

ORIGINAL ARTICLE

Values of Blood Coagulation Parameters in Distinguishing Esophagogastric Variceal Bleeding from Peptic Ulcer Bleeding

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ABSTRACT

Background: Esophagogastric variceal bleeding (EGVB), manifested with similar symptoms of hematemesis and/or melaena, is often difficult to differentiate from peptic ulcer bleeding (PUB). It remains unclear whether blood coagulation parameters can be used to distinguish between EGVB and PUB.

Methods: A total of 37 EGVB patients (EGVB group) and 89 cases with PUB (PUB group), were enrolled for final analysis retrospectively. The levels of coagulation parameters, including prothrombin time (PT), activated partial thromboplastin time (APTT), Fibrinogen, and D-dimer, were tested in the emergency department and compared between the two groups. Student's *t*-test was adopted for comparing the mean. Model discrimination was evaluated by using the area under the receiver operating characteristic curve (AUC).

Results: Compared with PUB group, PT, APTT, and D-dimer were significantly increased, while fibrinogen was significantly decreased in EGVB group (all $p < 0.01$); moreover, binary logistic regression analysis adjusted for covariate showed that PT, APTT, fibrinogen, and D-dimer remained independent risk factors for predicting EGVB; next, the AUC in distinguishing EGVB from PUB were 0.843, 0.725, 0.766, and 0.821 for PT, APTT, fibrinogen, and D-dimer, respectively; finally, the cutoff values (specificity, sensitivity, and Youden index) in distinguishing EGVB from PUB were 12.9 s (80.9%, 78.4%, 0.593) for PT, 25.1 s (68.5%, 78.4%, 0.469) for APTT, 1.99 g/L (67.4%, 75.7%, 0.431) for fibrinogen, and 0.31 mg/L (75.3%, 78.4%, 0.537) for D-dimer, respectively.

Conclusions: PT, APTT, fibrinogen, and D-dimer, useful and potential biomarkers in distinguishing EGVB from PUB, can demonstrate accurate and reliable diagnostic values.

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KEYWORDS

coagulation, peptic ulcer bleeding, EGVB, PT, D-dimer

INTRODUCTION

Upper gastrointestinal bleeding (UGIB), defined as intraluminal bleeding from an intestinal source originating proximal to the ligament of Treitz, is a common reason for presentation to the emergency department (ED) [1]. It was estimated that annual incidence of UGIB was approximately 84 - 160 cases per 100,000 adults in European populations, with incidence highest reported among men, lower socioeconomic groups and the elder-

ly [2]. In the United States, over 300,000 hospital admissions annually are due to patients with UGIB [3]. The hospital mortality of patients with UGIB is approximately 10% - 14% and has not changed over half a century [4].

UGIB results from a variety of conditions varying in severity from mild and asymptomatic to imminently life-threatening [5]. Peptic ulcer bleeding (PUB) is the most common cause of UGIB, responsible for about 50% of all cases [6,7], followed by esophagogastric variceal bleeding (EGVB) with a percentage of around 15% [8,9]. EGVB, manifested with similar symptoms of hematemesis and/or melaena, is often difficult to differentiate from PUB. Currently, endoscopic evaluation remains the gold standard for distinguishing between EGVB and PUB [10-13]. But it is not practical to perform endoscopy for all UGIB patients due to hemodynamic instability, high risk, compliance issues, and many other factors [14]. Hence, it remains a challenge for clinicians how to distinguish EGVB from PUB in a timely and accurate manner. In clinical practice, appropriate diagnostic laboratory tests may be helpful to support specific diagnoses, which can enable choosing the most appropriate pharmacological treatment before performing endoscopy. Our previous study confirmed that blood count values and ratios could differentiate EGVB from PUB [15]. On the other hand, we often discovered changes of blood coagulation parameters in EGVB and PUB [16-20]. A study, published in Romania [20], reported that there were significant differences of prothrombin time (PT), thrombin time, fibrinogen, and D-dimer levels except activated partial thromboplastin time (APTT) between non-variceal UGIB patients' groups with and without recurrent bleeding episodes ($p < 0.05$ shown for all parameters). Yue et al. [18] also came to a similar conclusion, in that they proved that the non-variceal UGIB patients with rebleeding exhibited higher D-dimer and lower fibrinogen than those without rebleeding. In addition, Matei et al. [16] investigated 154 patients with variceal bleeding and 363 cases of non-variceal bleeding and concluded that patients with variceal bleeding had significantly higher PT than those with non-variceal bleeding.

However, it remains uncertain whether these coagulation parameters could be used to differentiate EGVB from PUB preliminarily. To the best of our knowledge, identifying the diagnostic values of blood coagulation parameters in distinguishing between EGVB and PUB have not been previously reported. Our study may provide new insights for whether PT, APTT, fibrinogen, and D-dimer could demonstrate accurate and reliable diagnostic values in distinguishing EGVB from PUB.

MATERIALS AND METHODS

Study population

A total of 1,580 patients with acute hematemesis and/or melaena from ED, admitted to the Fourth Affiliated Hospital Zhejiang University School of Medicine, were consecutively enrolled in this study between January 2020 and July 2025. Confirmed by endoscopy, a total of 37 inpatients were diagnosed with EGVB (EGVB group) and 89 cases were inpatients with PUB (PUB group) according to the guidelines [12,21]. Inclusion criteria were adults ≥ 30 years old; symptoms onset within 72 hours; all patients who underwent endoscopy and blood coagulation tests. Exclusion criteria were patients with venous thromboembolism, atrial fibrillation, acute inflammatory diseases, cancers, autoimmune diseases, intracranial hemorrhage, acute ischemic stroke, acute coronary syndrome, other trauma diseases or other causes of UGIB; comorbidities of EGVB and PUB; pregnant women; patients whose symptoms onset were beyond 72 hours; patients who were treated by anticoagulant drugs before laboratory tests; patients whose blood drawing were not carried out before emergency treatment; and patients whose clinical data were incomplete. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Fourth Affiliated Hospital Zhejiang University School of Medicine.

Clinical data

Baseline data were gathered from medical records of patients admitted to the Fourth Affiliated Hospital Zhejiang University School of Medicine, including age, gender, blood coagulation tests before any treatment in the ED and endoscopy results in the ED or during hospitalization. CS-5100 coagulation analyzer (Sysmex, Kakogawa, Hyōgo Prefecture, Japan) was used to determine PT, APTT, fibrinogen, and D-dimer.

Statistical analysis

Statistical analysis was performed using SPSS software (version 19.0 for Windows, IBM Corp., Armonk, NY, USA). Descriptive analyses for continuous variables were used to calculate mean values and standard deviations. The qualitative data were compared with chi-squared test. The student's *t*-test of independent samples was adopted for comparing the mean between the two groups. Multivariate analysis was performed using binary logistic regression analysis. Prognostic performance was tested by calculation of the receiver operating characteristic (ROC) curve and displayed in the AUC using the software MedCalc version 18.2.1 (MedCalc Software bvba, Ostend, Belgium). From ROC coordinates, the cutoff values for the aforementioned scores using the score value with the best Youden index (sensitivity + specificity -1) were identified. $p < 0.05$ was considered statistically significant.

Table 1. Comparison of the levels of different variables between the two groups.

Variables	EGVB group (n = 37)	PUB group (n = 89)	p-value
Age (years)	53.84 ± 14.21	48.54 ± 14.20	0.059
Gender (female/male)	18/71	9/28	0.610 *
Hypertension (n (%))	22 (17.5%)	4 (3.2%)	0.094 *
Diabetes mellitus (n (%))	11 (8.7%)	7(5.6%)	0.338 *
Coronary heart disease (n (%))	1 (0.8%)	3 (2.4%)	0.076 *
Stroke history (n (%))	4 (3.2%)	2 (1.6%)	1.000 *
PT (s)	14.40 ± 2.26	11.91 ± 1.17	< 0.001
APTT (s)	28.59 ± 5.05	25.18 ± 4.86	0.001
Fibrinogen (g/L)	1.75 ± 0.45	2.32 ± 0.69	< 0.001
D-dimer (mg/L)	1.45 ± 1.84	0.40 ± 0.61	0.002

Quantitative data were present as mean ± standard deviations. EGVB: esophagogastric variceal bleeding, PUB: peptic ulcer bleeding, PT: prothrombin time, APTT: activated partial thromboplastin time, Student's *t*-test or chi-squared test *.

Table 2. Predictors for EGVB in the binary logistic regression analysis.

Variables	aOR ^a	95% CI	p-value
PT	0.406	0.280 - 0.589	< 0.001
APTT	0.901	0.831 - 0.976	0.011
Fibrinogen	6.540	2.494 - 17.148	< 0.001
D-dimer	0.259	0.119 - 0.562	0.001

CI: confidence interval, PT: prothrombin time, APTT: activated partial thromboplastin time, aOR: adjusted odds ratio, ^a adjusted for age, gender, hypertension, diabetes mellitus, coronary heart disease, and stroke history.

RESULTS

Characteristics of total population

A total of 37 inpatients were diagnosed with EGVB (EGVB group) and 89 cases were inpatients with PUB (PUB group) available for final analysis (Figure 1). The mean age of the study sample was (50.10 ± 14.35) years. Of them, 27 (21.4%) were females and 99 (78.6%) were males. There were no significantly statistical differences of age and the rate of gender, hypertension, diabetes mellitus, coronary heart disease, and stroke history (all *p* > 0.05) (Table 1).

Comparison of PT, APTT, fibrinogen, and D-dimer between the two groups

As shown in Table 1, Figure 2A, Figure 2B, Figure 2C, and Figure 2D, PT, APTT, and D-dimer were significantly increased in EGVB group compared with PUB group, while fibrinogen was significantly decreased (all *p* < 0.01).

Predictors for EGVB in the binary logistic regression analysis

Binary logistic regression analysis adjusted for age, gender, hypertension, diabetes mellitus, coronary heart disease, and stroke history, showed that PT, APTT, fibrinogen, and D-dimer remained independent risk factors for predicting EGVB (all *p* < 0.05) (Table 2).

ROC curves of PT, APTT, fibrinogen, and D-dimer in distinguishing between EGVB and PUB

The AUC in distinguishing between EGVB and PUB were 0.843 (95% confidence interval (CI), 0.768 to 0.902) for PT, 0.725 (95% CI, 0.638 to 0.800) for APTT, 0.766 (95% CI, 0.682 to 0.837) for fibrinogen, and 0.821 (95% CI, 0.743 to 0.884) for D-dimer, respectively (Figure 3). The cutoff values (specificity, sensitivity, and Youden index) in distinguishing EGVB from PUB were 12.9 s (80.9%, 78.4%, 0.593) for PT, 25.1 s (68.5%, 78.4%, 0.469) for APTT, 1.99 g/L (67.4%, 75.7%, 0.431) for fibrinogen, and 0.31 mg/L (75.3%, 78.4%, 0.537) for D-dimer, respectively.

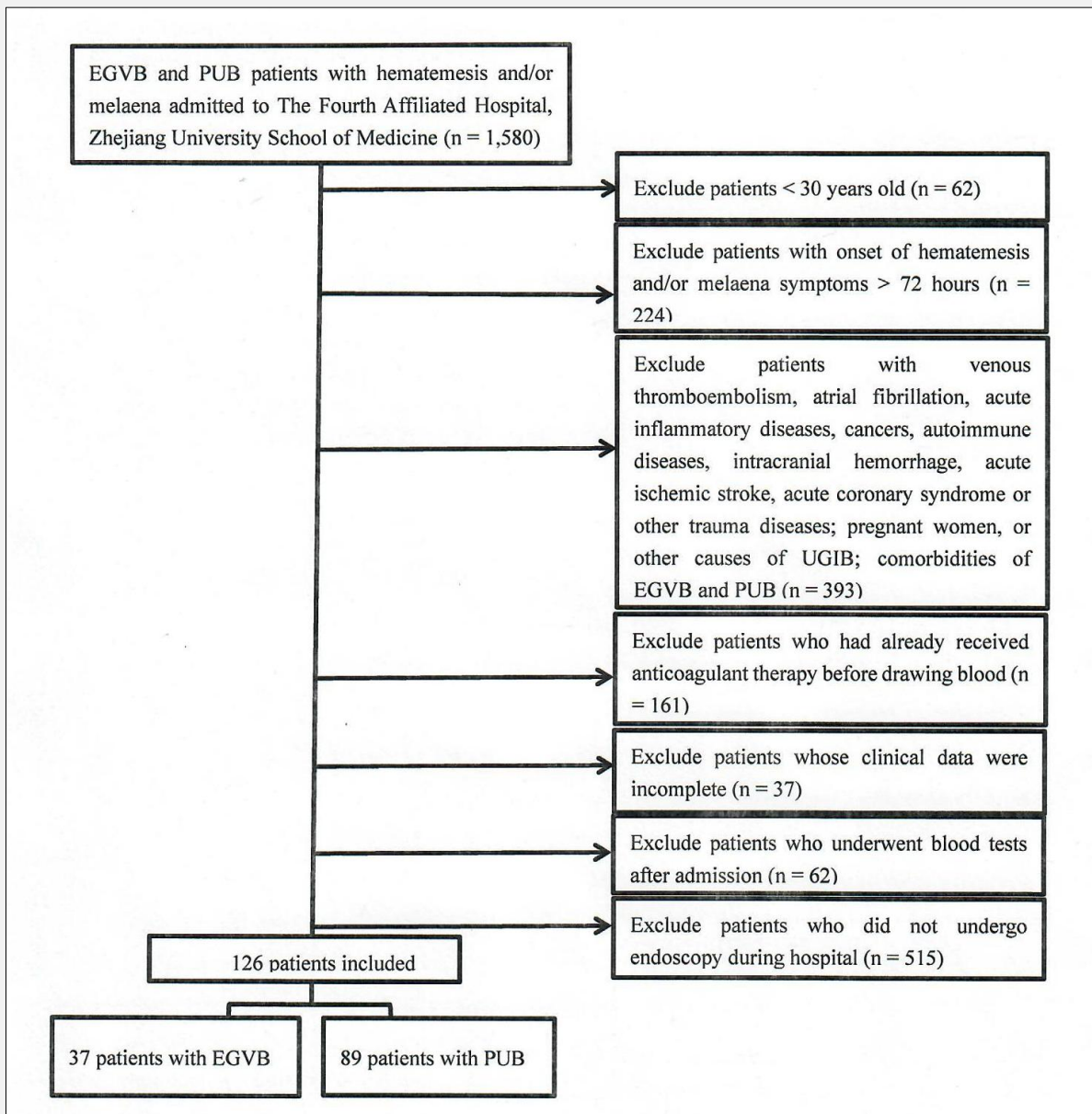


Figure 1. Study flow chart.

EGVB: esophagogastric variceal bleeding, PUB: peptic ulcer bleeding, UGIB: upper gastrointestinal bleeding.

DISCUSSION

Despite major advances in diagnosis and treatment, UGIB remains a serious problem and considerable healthcare burden, with considerable mortality and morbidity rates and high medical expenses [11,22]. Unfortunately, due to atypical abdominal signs and the absence of previous medical history, it is often difficult to

differentiate between EGVB and PUB before performing endoscopy. Therefore, before performing endoscopy, guidelines have recommended the administration of medication empirically. The treatment with vasoactive agents and antibiotics is recommended for patients with a suspicion of EGVB [23]. Whereas, in cases of high possibility of PUB, administration of proton pump inhibitors is indicated [24]. Blood coagulation test, com-

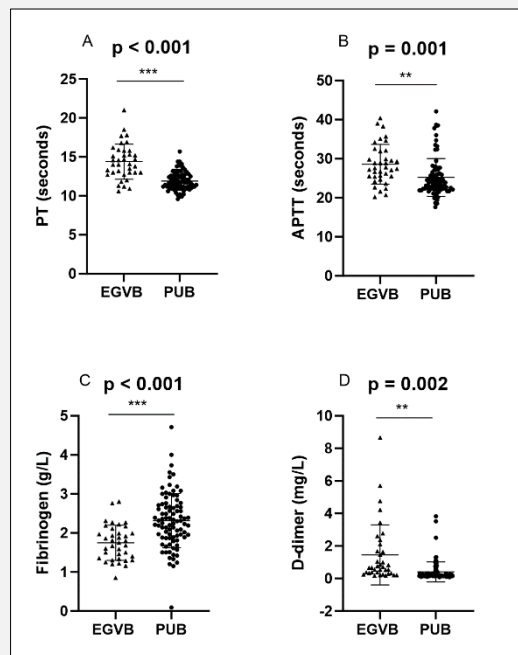


Figure 2. Comparison of PT (A), APTT (B), fibrinogen (C), and D-dimer (D) between the two groups. ** $p < 0.01$, *** $p < 0.001$.

EGVB: esophagogastric variceal bleeding, PUB: peptic ulcer bleeding, PT: prothrombin time, APTT: activated partial thromboplastin time.

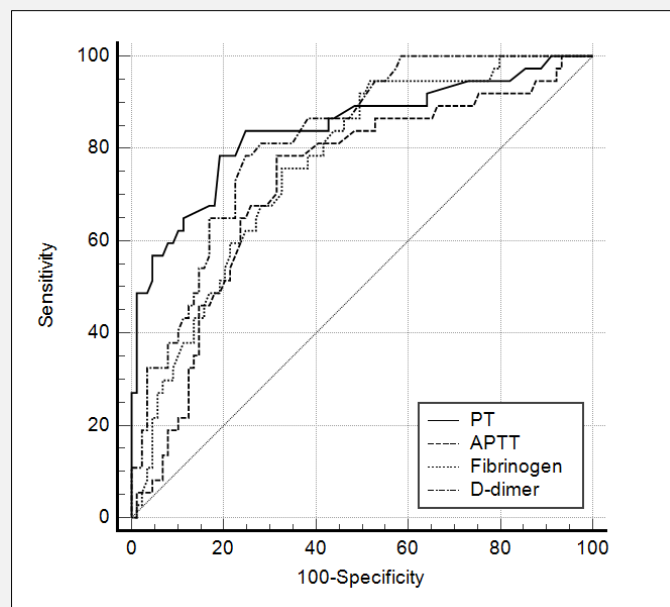


Figure 3. ROC curves of PT, APTT, fibrinogen, and D-dimer in distinguishing between EGVB and PUB.

EGVB: esophagogastric variceal bleeding, PUB: peptic ulcer bleeding, PT: prothrombin time, APTT: activated partial thromboplastin time.

pared with endoscopy, can be performed more rapidly and simply in ED without additional risks or time constraints. The specific mechanisms of coagulopathy in patients with PUB are unclear and may be related to factors such as hypoxia, acidosis, hypothermia, anemia, and consumption. Alternatively, activating the coagulation cascade on the causal pathway to death through a different cellular mechanism may play a certain role [25]. While coagulopathy in EGVB is a composite condition where liver synthetic deficit rebalances coagulation to a parallel reduction of both pro- and anticoagulant factors [26, 27].

In the present study, we have proved that PT was significantly increased in EGVB group compared with PUB group (14.40 ± 2.26 s vs. 11.91 ± 1.17 s, $p < 0.001$), suggesting that PT could be used to distinguish between EGVB and PUB. Our study result was also consistent with the conclusions of Matei et al. [16], as they found that variceal bleeding group had significantly higher PT than non-variceal bleeding group (mean: 24.05 s vs. 18 s, $p < 0.001$). Another study [28], enrolling 261 patients with UGIB (variceal: $n = 47$; nonvariceal: $n = 214$), discovered that UGIB patients with variceal had significantly higher PT than those with nonvariceal (21 ± 11 s vs. 16 ± 8 s, $p = 0.002$), which further supported our conclusions. In addition, we also observed that the AUC in distinguishing between EGVB and PUB was 0.843 for PT ($p < 0.001$), which further verified that PT could demonstrate accurate and reliable diagnostic value.

Next, we also discovered that APTT was significantly elevated in EGVB group compared with PUB group (28.59 ± 5.05 s vs. 25.18 ± 4.86 s, $p = 0.001$), suggesting that APTT could also be used to distinguish EGVB from PUB. Furthermore, we also confirmed that the AUC in distinguishing EGVB from PUB was 0.725 for APTT ($p < 0.001$), which further verified that APTT could demonstrate accurate and reliable diagnostic value, similarly.

In addition, we discovered fibrinogen was significantly lower in EGVB group compared with PUB group (1.75 ± 0.45 g/L vs. 2.32 ± 0.49 g/L, $p < 0.001$), suggesting that fibrinogen could be used to distinguish EGVB from PUB, similarly. We also confirmed that the AUC for fibrinogen was 0.766 in distinguishing EGVB from PUB ($p < 0.001$), which further verified that fibrinogen could demonstrate accurate and reliable diagnostic value.

In the present study, we also found that D-dimer was significantly increased in EGVB group compared with PUB group (1.45 ± 1.84 mg/L vs. 0.40 ± 0.61 mg/L, $p = 0.002$), suggesting that D-dimer could also be used to distinguish EGVB from PUB. We also confirmed that the AUC in distinguishing EGVB from PUB was 0.821 for D-dimer ($p < 0.001$), which further verified that D-dimer could demonstrate accurate and reliable diagnostic value, similarly.

Furthermore, we found that the cutoff values (specificity, sensitivity, and Youden index) in distinguishing EGVB from PUB were 12.9 s (80.9%, 78.4%, 0.593) for PT, 25.1 s (68.5%, 78.4%, 0.469) for APTT, 1.99 g/L

(67.4%, 75.7%, 0.431) for fibrinogen, and 0.31 mg/L (75.3%, 78.4%, 0.537) for D-dimer, respectively.

Finally, even adjusted for age, gender, hypertension, diabetes mellitus, coronary heart disease, and stroke history, binary logistic regression analysis showed that PT, APTT, fibrinogen, and D-dimer remained independent risk factors for predicting EGVB (aOR: 0.406 (0.280 - 0.589), 0.901 (0.831 - 0.976), 6.540 (2.494 - 17.148), 0.259 (0.119 - 0.562), respectively, all $p < 0.05$).

We recognized limitations of this study. First, it was a retrospective analysis and thus we did not perform a more rigorous design. Second, the sample size from a single-center was small. Third, there was heterogeneity of the sample (such as different hemorrhage volumes and different degrees of disease severities). Larger and more homogeneous samples from a multicenter study are needed to verify the conclusions.

CONCLUSION

PT, APTT, fibrinogen, and D-dimer, useful and potential biomarkers in distinguishing EGVB from PUB, can demonstrate accurate and reliable diagnostic values.

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Declaration of Interest:

The authors report no competing financial interests.

References:

- Long B, Gottlieb M. Emergency medicine updates: Upper gastrointestinal bleeding. *Am J Emerg Med* 2024;81:116-23. (PMID: 38723362)
- Kurien M, Lobo AJ. Acute upper gastrointestinal bleeding. *Clin Med (Lond)* 2015;15(5):481-5. (PMID: 26430191)
- Kavitt RT, Gralnek IM. Ideal strategy for nonvariceal upper gastrointestinal bleeding. *Curr Opin Gastroenterol* 2024;40(5):342-7. (PMID: 38967918)
- Palmer K. Management of haematemesis and melaena. *Postgrad Med J* 2004;80: 399-404. (PMID: 15254304)
- DeLaney M, Greene CJ. Emergency Department Evaluation And Management Of Patients With Upper Gastrointestinal Bleeding. *Emerg Med Pract* 2015;17(4):1-18. (PMID: 26291048)
- Kamboj AK, Hoversten P, Leggett CL. Upper Gastrointestinal Bleeding: Etiologies and Management. *Mayo Clin Proc* 2019; 94(4):697-703. (PMID: 30947833)
- Wuerth BA, Rockey DC. Changing epidemiology of upper gastrointestinal hemorrhage in the last decade: a nationwide analysis. *Dig Dis Sci* 2018;63:1286-93. (PMID: 29282637)

8. van Leerdam ME. Epidemiology of acute upper gastrointestinal bleeding. *Best Pract Res Clin Gastroenterol* 2008;22(2):209-24. (PMID: 18346679)
9. Jemilohun AC, Akande KO, Ngubor TD, Oku O, Ogunmola MI, Adesuyi YO. Endoscopic Findings in Patients With Upper Gastrointestinal Bleeding in Ogun State, Nigeria. *Cureus* 2022;14(3):e23637. (PMID: 35510020)
10. Barkun AN, Almadi M, Kuipers EJ, et al. Management of Non-variceal Upper Gastrointestinal Bleeding: Guideline Recommendations From the International Consensus Group. *Ann Intern Med* 2019;171(11):805-22. (PMID: 31634917)
11. Samuel R, Bilal M, Tayyem O, Guturu P. Evaluation and management of Non-variceal upper gastrointestinal bleeding. *Dis Mon* 2018;64:333-43. (PMID: 29525375)
12. Gralnek IM, Camus Duboc M, Garcia-Pagan JC, et al. Endoscopic diagnosis and management of esophagogastric variceal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2022; 54(11):1094-120. (PMID: 36174643)
13. Stanley AJ, Laine L. Management of acute upper gastrointestinal bleeding. *BMJ* 2019;364:l536. (PMID: 30910853)
14. Kim J, Gong EJ, Seo M, et al. Timing of endoscopy in patients with upper gastrointestinal bleeding. *Sci Rep* 2022;12(1):6833. (PMID: 35477727)
15. Zhang L, Zhang Y. Diagnostic Values of Blood Count Values and Ratios in Distinguishing between Peptic Ulcer Bleeding and Esophagogastric Variceal Bleeding. *Clin Lab* 2020;66(4):655-60. (PMID: 32255300)
16. Matei D, Groza I, Furnea B, et al. Predictors of variceal or non-variceal source of upper gastrointestinal bleeding. An etiology predictive score established and validated in a tertiary referral center. *J Gastrointestin Liver Dis* 2013 ;22(4): 379-84. (PMID: 24369318)
17. Ragni MV, Lewis JH, Spero JA, Hasiba U. Bleeding and coagulation abnormalities in alcoholic cirrhotic liver disease. *Alcohol Clin Exp Res* 1982;6(2):267-74. (PMID: 7048981)
18. Yue W, Liu Y, Jiang W, Huang J, Liu J. Prealbumin and D-dimer as Prognostic Indicators for Rebleeding in Patients with Nonvariceal Upper Gastrointestinal Bleeding. *Dig Dis Sci* 2021;66(6):1949-56. (PMID: 32583220)
19. Primignani M, Dell'Era A, Bucciarelli P, et al. High-D-dimer plasma levels predict poor outcome in esophageal variceal bleeding. *Dig Liver Dis* 2008;40(11):874-81. (PMID: 18329968)
20. Li X, Zheng X, Wang Y, Shao L, Xiao Y, Lv X. Construction of a risk prediction model for non-variceal upper gastrointestinal bleeding and rebleeding based on multi-dimensional indicators and its application research. *Am J Transl Res* 2023;15(5):3697-704. (PMID: 37303679)
21. Gralnek IM, Stanley AJ, Morris AJ, et al. Endoscopic diagnosis and management of nonvariceal upper gastrointestinal hemorrhage (NVUGIH): European Society of Gastrointestinal Endoscopy (ESGE) Guideline - Update 2021. *Endoscopy* 2021;53(3):300-32. (PMID: 33567467)
22. Abougergi MS, Travis AC, Saltzman JR. The in-hospital mortality rate for upper GI hemorrhage has decreased over 2 decades in the United States: a nationwide analysis. *Gastrointest Endosc* 2015;81(4):882-8.e.1. (PMID: 25484324)
23. Garcia-Tsao G, Sanyal AJ, Grace ND, et al. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Hepatology* 2007;46:922-38. (PMID: 17879356)
24. Barkun AN, Bardou M, Kuipers EJ, et al. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding in the United Kingdom. *Transfusion* 2013;53(5):1069-76. (PMID: 22897615)
25. Jairath V, Kahan BC, Stanworth SJ, et al. Prevalence, management, and outcomes of patients with coagulopathy after acute nonvariceal upper gastrointestinal bleeding in the United Kingdom. *Transfusion* 2013;53(5):1069-76. (PMID: 22897615)
26. Bianchini M, De Pietri L, Villa E. Coagulopathy in liver diseases: complication or therapy? *Dig Dis* 2014;32(5):609-14. (PMID: 25034295)
27. Lisman T, Caldwell SH, Intagliata NM. Haemostatic alterations and management of haemostasis in patients with cirrhosis. *J Hepatol* 2022;76(6):1291-305. (PMID: 35589251)
28. Pongprasobchai S, Nimitvilai S, Chasawat J, Manatsathit S. Upper gastrointestinal bleeding etiology score for predicting variceal and non-variceal bleeding. *World J Gastroenterol* 2009;15(9):1099-104. (PMID: 19266603)