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Risk Factors of Postoperative Upper Gastrointestinal Bleeding Following Colorectal Resections

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Abstract There is limited data regarding the risk factors of postoperative upper GI bleeding (UGIB) in patients undergoing colorectal resection. We sought to identify risk factors of UGIB after colorectal resection. The NIS database was used to evaluate all patients who had colorectal resection complicated by UGIB between 2002 and 2010. Multivariate analysis using logistic regression was performed to quantify the association of preoperative variables with postoperative UGIB. We sampled a total of 2,514,228 patients undergoing colorectal resection, of which, 12,925 (0.5 %) suffered a postoperative UGIB. The mortality of patients who had UGIB was significantly greater than patients without UGIB (14.9 vs. 4.7 %; OR, 3.57; CI, 3.40–3.75; P<0.01). Patients suffering from UGIB had an associated 14.9 % inhospital mortality. History of chronic peptic ulcer disease (6.75; CI, 5.75–7.91; P<0.01) and emergency admission (OR, 4.27; CI, 4.09–4.45; P<0.01) are associated with UGIB. Duodenal ulcer as the source of bleeding is a mortality predictors of patients (OR, 1.71; CI, 1.49–1.97; P<0.01). Postoperative UGIB occurs in less than 1 % of colorectal resections. However, patients suffering from postoperative UGIB are over three times more likely to die. Chronic peptic ulcer disease and emergency admission are respectively the strongest predictors of postoperative UGIB.

Introduction

Postoperative upper GI bleeding (UGIB) is associated with significant morbidity and increase in expenditures, prolonged hospital stay, and greater than 50 % mortality rate.[1–6] It is important to recognize risk factors prior to operation to attempt to decrease the morbidity and mortality of these patients. A number of previous studies have identified risk factors influencing UGIB rate in critically ill patients, with the goal of controlling morbidity and mortality. Some of the UGIB predictors include male gender, age greater than 60, sepsis, liver disease, coagulopathy, chronic active gastritis, chronic renal failure, respiratory failure, glucocorticoid administration, history of peptic ulcer, diabetes mellitus, Helicobacter pylori infection, intensive care unit hospitalization, and mechanical ventilation more than 24 h.[5, 7–11] Most previous studies are limited in their conclusions due to the small size of the index population. Hence, there is limited information regarding postoperative UGIB predictors in surgical patients.[12, 13] The incidence of postoperative UGIB has been reported between 0.22 and 8 % in surgical procedures.[3, 4] The wide variance of incidence of postoperative UGIB is related to the difference in the prevalence of risk factors in the patients according to the patient's pathology or procedure.[14] Additionally, many of the reports are from an era when nasogastric tubes and prolonged NPO states were routine. A large nationwide study analyzing the contemporary rate of UGIB in postoperative colorectal surgery is lacking. Therefore, we

aim to report on the incidence, risk factors, and outcomes of UGIB in patients undergoing colorectal surgery.

Materials and Methods

This study was performed utilizing the nationwide inpatient sample (NIS) database from January 1, 2002 to December 31, 2010. The health-care cost and utilization project NIS is an inpatient care database that contains information from nearly eight million hospital stays each year across the USA with an approximately 20 % stratified sample of the American community, nonmilitary, and nonfederal hospitals, resulting in a sampling frame that approximates 95 % of all hospital discharges in the USA.15 Approval for use of the NIS patient level data in this study was obtained from the NIS. We evaluated patients who had undergone colorectal resections for the diagnosis of benign or malignant colorectal tumors, diverticular diseases, and ulcerative colitis using the appropriate procedural and diagnosis codes as specified by the International Classification of Diseases, 9th Revision, Clinical Modifications (ICD-9-CM). Patients who had colorectal procedures were defined based on the following ICD-9 codes: 17.31–17.39, 45.71–45.79, 45.81–45.83, 48.50–48.52, 48.59, 48.62, and 48.63. Patients who underwent colorectal surgery without colon or rectal resection (e.g., ostomy creation) were excluded from this study. Patients' diagnosis was defined based on the following ICD-9 codes: malignant neoplasm of colon and rectum (153.0–153.9, 154.0, 154.1, 230.3, and 230.4), benign neoplasm of the colon and rectum (211.3, 211.4), diverticulosis or diverticulitis of colon (562.10– 562.13), and ulcerative colitis (556.0–556.9). Inhospital postoperative UGIB was defined as the presence of postoperative UGIB defined based on the following ICD-9 diagnosis codes: gastric ulcer with hemorrhage (531.20, 531.21, 531.40, 531.41, 531.60, and 531.61), duodenal ulcer with hemorrhage (532.20, 532.21, 532.40, 532.41, 532.60, and 532.61), gastritis with hemorrhage (535.01, 535.11, 535.21, 535.31, 535.41, 535.51, and 535.71), duodenitis with hemorrhage (535.51 and 535.61), angiodysplasia of the stomach and duodenum with hemorrhage (537.83), Dieulafoy's lesion (hemorrhagic) of the stomach and duodenum (537.84), and esophageal hemorrhage (530.82, 530.21, and 530.7).

Preoperative factors that were analyzed include patient characteristics (age, sex, and race), admission type (emergent vs. elective), patient comorbidities (history of peripheral vascular disorders, congestive heart failure, chronic peptic ulcer disease, chronic pulmonary disease, chronic renal failure, hypertension, diabetes mellitus with or without complications, liver disease, chronic lung disease, coagulopathy, alcohol abuse, and weight loss more than 10 % in last 6 months), pathologic conditions (colorectal cancer, diverticulosis or diverticulitis, ulcerative colitis, and benign colorectal tumor), surgical type (total colectomy, right colectomy, transverse colectomy, left colectomy, sigmoidectomy, multiple segmental resections of the colon, cecectomy, abdominoperineal resection of the rectum, and anterior resection of the rectum), surgical techniques (laparoscopic vs. open), and sources of the bleeding (gastric ulcer, duodenal ulcer, gastritis or duodenitis, Dieulafoy's lesion, and angiodysplasia). The overall rate of postoperative UGIB following colorectal resection, the rate of postoperative UGIB by procedure type, and admission type were examined. Risk adjusted analysis was performed to identify independent predictors of postoperative UGIB following colorectal

surgery and relation between the source of the bleeding and mortality of the patients. Female gender, age less than 70 and 54 years, Caucasian race, abdominoperineal resection of the rectum, open surgery technique, benign colorectal tumor, gastric ulcer, and elective admission were used as reference data points for comparison in line with the literature.[5, 7, 10, 12, 16]

Statistical Analysis

Statistical analysis was performed with SPSS® software, Version 19 (SPSS Inc., Chicago, IL). The chi-square test and t test were used to evaluate relationships between variables and postoperative UGIB. P values less than 0.05 were considered statistically significant and the adjusted odds ratio (OR) with a 95 % confidence interval was calculated to determine the combined effect of various preoperative factors on postoperative UGIB. Logistic regression analysis was used for inhospital mortality. Patients with missing data points were excluded from final analysis. Univariate and multivariate statistical analysis were conducted on unweighted numbers.
Discharge weight (DISCWT) was used to create national estimates for all analysis.

Results

A total of 2,514,228 patients underwent colorectal resection during January 1, 2002 and December 31, 2010. The mean age of patients was 63 years and 37.9 % of the patients were ≥70 years old. The majority of the patients were white (79.3 %) and female (53.3 %). Most common comorbidities include chronic lung disease (15.4 %) and diabetes mellitus (15.1 %). Demographic data of patients are reported in Table 1.

Table 1 Risk-adjusted analysis for postoperative upper gastrointestinal bleeding based on preoperative factors in colorectal surgery

Patients characteristics		Patients without bleeding (sample size=2,501,303)	Patients with bleeding (sample size=12,925)	*P* value	Odds ratio and 95 % confidence interval
Age	Mean, year	63	70	–	–
	Median, year	65	73	–	–
	Age without cutoff point	–	–	<0.0001	1.03 (1.02–1.031)
	<54/year	662,137 (26.5 %)	1,632 (12.6 %)	Reference	Reference
	≥54/year	1,839,166 (73.5 %)	11,292 (87.4 %)	<0.0001	2.49 (2.36–2.62)
	<70/year	1,555,277 (62.2 %)	5,490 (42.5 %)	Reference	Reference
	≥70/year	946,026 (37.8 %)	7,435 (57.5 %)	<0.0001	2.22 (2.15–2.30)
Race	White	1,518,776 (79.3 %)	7,286 (73.3 %)	Reference	Reference
	Black	178,095 (9.4 %)	1,270 (12.8 %)	<0.0001	1.47 (1.39–1.56)
	Hispanic	129,219 (6.7 %)	825 (8.3 %)	0.009	1.33 (1.23–1.43)
	Asian or Pacific Islander	35,703 (1.9 %)	305 (3.1 %)	<0.0001	1.78 (1.58–1.99)
	Native American	7,870 (0.4 %)	24 (0.2 %)	0.026	0.63 (0.42–0.95)
	Other	44,059 (2.3 %)	227 (2.3 %)	0.29	1.07 (0.94–1.22)
Sex	Female	1,332,532 (53.3 %)	6,220 (48.1 %)	Reference	Reference
	Male	1,166,191 (46.7 %)	6,704 (51.9 %)	<0.0001	1.23 (1.19–1.27)
Admission	Nonemergent admission	1,385,495 (55.5 %)	2,921 (22.6 %)	Reference	Reference
	Emergency admission	1,109,069 (44.5 %)	9,984 (77.4 %)	<0.0001	4.27 (4.09–4.45)
Comorbidity	Chronic lung disease	385,185 (15.4 %)	2,786 (21.6 %)	<0.0001	1.51 (1.44–1.57)
	Diabetes	376,374 (15 %)	2,177 (16.8 %)	<0.0001	1.14 (1.09–1.19)
	Diabetes without complication	341,224 (13.8 %)	1,763 (13.8 %)	0.92	0.99 (0.94–1.04)
	Congestive heart failure	194,545 (7.9 %)	2,427 (19 %)	<0.0001	2.74 (2.62–2.86)
	Preoperational weight loss	181,398 (7.3 %)	2,386 (18.5 %)	<0.0001	2.89 (2.76–3.02)
	Chronic renal failure	109,310 (4.4 %)	1,593 (12.3 %)	<0.0001	3.07 (2.91–3.24)
	Coagulopathy	85,833 (3.5 %)	1,610 (12.6 %)	<0.0001	4 (3.79–4.21)
	Alcohol abuse	48,012 (1.9 %)	508 (3.9 %)	<0.0001	2.09 (1.91–2.28)
	Liver disease	39,320 (1.6 %)	381 (3 %)	<0.0001	1.89 (1.71–2.10)
	Diabetes with complication	35,150 (1.4 %)	414 (3.2 %)	<0.0001	2.31 (2.10–2.55)
	Chronic peptic ulcer disease	4,654 (0.2 %)	161 (1.3 %)	<0.0001	6.75 (5.75–7.91)

Among patients undergoing colorectal resection, 12,925 (0.5 %) had a postoperative UGIB. Compared to the rate of postoperative UGIB in elective admission emergent admission was associated with a nearly five times higher rate of postoperative UGIB (0.9 vs. 0.2 %; OR, 4.27; P<0.01). The overall hospitalization length for colorectal resection patients was 11±12 days. The mean length of stay in the hospital for patients with postoperative UGIB was 24±18 days compared to 11±8 days in patients who did not suffer from a postoperative UGIB (P<0.01).

The mortality rate in patients with postoperative UGIB group was 14.9 vs. 4.7 % for patients who did not experience postoperative UGIB (OR, 3.57; CI, 3.40–3.75; P<0.01). When compared to patients without postoperative UGIB, patients who experienced postoperative UGIB had a higher mean total hospital charge ($168,509 vs. $68,003, P<0.01). The risk-adjusted analysis for factors associated with postoperative UGIB is reported in Tables 1 and 2.

Table 2 Risk-adjusted analysis for postoperative upper gastrointestinal bleeding based on type of the procedure and diagnosis in colorectal surgery

Patient characteristics		Patients without bleeding (sample size=2,501,303)	Patients with bleeding (sample size=12,925)	P value	Odds ratio and 95 % confidence interval
Procedure	Abdominoperineal resection of the rectum	21,925 (0.9 %)	52 (0.4 %)	Reference	Reference
	Right colectomy	822,536 (32.9 %)	5,556 (43 %)	<0.0001	2.81 (2.14–3.70)
	Sigmoidectomy	747,976 (29.9 %)	2,467 (19.1 %)	0.024	1.37 (1.04–1.80)
	Left colectomy	281,532 (11.3 %)	1,921 (14.9 %)	<0.0001	2.85 (2.16–3.75)
	Anterior resection of the rectum	259,149 (10.4 %)	754 (5.8 %)	0.16	1.22 (0.92–1.61)
	Cecectomy	123,863 (5 %)	496 (3.8 %)	<0.0001	1.68 (1.26–2.24)
	Transverse colectomy	114,437 (4.6 %)	899 (7 %)	<0.0001	3.30 (2.49–4.37)
	Total colectomy	31,538 (1.3 %)	307 (2.4 %)	<0.0001	4.19 (3.07–5.72)
	Multiple segmental resection of the colon	14,814 (0.6 %)	111 (0.9 %)	<0.0001	3.15 (2.27–4.39)
Procedure technique	Laparoscopic procedures	12,664 (0.5 %)	40 (0.3 %)	Reference	Reference
	Open procedures	2,488,639 (99.5 %)	12,885 (99.7 %)	<0.0001	1.63 (1.20–2.23)
Pathology	Benign colorectal tumor	301,748 (12.1 %)	1,409 (10.9 %)	Reference	Reference
	Colorectal cancer	923,534 (36.9 %)	4,885 (37.8 %)	<0.0001	1.59 (1.47–1.71)
	Diverticulosis or diverticulitis	535,865 (21.4 %)	1,473 (11.4 %)	<0.0001	0.58 (0.54–0.63)
	Ulcerative colitis	31,783 (1.3 %)	195 (1.5 %)	<0.0001	1.31 (1.12–1.52)

Patient demographic factors associated with higher mortality rate and increased postoperative UGIB were age ≥54 (OR, 2.49; CI, 2.36–2.62; P<0.01) and male sex (OR, 1.23; CI, 1.19–1.27; P<0.01). Comorbidities showing higher rates of postoperative UGIB include chronic peptic ulcer disease (OR, 6.75; CI, 5.76–7.91; P<0.01), coagulopathy (OR, 4; CI, 4.79–4.21; P<0.01), and chronic renal failure (OR, 3.07; CI, 2.91–3.24, P<0.01). Procedure-type total colectomy (OR, 4.19; CI, 3.07–5.72; P<0.01) and transverse colectomy (OR, 3.30; CI, 2.49–4.37; P<0.01) were factors that resulted in higher rates of postoperative UGIB. Also, emergent admission (OR, 4.27; CI, 4.09–4.45; P<0.01) and colorectal cancer (OR, 1.59; CI, 1.47–1.71; P<0.01) were independently associated with increased incidence of postoperative UGIB.

There was a statistical correlation between the age of patients and postoperative UGIB as shown in Fig. 1. The incidence of UGIB in patients younger than 50 years old is 0.2 % and this rate increases to 0.4 % in patients between 50 and 70 years old and reaches 0.8 % in patients older than 70 years (P<0.01).
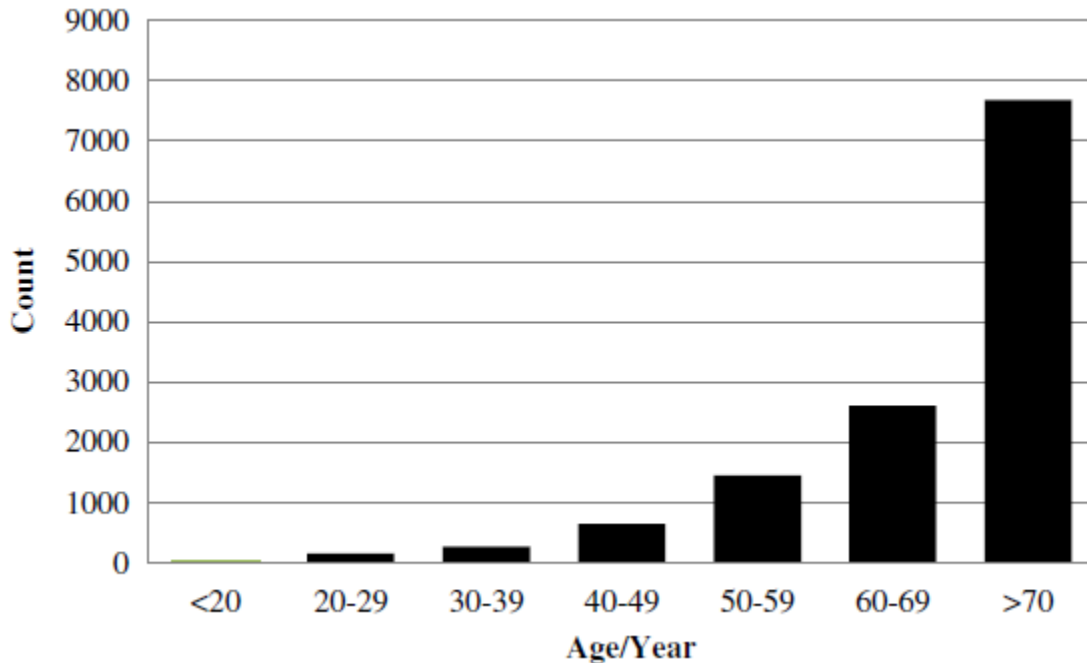
Fig. 1 Distribution of age in patients with postoperative upper gastrointestinal bleeding

The most common source of bleeding in the upper GI tract was gastritis or duodenitis (35.1 %) followed by gastric ulcer (27.8 %), and duodenal ulcer (15.6 %). The highest mortality rate associated with source of bleeding was duodenal ulcer (24.1 %), and there was an association between duodenal ulcer as the source of the bleeding and mortality of patients. (OR, 1.71; CI, 1.49–1.97; $P<0.01$) (Table 3).

Discussion

Postoperative UGIB following colorectal resection operations is associated with a poor prognosis, significant mortality rate, and an observed increase in hospital charges and hospitalization period. The inhospital mortality rate of patients undergoing colorectal operation who suffer postoperative UGIB was more than three times higher than in patients who did not experience postoperative UGIB (14.9 vs. 4.7 %). Also, postoperative UGIB is associated with more than double the mean hospital charges ($167,392 vs. $68,003) and hospitalization length of the patients (24 vs. 11 days).

We found a 0.6 % incidence rate of postoperative UGIB in colorectal resections which is in the line of 0.7 % previously reported in the literature.[5] The overall mortality rate of patients undergoing colorectal resection was 4.7 %, which is similar to the previously reported mortality rates of 4.5 % and 4.6 % in the literature.[17, 18] Callahan with a study of 48,582 patients who underwent colorectal resection reported inhospital mortality of 4.6 %.[17] Also, this study found that the mortality rate increases to 14.9 % in patients who suffered from postoperative UGIB.

The mortality rate of patients with postoperative UGIB in this study (14.9 %) is higher than the overall mortality rate reported for upper gastrointestinal bleeding (5.4 %).[19] This could be related to the higher prevalence of mortality predictors in colorectal patients or more likely is due to the added stress of the index operation.[6] Marmo et al., in

an evaluation of 1,263 patients, introduced predictive factors of mortality in upper gastrointestinal hemorrhage. They reported that in the absence of any risk factors, the mortality rate is 0.7 % and the mortality rate increases to 23.1 % in the presence of two or more predictors.[6]

The overall hospitalization length for patients who underwent colorectal resection was 11 days, and this is lower than the previously reported length of hospital stay for colorectal resection patients in select literature.[20] Kelly et al. with a study of 8,192 patients who underwent colorectal resection between 2002 and 2010 reported a mean hospitalization length of 21 and 14 days, respectively, for patients with emergent and elective admission.[20] Also, we found that the mean length of stay in the hospital is doubled in patients with UGIB.

Utilizing the power of the large NIS database, this study identified significant predictors of postoperative UGIB for colorectal resection operations. These predictors are divided into five subgroups which include patient-specific factors [age, male sex, race (Asian, Pacific Islander, Black, and Hispanic)], comorbidities (chronic peptic ulcer disease, coagulopathy, chronic renal failure,, weight loss, congestive heart failure, diabetes with complication, alcohol abuse, liver disease, and chronic lung disease), procedures (total colectomy and transverse colectomy), pathology (colorectal cancer), admission type (emergent admission), and procedure technique (open surgery).

This study confirms the previously reported risk factors of postoperative UGIB of male sex, liver disease, coagulopathy, chronic renal failure, and history of peptic ulcer as significant risk factors of postoperative UGIB. Our data also confirms the Klebl study which reported diabetes as a risk factor of UGIB[10]; however, the association between diabetes and postoperative UGIB only exists in diabetes with complications, and there is no correlation between postoperative UGIB with diabetes without complication in colorectal patients.

Our data on patient-specific factors shows that an Asian or Pacific Islander man older than 70 years has the highest chance of postoperative UGIB. This is in line with the literature.[11] Our study identified race (Asian or Pacific Islander, Black, and Hispanic) as a predictor of postoperative UGIB most likely due to the large number of patients in the database.

The highest risk of postoperative UGIB in colorectal resection exists in total colectomy procedures followed by transverse colectomy. Perhaps, this can be partially related to the interruption of the blood supply to the stomach and resultant relative ischemia during these two procedures.

The presence of colorectal cancer is a predictor of postoperative UGIB in this study. Using benign colorectal tumor as the reference, this study shows obvious correlation between postoperative UGIB and malignancy, with an odds ratio of 1.59. The risk decreases in benign diseases such as diverticulitis. Patients with risk factors of postoperative UGIB who will have colorectal procedures for malignancy warrant consideration of specific preventive methods of UGIB before surgery.

The most common pathology of UGIB in this study was gastroduodenitis followed by gastric ulcer. Furthermore, amongst patients with previous history of gastric ulcer, the most common source of the UGIB was gastric ulcer and this is in line with the literature.16 Dixon et al., in a review of 409 patients with bile duct obstruction, introduced gastric erosions as the most common site of bleeding.[16] Importantly, our data

shows that the duodenal ulcer as a source of UGIB is a predictor of UGIB mortality (Table 3).

Table 3 Risk-adjusted analysis of mortality of upper gastrointestinal bleeding in colorectal surgery

Sources of upper gastrointestinal bleeding	Frequency	Mortality rate (%)	P value	Odds ratio	95 % Confidence interval
Gastric ulcer	2,593 (27.8 %)	15.8	Reference	Reference	Reference
Gastritis or duodenitis	4,539 (35.1 %)	12.5	$P<0.0001$	0.73	0.64–0.83
Duodenal ulcer	2,018 (15.6 %)	24.1	$P<0.0001$	1.71	1.49–1.97
Esophageal bleeding	1,999 (15.5 %)	10.8	$P<0.0001$	0.64	0.54–0.76
Angiodysplasia of the stomach and duodenum	758 (5.9 %)	7.8	$P<0.0001$	0.44	0.33–0.59
Dieulafoy's lesion of stomach and duodenum	214 (1.7 %)	18.3	$P>0.05$	1.19	0.83–1.71

Our data also shows that emergency admission increases the risk of postoperative UGIB to fivefold. Because of the restriction of our data, we could not distinguish emergent vs. urgent/nonemergent operation in patients with emergency admission; however, there is obvious correlation between emergency admission and postoperative UGIB.

Open surgery is an independent risk factor of postoperative UGIB compared to laparoscopic surgery in colorectal resections. Kang et al., in a nationwide review of laparoscopic surgery, observed that the rates of postoperative pulmonary and urinary complications are lower in laparoscopic colorectal procedures compared to open procedures.[21] According to our data, the chance of postoperative UGIB decreases in laparoscopic procedures is decreased as well.

Age is a predictor of postoperative UGIB in colorectal surgery. Each year increase in age of patient was found to be associated with a 3 % increase rate of postoperative UGIB. In an analysis of the age cutoff points, patients older than 69 years had 2.22 times higher risk of UGIB than patients younger than 69 years. The highest increase in the rate of UGIB exists at the cutoff point of 54 years (OR, 2.49; $P<0.001$).

Based on the study findings, we recommend intensive prophylaxis treatment for UGIB in patients who undergo total colectomy and transverse colectomy procedures, emergently admitted patients, and patients with a history of peptic ulcer disease, CRF, or coagulopathy. The age of 55 years is recommended by this study as the cutoff point to distinguish high risk patients for postoperative UGIB in colorectal resection. Specific considerations for decreasing the risk factors in highrisk patients are recommended when possible. Also, intensive prophylaxis treatment is suggested for patients with multiple risk factors.

Study Limitations

This study is a large retrospective review and is therefore subject to typical inherent biases for retrospective studies such as selection bias. Data in this study was extracted from the NIS database that collects information from over a thousand hospitals and surgeons in the USA, and there is a wide variety in hospital setting and surgeons' expertise that can affect the study. Due to the restriction of the database, some potentially important preoperative risk factors of postoperative UGIB were not included in this study (i.e., glucocorticoid administration, sepsis, intensive care unit hospitalization, and

H. pylori infection).12, 13 Patients cannot be tracked, we do not have data beyond the index hospital admission, and we lack outpatient follow-up data and long-term outcomes. Also, coding errors may exist because of the use of discharge data (ICD-9 codes).22 Mortality rates of patients may be underestimated since the NIS only has information about inhospital mortality and the 30-day mortality rate is unknown. Although an admission may be designated as emergent/emergent, we cannot discern if this equates to an emergent/emergent operation. Despite these limitations, this study is the first to report on postoperative UGIB in colorectal resection procedures specifically in this population subset.

Conclusion

Colorectal resection operations complicated by postoperative UGIB are uncommon (incidence rate of 0.5 %) but carry an associated mortality rate of 14.9 %. We identified 21 significant predictors of UGIB for colorectal resection operations. Specific considerations to decrease risk factors when possible and intensive prophylaxis treatment for UGIB in patients with multiple risk factors are recommended.

Age is an independent predictor of postoperative UGIB following colorectal resection. Total colectomy and transverse colectomy carry a higher relative risk of postoperative UGIB compared to other colorectal procedures. Operation for malignancy is an independent predictor of postoperative UGIB. The most common sources of postoperative UGIB in colorectal resection procedures are erosions in the gastric or duodenal area. Duodenal ulcer as a source of postoperative UGIB is a poor prognostic factor with the highest mortality rate compared to other sources of the postoperative UGIB.

Conflict of Interest The authors declare no potential conflicts of interest.

Financial Disclosure None.

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