CLINICAL RESEARCH STUDY

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Outcomes and Resource Utilization in Patients Hospitalized with Gastrointestinal Bleeding Complicated by Types 1 and 2 Myocardial Infarction

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ABSTRACT

BACKGROUND: Types 1 and 2 myocardial infarction (MI) may occur in the setting of gastrointestinal bleeding (GIB). There is a paucity of data pertinent to the contemporary prevalence and impact of types 1 and 2 MI following GIB. We examined clinical profiles and the prognostic impact of both MI types on outcomes of patients hospitalized with GIB.

METHODS: The 2018 Nationwide Readmission Database was queried for patients hospitalized for the primary diagnosis of GIB and had concomitant diagnoses of type 1 or type 2 MI. Baseline characteristics, in-hospital mortality, resource utilization, and 30-day all-cause readmissions were compared among groups.

RESULTS: Of 381,867 primary GIB hospitalizations, 2902 (0.75%) had type 1 MI and 3963 (1.0%) had type 2 MI. GIB patients with type 1 and type 2 MI had significantly higher in-hospital mortality compared to their counterparts without MI (adjusted odds ratios [aOR]: 4.72, 95% confidence interval [CI] 3.43-6.48; and aOR: 2.17, 95% CI 1.48-3.16, respectively). Both types 1 and 2 MI were associated with higher rates of discharge to a nursing facility (aOR of type 1 vs. no MI: 1.65, 95% CI 1.45-1.89, and aOR of type 2 vs no MI: 1.37, 95% CI 1.22-1.54), longer length of stay, higher hospital costs, and more 30-day all-cause readmissions (aOR of type 1 vs no MI: 1.22, 95% CI 1.08-1.38; aOR of type 2 vs no MI: 1.17, 95% CI 1.05-1.30).

CONCLUSION: Types 1 and 2 MI are associated with higher in-hospital mortality and resource utilization among patients hospitalized with GIB in the United States.

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KEYWORDS: GI Bleeding; Outcomes; Type 1 myocardial infarction; Type 2 myocardial infarction

INTRODUCTION

Gastrointestinal bleeding is the most common primary gastrointestinal etiology for admission in the United States. It is estimated to result in more than 500,000 annual hospital admissions, with accrual of more than 2 million hospital days and $5 billion in direct annual costs in 2015.[1] Gastrointestinal bleeding constitutes not only a substantial economic burden but also carries a significant morbidity and mortality rate with an estimated 11,000 in-hospital deaths in 2015 alone.[1]

Although there is a significant literature available on the outcomes of gastrointestinal bleeding following acute myocardial infarction,[2,3] there is a paucity of data on the incidence and outcomes associated with in-hospital myocardial

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infarction following gastrointestinal bleeding. In a previous small, single-center study, the incidence of myocardial infarction was 13% in patients admitted with gastrointestinal bleeding in the intensive care unit.[4] Severe gastrointestinal bleeding leads to hypovolemia, hemodynamic compromise, myocardial hypoperfusion with oxygen supply-demand mismatch causing type 2 myocardial infarction, or less commonly to atherosclerotic plaque disruption and thrombosis, in part due to discontinuation of antiplatelet therapy, causing a type 1 myocardial infarction.[5] Both myocardial infarction subtypes have distinct clinical phenotype, pathophysiological mechanisms, therapeutic approaches, and clinical outcomes.[6] Hospitalized patients with types 1 and 2 myocardial infarction have high rates of mortality, resource utilization, and 30-day readmissions.[5,6] However, their impact in patients hospitalized with a primary diagnosis of gastrointestinal bleeding is not well characterized. Therefore, we conducted this large national database analysis to assess the prevalence, patient characteristics, outcomes, and 30-day readmissions for patients admitted with gastrointestinal bleeding complicated by type 1 and type 2 myocardial infarction.

CLINICAL SIGNIFICANCE

- Types 1 and 2 myocardial infarction in patients admitted with gastrointestinal bleeding are associated with higher in-hospital mortality, resource utilization, and 30-day all-cause readmission compared with their counterparts without myocardial infarction.
- The use of coronary angiography and percutaneous coronary intervention were low in patients with gastrointestinal bleeding with type 1 myocardial infarction.
- Heart failure is a more common cause of readmission for patients with types 1 and 2 myocardial infarction.

METHODS

Data Source

The Nationwide Readmission Database (NRD) was used to extract relevant patient information from January 1, 2018, to December 31, 2018. The NRD is developed by the Agency for Healthcare Research and Quality (AHRQ) as part of the Health Care Cost and Utilization Project (HCUP).[7] The NRD was used given its nationally representative large sample size that provides in-hospital outcomes and readmission rate following discharge. The NRD is drawn from the State Inpatient Databases that contain verified patient linkage numbers that can be used to track individual patients across hospitals within a state while adhering to strict privacy guidelines. The 2018 NRD includes data from 28 geographically dispersed states, accounting for 59.7% of the total U.S. resident population and 58.7% of all U.S. hospitalizations. The database captures demographics, comorbidities, inpatient procedures, in-hospital morality, in-hospital complications, expected payer, length of stay, total charges and hospital costs, discharge disposition, and postdischarge readmissions. Discharge weights are provided to obtain national estimates. The study is exempt from the institutional review board because it uses publicly available deidentified data.

Study Population

We used the *International Classification of Diseases, Tenth Revision-Clinical Modification* (ICD-10-CM) diagnosis codes listed in Supplementary Table 1 (available online) to identify all primary hospitalizations with gastrointestinal bleeding (upper, lower, and unspecified source of bleeding [weighted national estimate = 577,993]). Prior validation studies have shown that ICD-10-CM codes for gastrointestinal bleeding have a sensitivity of 95.7%, a positive predictive value of 75%-100%, a specificity of 97.2%, and a negative predictive value of 99.8%.[8,9] We excluded patients <18 years of age and those with missing information on death, elective admission, end-stage renal disease, myocardial infarction (types 3, 4, 5, combined types 1 and 2, and unspecified), acute heart failure, shock (ie, septic, cardiogenic, anaphylactic, and unspecified/other), cardiac arrest, Takotsubo syndrome, myocarditis, pulmonary embolism, severe sepsis, as well as those who underwent percutaneous left atrial appendage atrial occlusion or other any percutaneous or surgical valvular procedures. The final study sample included 381,867 gastrointestinal bleeding hospitalizations (Figure). Patients with type 1 myocardial infarction (I2101, I2102, I2109, I2111, I2119, I2121, I2129, I213, I220, I221, I228, I229, I214, and I222) and type 2 myocardial infarction (I21.A1) were identified by ICD-10-CM codes. These codes have been used in previous studies to identify patients with type 1 and type 2 myocardial infarction.[6,10-12]

Patient and Hospital Characteristics

Data on patient demographics (age, sex), admission status (weekend vs weekday admission), underlying comorbidities (ie, Elixhauser comorbidity score, diabetes mellitus, dyslipidemia, hypertension, smoking, atrial fibrillation, chronic heart failure, valvular heart disease, prior myocardial infarction, prior percutaneous coronary intervention, prior coronary artery bypass grafting, prior implantable cardioverter defibrillator/permanent pacemaker, prior cerebrovascular accident, peripheral vascular disease, carotid artery disease, obesity, weight loss, hypothyroidism, iron-deficiency anemia, neurological disorders, alcohol use disorder, drug abuse, liver disease, chronic kidney disease, chronic lung disease), treatment variables (ie, coronary angiography, percutaneous coronary intervention, and coronary artery bypass

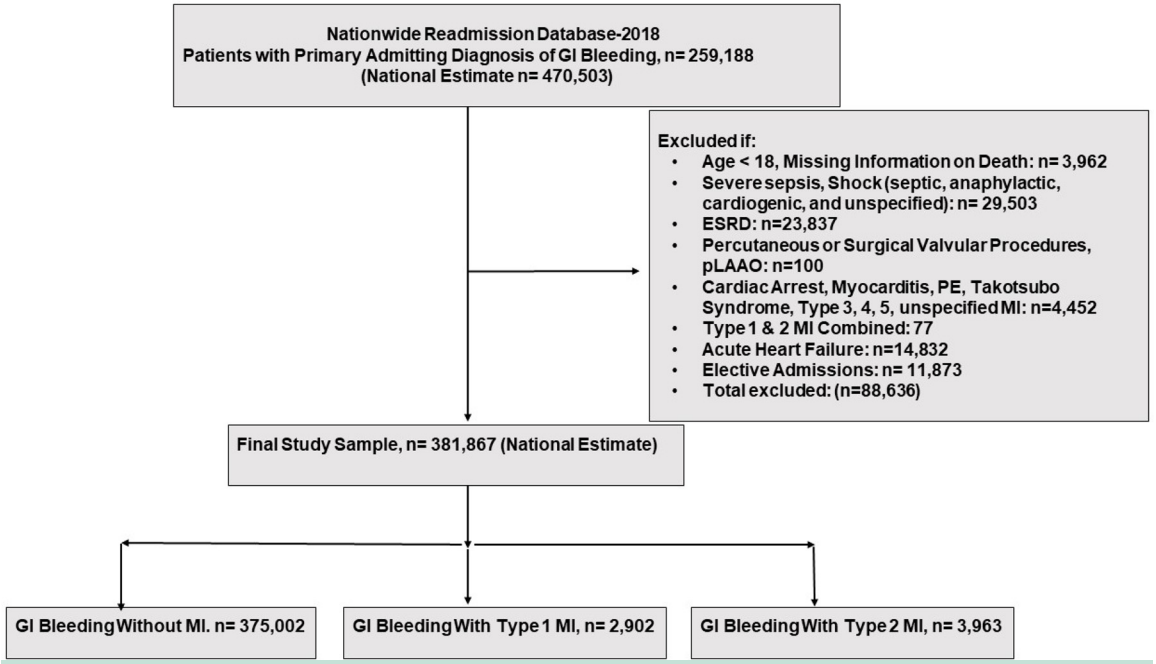

Figure Study population selection flowchart. ESRD = end-stage renal disease; GI = gastrointestinal; MI = myocardial infarction; PE = pulmonary embolism; pLAAO = percutaneous left atrial appendage occlusion.

graft surgery), hospital characteristics (ie, bed size, location, and teaching status), and expected primary payer source (ie, Medicare, Medicaid, private insurance, self-pay/no charge/other) were extracted. ICD-10-CM codes used to define these variables were extracted from the Elixhauser comorbidity approach and additional covariates listed in Supplementary Tables 1 and 2, available online.

Measures and Outcomes

The primary outcome of interest was in-hospital mortality. Secondary outcomes included index length of stay (LOS), hospital costs, discharge to a facility (ie, skilled nursing, intermediate care, and other facility), and 30-day all-cause readmission. We also examined the top 10 causes of 30-day readmissions in the 3 groups, using the HCUP Clinical Classification Software-Refined (CCSR), which bundles multiple ICD-10 codes into clinically meaningful categories (Clinical Classifications Software Refined[13] 2021). Readmissions were identified according to the methodology outlined by the HCUP.[14] For the readmission analyses, we excluded records of patients discharged in December 2018 due to unavailability of 30-day follow-up data on these cases, those who died during hospitalization, those with missing discharge disposition, and those who left against medical advice during the index hospitalization. For patients who had multiple readmissions within 30 days after index discharge, only the first readmission was counted.

Statistical Analyses

All statistical analyses were performed using discharge weights provided by the AHRQ to obtain national estimates. We used complex survey methods to account for stratification and clustering of data in the NRD, as recommended by the AHRQ.[14] For baseline characteristics, categorical variables are presented as frequencies and percentages and continuous variables as mean ± standard error (SE). Baseline patient characteristics as well as hospital, treatment, and primary expected payer variables were compared among patients with gastrointestinal bleeding with no myocardial infarction, type 1 myocardial infarction, and type 2 myocardial infarction using the Rao-Scott χ^2 test for categorical variables and linear regression for continuous variables. Multivariable logistic and linear regression models were used to determine the association of type 1 and type 2 myocardial infarction with clinical outcomes in patients with gastrointestinal bleeding, using the no myocardial infarction group as reference. The multivariable adjustment models included age, sex, admission status, and all the aforementioned baseline comorbidities, hospital characteristics, and insurance status. Similar statistical analyses were undertaken to compare outcomes of gastrointestinal bleeding patients with type 1 versus type 2 myocardial infarction. In these analyses, we compared rates of coronary angiography, percutaneous coronary intervention, and coronary artery bypass grafting, in addition to the predefined primary and secondary outcomes. In cases with missing covariates, multivariable regression analyses were performed only on hospitalizations with complete data. Hospital charges were converted to cost using the HCUP cost-to-charge ratio files. Effect sizes were expressed using odds ratios (ORs) and their 95% confidence intervals (CIs). Associations were considered significant if the P value was <.05. All statistical analyses were performed using Stata 16.0 (StataCorp).

RESULTS

Baseline Characteristics

A total of 381,867 patient hospitalizations with a primary admission diagnosis of gastrointestinal bleeding were included in the study (177,675 [46.5%] upper, 115,843 [30.3%] lower, 88,349 [23.1%] unspecified gastrointestinal source of bleeding). Of those, 2902 (0.75%) had type 1 myocardial infarction, and 3963 (1.0%) had type 2 myocardial infarction.

Compared to patients without myocardial infarction, patients with type 1 myocardial infarction were older, less likely to be women, had higher Elixhauser comorbidity scores, and higher prevalence of hypertension, diabetes mellitus, dyslipidemia, prior myocardial infarction, prior percutaneous coronary intervention, prior coronary artery bypass grafting, atrial fibrillation, chronic heart failure, long-term use of aspirin/antiplatelet/anticoagulants, peripheral vascular disease, carotid artery disease, chronic kidney disease, and chronic lung disease (Table 1). Patients with type 1 myocardial infarction were more likely to be insured by Medicare.

Compared to patients without myocardial infarction, patients with type 2 myocardial infarction were also older, less likely to be women, had higher Elixhauser comorbidity scores, and higher prevalence of hypertension, diabetes mellitus, dyslipidemia, prior myocardial infarction, prior percutaneous coronary intervention, long-term use of aspirin/antiplatelet/anticoagulants, and other comorbidities listed in Table 1. Like patients with type 1 myocardial infarction, those with type 2 myocardial infarction were also more likely to be insured by Medicare.

In-Hospital Mortality

In patients admitted with gastrointestinal bleeding, type 1 myocardial infarction was associated with higher in-hospital mortality compared with no myocardial infarction). Similarly, type 2 myocardial infarction was associated with higher in-hospital mortality compared with no myocardial infarction

In the subgroup analyses stratified by gastrointestinal bleeding source (upper vs lower), type 1 myocardial infarction and type 2 myocardial infarction were both associated with an increased risk of in-hospital mortality compared to gastrointestinal bleeding with no myocardial infarction; however, the effect size was larger in patients with lower gastrointestinal bleeding for both types 1 and 2 myocardial infarction ($P_{interaction} < .05$ for both) (Supplementary Table 3 and 4, available online).

Length of Stay, Costs, and Discharge to Facility

After multivariable adjustment, patients with type 1 and type 2 myocardial infarction had longer mean hospital LOS, higher mean hospital costs, and were more likely to be discharged to a facility compared to their counterparts without myocardial infarction (Table 2).

Risk of 30-Day All-Cause Readmission

Gastrointestinal bleeding patients with types 1 and 2 myocardial infarction had increased risk of 30-day all-cause readmission compared to patients without myocardial infarction (Table 2). Recurrent gastrointestinal bleeding (15.1%) followed by sepsis (7.8%) were the leading causes of readmission at 30 days among patients with gastrointestinal bleeding without myocardial infarction. In contrast, heart failure was the leading cause of readmission for patients with gastrointestinal bleeding with type 1 myocardial infarction (15.17%) and was the second-leading cause of readmission for patients with gastrointestinal bleeding with type 2 myocardial infarction (14.2%) (Table 3).

Comparative Outcomes of Gastrointestinal Bleeding Patients with Type 1 Versus Type 2 Myocardial Infarction

After multivariate adjustment, gastrointestinal bleeding patients with type 1 myocardial infarction had significantly higher in-hospital mortality, longer mean hospital LOS, and higher mean hospital costs, compared to gastrointestinal patients with type 2 myocardial infarction (Table 4). Further, use of coronary angiography and percutaneous coronary intervention were higher for patients with gastrointestinal bleeding and type 1 myocardial infarction compared to their counterparts with type 2 myocardial infarction. There was no significant difference in discharge to facility and 30-day all-cause readmission rates among patients with type 1 versus type 2 myocardial infarction.

DISCUSSION

In this large nationwide observational analysis of patients with primary admission diagnosis of gastrointestinal bleeding, we report several key findings. First, types 1 (0.75%) and 2 (1.0%) myocardial infarction occurred infrequently during gastrointestinal bleeding hospitalizations, and these patients were more likely to be males with a distinct and higher burden of cardiovascular comorbidities. Second, types 1 and 2 myocardial infarction were both associated with higher in-hospital mortality, more resource utilization (ie, LOS, hospital costs, and discharge to facility), and higher risk of 30-day all-cause readmission. Third, heart failure was a more common cause of readmission for patients with gastrointestinal bleeding with types 1 (15.17%) and 2 (14.1%) myocardial infarction compared to their counterparts without myocardial infarction (5.5%). Similar trend was observed for myocardial infarction readmissions. Fourth, patients with type 1 myocardial infarction had higher in-hospital mortality and resource utilization than those with type 2 myocardial infarction. Last, the use of coronary angiography and percutaneous coronary intervention were overall low but higher in patients with type 1 compared with type 2 myocardial infarction.

The overall prevalence of types 1 and 2 myocardial infarction after gastrointestinal bleeding (1.75%) was lower

Table 1 Baseline Characteristics of Patients with Gastrointestinal Bleeding Stratified by Presence of Type 1 and Type 2 MI

Variables	No MI N = 375,002	Type 1 MI N = 2902	Type 2 MI N = 3963	*P* Value Type 1 MI versus no MI	*P* Value Type 2 MI versus no MI
Demographics					
Age, years (mean ± SE)	69 (0.1)	75 (0.27)	75 (0.27)	<.001	<.001
Age, N (%)				<.001	<.001
18-40	25,965 (7.0)	12 (0.4)	28 (0.7)		
40-64	99,395 (27.0)	452 (15.9)	616 (15.9)		
65-84	176,170 (47.8)	1672 (58.9)	2312 (59.5)		
≥85	66,451 (18.0)	712 (25.0)	926 (23.9)		
Woman	182,310 (48.6)	1196 (41.2)	1724 (43.5)	<.001	<.001
Weekend admission	92,035 (24.5)	770 (26.5)	1019 (25.7)	.08	.23
Elixhauser Comorbidity Score				<.001	<.001
<4	180,601 (48.1)	785 (27.0)	979 (24.7)		
≥4	194,400 (51.8)	2117 (72.9)	2984 (75.3)		
Comorbidities					
Hypertension	261,514 (69.7)	2444 (84.2)	3317 (83.7)	<.001	<.001
Dyslipidemia	156,513 (41.7)	1806 (62.2)	2248 (56.7)	<.001	<.001
Diabetes mellitus	110,268 (29.4)	1207 (41.9)	1504 (37.9)	<.001	<.001
Obesity	49,583 (13.22)	420 (14.4)	518 (13.0)	.16	.84
History of smoking	154,834 (41.3)	1247 (43)	1687 (42.6)	.20	.33
Atrial fibrillation	83,285 (22.2)	896 (30.9)	1334 (33.7)	<.001	<.001
Chronic heart failure	68,271 (18.2)	1218 (42.0)	1544 (39)	<.001	<.001
Previous myocardial infarction	28,078 (7.5)	550 (18.9)	549 (13.8)	<.001	<.001
Prior CABG	26,194 (7.0)	486 (16.7)	710 (17.9)	<.001	<.001
Prior PCI	33,706 (9.0)	756 (26.0)	706 (17.8)	<.001	<.001
Prior CVA	44,021 (11.7)	337 (11.6)	597 (15.0)	.89	<.001
Peripheral vascular disease	35904 (9.6)	487 (16.7)	611 (15.4)	<.001	<.001
Carotid artery disease	4055 (1.0)	74 (2.5)	106 (2.7)	<.001	<.001
Valvular heart disease	32,827 (8.7)	580 (20.0)	908 (22.9)	<.001	<.001
Renal failure	75,877 (20.2)	1046 (36.0)	1450 (36.6)	<.001	<.001
Prior ICD or PPM	22,851 (6.1)	197 (6.8)	342 (8.6)	.258	<.001
Chronic pulmonary disease	81,540 (21.7)	784 (27.0)	1056 (26.6)	<.001	<.001
Liver disease	48376 (13.0)	247 (8.5)	383 (9.7)	<.001	<.001
Neurological disorders	27,345 (7.3)	263 (9.0)	389 (9.8)	.008	<.001
Deficiency anemia	34,119 (9.1)	234 (8.0)	380 (9.6)	.19	.48
Hypothyroidism	55,941 (14.9)	489 (16.8)	610 (15.4)	.05	.55
Weight loss	31810 (8.4)	263 (9.0)	400 (10.0)	.43	.021
Alcohol abuse	45418 (12.11)	196 (6.75)	362 (9.13)	<.001	<.001
Drug abuse	15894 (4.2)	78 (2.6)	123 (3.1)	.002	.018
Long-term aspirin/antiplatelet/ antithrombotic use	131,331 (35.0)	1359 (46.8)	1662 (41.9)	<.001	<.001
Hospital location				.35	.001
Metropolitan-nonteaching	90,118 (24.0)	675 (23.2)	753 (19.0)		
Metropolitan-teaching	252,047 (67.2)	1999 (68.9)	2911 (73.4)		
Nonmetropolitan hospital	32,837 (8.7)	228 (7.8)	299 (7.5)		
Bed size of the hospital				.6	.12
Small	68,626 (18.3)	540 (18.6)	708 (17.9)		
Medium	110,104 (29.3)	885 (30.5)	1032 (26.0)		
Large	196,272 (52.3)	1477 (50.9)	2223 (56.1)		
Insurance status				<.001	<.001
Medicare	248,551 (66.3)	2344 (80.8)	3231 (81.6)		
Medicaid	37,797 (10.1)	154 (5.3)	175 (4.4)		
Private insurance	65,347 (17.4)	298 (10.3)	410 (10.3)		
Self-pay, no charge, or other	22,674 (6.0)	102 (3.5)	145 (3.6)		
Treatment received					
Coronary angiography	—	334 (11.5)	130 (3.3)	N/A	N/A
PCI	—	96 (3.3)	18 (0.4)	N/A	N/A
CABG	—	13 (0.4)	0 (0)	N/A	N/A

CABG = coronary artery bypass grafting; CAD = coronary artery disease; CVA = cerebrovascular accident; GIB = gastrointestinal bleeding; ICD = implantable cardiac defibrillator; MI = myocardial infarction; PCI = percutaneous coronary intervention; PPM = percutaneous pacemaker; SE = standard error.

Numbers are frequency (%), unless otherwise specified.

Table 2 Outcomes and Resource Utilization in Patients with Gastrointestinal Bleeding Stratified by the Presence of Type 1 and Type 2 MI

Outcomes	No MI N = 375,002	Type 1 MI N = 2902	Type 2 MI N = 3963
In-hospital mortality			
N (%)	2347 (0.63)	103 (3.55)	72 (1.82)
Unadjusted OR (95% CI)	Ref.	5.85 (4.35-7.85)	2.95 (2.05-4.23)
Adjusted OR (95% CI)†	Ref.	4.72 (3.43-6.48)	2.17 (1.48-3.16)
LOS, days (mean [SE])			
(Mean [SE])	3.9 (0.02)	6.01 (0.16)	5.45 (0.1)
Unadjusted β coefficient (95% CI)	Ref.	2.16 (1.84-2.48)	1.55 (1.36-1.73)
Adjusted β coefficient (95% CI)†	Ref.	1.90 (1.60-2.20)	1.18 (1.01-1.36)
Hospital costs, (mean [SE]) US$			
(Mean [SE])	9785 (77)	15,802 (493.38)	14,255 (298.45)
Unadjusted β coefficient (95% CI)	Ref.	6017 (5077-6958)	4471 (3923-5018)
Adjusted β coefficient (95% CI)†	Ref.	5554 (4661-6446)	3843 (3302-4385)
Discharge to facility*			
N (%)	48,574 (13.6)	597 (22)	824 (21.5)
Unadjusted OR (95% CI)	Ref.	1.79 (1.58-2.04)	1.74 (1.56-1.94)
Adjusted OR (95% CI)†	Ref.	1.52 (1.32-1.75)	1.38 (1.22-1.55)
30-day all-cause readmission*			
N (%)	48,776.85 (15.06)	515.23 (20.67)	675.81 (20.06)
Unadjusted OR (95% CI)	Ref.	1.42 (1.26-1.61)	1.37 (1.23-1.52)
Adjusted OR (95% CI)†	Ref.	1.22 (1.08-1.38)	1.17 (1.05-1.30)

CI = confidence interval; LOS = length of stay; MI = myocardial infarction; OR = odds ratio; SE = standard error.

*Among patients discharged alive.

†Multivariate model adjusted for age, sex, admission status (weekend vs. weekday), baseline characteristics (chronic pulmonary disease, atrial fibrillation, dyslipidemia, diabetes mellitus, hypertension, obesity, peripheral vascular disease, renal disease, liver disease, neurological disorders, anemia, hypothyroidism, weight loss, chronic heart failure, carotid artery disease, valvular heart disease, history of smoking, alcohol abuse, drug abuse, prior myocardial infarction, prior coronary artery bypass graft surgery, prior percutaneous coronary intervention, prior implantable cardiac defibrillator or percutaneous pacemaker placement, prior cerebrovascular accident) and hospital characteristics (hospital location and bed size), and insurance status.

Table 3 Top 10 Causes of Readmission for Patients with Gastrointestinal Bleeding with and Without Type 1 or Type 2 Myocardial Infarction

Type 1 Myocardial Infarction	Type 2 Myocardial Infarction	No Myocardial Infarction
Heart failure (15.17%)	GI bleeding (15.9%)	GI bleeding (15.1%)
Recurrent GI bleeding (10.11%)	Heart failure (14.2%)	Sepsis (7.8%)
Acute myocardial infarction (8.34%)	Sepsis (7.7%)	Heart failure (5.5%)
Sepsis (8.22%)	Acute myocardial infarction (4.8%)	Diverticulosis and diverticulitis (5.4%)
Diverticulosis and diverticulitis (4.29%)	Diverticulosis and diverticulitis (3.7%)	Regional enteritis and ulcerative colitis (3.0%)
Coronary atherosclerosis and other heart disease (4.19%)	Other GI disorders (3.0%)	Other disorders of stomach and duodenum (2.7%)
Other GI disorders (4.11%)	Cardiac dysrhythmias (2.8%)	Liver disease (2.6%)
Other disorders of stomach and duodenum (3.08%)	Renal failure (2.6%)	Renal failure (2.4%)
Cerebral infarction (2.6%)	Coronary atherosclerosis and other heart disease (2.5%)	Other gastrointestinal disorders (2.3%)
Acute posthemorrhagic anemia (1.87%)	Other disorders of stomach and duodenum (2.0%)	Pneumonia (1.8%)

GI = gastrointestinal.

in our study than previous epidemiologic studies, which ranged from 7.7% to 14%.[4,15,16] However, these studies were limited by small sample size, single-center design, and lack of stratification of myocardial infarction into types 1 and 2. In addition, our exclusions of several conditions that are known to cause myocardial injury and of other myocardial infarction types may possibly explain the lower prevalence of myocardial infarction in our analysis but ascertain a higher specificity of the MI diagnosis codes. To our knowledge, this is the first large-scale report analyzing gastrointestinal bleeding complicated by types 1 and 2 myocardial infarction. In our study, type 1 myocardial infarction

Table 4 Outcomes and Resource Utilization of Gastrointestinal Bleed in Patients with Type 1 Versus Type 2 MI

Outcomes	Type 1 MI (n = 2902)	Type 2 MI (n = 3963)	OR (95% CI)	
			Unadjusted	Adjusted*
In-hospital mortality	103 (3.55)	72 (1.82)	1.98 (1.32-2.97)	2.23 (1.45-3.41)
LOS, days (mean [SE])	6 (0.16)	5 (0.1)	0.62 (0.26-0.97)†	0.8 (0.46-1.15)†
Hospital costs, (mean [SE]) US$	15,802 (493.38)	14,255 (298.45)	1547 (477-2617)†	1971 (890-3052)†
Discharge to facility‡	597 (22)	824 (21.5)	1.03 (0.87-1.21)	1.11 (0.93-1.32)
30-day all-cause readmission‡	515 (20.67)	676 (20.06)	1.04 (0.89-1.22)	1.03 (0.88-1.21)
Coronary angiography	334 (11.5)	130 (3.28)	3.83 (2.85-5.14)	4.10 (3.04-5.54)
Percutaneous coronary intervention	96 (3.29)	18 (0.46)	7.31 (3.42-15.64)	7.61 (3.67-15.81)
Coronary artery bypass graft	13 (0.44)	0 (0)	0 (0-0)	0 (0-0)

CI = confidence interval; LOS = length of stay; MI = myocardial infarction; OR = odds ratio; SE = standard error.

*Multivariate model adjusted for age, sex, admission status (weekend vs. weekday), baseline characteristics (chronic pulmonary disease, atrial fibrillation, dyslipidemia, diabetes mellitus, hypertension, obesity, peripheral vascular disease, renal disease, liver disease, neurological disorders, anemia, hypothyroidism, weight loss, chronic heart failure, carotid artery disease, valvular heart disease, history of smoking, alcohol abuse, drug abuse, prior myocardial infarction, prior coronary artery bypass graft surgery, prior percutaneous coronary intervention, prior implantable cardiac defibrillator or percutaneous pacemaker placement, prior cerebrovascular accident) and hospital characteristics (hospital location and bed size), and insurance status.

†β coefficient and corresponding 95% CI.

‡Among patients discharged alive.

was associated with a ~4-fold increase in in-hospital mortality, whereas type 2 myocardial infarction was associated with a ~2-fold increase in in-hospital mortality. Similarly, in a prior single-center study of 230 patients with gastrointestinal bleeding admitted to the intensive care unit, myocardial infarction was associated with a ~2 fold higher risk of in-hospital mortality.[15] Overall, inpatient mortality among patients admitted for gastrointestinal bleeding in the current study was 0.66%, which is lower than previously reported mortality rate of 2%-3% in all-comer patients with gastrointestinal bleeding.[1,17] This is also possibly explained by the exclusion of sicker patients with shock, cardiac arrest, end-stage renal disease, and sepsis. Although there are no prior studies comparing outcomes of type 1 versus type 2 myocardial infarction after gastrointestinal bleeding, there are numerous studies that compare outcomes of all-comer patients with types 1 and 2 myocardial infarction with conflicting results. McCarthy et al[6] found that patients with type 2 myocardial infarction had a significantly lower risk of in-hospital mortality compared to those with type 1 myocardial infarction ([adjusted OR 0.57 (95% CI 0.54-0.60) from the NRD. However, contradictory findings have been reported in other studies, including a meta-analysis of 9 observational studies.[18,19]

In addition to poor clinical outcomes, gastrointestinal bleeding hospitalizations are associated with substantial economic burden in the United States.[1] Discharge to skilled nursing facility is independently associated with higher risk of readmissions, health care cost, and death.[20,21] Moreover, a substantial proportion of patients discharged to these facilities never return home.[20] In this study, we identified a vulnerable group of patients with gastrointestinal bleeding, namely those with either types 1 or 2 myocardial infarction, who had higher rates of discharge to short- or long-term facilities and increased hospital costs compared to patients without myocardial infarction. Thirty-day readmission rates for patients with myocardial infarction and heart failure are considered a quality performance measure by the Centers of Medicare and Medicaid Service (CMS) due to rising health care costs, and are included in the hospital readmission reduction program by Centers of Medicare and Medicaid Service (Hospital Readmissions Reduction Program[22] 2020). Similar to previous studies, we have reported a 30-day readmission rate of ~15.1% for all-comer patients with upper or lower gastrointestinal bleeding.[1,23,24] However, readmission rates increased to 20.7% and 20.1% when gastrointestinal bleeding was complicated by types 1 or 2 myocardial infarction, respectively. Furthermore, the presence of either types 1 or 2 increased the likelihood of readmission for cardiovascular causes. Patients with gastrointestinal bleeding and either types 1 or 2 myocardial infarction were more likely to be readmitted with a primary diagnosis of acute heart failure decompensation compared to those with gastrointestinal bleeding without myocardial infarction. In addition, myocardial infarction was the third and fourth leading cause of 30-day readmission among patients with gastrointestinal bleeding with types 1 or 2 myocardial infarction, respectively, whereas it was not among the top 10 causes of readmission for gastrointestinal bleeding without myocardial infarction. This is likely attributable to the complications associated with the myocardial infarction event or the lower rates of invasive therapies after gastrointestinal bleeding, as seen in previous studies.[6,10,12] Early follow-up after discharge and intensification of interventions proven to be effective in reducing the burden of heart failure and myocardial infarction rehospitalizations may be valuable in reducing 30-day readmissions after gastrointestinal bleeding complicated by types 1 and 2 myocardial infarction.[25,26]

The rate of use of coronary angiography and percutaneous coronary intervention among patients with gastrointestinal bleeding and type 1 myocardial infarction was

significantly lower compared to previously reported rates in the literature from administrative databases. In the study by McCarthy et al,[6] 57% of patients with type 1 underwent coronary angiography and 38.5% had percutaneous coronary intervention. In our study, only 11.5% of patients with gastrointestinal bleeding and type 1 myocardial infarction underwent coronary angiography with only 3.29% undergoing percutaneous coronary intervention. The presence of gastrointestinal bleeding has likely deterred providers from recommending invasive coronary angiography given a higher risk of bleeding with peri- and postprocedural antithrombotic therapy. Given the increased mortality and readmission rates for heart failure, diagnostic coronary angiography following type 1 myocardial infarction (characterized often by plaque disruption and superimposed thrombosis) may at least provide a better risk stratification and allow providers to assess the balance of risks and benefits of coronary revascularization after gastrointestinal bleeding, including antithrombotic regimen, in a shared decision-making process with patients admitted with gastrointestinal bleeding. Given the limitations of administrative database, we are not able to identify which group of patients would benefit from such approach or the appropriateness of the markedly lower rates of percutaneous coronary intervention observed. The higher rates of coronary angiography and percutaneous coronary intervention in patients with gastrointestinal bleeding and type 1 myocardial infarction compared with those with type 2 myocardial infarction are not surprising given the differences in the pathophysiology and management of both myocardial infarction types. There are currently no data to support the role of coronary angiography and revascularization in type 2 myocardial infarction, and management should instead focus on relieving the provoking factor(s) leading to the supply-demand mismatch.[19] Given the high rate of multivessel coronary artery disease and risk for recurrent myocardial infarction in patients with type 2 myocardial infarction, these patients can be risk stratified by noninvasive testing with structural or functional imaging, and consideration should be given to treatment with beta-blockers, angiotensin-converting enzyme inhibitors, statins, and aspirin based on previous observational studies.[19,27-29]

The main strength of this study includes its large nationally representative sample size that provide clinically important information about the prevalence and prognostic impact of types 1 and 2 myocardial infarction in patients admitted with gastrointestinal bleeding. Our study also has important limitations. First, the ICD-10-CM code for type 2 myocardial infarction was introduced in October 2017, and it is possible that some of these patients had acute or chronic myocardial injury, as demonstrated by a prior study.[30] There are no ICD-10-CM codes for acute or chronic myocardial injury. However, we excluded many potential causes of myocardial injury (Figure) as was done in prior studies.[10-12] Due to our stringent exclusion criteria for causes of myonecrosis, it is plausible that we potentially excluded patients with true myocardial infarction and may have therefore underestimated the true prevalence of types 1 and 2 myocardial infarction after gastrointestinal bleeding. Second, the NRD is an administrative database prone to miscoding errors and lacks granularity and robust adjudication of clinical outcomes. Third, the database does not contain information on important variables such as the severity of gastrointestinal bleeding (ie, hemoglobin/hemodynamic instability), its hospital management, timing of myocardial infarction in relation to gastrointestinal bleeding, biomarkers, echocardiographic results, laboratory variables, and medications at discharge. Given that the severity of gastrointestinal bleeding is difficult to ascertain from the database, we only included primary gastrointestinal bleeding hospitalizations to capture clinically significant hospitalizations. Last, the NRD lacks long-term follow-up data, and we were therefore unable to establish the impact of types 1 and 2 myocardial infarction on mid- and long-term outcomes.

CONCLUSIONS

Our findings suggest that gastrointestinal bleeding patients with types 1 and 2 myocardial infarction have distinct clinical phenotype with higher burden of cardiovascular comorbidities. Types 1 and 2 myocardial infarction in the setting of gastrointestinal bleeding were associated with higher in-hospital mortality, resource utilization, and 30-day readmission. Further studies are needed to address the optimal management strategies in these patients to improve outcomes and assess the mid- and long-term outcomes of gastrointestinal bleeding complicated by types 1 and 2 myocardial infarction.

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SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjmed.2022.04.001.

Supplementary Table 1 International Classification of Diseases Diagnoses Codes Used in the Study Design and to Identify Baseline Variables

Diagnosis codes	ICD-10 codes
Upper GI bleed	I8501, I8511, K2211, K2901, K2921, K2931, K2941, K2951, K2961, K2971, K2981, K2991, K31811, K226, K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K282, K286, K284, K31811, K2081, K2091, K2101, K3182
Lower GI bleed	K50011, K50111, K50811, K51011, K51211, K51311, K51411, K51511, K51811, K51911, K5701, K5711, K5713, K5721, K5731, K5733, K5741, K5751, K5753, K5781, K5791, K5793, K5521, K625
Unspecified GI bleed	K922
Septic shock	R65.21, T8112XA
Type 1 myocardial infarction	I2101, I2102, I2109, I2111, I2119, I2121, I2129, I213, I220, I221, I228, I229, I214, I222
Type 2 myocardial infarction	I21A1
Type 3,4,5 myocardial infarction	I21A9
Acute heart failure	I5021, I5023, I5031, I5033, I5041, I5043, I50811, I50813
Atrial fibrillation	I48.0, I48.1, I48.2, I48.91
Previous myocardial infarction	I25.2, I22.0, I22.1, I22.2, I22.8, I22.9
Previous CABG	Z95.1, I25.7xx, I25.810, I25.812
Previous PCI	Z95.5, Z98.61
Prior ICD or PPM	Z950, Z4501xx, Z95810, Z4502xx
Prior CVA	Z867.3, I690xx, I691xx, I692xx, I693xx
Dyslipidemia	E78.XX
Carotid artery disease	I6303XX, I6313XX, I652XX
History of smoking	Z72.0, Z87.891, F172XX, O9933xx
ESRD	N186, Z992, Z9115
Takotsubo syndrome	I51.81
Acute pulmonary embolism	I26XX
Myocarditis	I012, I40XX, A381, A3952, B2682, B3322, B5881, D8685, I090, I41, I514, J1082, J1182
Cardiogenic shock	R570, T8111XA
Hypovolemic shock	R571
Anaphylactic shock	T782, T782XXA
Other/Unspecified shock	R578, R579
Cardiac arrest	I46, I9712XX, I9771XX, 5A12012
Severe sepsis	R6520

CABG = coronary artery bypass grafting; CVA = cerebrovascular accident; ESRD = end-stage renal disease; GI = gastrointestinal; ICD = implantable cardioverter defibrillation; PCI = percutaneous coronary intervention; PPM = permanent pacemaker.

Supplementary Table 2 International Classification of Diseases Procedure Codes Used in the Study Design and to Identify Baseline Variables

Procedure Codes	
Percutaneous left atrial appendage occlusion	02L73CK, 02L73DK, 02L73ZK
Transcatheter mitral valve repair	02UG3JZ
Transcatheter mitral valve replacement	02RG37Z, 02RG38Z, 02RG3JZ, 02RG3KZ
Transcatheter aortic valve replacement	02RF37Z, 02RF38Z, 02RF3JZ, 02RF3KZ, 02RF37H, 02RF38H, 02RF3JH, 2RF3KH
Percutaneous coronary intervention	02703XX, 02704XX, 02713XX, 02714XX, 02723XX, 02724XX, 02733XX, 02734XX, 02C03XX, 02C04XX, 02C13XX, 02C14XX, 02C23XX, 02C24XX, 02C33XX, 02C34XX
Coronary artery bypass grafting	0210XXX,0211XXX,0212XXX,0213XXX
Valvular surgery/repair (aortic, mitral, tricuspid, and pulmonic)	024XXXX, 027FXXX, 027GXXX, 027HXXX, 027JXXX, 02CFXXX, 02CGXXX, 02CJXXX, 02CHXXX, 02LHXXX, 02NFXXX, 02NGXXX, 02NJXXX, 02NHXXX, 02QFXXX, 02QGXXX, 02QJXXX, 02QHXXX, 02RF0XX, 02RF4XX, 02RG0XX, 02RG37H, 02RG38H, 02RG3JH, 02RG3KH, 02RG4XX, 02RJXXX, 02RHXXX, 02THXXX, 02UFXXX, 02UG0XX, 02UG4XX, 02UG37X, 02UG38X, 02UG3KX, 02UG37E, 02UJXXX, 02UHXXX, 02WFXXX, 02WGXXX, 02WJXXX, 02WHXXX, X2RFXXX,
Invasive mechanical ventilation	5A1935Z, 5A1945Z, 5A1955Z, 0BH17EZ, 0BH18EZ

Supplementary Table 3 Subgroup Analyses of In-Hospital Mortality of Patients with Upper versus Lower Gastrointestinal Bleed for Patients with Type 1 Myocardial Infarction

Subgroup	Type 1 Myocardial Infarction		Adjusted OR (95% CI)*	*P* Value	Interaction *P* Value
	No	Yes			
Upper GI bleed	901 (0.52)	31 (2.17)	3.48 (2.07-5.85)	<.001	.048
Lower GI bleed	376 (0.33)	20 (3.24)	8.51 (4.19-17.29)	<.001	

GI = gastrointestinal; OR = odds ratio.

*Multivariate model adjusted for age, sex, admission status (weekend vs. weekday), baseline characteristics (chronic pulmonary disease, atrial fibrillation, dyslipidemia, diabetes mellitus, hypertension, obesity, peripheral vascular disease, renal disease, liver disease, neurological disorders, anemia, hypothyroidism, weight loss, chronic heart failure, carotid artery disease, valvular heart disease, history of smoking, alcohol abuse, drug abuse, prior myocardial infarction, prior coronary artery bypass graft surgery, prior percutaneous coronary intervention, prior implantable cardiac defibrillator or percutaneous pacemaker placement, prior cerebrovascular accident) and hospital characteristics (hospital location and bed size), and insurance status.

Supplementary Table 4 Subgroup Analysis of In-Hospital Mortality of Patients with Upper or Lower Gastrointestinal Bleed for Patients with Type 2 Myocardial Infarction

Subgroup	Type 2 Myocardial Infarction		Adjusted OR (95% CI)*	*P* Value	Interaction *P* Value
	No	Yes			
Upper GI bleed	901 (0.52)	29 (1.31)	1.74 (1.00-3.05)	0.052	0.001
Lower GI bleed	376 (0.33)	21 (2.97)	6.20 (3.15-12.20)	<0.001	

GI = gastrointestinal; OR = odds ratio.

*Multivariate model adjusted for age, sex, admission status (weekend vs. weekday), baseline characteristics (chronic pulmonary disease, atrial fibrillation, dyslipidemia, diabetes mellitus, hypertension, obesity, peripheral vascular disease, renal disease, liver disease, neurological disorders, anemia, hypothyroidism, weight loss, chronic heart failure, carotid artery disease, valvular heart disease, history of smoking, alcohol abuse, drug abuse, prior myocardial infarction, prior coronary artery bypass graft surgery, prior percutaneous coronary intervention, prior implantable cardiac defibrillator or percutaneous pacemaker placement, prior cerebrovascular accident) and hospital characteristics (hospital location and bed size), and insurance status.