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RESEARCH ARTICLE

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Forrest-type IIb increases the risk of rebleeding after endoscopic treatment in patients with Dieulafoy's lesion of the upper gastrointestinal tract

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ABSTRACT

Background: Dieulafoy's lesion (DL) is a rare cause of nonvariceal upper gastrointestinal bleeding (NVUGIB) and represents a significant clinical challenge. This research aimed to identify the potential risk factors contributing to DL rebleeding after endoscopic hemostasis, including patient characteristics and laboratory and endoscopic findings such as the Forrest classification.

Methods: This retrospective study encompassed patients diagnosed with upper gastrointestinal DL who received standard endoscopic hemostasis between April 2007 and June 2024. Patients included in this study were categorized into the rebleeding and non-rebleeding groups. Univariate and multivariate logistic regression analyses were used to identify risk factors for DL rebleeding.

Results: Of the 272 patients included in this study, rebleeding occurred in 46 (16.9%). Multivariate logistic regression demonstrated that Forrest-type IIb lesions (odds ratio [OR] 3.86, 95% confidence intervals [CI] 1.16–12.83, $p=0.027$) and less experienced endoscopists (OR 3.74, 95%CI 1.82–7.66, $p<0.001$) were recognized as independent risk factors for rebleeding of DL in the upper gastrointestinal tract after endoscopic hemostasis. Compared with the non-rebleeding group, patients in the rebleeding group had received more transfusion units, a longer length of hospitalization, and higher rates of intensive care unit (ICU) transfer, embolization or surgery, and mortality ($p<0.005$).

Conclusion: Forrest-type IIb lesions and less experienced endoscopists were independent risk factors for DL rebleeding in the upper gastrointestinal tract after endoscopic hemostasis. More attention should be given to DL presenting as Forrest-type IIb, as rebleeding is often closely associated with a worse clinical prognosis.

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Dieulafoy's lesion; nonvariceal upper gastrointestinal bleeding; forrest classification; rebleeding; risk factor

1. Introduction

Dieulafoy's lesion (DL) is a rare but potentially life-threatening cause of nonvariceal upper gastrointestinal bleeding (NVUGIB), accounting for approximately 2-5% of all cases of acute upper gastrointestinal hemorrhage [1,2]. DL was first recognized and described in stomach as "exulceratio simplex" by George Dieulafoy in 1898 [3,4], and subsequently was also found in other locations including esophagus, duodenum, small intestine, colorectum and bronchus [5–9]. Among them, the most common site for DL is the lesser curvature of the stomach [10]. DL is pathologically characterized by abnormally large-caliber submucosal arteries that fail to taper, as they approach the mucosal surface. Due to the proximity of the arteries to the gastrointestinal lumen, which is separated only by a thin mucosal layer, making them vulnerable to rupture, even minor mucosal erosion can be associated with massive and fatal bleeding that may result in hemodynamic instability [10].

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With advancements in endoscopic techniques, endoscopic therapy has become the first-line treatment for diagnosing and managing DL, offering minimally invasive options for achieving hemostasis [11]. Techniques such as thermal coagulation, mechanical clipping, and injection therapy are commonly employed and have shown a high hemostasis success rate [12,13]. However, even with an initial successful endoscopic intervention, rebleeding remains a significant challenge, with reported rates ranging from approximately 5–30% depending on patient characteristics and therapeutic modalities [1,2,13]. Rebleeding within 30 days after endoscopic treatment of NVUGIB is associated with worse clinical outcomes, including increased mortality, longer hospital stays, and higher healthcare costs [14]. Therefore, identifying risk factors for DL rebleeding in the upper gastrointestinal tract is critical to guide clinicians in risk stratification and contribute to the development of evidence-based therapeutic management for this high-risk patient population.

At present, there are few large sample size studies on the risk factors for DL rebleeding in the upper gastrointestinal tract. Previous studies have suggested that the active stage (Ia–Ib) in the Forrest classification of DL bleeding is positively associated with the occurrence of re-bleeding [2,15]. Therefore, the objective of this study was to investigate the potential risk factors for rebleeding of DL in the upper gastrointestinal tract following endoscopic hemostasis, with a focus on patient characteristics and laboratory and endoscopic findings, such as the Forrest classification.

2. Methods

2.1. Patient selection

This retrospective study, conducted at the First Affiliated Hospital of Nanchang University in China, analyzed the endoscopic records and medical data of patients who underwent standard endoscopic hemostasis for DL in the upper gastrointestinal tract. This study included 312 patients treated between April 2007 and June 2024. Eligibility criteria were defined as follows: (a) patients diagnosed with upper gastrointestinal DL *via* endoscopy and (b) patients who received standard endoscopic treatment for NVUGIB in accordance with recent guidelines, excluding epinephrine injection monotherapy, which is not recommended by these guidelines for its insufficient hemostatic effect [16]. The exclusion criteria were as follows: (a) patients with other coexisting causes of NVUGIB, (b) patients with incomplete clinical records, and (c) patients experiencing initial hemostatic failure for DL. After applying these criteria, 272 patients were included in the final analysis and further classified into 'Rebleeding' group and 'non-Rebleeding' group based on the occurrence of rebleeding after endoscopic hemostasis within 30 days.

2.2. Data collection

The following data were obtained from the patients: (a) patient characteristics: sex, age, smoking and alcohol history, antithrombotics, immunosuppressants and non-steroidal anti-inflammatory drug (NSAIDs) use history, heart failure, liver damage, chief complaint (melena and hematemesis), Charlson comorbidity index (CCI), hemorrhagic shock, gastrointestinal bleeding related score (Rockall, Blatchford and AIMS65 score); (b) laboratory findings: white blood cell count (WBC), hemoglobin (Hb), platelet (PLT), prothrombin time (PT), activated partial thromboplastin time (APTT), international normalized ratio (INR), albumin (Alb), blood urea nitrogen (BUN), creatinine (Cr); (c) endoscopic related findings: use of general anesthesia, Forrest classification (Ia, Ib, IIa, IIb, IIc and III), location of DL (esophagus, stomach, duodenum and remnant stomach), endoscopic hemostasis therapy (injection alone, mechanical therapy alone, thermal coagulation alone and combination), experience of endoscopist (higher and less) and the timing of endoscopic hemostasis; (d) clinical outcomes: transfusion, intensive care unit (ICU) transfer, embolization or surgery, length of hospitalization and mortality rate. The research protocol was conducted in compliance with the guidelines outlined in the Declaration of Helsinki, and approved by the Ethics Committee of the First Affiliated Hospital of Nanchang University, with the approval number 2024-094. Informed consent for study participation was waived by the Ethics Committee of the First Affiliated Hospital of Nanchang University due to the retrospective and anonymous design of the study.

2.3. Dieulafoy's lesion diagnosis and management

The diagnostic criteria for DL based on endoscopic findings were defined as follows [2,13]: (a) active arterial pulsation or spurt originating from the surrounding normal mucosa or minute mucosal defects; (b) visible protrusion of blood vessels within the normal-appearing mucosa or minor mucosal defects, with or without active bleeding; and (c) fresh and densely adherent clots punctate attached to the normal mucosa or tiny mucosal defects. Written informed

consent for the endoscopic procedures was obtained from all patients before the endoscopic procedures in accordance with standard clinical practice.

Upon the identification of DL, the endoscopists determined the method of endoscopic hemostasis, which included monotherapy with injection, mechanical therapy, thermal coagulation, or a combination of these methods [17]. For Forrest-type IIb lesions, whether to remove the adherent blood clot were determined by endoscopists. Following endoscopic hemostasis, all patients received intravenous proton pump inhibitors (PPIs) (omeprazole and pantoprazole) at an initial dose of 80 mg, followed by continuous infusion at 8 mg/h for a minimum of 72 h. In the event of rebleeding, the need for endoscopic intervention or surgical treatment was determined based on the patient's clinical condition. Additionally, if required, patients were transferred to the intensive care unit (ICU) for further management.

2.4. Definitions

Initial hemostatic failure of DL was defined as persistent active bleeding despite successful initial endoscopic hemostasis or the presence of symptomatic evidence of ongoing active bleeding within 12 h of the initial endoscopic procedure [15,18]. Rebleeding was defined as the manifestation of one or more clinical symptoms occurring within 12 h to 30 days after the initial endoscopic intervention for hemostasis [18,19]: (a) hematemesis or the presence of bloody aspirate in a nasogastric tube; (b) melena or hematochezia occurring after stool color had normalized; (c) hemodynamic instability, defined as a heart rate ≥ 100 beats per minute or systolic blood pressure ≤ 90 mmHg, observed one hour after achieving initial hemodynamic stabilization, in the absence of other identifiable causes; (d) a reduction in hemoglobin levels exceeding 2 g/dL following two consecutive stable measurements; (e) a persistent decline in hemoglobin levels of more than 3 g/dL within 24 h, accompanied by melena or hematochezia; (f) evidence of recurrent bleeding from a previously treated DL, as confirmed by a second endoscopic evaluation. CCI scores were determined by evaluating the presence of various comorbid conditions in patients [20]. Hemorrhagic shock was defined as the presence of tachycardia, characterized by a heart rate ≥100 beats per minute or hypotension, indicated by a systolic blood pressure ≤90 mmHg [19]. General anesthesia was determined by anesthesiologists and endoscopists after assessing the patient's condition and considering the actual situation. The Forrest classification of DL was determined as follows [21]: (a) spurting bleeding (Forrest Ia); (b) oozing bleeding (Forrest Ib); (c) non-bleeding visible vessel (Forrest IIa); (d) adherent clot (Forrest IIb); (e) flat pigmented spot on the base (Forrest IIc); and (f) clean ulcer base (Forrest III). The experience of endoscopists was determined by their professional titles at our center. Endoscopists with senior professional titles were classified as highly experienced, whereas those with intermediate or junior titles were categorized as less experienced. The timing of endoscopic hemostasis was defined as the interval between patient admission and the initial endoscopic intervention [22].

2.5. Outcome assessment

The primary outcome of this study was to determine the potential risk factors associated with DL rebleeding in the upper gastrointestinal tract following endoscopic hemostasis. The secondary outcome was to evaluate and compare the clinical outcomes between patients with upper gastrointestinal DL with and without rebleeding.

2.6. Statistical analysis

Categorical variables were expressed as frequencies and percentages and analyzed using either the chi-square test or Fisher's exact test, as appropriate. Continuous variables that followed a normal distribution were presented as mean ± standard deviation (SD) and compared using Student's t-test. Non-normally distributed continuous variables are presented as median with interquartile range (IQR) and analyzed using the Mann–Whitney *U* test.

Based on the occurrence of rebleeding within 30 days, all enrolled patients were classified into two groups: rebleeding and non-rebleeding. Univariate analysis was performed to compare the differences between the two groups. Furthermore, multivariate logistic regression was conducted to identify independent risk factors associated with DL rebleeding in the upper gastrointestinal tract following endoscopic hemostasis. Variables associated with DL rebleeding ($p < 0.05$) in the univariate analysis were included in the multivariate logistic regression analysis to identify the independent risk factors that were most predictive of DL rebleeding. The results are expressed as odds ratios (OR) with 95% confidence intervals (CI) to quantify the degree of risk associated with each risk factor. A two-sided $p < 0.05$ was considered statistically significant. All statistical analyses were performed using the R software version 4.1.0 (www.r-project.org) and SPSS software version 25.0 (IBM, Chicago, IL, USA).

3. Results

3.1. Baseline characteristics of patients and lesions

We retrospectively analyzed 312 patients with DL who underwent standard endoscopic hemostasis at our center between April 2007 and June 2024. After excluding 40 patients based on the predefined exclusion criteria, 272 patients were ultimately included in the analysis (Figure 1). The baseline patient characteristics are shown in Table 1. Among the 272 patients included in the study, the mean age was 55.1 ± 17.6 years, with a predominance of male patients (79.8%). There were 82 (30.2%) patients were smokers, and 79 (29.0%) patients were alcohol users. Most patients (61.0%) presented with hematemesis and melena as chief symptoms upon

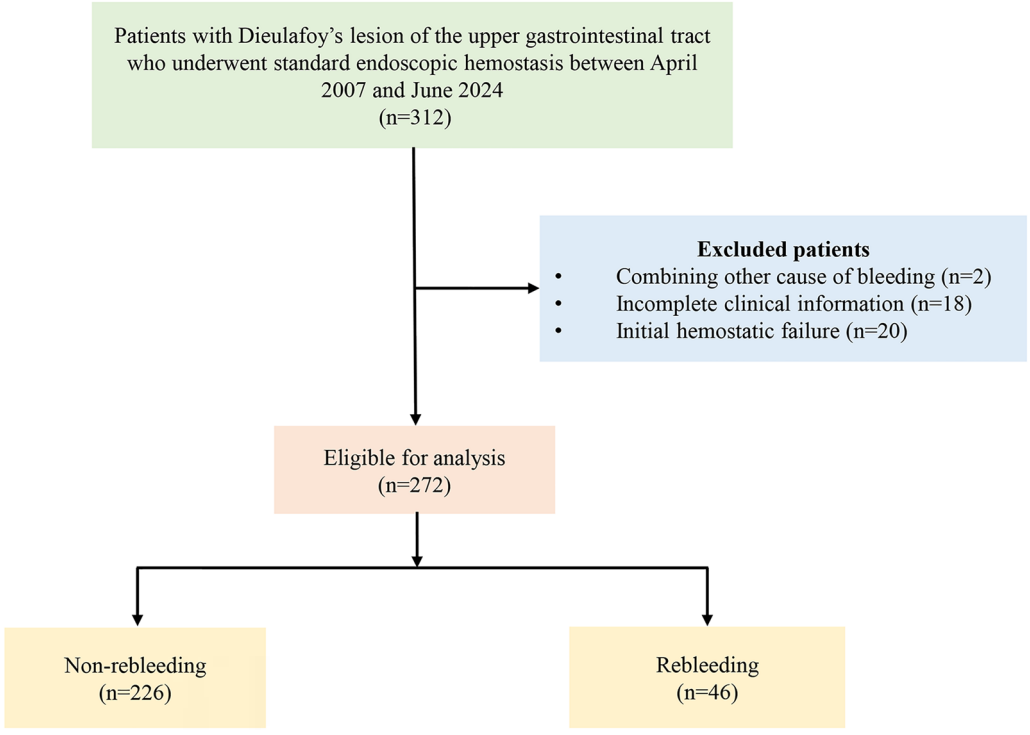

Figure 1. The flowchart of patients included in this study.

Table 1. Clinical characteristics between non-rebleeding and rebleeding groups.

Variables	All subjects (*N* = 272)	Non-rebleeding (*N* = 226)	Rebleeding (*N* = 46)	*P* value
Sex (*n* [%])				0.227
Male	217 (79.8)	183 (81.0)	34 (74.0)	
Female	55 (20.2)	43 (19.0)	12 (26.1)	
Age (years), (mean ± SD)	55.1 ± 17.6	54.2 ± 17.7	59.8 ± 16.1	0.047*
Smokers (*n* [%])	82 (30.2)	68 (30.1)	14 (30.4)	0.963
Alcoholics (*n* [%])	79 (29.0)	68 (30.1)	11 (23.9)	0.400
Medication history (*n* [%])				
Use of antithrombotics	19 (7.0)	15 (6.6)	4 (8.7)	0.856
Use of immunosuppressants	2 (0.7)	2 (0.9)	0 (0.0)	1.000
Use of NSAIDs	10 (3.7)	8 (3.5)	2 (4.7)	1.000
Heart failure (*n* [%])	3 (1.1)	3 (1.3)	0 (0.0)	1.000
Liver damage (*n* [%])	14 (5.2)	13 (5.7)	1 (2.3)	0.592
Chief complaint (*n* [%])				0.213
Melena	81 (29.8)	70 (31.0)	11 (23.9)	
Hematemesis	25 (9.2)	23 (10.2)	2 (4.4)	
Both	166 (61.0)	133 (58.8)	33 (71.7)	
CCI, (mean ± SD)	2.5 ± 1.8	2.4 ± 1.7	3.2 ± 2.1	0.007*
Hemorrhagic shock (*n* [%])	93 (34.2)	77 (34.1)	16 (34.8)	0.926
Rockall score ≥ 5 (*n* [%])	140 (51.5)	112 (49.6)	28 (60.9)	0.162
Blatchford score ≥ 6 (*n* [%])	254 (93.4)	210 (92.9)	44 (95.7)	0.723
AIMS65 score ≥ 2 (*n* [%])	104 (38.2)	79 (35.0)	25 (54.4)	0.014*

SD: standard deviation; NSAIDs: non-steroidal anti-inflammatory drugs; CCI: Charlson Comorbidity Index.
*P-value < 0.05.

Table 2. Laboratory and endoscopic related findings between non-rebleeding and rebleeding groups.

Variables	All subjects ($N=272$)	Non-rebleeding ($N=226$)	Rebleeding ($N=46$)	P value
Laboratory findings				
WBC $\times 10^9$/L, (mean ± SD)	9.2 ± 4.8	9.0 ± 4.9	9.9 ± 4.4	0.247
Hb (g/L), (mean ± SD)	78.8 ± 24.6	80.5 ± 25.0	70.1 ± 20.7	0.009*
PLT < 100×10^9/L (n [%])	47 (17.3)	40 (17.7)	7 (15.2)	0.685
PT (s), (mean ± SD)	13.3 ± 9.2	13.3 ± 10.1	13.38 ± 2.01	0.931
APTT (s), (mean ± SD)	28.8 ± 10.4	28.6 ± 10.2	29.81 ± 11.52	0.470
INR, (mean ± SD)	1.2 ± 1.1	1.2 ± 1.2	1.16 ± 0.17	0.903
Alb (g/L), (mean ± SD)	31.3 ± 7.1	31.9 ± 7.0	28.3 ± 7.0	0.002*
BUN (mmol/L), (mean ± SD)	11.4 ± 8.9	10.9 ± 8.0	13.4 ± 12.4	0.192
Cr > 97 umol/L (n [%])	54 (19.9)	42 (18.6)	12 (26.1)	0.245
General anesthesia (n [%])	126 (46.3)	109 (48.2)	17 (37.0)	0.162
Forrest classification (n [%])				0.043*
Ia	56 (20.6)	45 (19.9)	11 (23.9)	
Ib	104 (38.2)	85 (37.6)	19 (41.3)	
IIa	87 (32.0)	79 (35.0)	8 (17.4)	
IIb	25 (9.2)	17 (7.5)	8 (17.4)	
Lesion location (n [%])				0.252
Esophagus and stomach	169 (62.1)	144 (63.7)	25 (54.4)	
Duodenum	58 (21.3)	44 (19.5)	14 (30.4)	
Remnant stomach	45 (16.6)	38 (16.8)	7 (15.2)	
Endoscopic hemostasis therapy (n [%])				0.603
Injection alone	43 (15.8)	35 (15.5)	8 (17.4)	
Mechanical therapy alone	116 (42.7)	95 (42.0)	21 (45.6)	
Thermal coagulation alone	3 (1.1)	2 (0.9)	1 (2.2)	
Combination therapy	110 (40.4)	94 (41.6)	16 (34.8)	
Experience of endoscopist (n [%])				< 0.001*
Higher	179 (65.8)	159 (70.4)	20 (43.5)	
Less	93 (34.2)	67 (29.6)	26 (56.5)	
Timing of endoscopic hemostasis (n [%])				0.847
≤24 h	174 (64.0)	144 (63.7)	30 (65.2)	
>24 h	98 (36.0)	82 (36.3)	16 (34.8)	

SD: standard deviation; WBC: white blood cell count; Hb: hemoglobin; PLT: platelet; PT: prothrombin time; APTT: activated partial thromboplastin time; INR: international normalized ratio; Alb: albumin; BUN: blood urea nitrogen; Cr: creatinine.
*P-value < 0.05.

admission. The mean CCI scores was 2.5 ± 1.8, and 93 (34.2%) patients experienced hemorrhagic shock upon admission. Regarding gastrointestinal bleeding risk scores, 140 (51.5%) cases had Rockall scores ≥ 5, 254 (93.4%) cases had a Blatchford score ≥ 6, and 104 (38.2%) cases had an AIMS65 score ≥ 2.

Baseline characteristics of the laboratory and endoscopic findings are presented in Table 2. Laboratory findings revealed a mean Hb level of 78.8 ± 24.6 g/L, with 47 (17.3%) patients exhibiting PLT < 100×10^9/L. Endoscopic hemostasis was performed under general anesthesia in 126 patients (46.3%). Furthermore, DL were classified as Forrest Ia, Ib, IIa, and IIb in 20.6%, 38.2%, 32.0%, and 9.2% of cases, respectively, while Forrest IIc and III were not found during the research. In addition, DL in the esophagus and stomach accounted for the majority (62.1%) of cases, and mechanical therapy alone and combined therapy were the main endoscopic hemostatic treatments, accounting for 42.7% and 40.4%, respectively. Endoscopic hemostasis was performed by endoscopists with more experience in 179 (65.8%) patients, and 174 (64.0%) patients received hemostasis within 24 h of admission.

3.2. Risk factors for rebleeding of Dieulafoy's lesion

Among the 272 patients, rebleeding within 30 days occurred in 46 (16.9%). To identify the potential risk factors for rebleeding of the DL in the upper gastrointestinal tract after endoscopic hemostasis, we compared the rebleeding and non-rebleeding groups in Tables 1 and 2. Patients in the rebleeding group were older (59.8 vs. 54.2 years, $p=0.047$), had higher CCI scores (3.2 vs. 2.4, $p=0.007$), and had a higher rate of AIMS65 score ≥ 2 (54.4% vs. 35.0%, $p=0.014$) (Table 1). In terms of laboratory and endoscopic related findings (Tables 2), patients in rebleeding group had lower Hb levels (70.1 vs. 80.5 g/L, $p=0.009$), lower Alb levels (28.3 vs. 31.9 g/L, $p=0.002$) and a higher rate of less experienced endoscopists (56.5% vs. 29.6%, $p<0.001$). Moreover, the difference in the Forrest classification between the two groups was statistically significant ($p=0.043$).

According to the identified potential risk factors, the variables with statistical differences were subsequently entered into a multivariate logistic regression analysis (Table 3). Among these variables, Forrest-type

Table 3. Multivariate analysis of risk factors for rebleeding of DL after endoscopic hemostasis.

Variables	B	OR	95% CI	*P* value
Age (years)	−0.01	0.99	0.95–1.02	0.427
CCI	0.23	1.25	0.95–1.65	0.111
AIMS65 score ≥ 2	0.42	1.52	0.67–3.44	0.317
Hb (g/L)	−0.01	0.99	0.97–1.01	0.536
Alb (g/L)	−0.06	0.94	0.88–1.00	0.057
Forrest classification				
Ia	–	–	–	ref
Ib	0.16	1.18	0.48–2.90	0.725
IIa	−0.47	0.62	0.22–1.77	0.374
IIb	1.35	3.86	1.16–12.83	0.027*
Experience of endoscopist (Less)	1.32	3.74	1.82–7.66	< 0.001*

DL: Dieulafoy's lesion; CCI: Charlson Comorbidity Index; Hb: hemoglobin; Alb: albumin.
*P-value < 0.05.

Table 4. Clinical outcomes between non-rebleeding and rebleeding groups.

Variables	All subjects (N = 272)	Non-rebleeding (N = 226)	Rebleeding (N = 46)	*P* value
Transfusion units, median (IQR)	3.5 (0.0, 7.6)	2.0 (0.0, 5.9)	10.0 (6.0, 18.0)	<0.001*
ICU transfer (n [%])	12 (4.4)	4 (1.8)	8 (17.4)	<0.001*
Embolization or surgery (n [%])	18 (6.6)	0 (0.0)	18 (39.1)	<0.001*
Hospitalization (d), median (IQR)	8.0 (6.0, 12.0)	8.0 (6.0, 10.0)	13.5 (11.0, 19.5)	<0.001*
Mortality (n [%])	7 (2.6)	3 (1.3)	4 (8.7)	0.018*

IQR interquartile range; *ICU* intensive care unit standard deviation.
*P value < 0.05.

IIb lesions (OR 3.86, 95%CI 1.16–12.83, $p = 0.027$) and less experienced endoscopists (OR 3.74, 95%CI 1.82–7.66, $p < 0.001$) were evaluated as independent risk factors for rebleeding of DL in the upper gastrointestinal tract after endoscopic hemostasis.

3.3. Clinical outcomes between rebleeding and non-rebleeding groups

To further understand the importance of exploring risk factors for DL rebleeding, we compared the clinical outcomes of patients with and without rebleeding. As shown in Table 4, compared with patients without rebleeding, patients in the rebleeding group received more transfusion units (10.0 vs. 2.0, $p < 0.001$), longer length of hospitalization (13.5 vs. 8.0 d, $p < 0.001$), and higher rates of ICU transfer (17.4% vs. 1.8%, $p < 0.001$), embolization or surgery (39.1% vs. 0.0%, $p < 0.001$), and mortality (8.7% vs. 1.3%, $p = 0.018$).

4. Discussion

As a rare and life-threatening cause of NVUGIB, it is essential to identify high-risk patients with upper gastrointestinal DL who are prone to rebleeding to prevent adverse clinical prognosis. To the best of our knowledge, this study represents the largest sample size to date to investigate the risk factors for rebleeding within 30 days of DL in the upper gastrointestinal tract after endoscopic hemostasis. Moreover, Forrest-type IIb lesions and less experienced endoscopists were identified for the first time as independent risk factors for DL rebleeding.

Characterized by arterial bleeding, patients with NVUGIB due to DL have a rebleeding rate nearly four times higher than that of patients with peptic ulcer-related NVUGIB [2]. Unlike typical peptic ulcers, DL typically does not present with a large, visible ulcer but instead involves a small arterial remnant that can bleed even in the absence of an obvious ulceration [1]. This makes it harder to pinpoint the bleeding source during hemostasis, especially when a large amount of blood clots and fresh blood obscure the precise localization of the bleeding vessel [2,23]. As a result, accurate identification and treatment are challenging, potentially leading to higher rebleeding rates compared to standard ulcer bleeding. In this study, the incidence of DL rebleeding within 30 days after endoscopic hemostasis was 16.9%, which is consistent with the incidence proposed in previous studies [2,13,24]. A few previous studies have recognized some factors associated with an increased risk of rebleeding in DL, such as Forrest-type Ia-Ib lesions, NSAIDs use, anticoagulant use, injection alone therapy, high levels of WBC or PT, and end-stage renal disease and diabetes [1,2, 15,24].

In 2009, Lim et al. conducted a retrospective study of 44 patients with DL and revealed that the active stage (Ia-Ib) in the Forrest classification of DL bleeding was a risk factor for rebleeding within 30 days in DL patients [15]. However, only six patients in this study experienced rebleeding, and the identification of risk factors for rebleeding of DL was only based on the comparison between the rebleeding and non-rebleeding groups, without a multivariate regression analysis. In contrast to this previous study, our study identified Forrest-type IIb as an independent risk factor for rebleeding after endoscopic hemostasis in DL.

The Forrest classification has been widely employed in the assessment of peptic ulcer bleeding, providing a system for predicting the risk of rebleeding and guiding therapeutic interventions [25]. Among the various Forrest classifications (III to Ia), Forrest-type Ia, Ib,

and IIa were recognized as high-risk rebleeding stigmata and generally require an emergency endoscopic hemostasis. Current guidelines recommend the following endoscopic hemostatic techniques for high-risk stigmata, involving mechanical methods (e.g. clips), injection therapies (e.g. sclerotherapy, epinephrine), and thermocoagulation (e.g. argon plasma coagulation), either as monotherapy or in combination. Among them, the use of epinephrine injection as a monotherapy is not recommended [16,17]. However, Forrest-type IIb, which refers to a peptic ulcer covered by an adherent blood clot, presents a particular controversy in endoscopic management [26–28]. Many previous studies have also classified Forrest-type IIb lesions as high-risk ulcers for rebleeding [29–31]. The blood clot adhering to the surface of the peptic ulcer always obscures the endoscopist's observation of the ulcer itself, thereby complicating the selection of appropriate endoscopic treatment. At present, there were no clear recommendation regarding the use of endoscopic or medical treatments for patients with Forrest-type IIb lesions in cases of peptic ulcer bleeding [16,17,32]. Some researchers support that endoscopic treatment in these patients would be beneficial, arguing that the adherent blood clot may conceal underlying lesions that require intervention and potentially lead to adverse outcomes [26–28,33]. However, other experts caution against endoscopic treatment in such patients, as they believe that attempting to remove the clot may precipitate significant hemorrhage [31,34]. In our center, most patients did not undergo clot removal to avoid the risk of active bleeding following the clot removal. Additionally, Forrest-type IIc and III stigmata do not typically require necessitate endoscopic hemostasis, as they are associated with a low risk of adverse outcomes [17].

Compared with bleeding caused by peptic ulcers, arterial hemorrhage associated with DL exhibits a significantly higher risk of rebleeding, which makes endoscopic hemostasis more necessary for effective management. As DL bleeding has been recognized as a high-risk hemorrhage [16], all patients in our study who presented with DL received standard endoscopic hemostasis. Forrest-type IIb lesions were identified as independent risk factors for DL rebleeding after endoscopic hemostasis. We hypothesize that the underlying reasons may be as follows: On one hand, when DL was classified as Forrest-type IIb during endoscopic hemostasis, the blood clot that adhered to the lesion was not entirely removed, as endoscopists often performed hemostasis with the blood clot still attached to the lesion because of concerns that removing it might trigger severe active bleeding. This may result in inaccurate identification of the bleeding site and compromise the effectiveness of hemostasis. DL bleeding is typically defined as severe arterial bleeding without the presence of large peptic ulcers. Consequently, active bleeding often results in significant blood accumulation within the cavity, complicating accurate localization of the bleeding site compared with ulcer-related bleeding. Therefore, these factors may contribute to a higher rebleeding rate in DL patients classified as Forrest-type IIb than in those with Forrest-type Ia-IIa, which is considered to be a more active stage for peptic ulcer bleeding.

Previous study demonstrated that less experience of endoscopists was an important independent risk factor for rebleeding after hemostasis of NVUGIB caused by ulcers, except DL, Mallory-Weiss tears, and malignant ulcers [35]. Experienced endoscopists are more skilled at identifying bleeding sources, selecting appropriate hemostatic techniques, and ensuring complete hemostasis, thus reducing rebleeding risk. In contrast, less experienced endoscopists may face challenges, leading to incomplete hemostasis and higher rebleeding rates. However, Mohammed et al. reported that endoscopist experience did not affect the clinical prognosis of patients with acute upper gastrointestinal bleeding caused by ulcers and varices [36]. At present, there has been no research investigating the relationship between the experience of endoscopists and DL rebleeding. In this study, we found that less experience of endoscopists was an independent risk factor for rebleeding within 30 days after endoscopic hemostasis. As an arterial hemorrhage, endoscopic hemostasis in DL cases presents significant challenges for endoscopists. Among less experienced endoscopists, insufficient understanding of DL coupled with the lack of hemostasis experience may lead to it becoming a risk factor for DL rebleeding.

Therefore, for DL classified as Forrest-type IIb, or in cases where hemostasis is performed by less experienced endoscopists, several measures might be considered to address these elevated risk factors and prevent rebleeding. In the Forrest classification of peptic ulcers, the risk of rebleeding generally decreases from Forrest-type Ia to IIb. However, this study suggests that in DL, the rebleeding risk for Forrest-type IIb may be higher than anticipated. This highlights the need for clinicians and endoscopists to remain highly vigilant when encountering Forrest-type IIb DL, as these cases may carry an increased risk of rebleeding. Emphasis should be placed on achieving high-quality initial endoscopic hemostasis to minimize this risk. Furthermore, close post-endoscopy monitoring is essential to promptly detect and manage potential

rebleeding episodes, thereby ensuring optimal patient outcomes. For less experienced endoscopists, additional training, supervision during complex cases, and adherence to standardized treatment protocols can improve outcomes. When a less experienced endoscopist encounters a DL and performs hemostatic intervention, having a higher experienced endoscopist present for guidance and oversight may help enhance procedural safety and effectiveness. Furthermore, second-look endoscopy within a short timeframe (e.g. 24–48 h) may be beneficial in high-risk cases [37].

In this study, the remnant stomach was analyzed separately due to its distinct characteristics. Previous studies have indicated higher rebleeding rates for ordinary ulcers in the remnant stomach, often requiring interventional procedures rather than endoscopic hemostasis [38,39]. Altered vascular anatomy from surgery may increase the risk of rebleeding, particularly in DL, which involve submucosal arteriovenous malformations. However, our study did not identify the remnant stomach as a risk factor for rebleeding in DL. We hypothesize that DL are primarily associated with congenital vascular abnormalities, whereas vascular changes in the remnant stomach result from surgical alterations. Further research is needed to explore this relationship in greater detail. Moreover, although cardiac, liver, and renal insufficiency, as well as the use of anticoagulants, NSAIDs, and steroids, have generally been considered significant contributors to rebleeding in various clinical studies [40–43], none of these factors were identified as significant risk factors for rebleeding in DL in our study. This may be due to the limited sample size, which reduced statistical power, and the potential variability in the function management of these factors across patients. Additionally, careful management of these factors in our cohort may have mitigated their impact on rebleeding risk. Larger, more homogenous studies are needed to further investigate these relationships.

The limitations of this study include potential biases inherent to retrospective analyses and the limited generalizability of findings due to the single-center design. Furthermore, the number of cases involving esophageal DL was relatively small compared to gastric, duodenal and remnant stomach DL, which may limit the statistical power and robustness of conclusions drawn for analyzing esophageal cases as a separate group. Hence, further multicenter studies with larger cohorts of esophageal DL are necessary to confirm and expand upon our findings. Finally, the majority of patients with Forrest-type IIb DL did not underwent blood clot removal to avoid the high-risk of active bleeding. Thus, this study was difficult to assess the difference in rebleeding rates between patients who had adherent blood clots removed and those who did not. Future research should focus on the prognosis of Forrest-type IIb DL patients with and without adherent clot removal to better understand its potential impact on rebleeding rates.

5. Conclusion

In conclusion, Forrest-type IIb lesions and less experienced endoscopists were identified as independent risk factors for DL rebleeding in the upper gastrointestinal tract after endoscopic hemostasis, and patients with DL rebleeding had worse clinical outcomes. The early identification and treatment of these risk factors can play a crucial role in preventing the recurrence of bleeding in patients with DL and improving their clinical prognosis. In the future, multicenter prospective clinical studies with larger sample sizes are needed to further validate these findings.

Ethics statement

The research protocol was conducted in compliance with the guidelines outlined in the Declaration of Helsinki, and approved by the Ethics Committee of the First Affiliated Hospital of Nanchang University. Informed consent to participate was waived by the Ethics Committee of the First Affiliated Hospital of Nanchang University due to the retrospective and anonymous design of the study.

Authors contributions

J.Y.Q. Y.H.X. and Q.P.O. collected the data, analyzed the relevant information, and drafted the manuscript. L.P.W. R.Y.D. Y.H. and Z.Z.Y. contributed to statistical analysis and manuscript revision. X.L.P. and X.S. managed the patients clinically. X.L.P. and Y.X.Z. designed the study, critically revised the manuscript, and approved the final submission. All authors have contributed to the manuscript and approved the submitted version.

Disclosure statement

No potential conflict of interest was reported by the author(s)

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Data availability statement

The data supporting the findings of this study are available from the corresponding author (Y.X.Z.) upon reasonable request.

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