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Peptic Ulcer Is the Most Common Cause of Non-Variceal Upper-Gastrointestinal Bleeding (NVUGIB) in China

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Background: This study aimed to discover the common cause of non-variceal upper-gastrointestinal bleeding (NVUGIB) by conducting a multi-center retrospective study from 2008 to 2012.

Material/Methods: Hospitalized patients ages ≥18 years old, from 8 hospitals in China, diagnosed with NVUGIB by endoscopy from 1 January 2008 to 31 December 2012 were enrolled. Questionnaires were developed and a data-entry graphical user interface was designed by using EpiData software.

Results: Total of 2977 hospitalized patients from 8 medical centers were included. A total of 95.47% (2842/2977) of patients were admitted to a general ward, 3.53% (105/2977) were admitted to an emergency ward, and 1.00% (31/2977) were admitted to an intensive care unit. Peptic ulcer remained the most common cause of NVUGIB (73.26%), but there was a declining trend in its constituent ratio, from 2008 to 2012. A total of 14.41% (429/2977) of patients had co-morbid conditions, 92.85% (2764/2977) used proton-pump inhibitors (PPIs) prior to endoscopic treatment, 19.65% (585/2977) underwent emergency endoscopy, and 23.45% (698/2977) received a transfusion of red blood cell suspensions. A total of 5.34% (159/2977) underwent endoscopic therapy, with a treatment rate of 16.9% in high-risk peptic ulcer patients (96/568). A total of 7.69% (237/2977) were administered aspirin, of whom 32.50% (77/237) resumed aspirin intake after gastrointestinal bleeding was controlled. The median length of hospitalization was 8 days (IQR, 5–11) and the mortality rate was 1.71% (51/2977).

Conclusions: Peptic ulcer was still the most common cause of NVUGIB in China. The proportion of patients with high-risk peptic ulcer bleeding who received endoscopic therapy was 16.9%. Only 19.65% of NVUGIB patients underwent emergency endoscopy.

MeSH Keywords: Blood Transfusion • Gastrointestinal Diseases • Non-Variceal Upper-Gastrointestinal Bleeding

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Background

Non-variceal upper-gastrointestinal bleeding (NVUGIB) refers to diseases of the digestive tract above the ligament of Treitz. Studies in Western countries showed that the incidence rate of NVUGIB is 20–60/100 000 and is particularly high among elderly patients with other systemic diseases, with a mortality rate for NVUGIB of about 7–14% [1–4]. Retrospective large-sample studies on the epidemiologic characteristics and clinical therapy status of NVUGIB have been conducted in Western countries. Peptic ulcer is still the primary cause of NVUGIB. The rate of surgery, length of hospitalization, and mortality rate have declined compared with previous years [5,6]. The incidence rate of peptic ulcer has been reduced with the help of oral proton-pump inhibitors (PPIs) and *Helicobacter pylori* eradication therapy. However, NVUGIB remains a common and clinically severe acute disease [7] with a re-bleeding rate of around 10% [8]. The use of anti-platelet agents to prevent cardiovascular and cerebrovascular diseases and the use of non-steroidal anti-inflammatory drugs (NSAIDs) for the treatment of various bone and joint diseases are increasing in parallel with socioeconomic development and the advent of an aging society. Since the incidence rate of upper-gastrointestinal bleeding induced by the use of aspirin, anticoagulants, and NSAIDs is increasing, the proportion of elderly people with comorbid diseases is also increasing. However, the data on this remain unclear in China. Therefore, this study aimed to discover the most common causes of non-variceal, upper-gastrointestinal bleeding (NVUGIB) by conducting a multi-center retrospective study from 2008 to 2012. This study also aimed to understand the epidemiologic characteristics, diagnostic and etiologic make up, endoscopic therapy, re-bleeding rate, rates of surgery and angiographic embolization, in-hospital mortality rate, and length of hospitalization in NVUGIB patients, as well as the other clinical issues.

Material and Methods

Study subjects

A total of 8 hospitals participated, and 2977 hospitalized patients endoscopically diagnosed with NVUGIB from 1 January 2008 to 31 December 2012 were included. The present study was approved by the Ethics Committee of the Chinese PLA General Hospital, Beijing, China.

Definitions

Definition: NVUGIB refers to non-variceal diseases of the digestive tract above the ligament of Treitz, including bleeding of the pancreatic or bile ducts, and bleeding proximal to the anastomosis after gastrojejunostomy. Adherent clots are blood clots that adhere to the surface of an ulcer. Hematemesis refers to vomiting of fresh blood or blood clots. Coffee ground refers to coffee ground vomiting that was confirmed positive by vomit occult blood test. Melena refers to tarry stools confirmed by a physician or nurse. Re-bleeding refers to recurrence of hematemesis, bloody stool, persistent hypotension/tachycardia, and progressive decline in hemoglobin levels after the first endoscopic diagnosis or therapy. Diagnosis by endoscopy includes esophageal ulcer, gastric cystic lesions, ectopic pancreas, gastric mucosal lesions in portal hypertension, duodenal inflammation, Henoch-Schönlein purpura (abdominal), angiodysplasia with hemorrhage, and hemorrhage after endoscopic therapy (various types of bleeding due to endoscopic therapy). Ischemic heart disease (IHD) includes conditions that patients previously had, such as myocardial infarction, angina, and arrhythmias, or coronary artery bypass grafting. Cardiac failure includes cardiac failure Class I, II, III, and IV, as per the New York Heart Association (NYHA) Functional Classification. Chronic obstructive pulmonary disease (COPD) refers to chronic bronchitis and emphysema with persistent airflow limitation determined by pulmonary function tests (PFTs). Cancer includes patients with advanced malignant tumors in various body systems within 12 months after surgery, as well as those whose metastasis cannot be treated with surgery. Renal disease refers to renal failure that had been diagnosed previously. Central nervous system disease refers to patients with a history of cerebral hemorrhage or infarction. Arthritis includes rheumatism/rheumatoid arthritis, osteoarthritis, and gouty arthritis.

Inclusion and exclusion criteria

Inclusion criteria were all hospitalized patients, aged ≥18 years old, diagnosed with NVUGIB by endoscopy (including newly admitted patients and those with NVUGIB occurring during hospitalization), diagnostically confirmed by endoscopy, and with at least 1 of the following clinical symptoms: (1) hematemesis and/or melena, (2) Drainage of coffee grounds or fresh blood in the gastric tube, (3) Positive fecal occult blood test (FOBT), and (4) Presence of varices, but endoscopy confirmed that bleeding was unrelated to varices.

Exclusion criteria were variceal bleeding and lower-gastrointestinal bleeding.

Data processing

EpiData entry software (version 3.1, EpiData Association, Odense, Denmark) was used to convert the questionnaire into a data-entry graphical user interface (GUI) that was consistent with the survey form. The data entry was controlled by two-pass verification on all collected data to ensure the quality of data entered. All collected data were classified and aggregated according to the needs of the survey, and the researchers were

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Table 1. Patient's characteristics.

Variable	Value (n=2,977), % (n)	
Gender		
Male	76.486	(2,277)
Female	23.514	(700)
Age years		
Median (IQR)	55	(40–68)
Mean (SD)	54.6451±14.3418	
Age group distribution		
<60	59.489	(1,771)
60–79	33.557	(999)
≥80	6.953	(207)
Education background		
Illiteracy	4.736	(141)
Primary education	14.108	(420)
Junior middle school education	24.118	(718)
High school graduate	26.402	(786)
Bachelor's degree	12.361	(368)
Master's or Doctoral degree	1.31	(39)
Not recorded	16.963	(505)
Type of ward		
General ward	95.465	(2,842)
Emergency ward	3.527	(105)
ICU	1.007	(30)
Hemoglobin concentration(g/L)		
>101	33.557	(999)
81–100	27.8	(827)
71–80	15.217	(453)
≤70	23.446	(698)
Hemodynamic status		
Normal (BP>100, HR<100)	77.09	(2,295)
Tachycardia only (HR>100)	9.17	(273)
70≤ BP <100	13.369	(398)
50≤ BP <70	0.269	(8)
BP <50	0.1	(3)
Urea mmol/L		
<3.0	4.199	(125)
3.0–6.9	43.87	(1,306)
7.0–11.9	28.720	(855)
12.0–19.9	12.999	(387)
≥20.0	3.325	(99)
Not recorded	6.886	(205)
Median urea (IQR)	6.78	(4.75–10.14)
Medication at presentation		
Aspirin	6.382	(190)
Clopidogrel	0.672	(20)
Aspirin + Clopidogrel	1.579	(47)
Warfarin	0.638	(19)
NSAID	1.108	(33)
LMWH	0.1	(3)
Comorbidity (%)		
IHD	3.964	(118)
Cardiac failure	0.168	(5)
COPD	0.974	(29)
Cancer	2.89	(86)
Renal disease	0.974	(29)
CNS disease	2.284	(68)
Arthritis	0.638	(19)
Two or more Comorbidities	2.519	(75)
Other		
Smoking history	28.96	(862)
History of drinking	16.023	(477)
History of upper gastrointestinal bleeding	12.832	(382)

BP – systolic blood pressure (mm Hg); HR – heart rate/min; LMWH – low molecular weight heparin; NSAID – non-steroidal anti-inflammatory drug.

contacted whenever required for verification and approval of individual data.

Statistical analysis

SPSS software (version 17.0, SPSS, Chicago, IL, USA) was used for all statistical analyses in this study. The characteristics and clinical demographic and epidemiologic features were analyzed by using a descriptive statistical method (mean ± standard deviation (SD), percentage, median, and interquartile range [IQR]). Univariate analysis for risk factors affecting mortality was performed by using the Pearson χ^2 test, and $p<0.05$ variables were incorporated into the multivariate analysis model; clinically significant factors were also incorporated into the multivariate analysis model, even if there was no statistically significant difference. The stepwise logistic regression model was used to perform multivariate analysis of factors affecting mortality, and $p<0.05$ was considered to indicate a statistically significant difference.

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Table 2. Clinical presentation by age group.

Clinical presentation	Age <60 (1,771)		Age 60–79 (999)		Age ≥80 (207)	
	%, (n)		%, (n)		%, (n)	
OB(+)	3.444	(61)	5.205	(52)	3.865	(8)
Melena alone	61.999	(1098)	54.354	(543)	49.758	(103)
Hematemesis alone	10.107	(179)	15.315	(153)	18.841	(39)
Hematemesis & melena	24.280	(430)	24.224	(242)	21.739	(45)
Coffee ground emesis or blood from NG tube	0.169	(3)	0.9	(9)	5.797	(12)

OB(+) – fecal occult blood is positive.

Table 3. Endoscopic diagnoses by age group.

Endoscopic diagnoses	Age <60 (1,771)		Age 60–79 (999)		Age ≥80 (207)	
	%, (n)		%, (n)		%, (n)	
Peptic ulcer	80.632	(1428)	64.965	(649)	50.242	(104)
Malignancy	4.122	(73)	10.11	(101)	9.662	(20)
Esophagitis	4.009	(71)	5.706	(57)	5.314	(11)
Acute gastric mucosal lesions	3.106	(55)	4.104	(41)	10.145	(21)
Mallory-Weiss	2.315	(41)	2.503	(25)	2.899	(6)
Dieulafoy lesions	1.016	(18)	0.9	(9)	0.483	(1)
Anastomotic bleeding	1.863	(33)	3.303	(33)	2.415	(5)
Other	1.073	(19)	5.706	(57)	16.908	(35)
No abnormality found	1.863	(33)	2.703	(27)	1.932	(4)

Results

A total of 8 hospitals participated and 2977 patients were included in this study. The median age of the patients was 55 years old (range, 40–68 years old), the average age was 54.65±14.34 years, and the male: female ratio was 3.25: 1.

Patient characteristics and drug use

Patient characteristics included age distribution, education levels, type of ward, medication history, laboratory tests, hemodynamics, Rockall score, and Blatchford score (Table 1). The median time from the onset of clinical symptoms to hospitalization was 48 h (IQR, 24–72). The proportion of patients administered PPIs prior to endoscopy was 92.85% (2764/2977); 18.95% (564/2977) were administered tranexamic acid to stop bleeding, of whom 11.52% (65/564) had different degrees of coagulation dysfunction. A total 1.24% (37/2977) of patients had a history of erythromycin intake, 0.30% (9/2977) were administered metoclopramide hydrochloride to improve the rate of endoscopic diagnosis, and 1.11% (33/2977) were administered NSAIDs. A total of 237 patients took aspirin prior to treatment, of whom 32.50% (77/237) resumed aspirin intake after the gastrointestinal bleeding was controlled; the average time until the resumption of intake was 25.92±11.31 days (5–60 days). A total of 0.91% (27/277) of the patients used a long-term oral PPI for NSAID prophylaxis and the potential risks of bleeding caused by anti-platelet drugs. The clinical presentations of different age groups are summarized in Table 2.

Diagnosis

A total of 19.65% (585/2977) of patients underwent emergency endoscopy and the median time from gastrointestinal bleeding to gastroscopy was 72 h (36–120 h). The endoscopy waiting time for the patients with peptic ulcer was 3.9±1.2 days. Peptic ulcer was the most common cause of NVUGIB (73.26%). A total of 6.52% (194/2977) of the cases were neoplastic lesions and 3.93% (117/2977) were acute gastric mucosal lesions (Table 3), of whom 19.66% (23/117) used aspirin and 4.27% (5/117) used aspirin and clopidogrel simultaneously.

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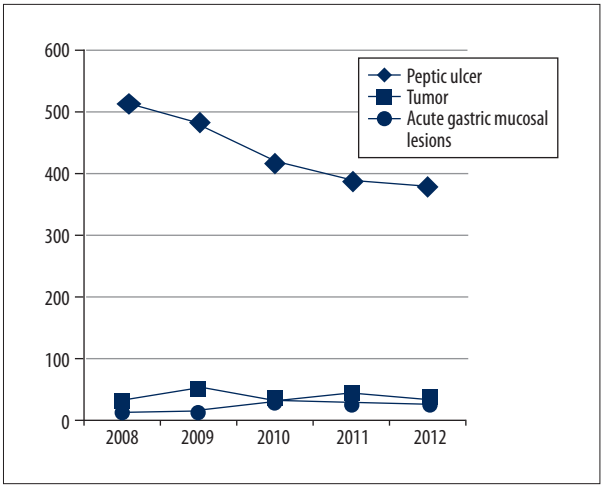

Figure 1. Trends in the main causes of NVUGIB.

The trends of peptic ulcer, tumor, and acute gastric mucosal lesions from 2008 to 2012 (5 years) are shown in Figure 1.

Blood transfusion

A total of 23.45% (698/2977) of patients received a transfusion of red blood cell suspension. Every patient received an average of 5.33±6.53 units of blood transfused. Moreover, the average hemoglobin level for the patients before the transfusion was 65.62±16.30 g/l.

Endoscopic therapy

A total of 5.34% (159/2977) of patients underwent endoscopic therapy, of whom 27.04% (43/159) underwent endoscopic combined therapy (Table 4). A total of 19.08% (568/2977) of patients had high-risk peptic ulcer bleeding (Table 5). A total of 159 patients had adherent clots. Ten patients underwent rinsing and subsequent exposure of basal lesions with physiological saline solution, of whom 2 patients had active ejection of blood, 4 had active errhysis, 1 had a vascular stump, and 3 had a fibrin-covered clean ulcer base. The patients were divided into 3 groups based on endoscopy waiting time: ≤24 h, 24–96 h, and ≥96 h. Our study showed that the frequency of endoscopic therapy in the ≤24 h group was higher than that in the 24–96 h and ≥96 h groups (p<0.05) (Table 6). There was no statistically significant difference in the length of hospitalization between the 3 groups (10.13±11.82, 8.87±7.31, and 9.64±7.33 days, respectively, p=0.92).

Re-bleeding

A total of 2.92% (87/2,977) of patients had re-bleeding. The patients were divided into ≤24 h, 24–96 h, and ≥96 h groups by endoscopy waiting time. Our study showed that the rates of re-bleeding in the ≤24 h group and 24–96 h group were higher than in the ≥96 h group (p<0.05), while there was no statistically significant difference between the ≤24 h group and 24–96 h group (Table 7). A further analysis found that the proportions of high-risk peptic ulcer bleeding in each group of patients with peptic ulcer were 288 (74%), 182 (23%), and 98 (10%), respectively (p<0.05). The average time from re-bleeding to the first endoscopic therapy was 49.61±53.45 h. A total of 4.60% (4/87) of patients were treated with medication and blood transfusion, 12.64% (11/87) of these underwent a second endoscopic treatment, 17.24% (15/87) underwent embolization, and 65.52% (57/87) underwent surgery, while a total of 7 patients (8.05%) died.

Angiographic intervention embolization

The proportion of patients undergoing angiographic embolization was 0.50% (15/2977), of whom 9 were found to have bleeding vessels (including 4 cases of the gastroduodenal artery, 3 of the pancreaticoduodenal artery, 1 of the dorsal pancreatic artery supplying the duodenum, and 1 of the short gastric arteries of the splenic artery) and underwent embolization, with 7 cases of successful hemostasis (77.78%). The 6 patients without a bleeding blood vessel underwent preventive embolization

Table 4. Endoscopic therapy.

Treatment method	n=159 (%)	
Endoscopic drug delivery by aerosol spray for hemostasis	24	(15.09)
Endoscopic injection of 1: 10,000 adrenaline	43	(27.04)
High-frequency electrocoagulation	2	(1.26)
Argon plasma coagulation	11	(6.92)
Hemoclip	36	(22.64)
Endoscopic injection of 1: 10,000epinephrine + thermal coagulation (any of which)	3	(1.89)
Endoscopic injection of 1: 10,000 epinephrine + Hemoclip	37	(23.27)
Endoscopic injection of 1: 10,000 epinephrine + thermal coagulation (any of which) + Hemoclip	3	(1.89)

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Table 5. Endoscopic therapy for high-risk peptic ulcer bleeding.

Forrest classification	No. of patients	Undergoing endoscopic therapy, n (%)
Forrest Ia	106	17 (16.04)
Forrest Ib	179	45 (27.93)
Forrest IIa	106	24 (22.64)
Forrest IIb	177	10 (5.65)

Table 6. The frequency of endoscopic therapy for lesions found at different times to endoscopy.

Time to endoscopy	No. of patients	Treatment frequency, n (%)	*p* Value
≤24 h	585	66 (11.28)	
24–96 h	1,014	36 (3.55)	
≥96 h	1,378	50 (3.63)	0.00

The multiple rate comparison (Scheffe's method), ≤24 h *vs.* 24–96 h, $p<0.05$; ≤24 h *vs.* ≥96 h, $p<0.05$; 24–96 h *vs.* ≥96 h, $p>0.05$.

Table 7. The rate of re-bleeding at different times to endoscopy.

Time to endoscopy	No. of patients	Rebleeding, n (%)	*p* Value
≤24 h	585	36 (6.15)	
24–96 h	1,014	33 (3.25)	
≥96 h	1,378	18 (1.31)	0.00

The multiple rate comparison (Scheffe's method), ≤24 h *vs.* 24–96 h, $p<0.05$; ≤24 h *vs.* ≥96 h, $p<0.05$; 24–96 h *vs.* ≥96 h, $p>0.05$.

that involved the pancreatic artery, hepatic artery-left gastric artery, hepatic artery, left gastric artery, left gastric and right gastroepiploic artery, and gastroduodenal artery, respectively, with 4 cases of successful hemostasis (66.67%).

Surgery

The proportion of patients undergoing surgery was 2.65% (79/2977), with an average age of 56.22±13.82 years, including 72.15% (57/79) male patients, among whom 67.09% (53/79) had tumors, 25.32% (20/79) had hemorrhage uncontrollable by medication or endoscopy, 3.80% (3/79) had vascular malformation, 2.53% (2/79) had uncontrollable bleeding caused by endoscopic therapy, and 1.27% (1/79) had an ectopic pancreas, with a postoperative mortality rate of 5.06% (4/79).

Comorbidities

The proportion of patients with comorbidities was 1.81% (54/2977) (Table 8). Among these comorbidities, 44.44% were pneumonia, 7.41% were cardiovascular events, 7.41% were liver failure, 18.52% were renal failure, 3.7% were stroke, 3.7% were deep vein thrombosis, 1.85% were perforation, 7.41% were pneumonia and renal failure, 1.85% were pneumonia and cardiovascular events, 1.85% were pneumonia and deep vein thrombosis, and 1.85% were cardiovascular events or liver and kidney failure. The results also showed that the pneumonia was the most frequently occurring comorbidity.

The length and costs of hospitalization

The median length of hospitalization was 8 days (IQR, 5–11), while the median cost of hospitalization was RMB 7363.55 (IQR, 4,574.76–12 521.37) and the median cost of endoscopy was RMB 330.00 (IQR, 250–430).

Multivariate analysis of mortality rate and factors associated with mortality

The mortality rate was 1.71% (51/2977), of whom 37.25% (19/51) completed endoscopy within 24 h and 25.49% (13/51) developed comorbidities. According to the results in Tables 9 and 10, the most significant risk factors associated with mortality were: age (p=0.0000), type of ward (p=0.0049), blood pressure level (p=0.0000), comorbidity (p=0.0000), endoscopy waiting time (p=0.0000), and re-bleeding (p=0.0008).

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Table 8. Comorbidities of the patients.

Complication (comorbidity)	n=54 (%)	
Pneumonia	24	(44.44)
Cardiovascular events	4	(7.41)
Liver failure	4	(7.41)
Renal failure	10	(18.52)
Stroke	2	(3.70)
Deep vein thrombosis	2	(3.70)
Perforation	1	(1.85)
Pneumonia and renal failure	4	(7.41)
Pneumonia and cardiovascular events	1	(1.85)
Pneumonia and deep vein thrombosis	1	(1.85)
Cardiovascular events, and liver and kidney failure	1	(1.85)

Table 9. Univariate analyses for mortality.

Variable	No. of patients	Mortality				χ^2 Value	*p* Value
	(n)	No, n (%)		Yes, n (%)			
Gender							
Male	2277	2,240	(98.38)	37	(1.62)		
Female	700	686	(98.00)	14	(2.00)	0.4473	0.5036
Age (years old)							
<60	1771	1,758	(99.27)	13	(0.73)		
60–79	999	978	(97.90)	21	(2.10)		
≥80	207	190	(91.79)	17	(8.21)	62.9121	0.0000
Type of ward							
General ward	2842	2,798	(98.45)	44	(1.55)		
Emergency ward	105	100	(95.24)	5	(4.76)		
ICU	30	28	(93.33)	2	(6.67)	10.6273	0.0049
Hemoglobin (g/l)							
>101	999	986	(98.70)	13	(1.30)		
81–100	827	816	(98.67)	11	(1.33)		
71–80	453	444	(98.01)	9	(1.99)		
≤70	698	680	(97.42)	18	(2.58)	5.0347	0.1693
Blood circulation							
Normal (BP >100, HR <100)	2295	2,268	(98.82)	27	(1.18)		
Tachycardia (HR >100)	273	265	(97.07)	8	(2.93)		
70≤ BP <100	398	384	(96.48)	14	(3.52)		
50≤ BP <70	8	6	(75.00)	2	(25.00)		
BP <50	3	3	(100.00)	0	(0.00)	39.8414	0.0000

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Table 9 continued. Univariate analyses for mortality.

Variable	No. of patients	Mortality		χ^2 Value	*p* Value
	(n)	No, n (%)	Yes, n (%)		
Comorbidity (%)					
Ischemic heart disease	118	114 (96.61)	4 (3.39)		
Heart failure	5	5 (100.00)	0 (0.00)		
COPD	29	28 (96.55)	1 (3.45)		
Tumor	86	77 (89.53)	9 (10.47)		
Kidney disease	29	27 (93.10)	2 (6.90)		
Central nervous system diseases	68	66 (97.06)	2 (2.94)		
Arthritis	19	19 (100.00)	0 (0.00)		
>2 comorbidities	75	67 (89.33)	8 (10.67)		
No comorbidities	2548	2,523 (99.02)	25 (0.98)	91.0814	0.0000
Time to endoscopy					
≤12 h	199	197 (98.99)	2 (1.01)		
12 h < T ≤24 h	386	383 (99.22)	3 (0.78)		
>24 h	2392	2,346 (98.08)	46 (1.92)	3.2269	0.1992
Hemoglobin levels before transfusion					
≤70	449	429 (95.55)	20 (4.45)		
70< Hb ≤90	187	175 (93.58)	12 (6.42)		
>90	62	58 (93.55)	4 (6.45)		
No transfusion	2279	2,264 (99.34)	15 (0.66)	67.9431	0.0000
Rebleeding					
Yes	87	81 (93.10)	6 (6.9)		
No	2890	2,845 (98.44)	45 (1.56)	11.3050	0.0008

BP – blood pressure; Hb – hemoglobin.

Discussion

In this nationwide, multi-center, retrospective study, we developed a preliminary understanding of the status of NVUGIB in China, and identified some issues and differences compared with Western studies. In this survey, the average age of the patients was 54.65±14.34 years old and the proportion of patients aged over 80 years old was 6.95%, which was lower than that of previous studies from the West [6,8–10]. Our study found that more than half of the total patients had middle and high school education levels, more than 95% were admitted to general wards, and 12.83% had a history of upper-gastrointestinal bleeding, which was slightly lower than that reported in Portugal [10]. Clinical symptoms were dominated by melena, which accounted for 58.58% of patients, higher than that reported by Zeitoun et al. [11]. The proportion of patients with a comorbidity was 14.41%, of which ischemic heart disease was the most common complication. In addition, central nervous system diseases and tumors were common comorbidities, and 22.91% of the patients had hemodynamic instability. Our study indicated that 58.45% (1740/2977) of patients had a completed Rockall score and 60.46% (1800/2977) had a Blatchford score. A total of 92.85% (2764/2977) of patients were administered PPIs prior to endoscopic examination. A total of 18.95% (564/2977) were administered tranexamic acid for hemostasis, of whom 11.52% (65/564) had varying degrees of coagulation disorders, while a higher proportion (88.48%) of the remaining patients had normal blood

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Table 10. Multivariate analysis of factors associated with mortality.

Independent variable	OR value	95% confidence interval	p Value
Age (years old)			
<60	1.00		
60–79	2.49	1.180–5.241	0.0166
≥80	11.00	4.799–25.237	0.0000
Type of ward			
General ward	1.00		
Emergency ward	4.70	1.719–12.865	0.0026
ICU	1.78	0.355–8.941	0.4834
Hemoglobin (g/l)			
>101	1.00		
81–100	1.05	0.450–2.450	0.9101
71–80	1.10	0.428–2.805	0.8480
≤70	1.88	0.866–4.060	0.1106
Blood circulation			
Normal (BP >100, HR <100)	1.00		
Tachycardia (HR >100)	0.00	0.000–3.163	0.9638
70≤ BP <100	2.67	1.041–6.866	0.0411
50≤ BP <70	2.81	1.343–5.898	0.0061
BP <50	9.58	1.330–68.958	0.0249
Comorbidity			
No comorbidity	1.00		
1	3.08	1.563–6.076	0.0012
≥2 comorbidities	7.71	3.016–19.699	0.0000
Time to endoscopy			
>24 h	1.00		
≤24 h	0.34	0.180–0.659	0.0013
Rebleeding			
No	1.00		
Yes	3.63	1.358–9.694	0.0101

coagulation. Meanwhile, a total of 237 patients took aspirin before treatment, of whom 32.50% (77/237) resumed aspirin intake after gastrointestinal bleeding was controlled; the average time to resumption of intake was 25.92±11.31 days (5–60 days), which is significantly different from a recent study in Japan [12] showing an average discontinuation period of 4.1±4.0 days for NVUGIB patients taking antithrombotic drugs, and from international consensus [1].

Previous studies [13–15] showed that endoscopy within 12 h did not improve the clinical prognosis. The 2011 Asia-Pacific Consensus [5] recommended a 24-h time frame for endoscopy, but it can be appropriately delayed for patients with severe cardiopulmonary dysfunction. Previous studies [16–18] show that failure to perform an endoscopy within 24 h may increase the mortality rate from 2.5% to 6.6%. Patients who did not undergo endoscopy were mostly aged over 80 years and had more than 3 comorbidities. This study found that 9.65% (585/2977) of patients underwent emergency endoscopy, with a median time from gastrointestinal bleeding to endoscopy of 72 h (36–120 h). We also divided the patients into ≤24 h, 24–96 h, and ≥96 h groups by the time to endoscopy and found that emergency endoscopy did not reduce the rate of re-bleeding. A further analysis found that a high proportion of patients

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in the emergency endoscopy group had high-risk peptic ulcer bleeding (Forrest Ia–IIb), which may be associated with the rate of re-bleeding. A study in Hong Kong [19] showed that the endoscopy waiting time for patients with peptic ulcer bleeding was 0.98±1.8 days, while the endoscopy waiting time in this study was 3.9±1.2 days. The lower proportion of emergency endoscopies and the longer endoscopy waiting time might be associated with the health care system in China, where critically ill patients are mostly concentrated in larger-scale hospitals that often require a longer waiting time for patient assessment and from examination to endoscopy, compared with that in Hong Kong and foreign countries. Peptic ulcer was still the most common cause of NVUGIB (73.26%), much higher than that reported in Western countries [4,20–22], and 61.71% (1346/2181) of patients underwent *H. pylori* testing. The incidence rate of peptic ulcer presented a declining trend each year from 2008 to 2012. The proportion of patients undergoing the transfusion of a red blood cell suspension was 23.45% (698/2977), which was lower than that reported in a previous study [5]. The average hemoglobin level prior to transfusion was 65.62±16.30 g/l. A randomized, controlled trial in Spain showed that a restrictive transfusion (Hb <70 g/l) can reduce the risk of re-bleeding, demand for salvage therapy, and comorbidities, as well as improve the survival rate [23].

A total of 5.34% (159/2977) of patients underwent endoscopic therapy, of whom 27.04% (43/159) underwent combination endoscopic therapy and 27.04% (43/159) only received endoscopic injection of 1: 10 000 adrenaline. The proportion of patients with high-risk peptic ulcer bleeding was 19.08% (568/2977), of whom 16.9% (96/568) underwent endoscopic therapy, which is less than that reported by a study in Portugal [10], while 6.34% (36/568) only received endoscopic injection of 1: 10 000 adrenaline and 4.58% (26/568) underwent combination endoscopic therapy. The treatment of adherent clots on the peptic ulcer remains controversial. In this study, only 6.29% (10/159) of patients received endoscopic lavage, including 7 patients who were found to have lesions and subsequently underwent endoscopic therapy. Hence, the pros and cons still require verification in a large-scale, randomized, controlled trial. Our study shows that 2.65% (79/2977) of patients received surgery, which was consistent with a study in the UK [5]. Such a low rate of surgery is attributed to recent advancements in endoscopic therapy. Surgery is often the last resort, with a higher mortality rate, and the postoperative mortality rate in this study was 5.06% (4/79). The proportion of patients undergoing angiographic embolization was 0.50% (15/2977), with a success rate of 77.78%, and the success rate of preventive embolization was 66.67% (4/6), which was consistent with that reported by Sildiroglu et al. [24]. The relatively low proportion of patients undergoing angiographic embolization is related to the technical requirement for equipment and expertise. A single-center retrospective study [25] showed that patients in the percutaneous intravascular embolization group were older and most had heart disease, compared with those receiving traditional surgery. A study reported by Beggs et al. [26] indicated that angiographic embolization possesses a higher risk of postoperative re-bleeding compared with surgery, but it does not affect the mortality rate.

Our study showed that the rate of re-bleeding was 2.92% (87/2977), lower than that reported in previous studies [8,27]. This might be related to the lower proportion of patients aged over 80 years old in this study. The proportion of patients with comorbidities was only 14.41%. The proportion of patients receiving a blood transfusion was also lower than that reported in previous studies. The study by Restellini et al. [28] showed that blood transfusions lead to an increase in the risk of re-bleeding but are unrelated to mortality. Studies reporting the mechanisms that lead to re-bleeding are rare. Re-bleeding may be caused by the disruption of a hypercoagulable state by a blood transfusion due to the elevation of coagulation factor VIII concentration after gastrointestinal bleeding; additionally, citrate as an anticoagulant may lead to further bleeding [29,30]. Previous studies have rarely focused on comorbidity in NVUGIB, but our study showed that 1.81% (54/2977) of patients developed comorbidities, of which pneumonia was the most common, followed by kidney failure. A previous study in the USA [31] showed that the lengths of hospitalization for patients with and without comorbidities were 4.4 days and 2.7 days, respectively, while the hospitalization cost was USD 5632 (equivalent to RMB 46 182.40 based on the currency exchange rate in 2004) and USD 3402 (RMB 27 896.40), respectively. In this study, the median length of hospitalization was 8 days (IQR, 5–11 days) and the average hospitalization cost was RMB 17 470±51 752. The relative hospitalization cost was inversely proportional to the length of hospitalization, which may be related to differences in the medical pricing system. Our study showed that the mortality rate was 1.71%, which was significantly lower than that reported by previous studies [1–3]. A further analysis indicated that this might be due to a higher proportion of patients aged below 60 years, accounting for nearly 60%. Meanwhile, patients with peptic ulcer also accounted for a higher proportion. Jairath [32] reported that the greater difference in the mortality rates of NVUGIB reported worldwide was mainly due to the different research methods and populations in the studies. Multivariate studies found that age ≥80 years, admission to the emergency ward, systolic blood pressure of 50 mmHg, the presence of 2 or more comorbidities, and re-bleeding led to a significant increase in the mortality risk, while emergency endoscopy can reduce the rate of mortality.

Through this study, we found that NVUGIB exhibits a declining trend in China, but the rate of endoscopic therapy for high-risk peptic ulcer still needs to be improved. The drug discontinuation

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period for patients using anti-platelet drugs while having gastrointestinal bleeding was longer than that in other countries. Patients admitted into the emergency ward have a higher risk of mortality and a lower rate of emergency endoscopy compared with patients admitted into the general wards and ICU. However, the proportions undergoing surgery and angiographic embolization are still low. The present study also has a few limitations. Firstly, we only described the non-variceal upper-gastrointestinal bleeding for the Chinese patients, but not for the other populations, which is also a limitation of this study. Secondarily, we analyzed the statistical results of a multi-center database, and there were a few limitations and bias in the data. Therefore, in a subsequent study, we would adjust the data and avoid the bias. Thirdly, each country has its own health insurance system, as well as cost effectiveness, but we did not discuss this point. We would also consider the health insurance system in a future study.

Conclusions

In China, peptic ulcer was still the most common cause of non-variceal upper-gastrointestinal bleeding (NVUGIB), but there was declining trend in the annual constituent ratio. Therefore, clinicians must suspect peptic ulcer in patients with high-risk factors associated with peptic ulcer.

Conflict of interest

None.

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