among patients with and without a history of gastrointestinal bleeding. Adjusted odds ratio in the matched cohort after adjusting for all variables in the propensity score was 1.19 with a 95% confidence interval of 0.89−1.59.

After matching, patients with a history of GIB appeared to have decreased survival early after PCI; however, the differences in survival were not statistically significant at 1 year (78% vs 80%; p = 0.217), 3 years (63% vs 64%; p = 0.409) or 5 years (54% vs 51%; p = 0.189) (Figure 4B).

Discussion

The main finding of this study is that a history of GIB prior to PCI was associated with a higher rate of post-PCI in-hospital bleeding complications including the need for transfusion. Although identified in only 1.1% of >30,000 patients undergoing PCI during this study, a history of GIB was associated with significantly higher risk of in-hospital post-PCI bleeding events. Patients with a history of GIB also had a high rate of 90-day readmission and mortality; however, after adjusting for baseline demographic and clinical characteristics, readmission and mortality rates did not significantly differ from patients without a history of GIB. This suggests that a history of GIB may be a proxy for overall clinical complexity and severity of illness. Our findings further underscore the importance of ensuring that all patients with a history of GIB on antithrombotic medications receive GIB prophylaxis with a proton pump inhibitor or histamine H_2 receptor antagonist.[22]

The absolute incidence of in-hospital post-PCI GIB in our study was low (0.43%), similar to findings from prior studies.[7,9,11] Although GIB after PCI is infrequent, prior studies indicated its clinical relevance with increased 30-day and long-term mortality.[11] Not only is GIB a common noncardiac cause of rehospitalization but prior work has found that any form of post-PCI bleeding readmissions were significantly associated with higher rates of death.[12] Our study differs in that we sought to evaluate patients with a history of GIB who may be at higher risk for post-PCI bleeding complications. Consistent with prior work,[7] our study revealed that a history of GIB is associated with an increased risk of post-PCI in-hospital bleeding.

Our findings demonstrate that patients with a history of GIB have high rates of 90-day readmission and mortality at baseline; however, these differences were not statistically different compared with similar matched patients without a history of GIB. One possible explanation for the increased risk of post-PCI bleeding among patients with a history of GIB may be related to the fact that the intra-procedural and acute post-procedural period is usually the state in which the most potent antithrombotic agents are used, including intravenous anticoagulants, intravenous antiplatelet agents and loading doses of P2Y12 inhibitors. Compared with clopidogrel, ticagrelor and prasugrel are known to be more

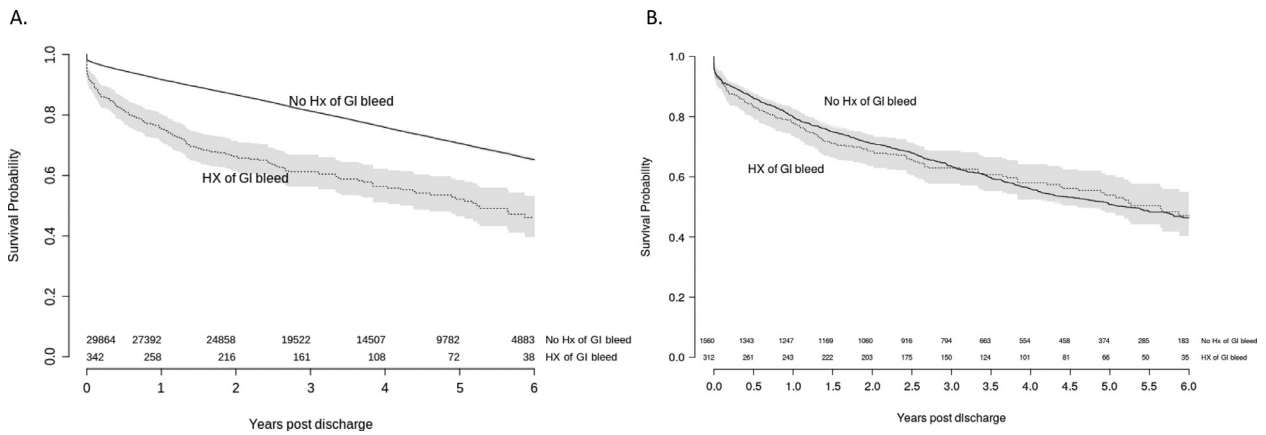

Figure 4. Kaplan-Meier curve of long-term mortality among patients discharged alive before (graph A) and after (graph B) matching. A. Before matching: Survival rate at 1 year with and without a history of GIB was 75% and 92% respectively, p < 0.0001. Survival rate at 3 years with and without a history of GIB was 61% and 81% respectively, p < 0.0001. Survival rate at 5 years with and without a history of GIB was 52% and 71% respectively, p < 0.0001. GIB indicates a gastrointestinal bleed. B. After matching: Survival rate at 1 year with and without a history of GIB was 78% and 80% respectively, p = 0.217. Survival rate at 3 years with and without a history of GIB was 63% and 64% respectively, p = 0.409. Survival rate at 5 years with and without a history of GIB was 54% and 51% respectively, p = 0.189. GIB indicates a gastrointestinal bleed.

potent antiplatelet agents. However, 1 in 9 patients in our cohort with a history of GIB were prescribed ticagrelor or prasugrel at discharge, identifying a subset of patients that may benefit from less potent P2Y12 inhibitor therapy (Supplemental Table 3).

These findings should be interpreted in the context of the following limitations. First, given the observational nature of the study, we were unable to account for all potential confounders including some variables that may be associated with a patient's risk of bleeding. We attempted to adjust for baseline differences with propensity score matching (Supplemental Figure 2). Second, the exposure variable of GIB was defined in the clinical PCI registry, as outlined in the methods section, but we could not define the magnitude or specific timing of this GIB. Although GIB occurring in the last 30 days might carry a higher risk of post-PCI bleeding than more remote episodes, additional studies will be required to assess this risk. Third, we were unable to assess out-of-hospital complications that did not lead to a readmission. Lastly, this study was limited to the BMC2 PCI clinical registry with a long history of focused quality improvement.[23] Thus, these findings may not be generalizable to other hospitals without a similar collaborative quality improvement environment.

In conclusion, a history of GIB was associated with a higher incidence of post-PCI bleeding complications including the need for transfusion. Overall, patients with a history of GIB had a higher rate of 90-day readmission and long-term mortality compared with patients without a history of GIB; however, after matching these differences were not statistically significant. Based on these findings, healthcare professionals caring for patients with a history of GIB in the peri-PCI period should counsel patients on their increased risks of adverse outcomes and ensure that steps are taken to reduce the incidence of post-PCI bleeding, including the use of proton pump inhibitors or histamine H_2 receptor antagonists and avoidance of NSAIDs.[22]

Disclosures

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2021.06.013.

1. Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, Chamberlain AM, Chang AR, Cheng S, Das SR, Delling FN, Djousse L, Elkind MSV, Ferguson JF, Fornage M, Jordan LC, Khan SS, Kissela BM, Knutson KL, Kwan TW, Lackland DT, Lewis TT, Lichtman JH, Longenecker CT, Loop MS, Lutsey PL, Martin SS, Matsushita K, Moran AE, Mussolino ME, O'Flaherty M, Pandey A, Perak AM, Rosamond WD, Roth GA, Sampson UKA, Satou GM, Schroeder EB, Shah SH, Spartano NL, Stokes A, Tirschwell DL, Tsao CW, Turakhia MP, VanWagner LB, Wilkins JT, Wong SS, Virani SS, On behalf of the American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2019 update: a report from the American Heart Association. *Circulation* 2019;139:e56–e528.
2. Levine GN, Bates ER, Bittl JA, Brindis RG, Fihn SD, Fleisher LA, Granger CB, Lange RA, Mack MJ, Mauri L, Mehran R, Mukherjee D, Newby LK, O'Gara PT, Sabatine MS, Smith PK, Smith SC. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease. *J Am Coll Cardiol* 2016;68:1082–1115.
3. Valgimigli M, Bueno H, Byrne RA, Collet J-P, Costa F, Jeppsson A, Jüni P, Kastrati A, Kolh P, Mauri L, Montalescot G, Neumann F-J, Petricevic M, Roffi M, Steg PG, Windecker S, Zamorano JL, Levine GN. ESC Scientific Document Group. ESC Committee for Practice Guidelines (CPG). ESC National Cardiac Societies. 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: the task force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2017;39:213–260.
4. Zhu P, Tang X, Xu J, Song Y, Liu R, Zhang Y, Gao L, Gao Z, Chen J, Yang Y, Gao R, Xu B, Yuan J. Predictors and consequences of postdischarge gastrointestinal bleeding after percutaneous coronary intervention. *Cardiovasc Ther* 2018;36:e12440.
5. Aronow HD, Steinhubl SR, Brennan DM, Berger PB, Topol EJ, Investigators CREDO. Bleeding risk associated with 1 year of dual antiplatelet therapy after percutaneous coronary intervention: insights from the clopidogrel for the reduction of events during observation (CREDO) trial. *Am Heart J* 2009;157:369–374.
6. Koskinas KC, Räber L, Zanchin T, Wenaweser P, Stortecky S, Moschovitis A, Khattab AA, Pilgrim T, Blöchlinger S, Moro C, Jüni P, Meier B, Heg D, Windecker S. Clinical impact of gastrointestinal bleeding in patients undergoing percutaneous coronary interventions. *Circ Cardiovasc Interv* 2015;8:e002053.
7. Patel NJ, Pau D, Nalluri N, Bhatt P, Thakkar B, Kanotra R, Agnihotri K, Ainani N, Patel N, Patel N, Shah S, Kadavath S, Arora S, Sheikh A, Badheka AO, Lafferty J, Alfonso C, Cohen M. Temporal trends, predictors, and outcomes of in-hospital gastrointestinal bleeding associated with percutaneous coronary intervention. *Am J Cardiol* 2016;118:1150–1157.
8. Abbas AE, Brodie B, Dixon S, Marsalese D, Brewington S, O'Neill WW, Grines LL, Grines CL. Incidence and prognostic impact of gastrointestinal bleeding after percutaneous coronary intervention for acute myocardial infarction. *Am J Cardiol* 2005;96:173–176.
9. Cholankeril G, Hu M, Cholankeril R, Khan MA, Gadiparthi C, Yoo ER, Perumpail RB, Nair S, Howden CW. Inpatient outcomes for gastrointestinal bleeding associated with percutaneous coronary intervention. *J Clin Gastroenterol* 2019;53:120–126.

10. Holroyd EW, Mustafa AH, Khoo CW, Butler R, Fraser DG, Nolan J, Mamas MA. Major bleeding and adverse outcome following percutaneous coronary intervention. *Interv Cardiol Rev* 2015;10:22.
11. Kwok CS, Sirker A, Farmer AD, Kontopantelis E, Potts J, Ayyaz Ul Haq M, Ludman P, Belder M, Townend J, Zaman A, Large A, Kinnaird T, Mamas MA, on behalf of the British Cardiovascular Intervention Society (BCIS) and National Institute of Cardiovascular Outcomes Research (NICOR). In-hospital gastrointestinal bleeding following percutaneous coronary intervention. *Catheter Cardiovasc Interv* 2020;95:109–117.
12. Valle JA, Shetterly S, Maddox TM, Ho PM, Bradley SM, Sandhu A, Magid D, Tsai TT. Postdischarge bleeding after percutaneous coronary intervention and subsequent mortality and myocardial infarction: insights from the HMO research network-stent registry. *Circ Cardiovasc Interv* 2016;9:e003519.
13. Abraham NS, Hlatky MA, Antman EM, Bhatt DL, Bjorkman DJ, Clark CB, Furberg CD, Johnson DA, Kahi CJ, Laine L, Mahaffey KW, Quigley EM, Scheiman J, Sperling LS, Tomaselli GF. ACCF/ACG/AHA 2010 expert consensus document on the concomitant use of proton pump inhibitors and thienopyridines: a focused update of the ACCF/ACG/AHA 2008 expert consensus document on reducing the gastrointestinal risks of antiplatelet therapy and NSAID use. *J Am Coll Cardiol* 2010;56:2051–2066.
14. Kline-Rogers E, Share D, Bondie D, Rogers B, Karavite D, Kanten S, Wren P, Bodurka C, Fisk C, Mcginnity J. Development of a multicenter interventional cardiology database: the blue cross blue shield of michigan cardiovascular consortium (BMC2) experience. *J Intervent Cardiol* 2002;15:387–392.
15. Moscucci M, Rogers EK, Montoye C, Smith DE, Share D, O'Donnell M, Maxwell-Eward A, Meengs WL, De Franco AC, Patel K, McNamara R, McGinnity JG, Jani SM, Khanal S, Eagle KA. Association of a continuous quality improvement initiative with practice and outcome variations of contemporary percutaneous coronary interventions. *Circulation* 2006;113:814–822.
16. Ellimoottil C, Syrjamaki JD, Voit B, Guduguntla V, Miller DC, Dupree JM. Validation of a claims-based algorithm to characterize episodes of care. *Am J Manag Care* 2017;23:e382–e386.
17. Sukul D, Seth M, Dupree JM, Syrjamaki JD, Ryan AM, Nallamothu BK, Gurm HS. Drivers of variation in 90-day episode payments after percutaneous coronary intervention: insights from Michigan hospitals. *Circ Cardiovasc Interv* 2019;12:e006928.
18. American College of Cardiology Foundation. "NCDR® CathPCI Registry® v4. 4 coder's data dictionary." 2016.
19. Sekhon JS. Multivariate and propensity score matching software with automated balance optimization: the matching package for R. *J Stat Softw Forthcom* 2008.
20. Gu XS, Rosenbaum PR. Comparison of multivariate matching methods: structures, distances, and algorithms. *J Comput Graph Stat* 1993;2:405–420.
21. R Core Team. R: A language and environment for statistical computing. 2013.
22. Kumbhani DJ, Cannon CP, Beavers CJ, Bhatt DL, Cuker A, Gluckman TJ, Marine JE, Mehran R, Messe SR, Patel NS, Peterson BE, Rosenfield K, Spinler SA, Thourani VH. 2020 ACC expert consensus decision pathway for anticoagulant and antiplatelet therapy in patients with atrial fibrillation or venous thromboembolism undergoing percutaneous coronary intervention or with atherosclerotic cardiovascular disease. *J Am Coll Cardiol* 2021;77:629–658.
23. Share DA, Campbell DA, Birkmeyer N, Prager RL, Gurm HS, Moscucci M, Udow-Phillips M, Birkmeyer JD. How a regional collaborative of hospitals and physicians in Michigan cut costs and improved the quality of care. *Health Aff (Millwood)* 2011;30:636–645.