ISSN 1948-5190 (online)

World Journal of *Gastrointestinal Endoscopy*

World J Gastrointest Endosc 2021 September 16; 13(9): 356-450

Published by Baishideng Publishing Group Inc

World Journal of Gastrointestinal Endoscopy

Contents

Monthly Volume 13 Number 9 September 16, 2021

Contents

World Journal of Gastrointestinal Endoscopy

Monthly Volume 13 Number 9 September 16, 2021

ABOUT COVER

Editorial Board Member of *World Journal of Gastrointestinal Endoscopy*, George Giannopoulos, MD, MSc, PhD, Surgeon, Department of Surgery, Asklepieio Voulas General Hospital, Athens 16673, Attiki, Greece. geogianno@hotmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Endoscopy* (*WJGE*, *World J Gastrointest Endosc*) is to provide scholars and readers from various fields of gastrointestinal endoscopy with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGE mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal endoscopy and covering a wide range of topics including capsule endoscopy, colonoscopy, double-balloon enteroscopy, duodenoscopy, endoscopic retrograde cholangiopancreatography, endosonography, esophagoscopy, gastrointestinal endoscopy, gastroscopy, laparoscopy, natural orifice endoscopic surgery, proctoscopy, and sigmoidoscopy.

INDEXING/ABSTRACTING

The *WJGE* is now abstracted and indexed in Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central, China National Knowledge Infrastructure (CNKI), and Superstar Journals Database. The 2021 edition of Journal Citation Reports® cites the 2020 Journal Citation Indicator (JCI) for *WJGE* as 0.36.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Xu Guo*; **Production Department Director:** *Yu-Jie Ma*; **Editorial Office Director:** *Jia-Ping Yan*.

NAME OF JOURNAL
World Journal of Gastrointestinal Endoscopy

ISSN
ISSN 1948-5190 (online)

LAUNCH DATE
October 15, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Sang Chul Lee, Bing Hu, Anastasios Koulaouzidis

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-5190/editorialboard.htm

PUBLICATION DATE
September 16, 2021

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Gastrointestinal Endoscopy

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Endosc 2021 September 16; 13(9): 391-406

DOI: 10.4253/wjge.v13.i9.391

ISSN 1948-5190 (online)

ORIGINAL ARTICLE

Retrospective Study

Gastrointestinal hemorrhage in the setting of gastrointestinal cancer: Anatomical prevalence, predictors, and interventions

Mohamad A Minhem, Ahmad Nakshabandi, Rabia Mirza, Mohd Amer Alsamman, Mark C Mattar

ORCID number: Mohamad A Minhem 0000-0002-1959-7826; Ahmad Nakshabandi 0000-0003-2207-9883; Rabia Mirza 0000-0003-4148-3339; Mohd Amer Alsamman 0000-0002-4041-959X; Mark C Mattar 0000-0002-9339-1607.

Author contributions: Minhem MA contributed to study concept and design, statistical analysis of data, and drafting of manuscript; Nakshabandi A supervised the report and contributed to interpretation of data and editing of manuscript; Mirza R contributed to interpretation of data and drafting of manuscript; Alsamman MA contributed to interpretation of data and editing of manuscript; Mattar MC supervised the report and provided critical revision of important intellectual concepts.

Institutional review board statement: Not required because study involves only de-identified data.

Informed consent statement: Not required because study involves only de-identified data.

Conflict-of-interest statement: All authors have no relevant disclosures.

Mohamad A Minhem, Internal Medicine, Loyola University Medical Center, Maywood, IL 60153, United States

Ahmad Nakshabandi, Mohd Amer Alsamman, Mark C Mattar, Department of Gastroenterology, Medstar Georgetown University Hospital, Washington, DC 20007, United States

Rabia Mirza, Mark C Mattar, School of Medicine, Georgetown University, Washington, DC 20007, United States

Corresponding author: Mark C Mattar, AGAF, FACG, Associate Professor, Department of Gastroenterology, Medstar Georgetown University Hospital, 3800 Reservoir Rd NW, Washington, DC 20007, United States. mark.c.mattar@medstar.net

Abstract

BACKGROUND

Gastrointestinal hemorrhage (GIH) is a common complication with gastrointestinal cancers (GIC). There is no comprehensive research that examines GIH in different types of GIC.

AIM

To study the prevalence, predictors, and interventions of GIH based on the anatomical location of GIC.

METHODS

This is a retrospective analysis of the 2016-2018 National Inpatient Sample database, the largest inpatient care database in the United States. All adult inpatients (≥ 18-year-old) were included. ICD-10-CM codes were used to identify patients with GIH and GIC. Prevalence of GIH was obtained based on the anatomical location of GIC. Predictors of GIH in the GIC population were studied using multivariate analysis. Interventions including endoscopy were compared to the non-intervention group to determine the differences in inpatient mortality.

RESULTS

Out of a total of 18173885 inpatients, 321622 (1.77%) cases had a diagnosis of GIC. Within GIC patients, 30507 (9.5%) inpatients had GIH, which was significantly (P < 0.001) more than the prevalence of GIH in patients without GIC (3.4%). The highest to lowest GIH rates are listed in the following order: Stomach cancer (15.7%), liver cancer (13.0%), small bowel cancer (12.7%), esophageal cancer

Manuscript source: Unsolicited manuscript

Specialty type: Gastroenterology and hepatology

Country/Territory of origin: United States

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

Received: April 21, 2021
Peer-review started: April 21, 2021
First decision: June 23, 2021
Revised: June 27, 2021
Accepted: August 6, 2021
Article in press: August 6, 2021
Published online: September 16, 2021

P-Reviewer: Yu X
S-Editor: Yan JP
L-Editor: A
P-Editor: Guo X

(9.1%), colorectal cancer (9.1%), pancreatic cancer (7.2%), bile duct cancer (6.0%), and gallbladder cancer (5.1%). Within gastric cancer, the GIH rate ranged from 14.8% in cardia cancer to 25.5% in fundus cancer. Within small bowel cancers, duodenal cancers had a higher GIH rate (15.6%) than jejunal (11.1%) and ileal cancers (5.7%). Within esophageal cancers, lower third cancers had higher GIH (10.7%) than the middle third (8.0%) or upper third cancers (6.2%). When studying the predictors of GIH in GIC, socioeconomic factors such as minority race and less favorable insurances (Medicaid and self-pay) were associated with significantly higher GIH on multivariate analysis (P < 0.01). Chemotherapy and immunotherapy were also identified to have a lower risk for GIH [odds ratios (OR) = 0.74 (0.72-0.77), P < 0.001]. Out of 30507 GIC inpatients who also had GIH, 16267 (53.3%) underwent an endoscopic procedure, *i.e.*, upper endoscopy or colonoscopy. Inpatient mortality was significantly lower in patients who underwent endoscopy compared to no endoscopy [5.5% *vs* 14.9%, OR = 0.42 (0.38-0.46), P < 0.001].

CONCLUSION

The prevalence of GIH in patients with GIC varies significantly based on the tumor's anatomical location. Endoscopy, which appears to be associated with a substantial reduction in inpatient mortality, should be offered to GIC patients with GIH. Nevertheless, the decision on intervention in the GIC population should be tailored to individual patient's goals of care, the benefit on overall care, and long-term survival.

Key Words: Gastrointestinal hemorrhage; Gastrointestinal cancer; Anatomy; Risk factors; Gastrointestinal endoscopy

Core Tip: This is a retrospective analysis of the National Inpatient Sample database aiming to study the prevalence, predictors, and interventions of gastrointestinal hemorrhage (GIH) in the setting of gastrointestinal cancer (GIC). The prevalence of GIH varies based on the anatomical location of cancer, ranging between 15.7% in gastric cancer and 5.1% in gallbladder cancer. Many risk factors, including socioeconomic factors such as insurance and race, can affect the rates of GIH. Endoscopy is significantly associated with lower inpatient mortality in bleeding patients with GIC.

Citation: Minhem MA, Nakshabandi A, Mirza R, Alsamman MA, Mattar MC. Gastrointestinal hemorrhage in the setting of gastrointestinal cancer: Anatomical prevalence, predictors, and interventions. *World J Gastrointest Endosc* 2021; 13(9): 391-406
URL: https://www.wjgnet.com/1948-5190/full/v13/i9/391.htm
DOI: https://dx.doi.org/10.4253/wjge.v13.i9.391

INTRODUCTION

Gastrointestinal hemorrhage (GIH) is a common complication in patients with gastrointestinal cancers (GIC). In terms of incidence and mortality, GICs are among the highest globally[1]; and thus remain an ongoing challenge as to management and treatment. GIH often serves as the initial symptom for GIC, locally invasive, and metastatic disease[2]. It can also carry a high mortality rate, as in the case of upper GIH [3]. An earlier study documented that bleeding gastrointestinal (GI) tumors accounted for roughly 12 percent of cases involving GIH[4]. Another analysis of studies purported that neoplasia constituted between 3%-11% of lower GIH[5]. On the other hand, in 5% of patients with upper GI bleeds, biopsy-proven tumors were the source of bleeding[6]. While existing literature studied the prevalence of GIC in GIH, and some assess GIH as a clinical symptom of a specific type of tumor[2,4,7,8], there are no inclusive studies that assess GIH in different types of GIC. Therefore, a more comprehensive and large sample size analysis is warranted to study GIH in all types of GIC.

Bleeding in GIC patients could be the result of many causes and risk factors. One study revealed that bleeding from the tumor site is the predominant source of upper GI bleeds in patients with cancer[9]. Another study found GIH common after chemoradiotherapy in patients with locally advanced pancreatic cancer[10]. Some existing literature examines the risk factors behind GIH in specific tumors, such as gastrointestinal stromal tumors[11]. In one study, risk factors implicated in GIH included initial tumor stage, smoking, and carbohydrate antigen 19-9 Levels at the time of pancreatic cancer diagnosis[8]. This current retrospective analysis assesses predictors of GIH in the setting of GIC. Another study found that GIH rate can vary based on pancreatic cancer location; however, the study was limited by the small sample size[8]. Therefore, further analysis on the prevalence of GIH regarding the anatomical location of neoplasm would assist in future clinical management of GIH in these patients.

Most importantly, investigating different interventions for GIH in the setting of GIC would provide vital information in developing treatment plans for these patients and preventing mortality. For example, literature reviews endoscopic hemostasis of GIH in both cancer and non-cancer settings, but data remains limited in specifically the setting of tumor bleeding[2,6,12,13]. Endoscopic therapy is often recommended for non-cancer related GIH, as it may decrease overall morbidity and the need for invasive surgery [14,15]. However, while hemostasis is often successfully achieved by endoscopic therapy for bleeding GIC, rebleeding rates, unfortunately, remain common[6,13].

This study's goals involve estimating the prevalence of GIH in patients with GIC based on the anatomical location of tumors, evaluating the predictors of GIH in GIC, and the outcomes of different procedure modalities used in bleeding GIC patients.

MATERIALS AND METHODS

Study setting

This study is a retrospective analysis of the 2016 to 2018 National (Nationwide) Inpatient Sample (NIS) database, the largest national inpatient database. NIS is drawn from 48 states and includes more than 97% of the United States population. The NIS does not contain any patient identifier; therefore, it does not require review by the institutional review board.

Inclusion/exclusion criteria

All adult inpatients (≥ 18-year-old) were included.

Outcomes

(1) Estimate GIH prevalence in patients with GIC based on the anatomical location of cancer; (2) Study the predictors of GIH in patients with GIC; and (3) Study the mortality outcome of various procedural modalities used in GIH patients with GIC: (a) Endoscopy; (b) Surgery; (c) Trans-arterial embolization; and (d) Radiation therapy.

Exposure

(1) In all adult inpatients, the prevalence of GIH was compared between patients with and without GIC; (2) In inpatients with GIC, the prevalence of GIH was determined according to the anatomic location of GIC; (3) In inpatients with GIC, demographics, socioeconomic factors, comorbidities, and other disease-related factors were compared based on GIH status; and (4) In inpatients with GIC and GIH, mortality outcome was compared between patients who underwent or did not undergo interventions such as endoscopy, surgery, embolization, and radiation therapy.

Definitions

All diagnoses and procedures were reported based on ICD-10-CM and PCS coding listed in Table 1. GIH was defined as the presence of upper or lower GIH or the presence of hematemesis, melena, hematochezia, or unspecified source of GIH.

Statistical analysis

Continuous variables were presented as mean and standard deviation. Categorical variables were presented as frequencies and percentages (%). Student *t*-test was used for the comparison of continuous variables, and Pearson's χ^2 test was used for categorical variables. *P* values were adjusted according to the Bonferroni method when pairwise comparisons were used. In a few instances, analysis was not performed

Table 1 ICD-10-CM and PCS codes for diagnoses and procedures

Diagnosis	ICD-10-CM
GI hemorrhage	Upper: I85.x1; (K25-K28).0,2,4,6; K29.x1; K318.11 K31.82
	Lower: K50.x11; K51.x11; K55.21; K57.x1; K57.x3
	Total = upper + lower + K62.5; K92.0-2
GI cancer	
Esophageal cancer	C15; C49.A1; D00.1
Upper third	C15.3
Middle third	C15.4
Lower third	C15.5
Other/unspecified	C15.8-9; C49.A1; D00.1
Gastric cancer	C16; C49.A2; D00.2
Cardia	C16.0
Fundus	C16.1
Body	C16.2
Pyloric antrum	C16.3
Pylorus	C16.4
GIST	C49.A2
Other/unspecified	C16.5-9; D00.2
Small bowel cancer	C17; C49.A3; D01.49
Duodenum	C17.0
Jejunum	C17.1
Ileum	C17.2
GIST	C49.A3
Other/unspecified	C17.3-9; D01.49
Liver cancer	C22; D01.5
Hepatocellular carcinoma	C22.0
Other primary liver	C22.2-8; D01.5
Biliary cancer	C22.1; C24
Intrahepatic	C22.1
Extrahepatic	C24.0
Ampulla of Vater	C24.1
Other/unspecified	C24.8-9
Gallbladder cancer	C23
Pancreatic cancer	C25
Head	C25.0
Body	C25.1
Tail	C25.2
Duct	C25.3
Endocrine	C25.4
Other/unspecified	C25.7-9
Colorectal cancer	C18; C19; C20; C26.0; C49.A4-5; D01.0-4
Cecum	C18.0

Appendix	C18.1
Ascending colon	C18.2
Hepatic flexure	C18.3
Transverse colon	C18.4
Splenic flexure	C18.5
Descending colon	C18.6
Sigmoid	C18.7
Rectosigmoid junction	C19
Rectum	C20
Other/unspecified	C188.9-9; C26.0; C49.A4-5; D01.0-4
Acute kidney injury	N17; N19; N99.0; O90.4
Chronic kidney disease	D63.1; (E08-E13).22; I12.0,9; I13.10,11,20; N18; R88.0; Z49
Congestive heart failure	I50; I97.13x; O29.12x; Z95.812; I09.81; I11.0; I13.0,2
Cirrhosis and liver failure	K70.4; K70.3; K72; K91.82; K71.7; K74; K76.(6,7); K65.2; I85
Radiation gastroenteritis/proctitis	K52.0; K62.7
Metastasis	C77; C78; C79; C80.0
Chemotherapy and immunotherapy	Z92.21; Z51.11-12; T45.1X; K12.31; D61.81; D64.81
Severe malnutrition and cachexia	E40-43; R64
Obesity	E66.01; E66.09; E66.(1,2,8,9); Z68.3-4
Palliative care	Z521.5
Aspirin/antiplatelets	Z79.82; Z79.02
Anticoagulants	Z79.01
Intestinal infection	A00-09; A18.32; A21.3; A22.2; B37.82; B25.8-9
Hypovolemic shock	R57.1
Procedures	ICD-10-PCS
Upper endoscopy	06L34CZ; 0D5(1-9)8ZZ; 0DB(1-9)8ZX; 0DB(1-9)8ZZ; 0DBA8ZX; 0DJ08ZZ; 0DQ(6,7,9)8ZZ; 3E0G8TZ
Colonoscopy	06LY4CC; 0D5(E-Q)8ZZ; 0DB(B-Q)8ZZ; 0DB(B-Q)8ZX; 0DJD8ZZ
Surgery	0D(1,5,B,J,T); 0F(5,B,T); OW(J,3) excluding endoscopic approach
Trans-arterial embolization	04(L,V)(1,2,3,5,6,7,9,B)3DZ
Radiation therapy	D(D,F,W)0(0-7)(0-6)Z(0,Z)

GI: Gastrointestinal; GIST: Gastrointestinal stromal tumor.

due to lack of enough sample size (≤ 10 patients in a table cell), and the affected cells were left unfilled in the table.

Binary multiple logistic regression was performed for the following outcomes: (1) GIH (to assess the predictors of GIH in patients with GIC); and (2) Inpatient mortality (to assess the association between mortality and interventions such as endoscopy, surgery, embolization, and radiation therapy).

Multivariate analysis was used in the backward stepwise regression to select statistically significant variables. The binary logistic regression results were represented with adjusted OR and 95% confidence interval. Statistical significance was set at the 5% level. Statistical analysis was performed using IBM SPSS, version 27 (IBM Inc., Armonk, NY, United States).

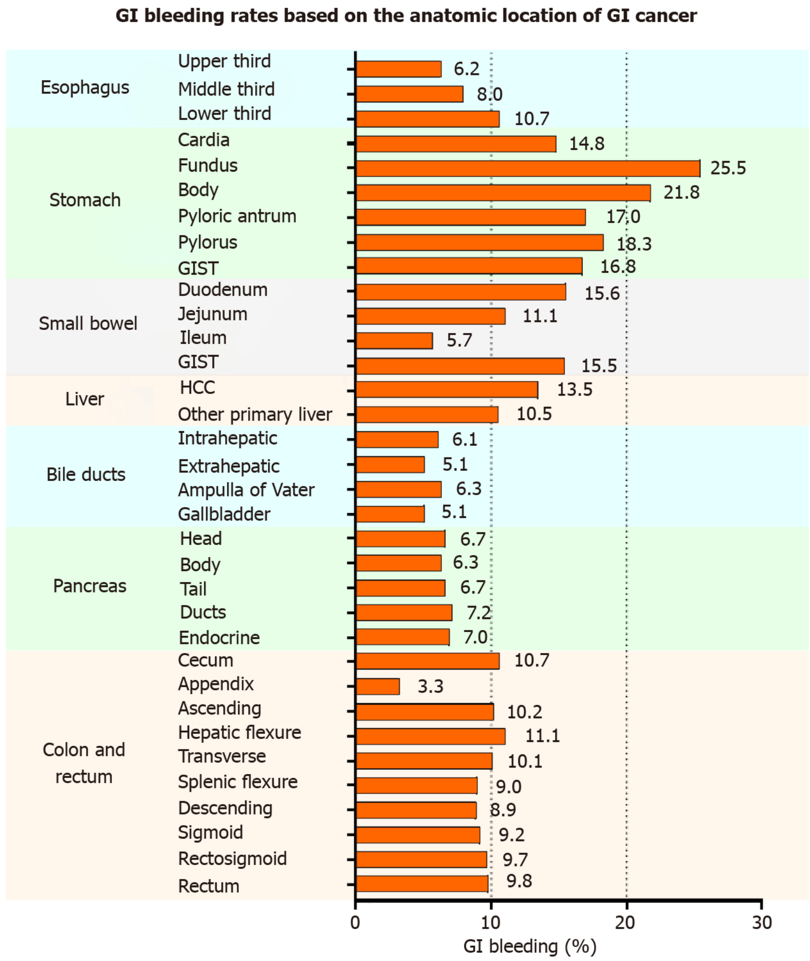

Figure 1 The proportion of gastrointestinal bleeding in inpatients according to the anatomical location of gastrointestinal cancer. GI: Gastrointestinal; GIST: Gastrointestinal stromal tumor; HCC: Hepatocellular carcinoma.

RESULTS

Prevalence of GIH in the setting of GIC

The prevalence of GIH in adult inpatients was compared based on GIC (Table 2). Out of a total of 18173885 inpatients, 321622 (1.77%) cases had a diagnosis of GIC. Within patients with GIC, 30507 (9.5%) inpatients had GIH, which was significantly (P < 0.001) more than the prevalence of GIH in patients without GIC (3.4%).

Prevalence of GIH based on the anatomical location of GIC

The highest to lowest GIH rates are listed in the following order: stomach cancer (15.7%), liver cancer (13.0%), small bowel cancer (12.7%), esophageal cancer (9.1%), colorectal cancer (9.1%), pancreatic cancer (7.2%), bile duct cancer (6.0%), and gallbladder cancer (5.1%). The prevalence of GIH was dissected more in detail by the anatomical location of GIC, as displayed in Figure 1. In esophageal cancer, GIH appears to become more prevalent in lower esophageal lesions (GIH in upper third esophageal cancer: 6.2% < middle third: 8.0% < lower third: 10.7%). Patients with stomach cancer have the highest GIH rates compared to other locations. The highest GIH rate occurs in patients with cancer of the stomach fundus (25.5%), and the lowest rate occurs in the cancer of the stomach cardia (14.8%). In the small bowel, cancer of the duodenum had the highest rate of GIH (15.6%), followed by jejunum (11.1%) and ileum (5.7%). Hepatocellular carcinoma was associated with a GIH rate of 13.5%, whereas biliary and gallbladder cancers had a GIH rate approximately 5%-6%, slightly differing by location. Patients with pancreatic cancers had GIH of approximately 6%-7%, slightly differing by location. Patients with cancers of the colon and rectum had comparable GIH rates (approximately 9%-11%) except for appendiceal cancer with a low bleeding rate (3.3%). The highest GIH rate in colorectal cancer patients belonged to hepatic flexure tumors (11.1%), and the lowest GIH (after appendiceal cancer) was for descending colon cancer (8.9%). Detailed data showing the patient counts

Table 2 Comparison of gastrointestinal hemorrhage between inpatients who have and do not have gastrointestinal cancer

		GI cancer				Total	
		No		Yes			
		Count	Within GI cancer (%)	Count	Within GI cancer (%)	Count	Within total (%)
GI bleeding	No	17242568	96.6	291115	90.5	17533683	96.5
	Yes	609695	3.4	30507	9.5	640202	3.5
	Total	17852263	100	321622	100	18173885	100

P < 0.001. GI: Gastrointestinal.

determining the percentages mentioned above are available in Table 3. No statistical comparison was performed between different anatomical locations due to the numerous possibilities for comparisons and combinations; however, assessing the clinical significance of percentages and their differences is still valuable in making comparisons.

Predictors of GIH in patients with GIC

In this section, the predictors of GIH were studied in the population of patients with GIC. Table 4 shows a comparison of various demographic, socioeconomic, and other disease-related factors based on GIH status. Patients with GIH were slightly older compared to patients without GIH (68.2 ± 13.2 *vs* 66.2 ± 12.8 years old, P < 0.001). Patients with GIH were less likely to be females (37.8% *vs* 43.3%, P < 0.001). While minority races, including Black, Hispanic, Asian, and Native American, were more prevalent in patients with GIH, White race was less common in GIH patients (63.0% *vs* 68.3%, P < 0.001). Socioeconomic factors also were associated with varying GIH rates. Patients with GIH were more likely to be Medicare (60.3% *vs* 55.5%, P < 0.001), Medicaid, or self-pay patients, and they were less likely to have private insurance (21.3% *vs* 28.1%, P < 0.001). Likewise, GIH patients had a lower median household income compared to patients without GIH. Comorbidities such as acute kidney injury, chronic kidney disease, heart failure, cirrhosis, and liver failure were more common in patients with GIH. For cancer-related variables, patients with GIH had less metastatic disease (39.7% *vs* 43.1%, P < 0.001), were less treated with chemotherapy or immunotherapy (14.1% *vs* 19.6%, P < 0.001), and had more radiation gastroenteritis or proctitis (0.6% *vs* 0.3%, P < 0.001). GIH patients were also less obese and were more diagnosed with severe malnutrition and cachexia compared to non-GIH patients.

Table 5 shows the multivariate analysis results, which validates the results of the bivariate analysis discussed above. In summary, predictors (in favor) of GIH were age, minority races (Black, Hispanic, Asian, Native American compared to White race), Insurance (Medicaid and Self-pay compared to Medicare), acute kidney injury, chronic kidney disease, heart failure, cirrhosis, and liver failure, radiation gastroenteritis or proctitis, severe malnutrition and cachexia, use of aspirin, antithrombotic and anticoagulants. Predictors against having GIH were female gender, private insurance (compared to Medicare), higher median household income, presence of metastatic disease, patient on chemotherapy or immunotherapy, and obesity. The factor with the highest OR for GIH was radiation gastroenteritis and proctitis [OR = 2.39 (2.02-2.81)]. The factor with the lowest OR for GIH was chemotherapy or immunotherapy [OR = 0.74 (0.72-0.77)].

Interventions for GIH

Interventions that have been proposed and utilized in GIH patients with GIC were studied. Inpatient mortality was the outcome of interest. The four studied interventions were endoscopy, surgery, trans-arterial embolization, and radiation therapy. Multivariate analysis, using stepwise binary logistic regression, accounted for the following factors: Age, female, race, income, acute kidney injury, chronic kidney disease, heart failure, cirrhosis and liver failure, intestinal infection, metastasis, chemotherapy and immunotherapy, radiation gastroenteritis, palliative care, hypovolemic shock, endoscopy, surgery, embolization, and radiation therapy.

Endoscopy

Out of 30507 inpatients with GIC who also had GIH, 16267 (53.3%) underwent an

Table 3 Tabulated representation of data of Figure 1 which shows to the prevalence of gastrointestinal hemorrhage according to the anatomic location of gastrointestinal cancer

Anatomic location of cancer		GI hemorrhage			
		No		Yes	
	n	Count	Row (%)	Count	Row (%)
Esophagus	23674	21508	90.90	2166	9.10
Upper third	773	725	93.80	48	6.20
Middle third	1467	1349	92.00	118	8.00
Lower third	6540	5843	89.30	697	10.70
Other/unspecified	15161	13842	91.30	1319	8.70
Stomach	27409	23103	84.30	4306	15.70
Cardia	6829	5815	85.20	1014	14.80
Fundus	471	351	74.50	120	25.50
Body	1284	1004	78.20	280	21.80
Pyloric antrum	1881	1561	83.00	320	17.00
Pylorus	398	325	81.70	73	18.30
GIST	2477	2060	83.20	417	16.80
Other/unspecified	14410	12256	85.10	2154	14.90
Small bowel	6469	5646	87.30	823	12.70
Duodenum	3270	2760	84.40	510	15.60
Jejunum	513	456	88.90	57	11.10
Ileum	540	509	94.30	31	5.70
GIST	872	737	84.50	135	15.50
Other/unspecified	1322	1228	92.90	94	7.10
Liver	33452	29111	87.00	4341	13.00
HCC	27601	23877	86.50	3724	13.50
Other primary liver	5988	5357	89.50	631	10.50
Bile ducts	18706	17577	94.00	1129	6.00
Intrahepatic	12515	11749	93.90	766	6.10
Extrahepatic	2749	2608	94.90	141	5.10
Ampulla of Vater	2143	2008	93.70	135	6.30
Other/unspecified	1464	1368	93.40	96	6.60
Gallbladder	4268	4049	94.90	219	5.10
Pancreas	63636	59063	92.80	4573	7.20
Head	17643	16469	93.30	1174	6.70
Body	3077	2882	93.70	195	6.30
Tail	3892	3630	93.30	262	6.70
Ducts	774	718	92.80	56	7.20
Endocrine	589	548	93.00	41	7.00
Other/unspecified	38379	35489	92.50	2890	7.50
Colon and rectum	148943	135410	90.90	13533	9.10
Cecum	12171	10863	89.30	1308	10.70
Appendix	3967	3835	96.70	132	3.30

Ascending	16104	14458	89.80	1646	10.20
Hepatic flexure	3280	2916	88.90	364	11.10
Transverse	7439	6687	89.90	752	10.10
Splenic flexure	2033	1851	91.00	182	9.00
Descending	4239	3862	91.10	377	8.90
Sigmoid	17602	15976	90.80	1626	9.20
Rectosigmoid	17199	15527	90.30	1672	9.70
Rectum	29634	26730	90.20	2904	9.80
Other/unspecified	40531	37341	91.50	3190	8.50

GI: Gastrointestinal; GIST: Gastrointestinal stromal tumor; HCC: Hepatocellular carcinoma.

endoscopic procedure, *i.e.*, upper endoscopy or colonoscopy. Figure 2 displays a significant decrease in mortality associated with endoscopy performance in patients with GIH and GIC (mortality with endoscopy: 5.5% *vs* no endoscopy: 14.9%, $P <$ 0.001). Multivariate adjusted analysis (Table 6) shows a mortality reduction associated with endoscopy [OR = 0.42 (0.38-0.46)]. This association also applied to cancer subtypes, particularly esophageal, gastric, primary hepatic, biliary, pancreatic, and colorectal cancer. Gallbladder and small bowel cancer patients did not show a statistically significant association between mortality and endoscopy.

Colorectal cancer had a sufficient patient population to study the types of endoscopy performed and their association with inpatient mortality. Figure 3 shows that, in colorectal cancer patients with GIH, the lowest mortality was reported in patients who underwent either colonoscopy (2.6%) or dual (upper and lower) endoscopy (2.6%). This was significantly lower compared to mortality in patients who underwent upper endoscopy (6.5%) or no endoscopy (9.0%) ($P < 0.001$ for colonoscopy or dual endoscopy *vs* upper endoscopy or non-endoscopy group). Eight percent of all GIH causes in colorectal cancer patients were attributed to upper GIH, including 4.1% peptic ulcer disease and 0.9% esophageal varices.

Surgery

Out of 30507 inpatients with GIC who also had GIH, 4568 (15.0%) underwent surgical exploration with or without bowel resection during hospitalization. Unadjusted analysis displays a significant decrease in mortality associated with the performance of surgery in GIH patients with GIC (total) (5.6% *vs* 10.6%, $P < 0.001$) and colorectal cancer (4.6% *vs* 6.5%, $P < 0.001$). On multivariate (adjusted) analysis shown in Table 6, results were different from unadjusted analysis. Surgery was not associated with any statistical difference decrease in mortality in GIC (total) but had increased odds of mortality in patients with gastric [OR = 1.73 (1.00-3.00)] and colorectal cancer [OR = 1.33 (1.09-1.62)]. Small bowel, hepatic, and pancreatic cancer patients did not show a statistical difference between surgery and non-surgery groups.

Trans-arterial embolization

Out of 30507 inpatients with GIC who also had GIH, 516 (1.7%) underwent trans-arterial embolization. Unadjusted analysis displays a significant increase in mortality associated with the performance of trans-arterial embolization in GIH patients with GIC (total) (14.7% *vs* 9.8%, $P < 0.001$). Gastric cancer (15.1% *vs* 8.7%, $P = 0.01$) and colorectal cancer (21.9% *vs* 5.9%, $P < 0.001$) were also associated with increased mortality in patients who underwent embolization. Similarly, on multivariate (adjusted) analysis in Table 6, embolization was associated with increased odds of mortality in GIC (total) [OR = 1.35 (1.02-1.80)] and colorectal cancer [OR = 2.52 (1.23-5.15)]. Gastric, hepatic, and pancreatic cancer patients did not show a statistical association between embolization and mortality on multivariate analysis.

Radiation therapy

Out of 30507 inpatients with GIC who also had GIH, radiation therapy was performed in 210 (0.7%) patients during the hospitalization. On bivariate analysis, the inpatient mortality of patients who underwent inpatient radiation therapy was lower than those who did not undergo radiation therapy (5.7% *vs* 9.9%, $P = 0.04$). On multivariate

Table 4 Bivariate analysis comparing various factors based on gastrointestinal hemorrhage status in a population of inpatients with gastrointestinal cancer

Inpatients with GI cancer		No GI hemorrhage		GI hemorrhage		*P* value
		n = 291115		*n* = 30507		
		Count/mean	Column%/SD	Count/mean	Column%/SD	
Demographic factors						
Age (yr)		66.2	± 12.8	**68.2**	**± 13.2**	< 0.001
Female		**125898**	**43.30**	11543	37.80	< 0.001
Race	White	**192544**	**68.30**	18633	63.00	< 0.001
	Black	37986	13.50	**4727**	**16.00**	< 0.001
	Hispanic	29010	10.30	**3462**	**11.70**	< 0.001
	Asian or Pacific Islander	11482	4.10	**1562**	**5.30**	< 0.001
	Native American	1494	0.50	**189**	**0.60**	0.015
	Other	9345	3.30	999	3.40	0.543
Socioeconomic factors						
Insurance	Medicare	161272	55.50	**18371**	**60.30**	< 0.001
	Medicaid	33523	11.50	**3859**	**12.70**	< 0.001
	Private	**81599**	**28.10**	6483	21.30	< 0.001
	Self-pay	6348	2.20	**894**	**2.90**	< 0.001
	No charge	628	0.20	71	0.20	0.544
	Other	7379	2.50	799	2.60	0.373
Median household income for patient ZIP Code	1st quartile	78840	27.60	**8905**	**29.70**	< 0.001
	2nd quartile	73759	25.80	7733	25.80	0.965
	3rd quartile	**69806**	**24.40**	7072	23.60	0.003
	4th quartile	**63693**	**22.30**	6241	20.80	< 0.001
Comorbidities						
Acute kidney injury		55007	18.90	**7849**	**25.70**	< 0.001
Chronic kidney disease		38425	13.20	**5766**	**18.90**	< 0.001
Heart failure		8704	3.00	**1289**	**4.20**	< 0.001
Cirrhosis and liver failure		32194	11.10	**6154**	**20.20**	< 0.001
Intestinal infection		6694	2.30	753	2.50	0.06
Cancer related						
Metastasis		**125345**	**43.10**	12120	39.70	< 0.001
Chemo and Immunotherapy		**57005**	**19.60**	4314	14.10	< 0.001
Radiation gastroenteritis/proctitis		849	0.30	**189**	**0.60**	< 0.001
Palliative care		38129	13.10	**5318**	**17.40**	< 0.001
Nutritional status						
Severe malnutrition and cachexia		41008	14.10	**4952**	**16.20**	< 0.001
Obesity		**32691**	**11.20**	3127	10.30	< 0.001
Use of antithrombotic/anticoagulants						
Aspirin/antiplatelets		30778	10.60	**3605**	**11.80**	< 0.001
Anticoagulants		22753	7.80	**3345**	**11.00**	< 0.001

Bold values represent a statistically significant higher column proportion. GI: Gastrointestinal.

analysis (Table 6), inpatient radiation therapy for GI bleeding patients with GIC was not significantly associated with any inpatient mortality difference. Analysis was not performed on individual GIC types (esophageal, gastric, small bowel, …) due to insufficient sample in the radiation group.

DISCUSSION

This was a retrospective review of the 2016-2018 NIS database, which is one of the largest national inpatient databases. Our results, as presented in Table 2, our results showed that hospitalized patients with GIC have a significantly higher prevalence of GIH (9.5%) compared to that of the general inpatient population (3.4%). This estimate underscores that GIH is a common complication of GIC and corroborates this study's importance.

Our study showed that GIH is note common in GIC patients and varies significantly based on the anatomical location of cancer. The highest to lowest GIH rates are listed in the following order: stomach cancer (15.7%), liver cancer (13.0%), small bowel cancer (12.7%), esophageal cancer (9.1%), colorectal cancer (9.1%), pancreatic cancer (7.2%), bile duct cancer (6.0%), and gallbladder cancer (5.1%). Figure 1 shows a more detailed representation of GIH rates based on the anatomical location of GIC. The rate of GIH can significantly vary with different tumor locations, even for locations within the same organ. The pattern of bleeding, displayed in Figure 1, shows the highest GIH rate in gastric cancers (ranging between 14.8% in the cardia and 25.5% in cancers of the fundus) followed by cancers adjacent to the stomach, such as cancer of the duodenum (15.6%) and lower third of the esophagus (10.7%). This could be related to the effect of the stomach's acidic medium that can cause erosion and ulceration of the friable intraluminal cancerous tissue and subsequently bleeding. Thus, the further the cancerous tissue from the stomach, the less risk of GIH. Following the same logic, jejunal (11.1%) and ileal cancers (5.7%) have lower GIH rate than duodenal cancers (15.6%), and cancers of the upper (6.2%) and middle third (8.0%) of the esophagus have lower GIH than lower third cancers (10.7%). The correlation between the high incidence of GIH in hepatocellular carcinoma and underlying severe liver cirrhosis with resultant variceal hemorrhage has been demonstrated in previous studies.[16] Colorectal cancer's GIH rates based on different anatomical locations were relatively comparable in the range between 9% to 11%. Appendiceal cancer was an exception with 3.3% GIH, which is similar to the general inpatient population (3.4%).

While our study reports the prevalence of GIH among GIC patients, prior studies have reported the reciprocal prevalence of GIC among patients with GIH[3,17,18]. For example, Sheibani *et al*[6] stated that tumor bleeding comprised 5% (106 cases) of all upper GIH with gastric cancer representing 73%, esophageal cancer 16%, and duodenal cancer 11%. The aforementioned study serves another purpose and cannot estimate the rates of GIH as it examines another parameter. In addition, the large sample size of our patients (30507 bleeding GIC) robustly increases the power of our GIH estimates and analysis.

Notable findings were also reported in the study of the predictors of GIH in GIC. Multivariate analysis results are shown in Table 5. A closer look at the prevalence of GIH in GIC, stratified by race, raises concerning questions on healthcare disparities. Compared to the White race, certain minority races (Black, Hispanic, Asian, and Native American) were predictors of GIH. Lower median household income was also a concerning predictor of GIH. GIH outcomes, stratified by race, have been studied before in various contexts. One study of patients hospitalized for upper GIH found that rebleeding rates were significantly lower in White patients than in Hispanic or Black patients[19]. In the instance of cancer, healthcare disparities also play a significant role in disease onset and outcome. Black patients are observed to have the highest incidence and mortality of many GI tract malignancies, including esophageal, gastric, small bowel, pancreas, colorectal, and anal cancer[20]. Despite the decline in colorectal cancer mortality rates in the past years, the reduction is not as prominent in Black patients. The causes of this are likely multifactorial, many of which are modifiable risk factors such as socioeconomic status, insurance coverage, education level, and consistent access to medical care[21]. The results of this study potentially reinforce these conclusions, as Medicaid patients and non-White patients with GIC

Table 5 The results of multivariate analysis showing the predictors of gastrointestinal hemorrhage in a population of patients with gastrointestinal cancer

Predictors of GI hemorrhage		aOR	95%CI	*P* value
Demographic factors				
Age (yr)		**1.01**	**(1.01-1.02)**	**< 0.001**
Female		0.84	(0.81-0.86)	< 0.001
Race	White- Reference	1.00	-	-
	Black	**1.27**	**(1.22-1.31)**	**< 0.001**
	Hispanic	**1.19**	**(1.14-1.24)**	**< 0.001**
	Asian or Pacific Islander	**1.42**	**(1.34-1.50)**	**< 0.001**
	Native American	**1.24**	**(1.06-1.46)**	**0.007**
	Other	**1.13**	**(1.05-1.21)**	**0.001**
Socioeconomic factors				
Insurance	Medicare- Reference	1.00	-	-
	Medicaid	**1.17**	**(1.12-1.22)**	**< 0.001**
	Private	0.91	(0.88-0.94)	< 0.001
	Self-pay	**1.44**	**(1.34-1.56)**	**< 0.001**
	No charge	1.21	(0.94-1.56)	0.148
	Other	1.03	(0.95-1.12)	0.468
Median household income for patient ZIP Code	1st quartile- Reference	1.00	-	-
	2nd quartile	0.98	(0.95-1.01)	0.246
	3rd quartile	0.96	(0.93-0.99)	0.022
	4th quartile	0.94	(0.90-0.97)	< 0.001
Comorbidities				
Acute kidney injury		**1.17**	**(1.13-1.20)**	**< 0.001**
Chronic kidney disease		**1.22**	**(1.18-1.26)**	**< 0.001**
Heart failure		**1.19**	**(1.12-1.27)**	**< 0.001**
Cirrhosis and liver failure		**1.84**	**(1.78-1.90)**	**< 0.001**
Cancer related				
Metastasis		0.93	(0.90-0.95)	< 0.001
Chemo and Immunotherapy		0.74	(0.72-0.77)	< 0.001
Radiation gastroenteritis/proctitis		**2.39**	**(2.02-2.81)**	**< 0.001**
Palliative care		**1.21**	**(1.17-1.26)**	**< 0.001**
Nutritional status				
Severe malnutrition and cachexia		**1.12**	**(1.08-1.15)**	**< 0.001**
Obesity		0.94	(0.90-0.98)	0.001
Use of antithrombotic/anticoagulants				
Aspirin/antiplatelets		**1.09**	**(1.05-1.13)**	**< 0.001**
Anticoagulants		**1.48**	**(1.42-1.54)**	**< 0.001**

Bold values represent a statistically significant odds ratio > 1 [in favor of gastrointestinal hemorrhage (GIH)]; multivariate logistic regression of outcome (GIH) was performed using the backward stepwise method to determine statistically significant factors; variables included in the analysis: Age, female, race, insurance, income, acute kidney injury, chronic kidney disease, heart failure, cirrhosis and liver failure, intestinal infection, metastasis, chemotherapy and immunotherapy, radiation gastroenteritis, palliative care, severe malnutrition and cachexia, obesity, aspirin/antiplatelet, and anticoagulant; intestinal infection was a statistically non-significant factor; GI: Gastrointestinal; CI: Confidence interval; OR: Odds ratio.

Table 6 The results of multivariate analysis showing the odds ratio of inpatient mortality associated with different interventions (endoscopy, surgery, embolization, radiation)

		GI bleeding patients with cancer								
		All GI Ca	Esophageal Ca	Gastric Ca	Hepatic Ca	Biliary Ca	Gallbladder Ca	Pancreatic Ca	Small bowel Ca	Colorectal Ca
Mortality aOR (95%CI)	Endoscopy	**0.42 (0.38-0.46)**	**0.42 (0.31-0.57)**	**0.42 (0.32-0.54)**	**0.36 (0.29-0.43)**	**0.43 (0.28-0.66)**	0.71 (0.24-2.11)	**0.36 (0.29-0.44)**	1.19 (0.59-2.43)	**0.45 (0.38-0.54)**
	Surgery	0.97 (0.84-1.13)	-	**1.73 (1.00-3.00)**	1.30 (0.67-2.53)	-	-	0.85 (0.49-1.48)	2.26 (0.95-5.36)	**1.33 (1.09-1.62)**
	Trans-arterial embolization	**1.35 (1.02-1.80)**	-	1.46 (0.81-2.62)	1.12 (0.55-2.30)	-	-	0.98 (0.56-1.69)	-	2.52 (1.23-5.15)
	Radiation therapy	0.55 (0.29-1.05)	-	-	-	-	-	-	-	-

Bold values: Statistically significant (P < 0.05). Adjusted odds ratio with 95% confidence interval; empty cells indicate that analysis for the corresponding intervention was not performed due to the insufficient sample size; multivariate logistic regression of outcome (mortality) was performed using the backward stepwise method to determine statistically significant factors; variables included in the analysis: Age, female, race, income, acute kidney injury, chronic kidney disease, heart failure, cirrhosis and liver failure, intestinal infection, metastasis, chemotherapy and immunotherapy, radiation gastroenteritis, palliative care, hypovolemic shock, endoscopy, surgery, embolization, and radiation therapy. GI: Gastrointestinal. CI: Confidence interval; Ca: Cancer; OR: Odds ratio.

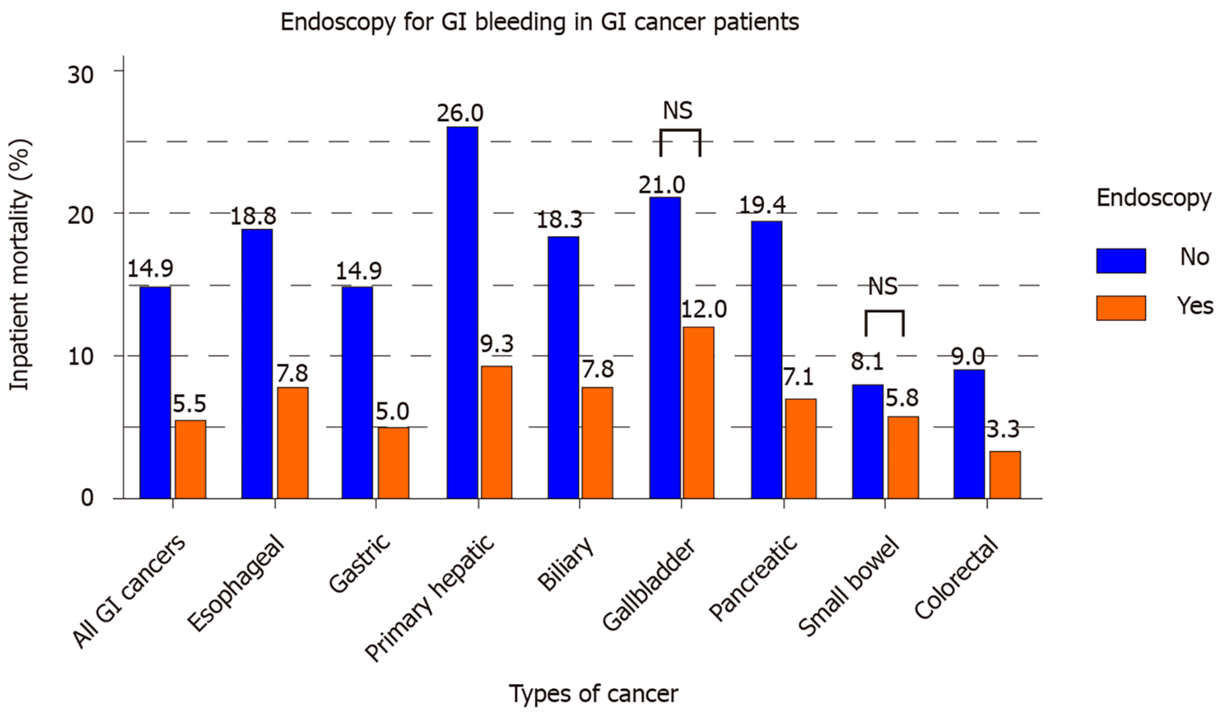

Figure 2 The mortality outcomes of endoscopy in gastrointestinal cancer patients who have gastrointestinal hemorrhage. GI: Gastrointestinal; NS: Not significant.

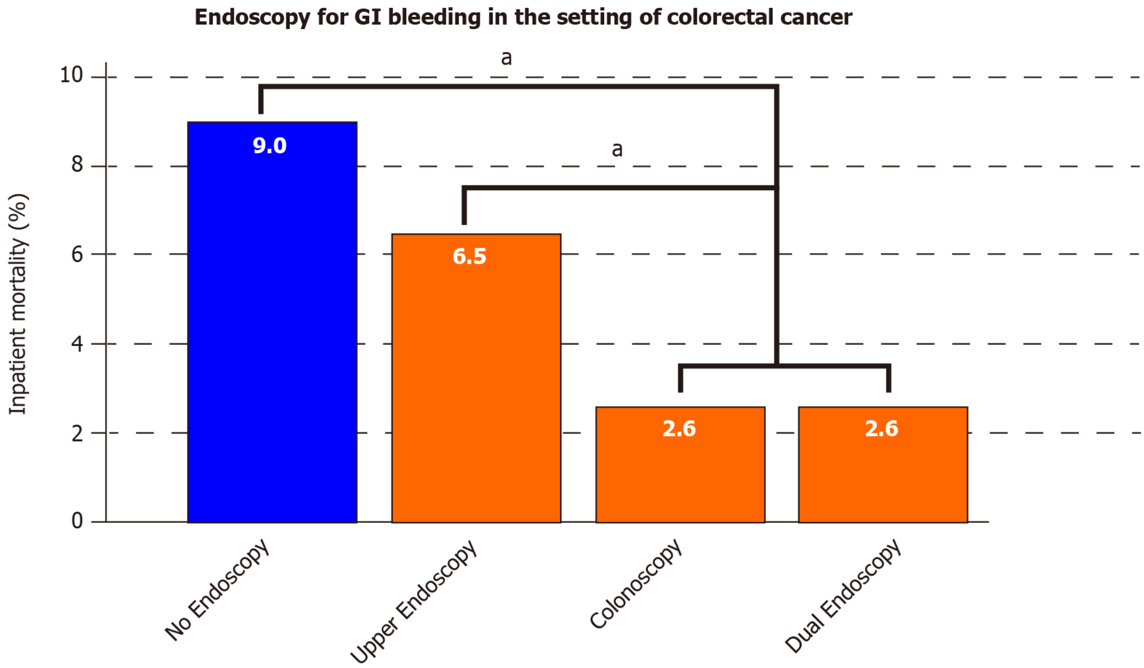

Figure 3 The mortality outcomes of different endoscopic approaches (upper, colonoscopy, or dual) in colorectal cancer patients who have gastrointestinal hemorrhage. $^a P < 0.05$. GI: Gastrointestinal.

experienced higher rates of GIH. Future studies should continue to examine outcomes of GIH in cancer patients, stratified by factors that would affect access to quality healthcare. Such data would be important in driving targeted screening and prevention efforts to high-risk populations. Our analysis also found other significant predictors of GIH, including cancer-related factors. Chemotherapy and immunotherapy were associated with lower risk for GIH [OR = 0.74 (0.72-0.77), $P < 0.001$]. We speculate that the associated decreased risk is related to tumor involution in response to chemotherapy. Radiation gastroenteritis and proctitis was the strongest predictor of GIH [OR = 2.39 (2.02-2.81), $P < 0.001$]. The presence of metastasis was associated with a lower risk of GIH [OR = 0.93 (0.90-0.95), $P < 0.001$]. This could be confounded by other factors that are not retrospectively available for analysis in this database, such as patients' prior surgical history related to the malignancy.

In examining interventions for GIH in the setting of GIC, our data support that endoscopic therapy is associated with a substantial reduction in mortality. Figure 2 highlights the marked difference in mortality between endoscopy and non-endoscopy groups in various GICs (esophageal, gastric, liver, biliary, pancreatic, and colorectal cancer). There was no statistical difference in the subset of gallbladder and small bowel cancers. The type of endoscopy was studied particularly in our cohort of bleeding colorectal cancer patients. Performing either dual endoscopy or colonoscopy resulted in a statistically significant reduction in mortality compared to no endoscopy or upper endoscopy alone (Figure 3). We also have reported that eight percent of all GIH causes in colorectal cancer patients were attributed to upper GIH, including 4.1% peptic ulcer disease and 0.9% esophageal varices. From this standpoint, we can argue in favor of performing dual endoscopy, as upper endoscopy is a fast procedure that can generally be performed with ease along with colonoscopy. As discussed before, endoscopic therapy for GIH may decrease overall morbidity and the need for surgical intervention[14]. Multiple endoscopic methods such as injection, mechanical, and ablative therapies were suggested to stop bleeding from GI tumors; however, literature is mainly based on limited small sample size (10-100 patients) studies[22,23]. Based on our current knowledge, this current study has the largest analysis of endoscopy in bleeding GIC patients. Future studies should examine the different modalities of endoscopic therapy for the treatment of hemorrhage in the specific setting of cancer.

Trans-arterial embolization for GIH in GIC patients was associated with increased inpatient mortality, particularly for colorectal cancers. Surgical exploration with or without resection was not associated with mortality difference in bleeding GIC total population. However, it was associated with increased gastric and colorectal cancer mortality on multivariate analyses (Table 6). Surgery is usually reserved as a last resort for rebleeding or hemorrhage refractory to endoscopic therapy, and these cancer patients usually have an initial poor prognosis or advanced disease[12]. Radiation therapy was not associated with mortality difference in patients with GIH and GIC. The limitations are mainly due to the retrospective nature of the study. Important factors, such as the severity of GIH, intensive care admission, rebleeding rates, tumor's size, and the stage and grade of cancer, were also not available for analysis in this database. Therefore, prospectively studying this patient population in the future would instead decrease potential information bias and would be able to fill in the gaps of the current research. However, our study's strength is numerous and related to its uniqueness, novelty, and robust analysis. The current study provides a detailed and comprehensive examination of the subject of GIH in GIC and provides evidence to support the use of endoscopy in this patient population.

CONCLUSION

The prevalence of GIH in patients with GIC varies significantly based on the anatomical location of the tumor. GICs with the highest to the lowest likelihood of GIH are stomach cancer, liver cancer, small bowel cancer, esophageal cancer, colorectal cancer, pancreatic cancer, bile duct cancer, and lastly, gallbladder cancer. Endoscopy is associated with a substantial reduction in inpatient mortality and therefore should be offered to GIH patients with GIC. Nevertheless, the decision on intervention in the GIC population should be tailored to individual patient's goals of care, the benefit on overall care, and long-term survival.

ARTICLE HIGHLIGHTS

Research background

Gastrointestinal hemorrhage (GIH) is a common complication with gastrointestinal cancers (GIC).

Research motivation

There is no comprehensive research that examines GIH in different types of GIC. Furthermore, endoscopic therapy is insufficiently studied in this setting.

Research objectives

We aim to study the prevalence, predictors, and interventions of GIH based on the anatomical location of GIC.

Research methods

This is a retrospective analysis of the 2016-2018 National Inpatient Sample database, the largest inpatient care database in the United States. Adult inpatients were evaluated for the prevalence and predictors of GIH in the setting of GIC. In addition, inpatient mortality was compared between patients who underwent or did not undergo endoscopy.

Research results

The highest to lowest GIH rates are listed in the following order: stomach cancer (15.7%), liver cancer (13.0%), small bowel cancer (12.7%), esophageal cancer (9.1%), colorectal cancer (9.1%), pancreatic cancer (7.2%), bile duct cancer (6.0%), and gallbladder cancer (5.1%). Inpatient mortality was significantly lower in patients who underwent endoscopy compared to no endoscopy [5.5% *vs* 14.9%, OR = 0.42 (0.38-0.46)], $P < 0.001$).

Research conclusions

The prevalence of GIH in patients with GIC varies significantly based on the tumor's anatomical location. Endoscopy appears to be associated with a substantial reduction in inpatient mortality and should be offered to GIC patients with GIH.

Research perspectives

Future studies, prospective and randomized trials, would help confirm the effectiveness of endoscopic therapy for GIH in patients with GIC.

REFERENCES

1 **Ferlay J**, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer* 2015; **136**: E359-E386 [PMID: 25220842 DOI: 10.1002/ijc.29210]

2 **Schatz RA**, Rockey DC. Gastrointestinal Bleeding Due to Gastrointestinal Tract Malignancy: Natural History, Management, and Outcomes. *Dig Dis Sci* 2017; **62**: 491-501 [PMID: 28032204 DOI: 10.1007/s10620-016-4368-y]

3 **Roberts SE**, Button LA, Williams JG. Prognosis following upper gastrointestinal bleeding. *PLoS One* 2012; **7**: e49507 [PMID: 23251344 DOI: 10.1371/journal.pone.0049507]

4 **Lightdale CJ**, Kurtz RC, Boyle CC, Sherlock P, Winawer SJ. Cancer and upper gastrointestinal tract hemorrhage. Benign causes of bleeding demonstrated by endoscopy. *JAMA* 1973; **226**: 139-141 [PMID: 4542315]

5 **Strate LL**. Lower GI bleeding: epidemiology and diagnosis. *Gastroenterol Clin North Am* 2005; **34**: 643-664 [PMID: 16303575 DOI: 10.1016/j.gtc.2005.08.007]

6 **Sheibani S**, Kim JJ, Chen B, Park S, Saberi B, Keyashian K, Buxbaum J, Laine L. Natural history of acute upper GI bleeding due to tumours: short-term success and long-term recurrence with or without endoscopic therapy. *Aliment Pharmacol Ther* 2013; **38**: 144-150 [PMID: 23710797 DOI: 10.1111/apt.12347]

7 **Wan W**, Xiong Z, Zeng X, Yang W, Li C, Tang Y, Lin Y, Gao J, Zhang P, Tao K. The prognostic value of gastrointestinal bleeding in gastrointestinal stromal tumor: A propensity score matching analysis. *Cancer Med* 2019; **8**: 4149-4158 [PMID: 31197969 DOI: 10.1002/cam4.2328]

8 **Wang YU**, Yuan C, Liu X. Characteristics of gastrointestinal hemorrhage associated with pancreatic cancer: A retrospective review of 246 cases. *Mol Clin Oncol* 2015; **3**: 902-908 [PMID: 26171204 DOI: 10.3892/mco.2015.563]

9 **Maluf-Filho F**, Martins BC, de Lima MS, Leonardo DV, Retes FA, Kawaguti FS, Sato CF, Hondo FY, Safatle-Ribeiro AV, Ribeiro U Jr. Etiology, endoscopic management and mortality of upper gastrointestinal bleeding in patients with cancer. *United European Gastroenterol J* 2013; **1**: 60-67 [PMID: 24917941 DOI: 10.1177/2050640612474652]

10 **Lee KJ**, Kim HM, Jung JW, Chung MJ, Park JY, Bang S, Park SW, Lee WJ, Seong JS, Song SY. Gastrointestinal hemorrhage after concurrent chemoradiotherapy in locally advanced pancreatic cancer. *Gut Liver* 2013; **7**: 106-111 [PMID: 23423146 DOI: 10.5009/gnl.2013.7.1.106]

11 **Yin Z**, Gao J, Liu W, Huang C, Shuai X, Wang G, Tao K, Zhang P. Clinicopathological and Prognostic Analysis of Primary Gastrointestinal Stromal Tumor Presenting with Gastrointestinal Bleeding: a 10-Year Retrospective Study. *J Gastrointest Surg* 2017; **21**: 792-800 [PMID: 28275959 DOI: 10.1007/s11605-017-3385-2]

12 **Heller SJ**, Tokar JL, Nguyen MT, Haluszka O, Weinberg DS. Management of bleeding GI tumors. *Gastrointest Endosc* 2010; **72**: 817-824 [PMID: 20883861 DOI: 10.1016/j.gie.2010.06.051]

13 **Ofosu A**, Ramai D, Latson W, Adler DG. Endoscopic management of bleeding gastrointestinal tumors. *Ann Gastroenterol* 2019; **32**: 346-351 [PMID: 31263356 DOI: 10.20524/aog.2019.0391]

14 **Cappell MS**, Friedel D. Acute nonvariceal upper gastrointestinal bleeding: endoscopic diagnosis and therapy. *Med Clin North Am* 2008; **92**: 511-550, vii [PMID: 18387375 DOI: 10.1016/j.mcna.2008.01.001]

15 **Barnert J**, Messmann H. Management of lower gastrointestinal tract bleeding. *Best Pract Res Clin Gastroenterol* 2008; **22**: 295-312 [PMID: 18346685 DOI: 10.1016/j.bpg.2007.10.024]

16 **Lang BH**, Poon RT, Fan ST, Wong J. Outcomes of patients with hepatocellular carcinoma presenting with variceal bleeding. *Am J Gastroenterol* 2004; **99**: 2158-2165 [PMID: 15554997 DOI: 10.1111/j.1572-0241.2004.40336.x]

17 **Savides TJ**, Jensen DM, Cohen J, Randall GM, Kovacs TO, Pelayo E, Cheng S, Jensen ME, Hsieh HY. Severe upper gastrointestinal tumor bleeding: endoscopic findings, treatment, and outcome. *Endoscopy* 1996; **28**: 244-248 [PMID: 8739741 DOI: 10.1055/s-2007-1005436]

18 **Loftus EV**, Alexander GL, Ahlquist DA, Balm RK. Endoscopic treatment of major bleeding from advanced gastroduodenal malignant lesions. *Mayo Clin Proc* 1994; **69**: 736-740 [PMID: 8035627 DOI: 10.1016/s0025-6196(12)61090-8]

19 **Wollenman CS**, Chason R, Reisch JS, Rockey DC. Impact of ethnicity in upper gastrointestinal hemorrhage. *J Clin Gastroenterol* 2014; **48**: 343-350 [PMID: 24275716 DOI: 10.1097/MCG.0000000000000025]

20 **Ashktorab H**, Kupfer SS, Brim H, Carethers JM. Racial Disparity in Gastrointestinal Cancer Risk. *Gastroenterology* 2017; **153**: 910-923 [PMID: 28807841 DOI: 10.1053/j.gastro.2017.08.018]

21 **Carethers JM**. Screening for colorectal cancer in African Americans: determinants and rationale for an earlier age to commence screening. *Dig Dis Sci* 2015; **60**: 711-721 [PMID: 25540085 DOI: 10.1007/s10620-014-3443-5]

22 **Thosani N**, Rao B, Ghouri Y, Batra S, Raju G, Shafi M, Guha S. Role of argon plasma coagulation in management of bleeding GI tumors: evaluating outcomes and survival. *Turk J Gastroenterol* 2014; **25** Suppl 1: 38-42 [PMID: 25910365 DOI: 10.5152/tjg.2014.4867]

23 **Kim YI**, Choi IJ. Endoscopic management of tumor bleeding from inoperable gastric cancer. *Clin Endosc* 2015; **48**: 121-127 [PMID: 25844339 DOI: 10.5946/ce.2015.48.2.121]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com