BMJ Open In-hospital gastrointestinal bleeding in patients with acute myocardial infarction: incidence, outcomes and risk factors analysis from China Acute Myocardial Infarction Registry

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ABSTRACT

Objective To investigate the incidence of gastrointestinal bleeding (GIB) in patients with acute myocardial infarction (AMI), clarify the association between adverse clinical outcomes and GIB and identify risk factors for in-hospital GIB after AMI.

Design Retrospective cohort study.

Setting 108 hospitals across three levels in China.

Participants From 1 January 2013 to 31 August 2014, after excluding 2659 patients because of incorrect age and missing GIB data, 23 794 patients with AMI from 108 hospitals enrolled in the China Acute Myocardial Infarction Registry were divided into GIB-positive (n=282) and GIB-negative (n=23 512) groups and were compared.

Primary and secondary outcome measures Major adverse cardiovascular and cerebrovascular events (MACCEs) are a composite of all-cause death, reinfarction and stroke. The association between GIB and endpoints was examined using multivariate logistic regression and Cox proportional hazards models. Independent risk factors associated with GIB were identified using multivariate logistic regression analysis.

Results The incidence of in-hospital GIB in patients with AMI was 1.19%. GIB was significantly associated with an increased risk of MACCEs both in-hospital (OR 2.314; p<0.001) and at 2-year follow-up (HR 1.407; p=0.0008). Glycoprotein IIb/IIIa (GPIIb/IIIa) receptor inhibitor, percutaneous coronary intervention (PCI) and thrombolysis were novel independent risk factors for GIB identified in the Chinese AMI population (p<0.05).

Conclusions GIB is associated with both in-hospital and follow-up MACCEs. Gastrointestinal prophylactic treatment should be administered to patients with AMI who receive primary PCI, thrombolytic therapy or GPIIb/IIIa receptor inhibitor.

Trial registration number NCT01874691.

INTRODUCTION

Gastrointestinal bleeding (GIB) is a common cause of haemorrhage in patients with acute myocardial infarction (AMI). The current

Strengths and limitations of this study

- We carried out a comprehensive study that identified independent risk factors for gastrointestinal bleeding after acute myocardial infarction using nationwide registry data.
- High-quality and complete data were used to examine the association between gastrointestinal bleeding and adverse outcomes and mortality.
- The large sample, broad representation and involvement of both the principal investigator, and clinical and research experts are the main strengths of this study.
- The relatively lower gastrointestinal bleeding rates in our study limit the division of the data into training (80%) and validation (20%) sets, increasing the risk of overfitting in our models.
- Despite some limitations making our findings less convincing, our study allows evaluation of the importance of demographic and geographical variations.

AMI guidelines recommend an initial high oral loading dose of dual antiplatelet therapy (DAPT), including aspirin (150–300 mg), a P2Y₁₂ inhibitor (60 mg of prasugrel 60 mg, 180 mg of ticagrelor or 600 mg of clopidogrel), and thrombolytic medications.¹ However, these medications aggravate GIB. Studies have reported GIB rates from 1.3% to 8.9% in patients with AMI, which is associated with an increased risk of early and late adverse clinical outcomes.^{2–4} Thus, it is important to identify independent risk factors for GIB.^{3 5} However, data about incidence and risk factors of GIB in China are scarce. Therefore, we examined the database from the prospective, nationwide, multi-centre, observational China Acute Myocardial Infarction (CAMI) Registry to analyse

the incidence, outcomes and predictors of GIB occurring during hospitalisation.

METHODS

The CAMI Registry has a broad representation of all provinces and different-level hospitals, allowing for the exploration of GIB in patients with AMI across diverse geographic regions and economic circumstances.⁶ This study was registered with ClinicalTrials.gov.

We collected, validated and submitted standardised data through a secure, password-protected, web-based electronic data capture system (<http://www.CAMIRegistry.org>) by the local investigators at each participating site. Data included patient demographics, clinical presentation, medical history, risk factors, triggering factors, physical examination findings, laboratory and imaging results, transfer facility therapies, reperfusion strategies, medications, clinical events and cost. All the information was collected using a standardised set of variables and standard definitions (element dictionary), systematic data entry and transmission procedures, and rigorous data quality control. CDISC (the Clinical Data Interchange Standards Consortium), ICD-10 (International classification of diseases), MedDra, and WHO-DD (World Health Organization-drug dictionary) codes were used to standardise the variables.

Trained research participants called the patients at 30 days, and 6, 12, 18 and 24 months and asked the patient about their lifestyle, medications and reasons for discontinuation, and clinical events (including death, cardiovascular events and bleeding), which were validated using source documents.

Other detailed descriptions about data management and quality control are found in the published methodological article of the CAMI Registry.⁶

Overall, patients with AMI from 108 hospitals were enrolled in the CAMI Registry from 1 January 2013 to 31 August 2014. A total of 2659 patients with incorrectly recorded age or missing GIB data were excluded (figure 1). GIB was defined as clinically evident GIB (gross haematemesis, haeme-positive coffee ground emesis and haeme-positive melena) accompanied by a decrease in haemoglobin level of ≥ 1 g/dL. Significant GIB was defined as clinically evident bleeding with a decrease in haemoglobin level of ≥ 3 g/dL without an identifiable extraintestinal source. Major adverse cardiovascular and cerebrovascular events (MACCEs) are a composite of all-cause death, reinfarction and stroke. Bleeding Academic Research Consortium types 3 or 5 were defined according to a consensus report.⁷

The study population was separated into GIB-positive and GIB-negative groups, and continuous variables were presented as either means with SD or medians with IQRs, and categorical variables were presented as percentages. Differences in baseline characteristics were assessed using the χ^2 test or Fisher's exact test for categorical variables and analysis of variance or Wilcoxon rank test

Figure 1 Flow chart for selection of study population. CAMI, China Acute Myocardial Infarction; GIB, gastrointestinal bleeding.

for continuous variables. Multivariate logistic regression analyses were conducted to evaluate independent risk factors for GIB. The association between GIB and clinical endpoints was examined using multivariate logistic regression analysis and Cox proportional hazards models. Clinical characteristics that significantly differed between the two groups, including age, clinical presentation and medicine therapy, were identified and included in the final adjusted model (detailed variables are presented further the relevant tables).

ORs and HRs were presented with 95% CIs. All statistical analyses were performed using SAS V.9.4, and a two-tailed p value of <0.05 was considered statistically significant.

Patient and public involvement

We did not involve patients or the public directly in the design, conduct, reporting or dissemination plans of our research.

RESULTS

GIB after AMI in China

The most frequent bleeding site in our study was gastrointestinal (n=282, 80.6%) (online supplemental table). Patients' baseline characteristics and clinical presentations are shown in table 1. Among the 23 794 patients with AMI included in the final analysis, the mean age was 62 years, 25% were females and 55% came from prefecture-level hospitals. Patients with GIB were more likely to be female, older, with a lower systolic pressure and haemoglobin but higher Killip class at admission, and had a history of hypertension, dyslipidaemia, congestive heart failure, peptic ulcer, prior bleeding and malignancy. They were often treated with thrombolytic therapy and glycoprotein IIb/IIIa (GPIIb/IIIa) receptor inhibitors during hospitalisation.

Our study reported an overall incidence of in-hospital GIB and SGIB (severe gastrointestinal bleeding) in

Table 1 Baseline clinical data in patients with and without GIB

Variables	Total (n=23 794)	GIB (n=282)	No GIB (n=23 512)	P value
Demographics				
Age	62.34±13.31	67.53±12.39	62.28±13.46	0.0000
Female, n (%)	6020 (25.3)	86 (30.5)	5934 (25.2)	0.0000
Hospital level, n (%)				0.0000
Province-level hospital	7569 (31.8)	71 (25.2)	7498 (31.9)	
Prefecture-level hospital	13075 (55.0)	162 (57.4)	12913 (54.9)	
County-level hospital	3150 (13.2)	49 (17.4)	3101 (13.2)	
Medical history, n (%)				
Hypertension	11 959 (50.3)	161 (57.1)	11 798 (50.3)	0.0225
Dyslipidaemia	1598 (6.7)	29 (10.3)	1569 (6.7)	0.0254
Diabetes mellitus	4548 (19.1)	56 (19.9)	4492 (19.2)	0.7473
Myocardial infarction	1693 (7.1)	25 (8.9)	1668 (7.1)	0.2739
PCI	1110 (4.7)	18 (6.4)	1092 (4.7)	0.1979
CABG	95 (0.4)	3 (1.1)	92 (0.4)	0.1035
Congestive heart failure	560 (2.4)	24 (8.5)	536 (2.3)	0.0000
Stroke	2169 (9.1)	39 (13.8)	2130 (9.1)	0.0101
Peripheral arterial disease	140 (0.6)	4 (1.4)	136 (0.6)	0.0856
Chronic kidney disease	299 (1.3)	12 (4.3)	287 (1.2)	0.0003
PUD/ <i>Helicobacter pylori</i>	676 (2.8)	29 (10.3)	647 (2.8)	0.0000
GIB	417 (1.8)	27 (9.6)	390 (1.7)	0.0000
Malignancy	298 (1.3)	11 (3.9)	287 (1.2)	0.0010
Admission features, n (%)				
Diagnosis				0.9716
NSTEMI	5928 (24.9)	70 (24.8)	5858 (24.9)	
STEMI	17 866 (75.1)	212 (75.2)	17 654 (75.1)	
Heart rate (beats/min)	78.05±18.94	78.69±20.90	78.05±18.81	0.6087
Systolic BP (mm Hg)	128.95±25.82	121.92±27.27	129.04±25.69	0.0000
Killip class IV	980 (4.1)	36 (12.8)	944 (4.0)	0.0000
Ccr (ml/(min·1.73 m ²))	92.23±607.28	84.60±161.04	92.32±610.15	0.5639
Hb (g/L)	135.90±21.69	124.34±28.66	136.03±21.41	0.0000
Hct (%) (Q1:Q3)	36.68;44.10	31.50;43.30	36.70;44.10	0.4466
LVEF (%)	53.46±11.09	51.91±12.45	53.48±10.93	0.0734
CRUSADE score	20.05±15.47	28.70±18.21	19.95±15.24	0.0000
Prehospital medications, n (%)				
Aspirin	2611 (11.0)	38 (13.5)	2573 (11.0)	0.1954
P2Y12 receptor inhibitor	871 (3.7)	11 (3.9)	860 (3.7)	0.8342
Oral anticoagulants	78 (0.3)	1 (0.4)	77 (0.3)	0.6072
Statin	2119 (8.9)	33 (11.9)	2086 (9.0)	0.1137
β-blockers	1376 (5.8)	21 (7.5)	1355 (5.8)	0.2582
ACEI/ARB	1572 (6.6)	28 (10.1)	1544 (6.6)	0.0304
In-hospital medications, n (%)				
Aspirin	22 970 (96.5)	236 (83.7)	22 734 (96.8)	0.0000
P2Y12 receptor inhibitor	22 933 (96.4)	248 (87.9)	22 685 (97.0)	0.0000
GPIIb/IIIa receptor inhibitor	7103 (29.9)	101 (36.5)	7002 (30.8)	0.0451
Oral anticoagulants	382 (1.6)	4 (1.4)	378 (1.6)	1.0000
Heparin/LMWH	21 097 (88.7)	219 (78.8)	20 878 (90.6)	0.0000

Continued

Table 1 Continued

Variables	Total (n=23 794)	GIB (n=282)	No GIB (n=23 512)	P value
Statin	21 726 (91.3)	243 (92.0)	21 483 (97.4)	0.0000
β-blockers	16 719 (70.3)	176 (62.4)	16 543 (70.5)	0.0039
ACEI/ARB	14 354 (60.3)	140 (49.6)	14 214 (60.6)	0.0002
Treatment, n (%)				
Primary PCI	8617 (36.2)	105 (46.7)	8512 (44.5)	0.5334
Primary CABG	38 (0.2)	0 (0.0)	38 (0.2)	1.0000
Thrombolysis	1759 (7.4)	32 (13.7)	1737 (8.7)	0.0121
Hospitalisation (Q1;Q3)				
LOS in ICU	0.00;6.00	1.00;8.00	0.00;6.00	0.0000
LOS in general wards	2.00;10.00	1.00;14.00	2.00;10.00	0.5350
Total cost	10845;48 831	11269;54 128	10763;48 799	0.1733

ACEI/ARB, ACE inhibitor/angiotensin receptor blocker; BP, blood pressure; CABG, coronary artery bypass grafting; Ccr, creatinine clearance rate; CRUSADE, Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines; GIB, gastrointestinal bleeding; GPIIb/IIIa, glycoprotein IIb/IIIa; Hb, haemoglobin; Hct, haematocrit; ICU, intensive care unit; LMWH, low molecular weight heparin; LSO, length of stay; LVEF, left ventricular ejection fraction; NSTEMI, non-STEMI; PCI, percutaneous coronary intervention; PUD, peptic ulcer disease; STEMI, ST-elevation myocardial infarction.

patients with AMI of 1.19% and 0.32%, respectively. The incidence of GIB in provincial, prefecture and county hospitals was 0.94%, 1.24% and 1.50%, respectively. The proportion of haemoglobin decrease caused by GIB in hospitals at different levels is shown in figure 2.

Outcomes of patients with GIB

As shown in table 2, GIB was associated with an increased risk for MACCE (OR 2.314; 95% CI 1.801 to 3.418; $p<0.0001$) and individual endpoints during hospitalisation. At the 2-year follow-up (table 3 and online supplemental figure 1), GIB-positive patients still had a significantly higher risk for MACCE (adjusted HR 1.4107; 95% CI 1.124 to 1.761; $p=0.0008$) and death (adjusted HR 1.392; 95% CI 1.105 to 1.764; $p=0.0071$).

Independent risk factors for GIB

Independent risk factors for GIB after adjusting for covariates were identified (table 4). Significant risk factors in the entire study population included older age (>65

years) (online supplemental figure 2A) higher Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines (CRUSADE) score (online supplemental figure 2B), dyslipidaemia, prior congestive heart failure, peptic ulcer disease (PUD)/*Helicobacter pylori*, or GIB, Killip VI class, glycoprotein IIb/IIIa (GPIIb/IIIa) receptor inhibitor, primary percutaneous coronary intervention (PCI) and thrombolytic therapy. In patients with SGIB, risk factors included male sex, higher CRUSADE score and prior GIB. In patients with GIB with a drop of haemoglobin ≥ 5 g/dL, risk factors included male sex and in-hospital aspirin.

DISCUSSION

In the CAMI Registry, GIB was the most frequent source of AMI-related bleeding in the entire population. Another large registry study involving 3.3 million PCI procedures

Figure 2 Proportion of haemoglobin drop caused by GIB in hospitals at different levels. GIB, gastrointestinal bleeding.

Table 2 Comparison of in-hospital outcomes between patients with GIB and without GIB

Clinical endpoint	GIB (n=282) (%)	No GIB (n=23512) (%)	P value	Adjusted OR (95% CI)	P value
MACCE	26.2	7.1	<0.0001	2.314 (1.801 to 3.418)	<0.0001
Death	22.0	6.3	<0.0001	2.194 (1.499 to 3.007)	<0.0001
MI	3.9	0.5	<0.0001	3.983 (2.012 to 7.741)	<0.0001
Stroke	5.7	0.7	<0.0001	5.063 (2.801 to 9.173)	<0.0001

Variables included in the model: age; hospital level; hypertension; diabetes mellitus; congestive heart failure; stroke; peripheral arterial disease; PUD/*Helicobacter pylori*; GIB; malignancy; STEMI; systolic BP; Hb; Ccr; aspirin; P2Y12 receptor; GPIIb/IIIa receptor inhibitor; oral anticoagulants; heparin/LMWH; steroids; β -blockers; ACEI/ARB; primary PCI; emergent CABG; and thrombolysis therapy. ACEI/ARB, ACE inhibitor/angiotensin receptor blocker; BP, blood pressure; CABG, coronary artery bypass grafting; Ccr, creatinine clearance rate; GIB, gastrointestinal bleeding; Hb, haemoglobin; LMWH, low molecular weight heparin; MACCE, major adverse cardiovascular and cerebrovascular event; MI, myocardial infarction; PCI, percutaneous coronary intervention; PUD, peptic ulcer disease; STEMI, ST-elevation myocardial infarction.

showed that entry-site bleeding was the first common cause of bleeding complications,⁸ because of a lower frequency of bleeding avoidance strategies, such as radial artery access and arterial closure devices. In China, transradial intervention was adopted as a safety entry site for PCI, which may have reduced the entry-site bleeding rate.

Moreover, GIB occurred in 282 (1.19%) patients during hospitalisation, consistent with several studies ranging from 1.1% to 3.0%.^{3,9} It seems that the GIB incidence in our study is lower than that in the ACUTY (acute catheterization and urgent intervention triage strategy) trial (1.3%),³ which studied acute coronary syndrome (ACS) patients treated with a combination of aspirin, clopidogrel and enoxaparin (2.5%).⁹ The population in our study was AMI patients, while the population in the previously mentioned two studies were selected patients with intense antiplatelet or antithrombotic therapy that might have contributed to a higher GIB rate. In addition, a temporal trend study for GIB indicated that the incidence of PCI-associated GIB decreased within a decade, despite aggressive therapies for ACS.⁵ Expert consensus recommendations focusing on decreasing bleeding events were discussed in 2010¹⁰ and issued since 2011,¹¹ which might exert a positive effect on gastrointestinal protection. Physicians in China tend to follow the guidelines and

prescribe proton-pump inhibitors against GIB, which may have alleviated the incidence in our study.

Previous studies have demonstrated an association between in-hospital GIB and adverse clinical outcomes.^{3,12} In our study, AMI patients with GIB had a risk of death and an increased risk of ischaemic events (reinfarction and stroke). In addition, those who suffered GIB in the hospital still had a higher risk of MACCE and all-cause death after 2 years. The mechanism behind the poor outcomes of patients with AMI experiencing GIB is multifactorial. These patients had worse baseline clinical characteristics, such as older age, higher prevalence of peptic ulcer and prior GIB, which are independent risk factors for GIB.³ In addition, one-fourth of patients had SGIB, which may cause bleeding-related haemodynamic instability and contribute to ischemia, resulting in reinfarction and stroke. Moreover, GIB is also a well-known signal for physicians to stop DAPT prescription (only 71.6% of GIB-positive patients quit DAPT), which may increase the risk for both in-hospital and out-hospital adverse clinical outcomes.¹³

Consistent with previous reports, the occurrence of GIB in patients with AMI was strongly associated with older age and prior congestive heart failure, PUD/*Helicobacter pylori* and GIB.^{3,5} Several studies had reported

Table 3 Thirty-day, 6-month and 2-year clinical outcomes of patients with and without GIB

Clinical endpoints	30 days		6 months		2 years	
	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
MACCE	1.383 (1.031 to 1.802)	0.0187	1.355 (1.026 to 1.763)	0.0102	1.407 (1.124 to 1.761)	0.0008
Death	1.377 (1.053 to 1.796)	0.0294	1.395 (1.081 to 1.792)	0.0008	1.392 (1.105 to 1.764)	0.0071
MI	3.931 (1.301 to 10.292)	0.0218	1.809 (0.703 to 4.614)	0.1836	1.981 (0.968 to 3.931)	0.0511
Stroke	–	–	–	–	0.477 (0.058 to 3.447)	0.4641
BARC 3/5	9.739 (2.018 to 42.318)	0.0009	4.211 (1.430 to 11.903)	0.0076	2.365 (0.815 to 6.618)	0.1022

Variables included in the model: age; hospital level; hypertension; diabetes mellitus; congestive heart failure; stroke; peripheral arterial disease; PUD/*Helicobacter pylori*; GIB; malignancy; STEMI; systolic BP; Hb; Ccr; aspirin; P2Y12 receptor; GPIIb/IIIa receptor inhibitor; oral anticoagulants; heparin/LMWH; steroids; β -blockers; ACEI/ARB; primary PCI; emergent CABG; and thrombolysis therapy. ACEI/ARB, ACE inhibitor/angiotensin receptor blocker; BARC, bleeding academic research consortium; BP, blood pressure; CABG, coronary artery bypass grafting; Ccr, creatinine clearance rate; GIB, gastrointestinal bleeding; GPIIb/IIIa, glycoprotein IIb/IIIa; Hb, haemoglobin; LMWH, low molecular weight heparin; MACCE, major adverse cardiovascular and cerebrovascular events; MI, myocardial infarction; PCI, percutaneous coronary intervention; PUD, peptic ulcer disease; STEMI, ST-elevation myocardial infarction.

Table 4 Independent risk factors of GIB in the entire CAMI population and in patients with a drop of haemoglobin ≥ 3 g/dL or ≥ 5 g/dL

Multivariable predictors	OR	95% CI	P value
All patients			
Age	1.018	1.007 to 1.030	0.0068
Dyslipidaemia	1.703	1.120 to 2.578	0.0124
Congestive heart failure	2.012	1.253 to 3.294	0.0057
Prior PUD/ <i>Helicobacter pylori</i>	2.051	1.289 to 3.253	0.0021
Prior GIB	2.149	1.300 to 3.562	0.0029
Killip VI	1.714	1.119 to 2.630	0.0128
GPIIb/IIIa receptor inhibitor	1.677	1.241 to 2.259	0.0073
Thrombolysis therapy	3.213	2.106 to 4.913	<0.0001
Patients with a drop of haemoglobin ≥ 3 g/dL			
Male	2.045	1.142 to 3.657	0.0161
Prior GIB	3.124	1.511 to 6.588	0.0021
Patients with a drop of haemoglobin ≥ 5 g/dL			
Male	2.502	1.099 to 5.704	0.0295
In-hospital aspirin	3.258	1.241 to 8.556	0.0109

Variables included in the model: age; hospital level; hypertension; diabetes mellitus; congestive heart failure; stroke; peripheral arterial disease; PUD/*Helicobacter pylori*; GIB; malignancy; STEMI; systolic BP; Hb; Ccr; aspirin; P2Y12 receptor; GPIIb/IIIa receptor inhibitor; oral anticoagulants; heparin/LMWH; steroids; β -blockers; ACEI/ARB; primary PCI; emergent CABG; and thrombolysis therapy. ACEI/ARB, ACE inhibitor/angiotensin receptor blocker; BP, blood pressure; CABG, coronary artery bypass grafting; CAMI, China Acute Myocardial Infarction; Ccr, creatinine clearance rate; CRUSADE, can rapid risk stratification of unstable angina patients suppress adverse outcomes with early implementation of the ACC/AHA guidelines; GIB, gastrointestinal bleeding; GPIIb/IIIa, glycoprotein IIb/IIIa; Hb, haemoglobin; LMWH, low molecular weight heparin; PCI, percutaneous coronary intervention; PUD, peptic ulcer disease; STEMI, ST-elevation myocardial infarction.

increasing age as an independent risk factor for GIB,^{3 14 15} and we identified that AMI patients aged >65 years had a high association with GIB risk (online supplemental figure 2), thus GI prophylaxis should be prescribed to them in a timely manner. The CRUSADE bleeding risk score is a quantitative tool used to stratify bleeding risk in patients with non-ST-elevation myocardial infarction (NSTEMI).¹⁶ A small population study demonstrated that the CRUSADE score was the most accurate quantitative tool for NSTEMI and ST-elevation myocardial infarction patients undergoing coronary arteriography among contemporary bleeding risk scores.¹⁷ However, the applicability of CRUSADE bleeding risk scores to predict GIB among patients with AMI remains uncertain. In our study, we found that patients with higher scores had a higher risk of GIB. Therefore, this tool could help physicians in risk stratification during clinical practice.

The latest myocardial revascularisation guidelines recommend GP IIb/IIIa antagonists for bail-out use if there is evidence of no-reflow or thrombotic complications.¹ In our study, 7103 patients received GP IIb/IIIa

antagonists during primary PCI and were identified as an independent risk factor for GIB (OR 1.671; 95% CI 1.238 to 2.255; $p=0.0008$). However, only 66.9% of patients treated with GP IIb/IIIa antagonists were prescribed with GI prophylactic medications. Moreover, patients who received thrombolysis as revascularisation had a higher risk of GIB (OR 3.206; 95% CI 2.095 to 4.907; $p<0.0001$), and a lower proportion (29.6%) received GI prophylaxis. It might be that GI prophylaxis use for patients treated with GP IIb/IIIa and thrombolysis was not recommended by the guidelines.^{12 18} To reduce the incidence of GIB, GI prophylaxis should be used before revascularisation, which had been verified useful in prospective, randomised studies.^{19 20}

Limitations

Our study has some limitations. First, although a large sample size could ensure a wide representation, the danger of overfitting in our models cannot be ignored. A small GIB population limited the division of data into training and validation sets. Second, the CAMI Registry is the first national study focusing on the management and therapy for AMI in China, and we noticed that the patients' treatment compliance in the CAMI Registry was worse than that in registries from other developed countries; thus, this might limit the global clinical relevance of the study. We recommend further research to provide more evidence.

CONCLUSION

As shown in our research, GIB is the most common cause of bleeding in the Chinese AMI population and is associated with poor clinical prognosis. After multivariate analysis, we confirmed that the independent risk factors for GIB during hospitalisation, advanced age, heart failure (Killip IV), and history of GIB, PUD or *Helicobacter pylori* infection were common high-risk groups for GIB. Moreover, GPIIb/IIIa receptor inhibitor or thrombolysis therapy were also independent risk factors for GIB, which were less reported in previous studies. Clinicians should identify the high-risk groups of GIB among the AMI population early based on the clinical characteristics and prescribe gastrointestinal prophylaxis as soon as possible to improve clinical endpoints.

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Contributors WS was responsible for literature search, study design, data management, data interpretation and writing. XF and LN were responsible for data analysis, data interpretation and writing. JY, SS, MeiY and HY were involved in study design, statistical analysis plan and data interpretation. MenY and YY were involved in data interpretation and writing of the manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval CAMI registry was approved by the institutional review board central committee at Fuwai Hospital, NCCD of China (No 2012-431). The institutional review board approved protocol that describes methods used to protect the privacy of patients and maintain confidentiality of data collected was maintained by the study group. Every eligible patient before registration signed a written informed consent.

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REFERENCES

- Neumann FJ, Sousa-Uva M, Ahlsson A. ESC/EACTS guidelines on myocardial revascularization. *Eur J Cardiothorac Surg* 2019;55:1435–534.
- Moscucci M, Fox KAA, Cannon CP, et al. Predictors of major bleeding in acute coronary syndromes: the global registry of acute coronary events (GRACE). *Eur Heart J* 2003;24:1815–23.
- Nikolsky E, Stone GW, Kirtane AJ, et al. Gastrointestinal bleeding in patients with acute coronary syndromes: incidence, predictors, and clinical implications: analysis from the acuity (acute catheterization and urgent intervention triage strategy) trial. *J Am Coll Cardiol* 2009;54:1293–302.
- Chua S-K, Liao C-S, Hung H-F, et al. Gastrointestinal bleeding and outcomes after percutaneous coronary intervention for ST-segment elevation myocardial infarction. *Am J Crit Care* 2011;20:218–25.
- Shivaraju A, Patel V, Fonarow GC, et al. Temporal trends in gastrointestinal bleeding associated with percutaneous coronary intervention: analysis of the 1998–2006 nationwide inpatient sample (NIS) database. *Am Heart J* 2011;162:1062–8.
- Xu H, Li W, Yang J, et al. The China acute myocardial infarction (CAMI) registry: a national long-term registry-research-education integrated platform for exploring acute myocardial infarction in China. *Am Heart J* 2016;175:193–201.
- Mehran R, Rao SV, Bhatt DL, et al. Standardized bleeding definitions for cardiovascular clinical trials: a consensus report from the bleeding academic research Consortium. *Circulation* 2011;123:2736–47.
- Chhatrivala AK, Amin AP, Kennedy KF, et al. National cardiovascular data registry, association between bleeding events and in-hospital mortality after percutaneous coronary intervention. *JAMA* 2013;309:1022–9.
- Ng F-H, Wong S-Y, Lam K-F, et al. Gastrointestinal bleeding in patients receiving a combination of aspirin, clopidogrel, and enoxaparin in acute coronary syndrome. *Am J Gastroenterol* 2008;103:865–71.
- Abraham NS, Hlatky MA, Antman EM, et al. 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: a report of the American College of cardiology Foundation Task force on expert consensus documents. *Circulation* 2010;122:2619–33.
- Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: a report of the American College of cardiology Foundation/American heart association Task force on practice guidelines and the Society for cardiovascular angiography and interventions. *Circulation* 2011;124:e574–651.
- Barthélémy O, Silvain J, Brieger D, et al. Bleeding complications in primary percutaneous coronary intervention of ST-elevation myocardial infarction in a radial center. *Catheter Cardiovasc Interv* 2012;79:104–12.
- Grines CL, Bonow RO, Casey DE, et al. Prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents: a science advisory from the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association, with representation from the American College of Physicians. *Circulation* 2007;115:813–8.
- Chen Y-L, Chang C-L, Chen H-C, et al. Major adverse upper gastrointestinal events in patients with ST-segment elevation myocardial infarction undergoing primary coronary intervention and dual antiplatelet therapy. *Am J Cardiol* 2011;108:1704–9.
- Al-Mallah M, Bazari RN, Jankowski M, et al. Predictors and outcomes associated with gastrointestinal bleeding in patients with acute coronary syndromes. *J Thromb Thrombolysis* 2007;23:51–5.
- Subherwal S, Bach RG, Chen AY, et al. Baseline risk of major bleeding in non-ST-segment-elevation myocardial infarction: the crusade (can rapid risk stratification of unstable angina patients suppress adverse outcomes with early implementation of the ACC/AHA guidelines) bleeding score. *Circulation* 2009;119:1873–82.
- Abu-Assi E, Raposeiras-Roubin S, Lear P, et al. Comparing the predictive validity of three contemporary bleeding risk scores in acute coronary syndrome. *Eur Heart J Acute Cardiovasc Care* 2012;1:222–31.
- Valgimigli M, Bueno H, Byrne RA. 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* 2018;39:213–60.
- Wu H, Jing Q, Wang J, et al. Pantoprazole for the prevention of gastrointestinal bleeding in high-risk patients with acute coronary syndromes. *J Crit Care* 2011;26:434.e1–6.
- Barada K, Karrowni W, Abdallah M, et al. Upper gastrointestinal bleeding in patients with acute coronary syndromes: clinical predictors and prophylactic role of proton pump inhibitors. *J Clin Gastroenterol* 2008;42:368–72.