Outcomes of Percutaneous Coronary Intervention in Patients With Crohn's Disease and Ulcerative Colitis (from a Nationwide Cohort)

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Patients with inflammatory bowel disease (IBD) are at an increased risk of ischemic heart disease. However, there is limited evidence on how their outcomes after percutaneous coronary intervention (PCI) compare with those without IBD. All PCI-related hospitalizations from the National Inpatient Sample from 2004 to 2015 were included, stratified into 3 groups: no-IBD, Crohn's disease (CD), and ulcerative colitis (UC). We assessed the association between IBD subtypes and in-hospital outcomes. A total of 6,689,292 PCI procedures were analyzed, of which 0.3% (n = 18,910) had an IBD diagnosis. The prevalence of IBD increased from 0.2% (2004) to 0.4% (2015). Patients with IBD were less likely to have conventional cardiovascular risk factors and more likely to undergo PCI for an acute indication, and to receive bare metal stents. In comparison to patients without IBD, those with IBD had reduced or similar adjusted odds ratios (OR) of major adverse cardiovascular and cerebrovascular events (CD OR 0.69, 95% confidence interval (CI) 0.62 to 0.78; UC OR 0.75, 95% CI 0.66 to 0.85), mortality (CD: OR 0.94, 95% CI 0.79 to 1.11; UC OR 0.35, 95% CI 0.27 to 0.45) or acute cerebrovascular accident (CD: OR 0.73, 95% CI 0.60 to 0.89; UC: OR 0.94, 95% CI 0.77 to 1.15). However, IBD patients had an increased odds for major bleeding (CD: OR 1.42 95% CI 1.23 to 1.63, and UC: OR 1.35 95% CI 1.16 to 1.58). In summary, IBD is associated with a decreased risk of in-hospital post-PCI complications other than major bleeding that was significantly higher in this group. Long term follow-up is required to evaluate the safety of PCI in IBD patients from both bleeding and ischemic perspectives. **(Am J Cardiol 2020;130:30−36)**

Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic inflammatory conditions with an estimated global prevalence of 0.2% to 0.8%.[1,2] Although their manifestations are mainly gastrointestinal, they are frequently associated with cardiovascular conditions such as atrial fibrillation (AF), heart failure, as well as ischemic heart disease (IHD).[3−6] The latter is primarily attributed to the autoinflammatory pathogenesis of IBD as well as some of its associated treatments such as corticosteroids, which promote atherogenesis and enhance the risk of IHD.[7−10] Despite previous reports of worse PCI-related outcomes with some chronic inflammatory conditions, there is limited evidence on procedural outcomes of PCI in patients with IBD.[11−15] we examined the prevalence of IBD, their clinical characteristics and in-hospital outcomes in patients who underwent PCI from a nationally representative sample in the United States (US).

Methods

The National Inpatient Sample (NIS) is the largest all-payer inpatient health care database in the United States developed by the Healthcare Cost and Utilization Project (HCUP) and sponsored by the Agency for Healthcare Research and Quality.[16,17] The NIS dataset contains hospital information on between 7 and 8 million yearly hospital discharges from 2004 onward. Since 2012, the NIS samples discharge from all hospitals participating in HUCP, approximating a 20% stratified sample of all discharges from US community hospitals. The sampling strategy has changed over time in order to produce more generalizable estimates by reducing sampling bias. Before 2012 the NIS retained all discharges, but only from a sample of hospitals.

All patients underwent PCI from January 2004 to September 2015 were included, identified using the following International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure codes: 00.66, 36.06, 36.07, 36.01, 36.02, and 36.05.

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See page 35 for disclosure information.

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All records were eligible for inclusion if discharge record showed that the patient had undergone a PCI procedure during their hospital stay and was over the age of 18 years. Information on patient demographics were recorded for each hospital discharge including age, gender, race, admission type (elective or emergent), admission day (weekday or weekend), expected primary payer and median household income according to ZIP code. Missing records for age, gender, elective or weekend admission and hospital location/ teaching status were excluded from the analysis. Patients with known primary connective tissue disease were also excluded from analysis. Each discharge record had information on up to 30 diagnoses (15 from 2004 to 2008, 25 from 2009 to 2013, and 30 in 2014). A full list of ICD 9-CM codes used to identify CD (555.×), UC (556.×), as well as other patient characteristics and complications is provided in Supplementary Table 1. ICD 9-CM codes were also used to identify procedural information including multivessel versus single-vessel procedure, bifurcation lesions, type of stent type deployed (bare metal (BMS) or drug eluting (DES)), use of adjunctive devices including intracoronary pressure wire, intravascular ultrasound, Optical Coherence Tomography, assist device or intra-aortic balloon pump.

The main outcome was to compare the in-hospital clinical outcomes, including major adverse cardiovascular and cerebrovascular events (MACCE) (composite of mortality, acute stroke or transient ischemic attack (TIA) and cardiac complications), all-cause mortality and major bleeding, between patients with and without IBD. Cardiac complications included coronary dissection, pericardial effusion or hemopericardium and cardiac tamponade. Major bleeding events were defined as a composite of diagnosis of gastrointestinal, retroperitoneal, intracranial, intracerebral hemorrhage, unspecified hemorrhage, and whether a blood transfusion was required.

Statistical analysis was performed on IBM SPSS version 25. Continuous variables are presented as median and interquartile range, due to skewed data, and categorical data are presented as frequencies and percentages. Missing data were assumed to be missing at random. For all analyses, cases were weighted. The use of sampling weights was required because the design of the study means that different observations may have different probabilities of selection. Sampling weights for each individual discharge that were provided by the Agency for Healthcare Research and Quality were used.

Multivariable logistic regression models were to examine the association between IBD and its subtypes to in-hospital complications. All models were adjusted for potential confounders. These included age, gender, elective admission, weekend admission, hospital location/teaching status, type of clinical syndrome (ST elevation myocardial infarction (STEMI), non-STEMI, unstable or stable angina), cardiogenic shock, use of assist device/intra-aortic balloon pump, diabetes, hypertension, dyslipidemia, renal failure, thrombocytopenia, coagulopathy, anemia, chronic liver and lung diseases, smoking status, malignancy, previous bowel resection, known ischemic heart disease or heart failure, previous myocardial infarction (MI) or cerebrovascular accident (CVA), multivessel PCI and type of stent (drug-eluting DES or BMS).

Results

A total of 6,689,292 PCI procedures were recorded from 2004 to 2015, of which 18,910 patients (0.28%) had a diagnosis of IBD. The number of patients with CD and UC were 10,367 (0.15%) and 8,543 (0.13%), respectively. From 2004 to 2015, the rate of IBD among all those who underwent PCI doubled from 0.2% to 0.4% (Figure 1).

In comparison to those without IBD, patients with CD were younger and more likely to be female whereas those with UC were more likely to be male (Table 1). Patients with IBD were more likely to be white and had a lower prevalence of certain conditions such as heart failure, diabetes, peripheral vascular disease and previous history of CVA, MI or coronary revascularization (PCI or CABG). In contrast, IBD patients had a higher prevalence of AF, malignancies (solid tumors and metastatic disease), bleeding diatheses (anemia, thrombocytopenia, coagulopathy), and chronic liver disease.

Patients with IBD were more likely to undergo PCI for an acute indication (STEMI and non-STEMI) compared with those without IBD (Table 1). The rates of single vessel PCI and BMS use were higher in the IBD groups. The median length of stay was similar in all groups, whereas the cost of admission for patients with UC was higher than CD or non-IBD patients (Table 1). From 2004 to 2015 the rates of BMS decreased from 23% to 14%.

Overall, the crude rates of in-hospital MACCE, mortality acute stroke/TIA and vascular complication were lower in UC and CD patients compared with non-IBD patients (Table 2 and Figure 2). However, in comparison to non-IBD patients, the rates of cardiac complications were lower in CD patients and higher in UC patients. In multivariable analysis, patients with UC and CD had reduced odds of MACCE (CD: OR 0.69, 95% CI 0.62 to 0.78; UC: OR 0.75, 95% CI 0.66 to 0.85), mortality (CD: OR 0.94, 95% CI 0.79 to 1.11; UC: OR 0.35, 95% CI 0.27 to 0.45), and acute stroke/TIA (CD: OR 0.73, 95% CI 0.60 to 0.89; UC: OR 0.94, 95% CI 0.77 to 1.15), compared with those without IBD (Figure 3).

The crude rates of major bleeding were higher in the IBD groups compared with the non-IBD group, mainly driven by higher rates of GI bleeding in the IBD groups (Table 2 and Figure 2). Patients with CD and UC had an increase in adjusted odds of major bleeding compared with those without IBD (CD: OR 1.42 95% CI 1.23 to 1.63 and UC: OR 1.35 95% CI 1.16 to 1.58; Figure 3).

Discussion

This is the first national-level analysis comparing procedural outcomes between patients with and without IBD who underwent PCI. First, we show that IBD patients represent a small proportion of those who underwent PCI, although their prevalence has doubled over the study decade. Second, we observe differences in risk profile and indications between patients with and without IBD. Patients with IBD have a lower prevalence of conventional cardiovascular risk factors compared with those without IBD, but also a higher prevalence of risk factors for bleeding. Furthermore, IBD patients were more likely to undergo PCI for

Table 1
Patients' demographics and procedural characteristics for included hospital records, stratified by a diagnosis

Patient Characteristics	No IBD (n = 6,670,383)	CD (n = 10,367)	UC (n = 8,543)	p Value
Age (years), median (IQR)	65 (56,74)	63 (55,72)	65 (58,74)	<0.001
Women	33.2%	39.8%	30.6%	<0.001
Ethnicity				<0.001
White	79%	89.3%	89.5%	
Black	8.2%	4.9%	3.7%	
Hispanic	6.6%	2.6%	2.6%	
Asian/Pacific Islander	2%	0.5%	0.9%	
Native American	0.5%	0.5%	0.1%	
Other	3.6%	2.1%	3.3%	
Hospital Location				<0.001
Northeast	8.5%	11.8%	15.1%	
Midwest	30.8%	34.8%	36.3%	
South	53.1%	46.2%	38.3%	
West	7.6%	7.2%	10.3%	
Hospital Size				<0.001
Small	10.1%	10.5%	11.8%	
Medium	24.2%	22.5%	20.8%	
Large	65.7%	66.9%	67.4%	
Hospital Location/ teaching Status				<0.001
Rural	6.1%	6.1%	5.7%	
Urban non-teaching	37.7%	36.1%	32.1%	
Teaching	56.2%	57.8%	62.2%	
Elective admission	26%	19.8%	18.4%	<0.001
Weekend Admission	16.6%	18.1%	20.2%	<0.001
Median ZIP income, quartile				<0.001
1st	25.6%	20.9%	19.6%	
2nd	26%	23.9%	24.4%	
3rd	24.6%	28.1%	27.3%	
4th	23.8%	27.1 %	28.7%	
Expected Primary Payer				<0.001
Medicare	51.1%	52.8%	51.9%	
Medicaid	5.9%	4.3%	3.4%	
Private	34.6%	37.1%	40.2%	
Uninsured	5.1%	3.1%	2.2%	
No charge	0.5%	0.3%	0.3%	
Other	2.8%	2.3%	2%	
Single vessel PCI	47.9%	54.1%	52.4%	<0.001
Bifurcation stenting	1.5%	1.5%	2.2%	<0.001
Stent Type				<0.001
Bare Metal	20.8%	25.8%	28.7%	
Drug Eluting	72%	67.1%	63.4%	
Both	1.9%	1.7%	2%	
Unknown	9.1%	8.8%	9.9%	
Use of assist device or IABP	3.3%	3.1%	3.7%	0.040
Fractional flow reserve	0.7%	1.1%	0.8%	<0.001
Intravascular ultrasound	3.9%	4%	4.3%	0.189
Optical Coherence Tomography	0.1%	<0.1%	0.1%	0.052
PCI indication:				<0.001
Stable Angina Pectoris	30.8%	23.2%	22.8%	
STEMI	23.6%	24.4%	25.6%	
NSTEMI	24.1%	27%	29.2%	
Unstable Angina Pectoris	21.5%	25.4%	22.4%	
Cardiogenic Shock	3%	2.8%	2.8%	0.201
Length of stay, (days), median (IQR)	2 (1,4)	2 (1,4)	2 (1,4)	0.052
Total charge, $, median (IQR)	45,372 (32,133, 68,818)	45,290 (32,938, 65,459)	48,175 (34,269, 70,834)	<0.001
Previous MI	10.4%	9.5%	7.7%	<0.001
Previous PCI	13.7%	11.2%	12.2%	<0.001
Previous CABG	8.4%	6.7%	7.2%	<0.001
Previous CVA	2.5%	2%	2%	<0.001
Heart failure	14.7%	12.5%	13%	<0.001

(*continued*)

Table 1 (***Continued***)

Patient Characteristics	No IBD (n = 6,670,383)	CD (n = 10,367)	UC (n = 8,543)	p Value
Valvular disease	0.3%	0.2%	0.3%	0.367
Atrial fibrillation/flutter	10.5%	11%	12.4%	<0.001
Hypertension	69.9%	68.4%	68%	<0.001
Hyperlipidemia	59.9%	51%	56.1%	<0.001
Diabetes Mellitus	33.7%	26.3%	28.5%	<0.001
Smoker	19.3%	19%	9%	<0.001
Peripheral vascular disorder	10.5%	9.8%	10.1	0.039
Renal Failure	9.9%	9.3%	9.8%	0.104
Chronic Pulmonary disease	15.7%	18.8%	15.5%	<0.001
Obesity	12.7%	10.2%	12.3%	<0.001
Previous bowel resection	0.1%	1.2%	0.4%	<0.001
Fluid & electrolyte disorders	9.7%	13.2%	11.3%	<0.001
Anemia	8.3%	13.2%	12.5%	<0.001
Hypothyroidism	7.8%	9.4%	10.7%	<0.001
Thrombocytopenia	1.4%	1.6%	2.2%	<0.001
Coagulopathy	2.3%	2.5%	3.4%	<0.001
Depression	5.5%	9.4%	7.4%	<0.001
Chronic Liver Disease	0.9%	1.6%	1.7%	<0.001
Alcohol abuse	2.1%	1.8%	1.7%	0.010
Drug abuse	1.4%	1.7%	0.7%	<0.001
AIDS	0.1%	0.1%	<0.1%	0.995
Other Neurological disorders	3%	4.6%	2.7%	<0.001
Paralysis	0.7%	0.3%	0.9%	<0.001
Psychoses	1.4%	2.5%	1.5%	<0.001
Pulmonary circulation disorders	0.2%	0.3%	0.3%	<0.001
Peptic ulcer disease without bleeding	<0.1%	<0.1%	<0.1%	0.129
Weight loss	0.9%	1.4%	1.4%	<0.001
Solid tumor without metastasis	0.9%	1.1%	1.5%	0.001
Lymphoma	0.3%	0.3%	0.5%	0.038
Metastatic cancer	0.3%	0.4%	0.5%	<0.001

ACS than stable angina. After adjustment for differences in risk profile and PCI indication, we find that IBD (UC and CD) was associated with reduced odds for MACCE, mortality and acute CVA, but was independently associated with an increased risk of major bleeding.

Patients with IBD are at a heightened risk of ischemic heart disease, for which they may require coronary revascularization, but little is known about their prevalence among patients who underwent PCI, and their clinical outcomes.[4] Although IBD patients represent a small proportion of those who underwent PCI, their prevalence has doubled over the study period. However, there is limited procedural outcomes data for this population, for example, an analysis of 131 patients with IBD and IHD, of which less than 30% underwent PCI, demonstrated no difference in overall complications between IBD and non-IBD subjects.[15]

We show that IBD, including CD and UC, was associated with a lower risk of MACCE, mortality, acute stroke and vascular complications. In the absence of established evidence on PCI outcomes in this group it is difficult to compare our findings with those in previous one. One previous study found lower mortality among IBD patients admitted with MI. The observed differences in the outcomes of UC and CD patients were not previously reported.[18] Although some factors such as pharmacotherapeutic use and angiographic findings were not adjusted for in our analysis, several reasons could explain why patients with IBD experience lower rates of ischemic and vascular complications. IBD patients are younger and, therefore, less likely to have complex lesions including diffuse atherosclerosis, calcific or multivessel coronary artery disease that are known to be associated with adverse outcomes Our analysis suggests that patients who underwent IBD are at greater risk of sustaining in-hospital major bleeding complications, mainly driven through increased gastrointestinal bleeding events. The latter finding is of great clinical significant since it provides insights in to the inherent bleeding risk in this patient group, who are currently not considered in high-bleeding risk definitions.[19] We observe higher rates of BMS use in IBD patients, which could be explained by physicians' recognition of the potential higher risk of long-term bleeding in this group and their possibility of early discontinuation of dual antiplatelet therapy.[20–22] However, BMS have been shown to be inferior to DES in the long-term with respect to outcomes such as target lesion and vessel revascularization and risk of reinfarction.[23] In the recent years, as an alternative to BMS in high bleeding risk groups, many studies reported favorable outcomes of new stent platforms, as well as new antiplatelet therapy strategies with shorter DAPT duration. The adoption of such may help to reduce the higher bleeding risk in this group.[24–26] Furthermore, use of less potent antiplatelet agents may serve to decrease the bleeding risk further.

The are several limitations to the present study. First, the NIS is an administrative dataset, and coding error may be a source of bias. The identification of PCI and IBD diagnoses as well as other comorbidities and procedural data was

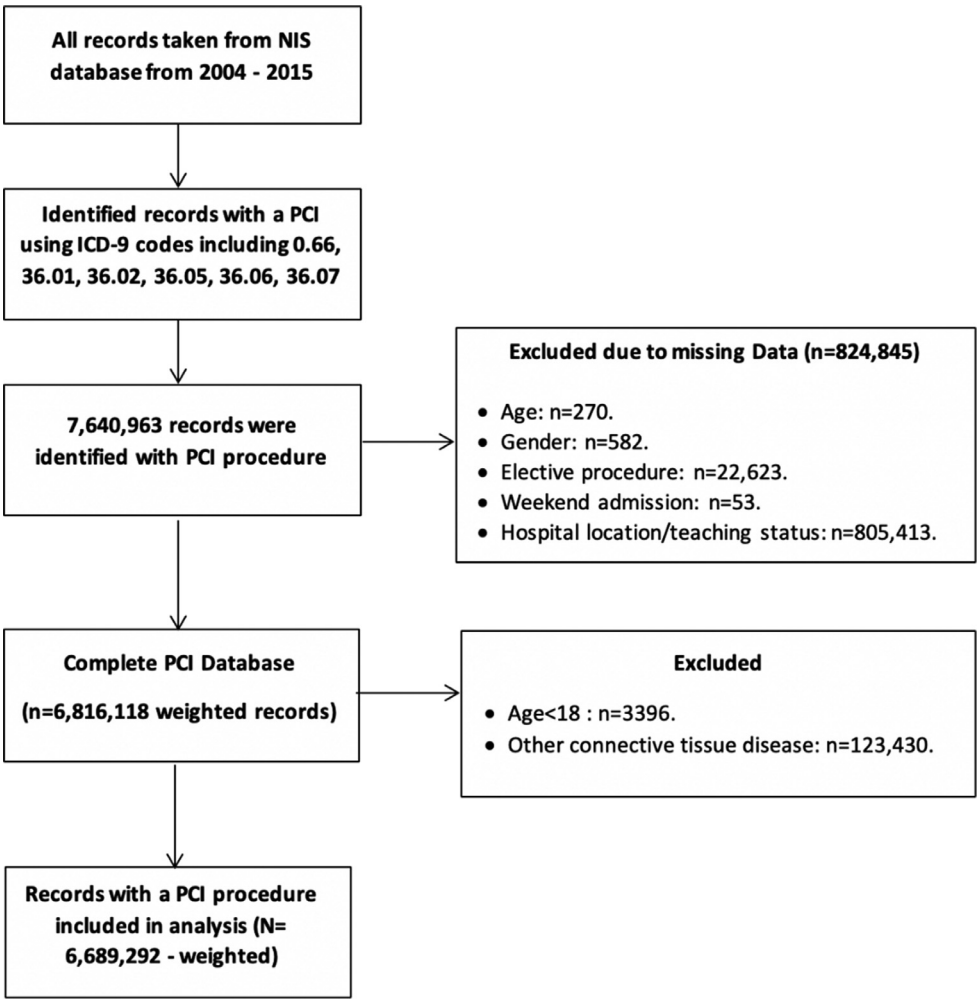

Figure 1. Flow diagram of study population. PCI = percutaneous coronary intervention; NIS = National Inpatient Sample; ICD-9 = International Classification of Diseases, Ninth Revision, Clinical Modification.

Table 2
In-hospital adverse events stratified by disease type

Variable	No IBD (n = 6,670,383)	CD (n = 10,367)		UC (n = 8,543)	
			p Value*		p Value*
MACCE†	4.3%	3.1%	<0.001	3.6%	<0.001
Mortality	1.7%	1.5%	0.216	0.9%	<0.001
Cardiac complications‡	1.2%	0.6%	<0.001	1.3%	0.220
Acute Stroke/TIA	1.7%	1.2%	<0.001	1.5%	0.198
Vascular complications	0.6%	0.4%	0.036	0.5%	0.104
Major Bleeding	1.2%	2%	<0.001	1.9%	<0.001
GI Bleeding	0.8%	1.4%	<0.001	1.7%	<0.001

* Reference group is "no IBD."
† composite of mortality, cardiac complication, and acute stroke/TIA.
‡ composite of coronary dissection, pericardial effusion or hemopericardium and cardiac tamponade.

based on the use of administrative codes. However, the NIS is a validated database, and the use of ICD-9 codes have been previously validated for the purposes of cardiovascular research.[27,28] Second, the NIS relate only to in-hospital outcomes and therefore longer-term follow-up of mortality and other adverse events are missing from our analysis. As IBD are chronic inflammatory conditions, the full extent of the risk related to it may be underestimated on short-term follow-up[11,12,29] Finally, the NIS database does not include data that may be relevant. It does not include

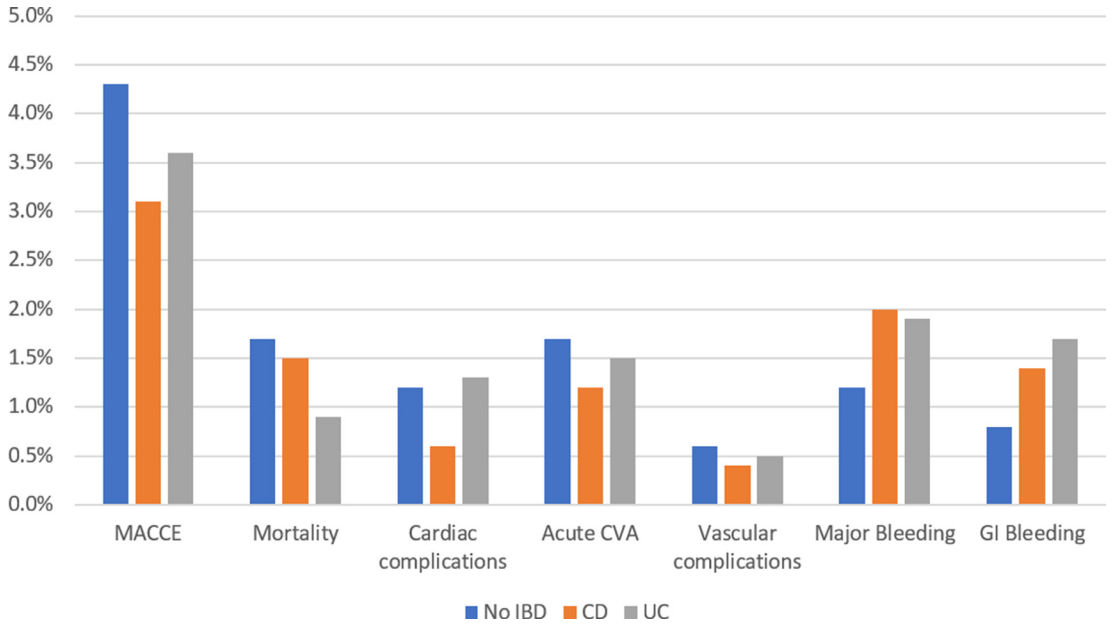

Figure 2. Crude rates of in-hospital outcomes.**Legend:** IBD = inflammatory bowel disease; CD = Crohn's Disease; UC = ulcerative colitis.

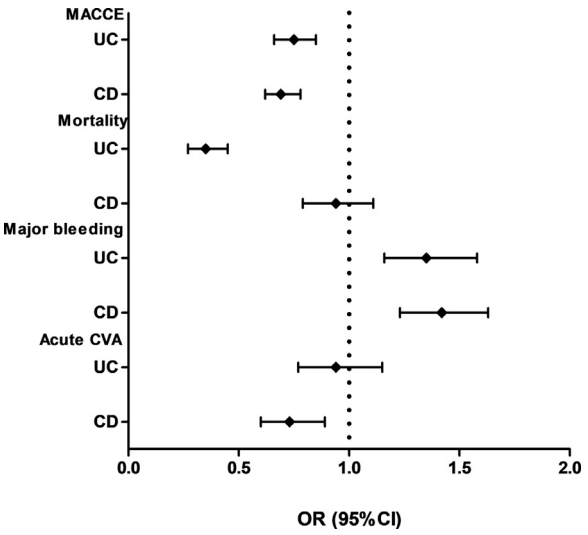

Figure 3. Adjusted odds ratios (OR) of in-hospital adverse outcomes*. *reference group: patients without IBD; CD = Crohn's disease; UC = ulcerative colitis.

pharmacotherapy; hence we were unable to determine differences in the use of antithrombotic therapy between the study groups or to determine the effect of baseline IBD treatment on clinical outcomes, which may both act as confounders.[3,8,20] The NIS also does not provide certain procedural information such as coronary lesion and procedural complexities, type of DES used (first vs second generation) and extent of revascularization. Laboratory results, including inflammatory markers, are also not included in the NIS database. Nevertheless, we believe that our findings provide insight into the "real world" in-hospital clinical outcomes of a large and unselected cohort of patients with inflammatory bowel diseases underwent PCI.

In conclusion, patients with IBD who underwent PCI have increased in prevalence over an eleven-year period. Patients with IBD are less likely to have conventional cardiovascular risk factors and are more likely to undergo PCI for an acute indication. Although this group was associated with a reduced risk of in-hospital mortality, acute stroke and vascular complications after PCI, they were more likely to experience major bleeding, specifically gastrointestinal in origin. The present findings emphasize the importance of incorporating IBD as part of the high bleeding risk criteria when risk-stratifying patients who underwent PCI as well as the need for long-term follow-up studies of post-PCI outcomes this patient group.

CRediT author statement

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Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2020.06.013.

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