SHORT-TERM TREATMENT OUTCOMES OF FORREST IIB GASTRIC AND DUODENAL ULCER BLEEDING USING HIGH-DOSE INTRAVENOUS NEXIUM

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ABSTRACT

Background: Among the causes of upper gastrointestinal bleeding, gastric and duodenal ulcers (GDU) are the most common. Forrest classification IIB (FIIB) is assessed as having a high risk of recurrent bleeding as FIA, FIB, FIIA, but treatment opinions differ. As of 2021, the European Society of Gastrointestinal Endoscopy recommends considering high-dose PPI treatment for patients in the FIIB group without endoscopic hemostasis as strong recommendation, high level of evidence. ***Objectives:*** To describe clinical and laboratory characteristics. To evaluate the short-term treatment outcomes of FIIB GDU bleeding using high-dose intravenous Nexium. ***Materials and methods:*** An uncontrolled clinical trial was conducted with 41 patients diagnosed gastrointestinal bleeding due to FIIB GDU admitted to Can Tho Central General Hospital from June 2022 to May 2024. ***Results:*** The research shows that the majority of patients responded well to treatment with high-dose intravenous Nexium (85.4%). The rates of rebleeding, surgical intervention, and mortality were relatively low at 7.3%, 2.4%, and 4.9%, respectively. Cumulative treatment failure risk was approximately 5% after 6 days of hospitalization and increased to 12.5% after 20 days of treatment. ***Conclusion:*** In patients with gastrointestinal bleeding due to FIIB peptic ulcers, treatment with high-dose intravenous Nexium has a relatively high success rate in short-term outcomes during hospitalization.

Keywords: *gastric and duodenal ulcers, Forrest IIB, high-dose intravenous Nexium.*

I. INTRODUCTION

Among the causes of upper gastrointestinal bleeding, GDU are the most common, accounting for 27-40% of bleeding episodes. Duodenal ulcers are more common than gastric ulcers, but the bleeding incidence of both is similar [1]. Currently, the Forrest classification is used to describe ulcerative lesions in GDU observed via esophagogastroduodenoscopy, with groups FIA, FIB, and FIIA having a very high risk of rebleeding, necessitating endoscopic hemostasis intervention [2]. Meanwhile, group FIIB is assessed as having a high risk of recurrent bleeding, but treatment opinions differ; some authors support endoscopic hemostasis intervention, while others advocate for medical treatment with high-dose intravenous PPIs. As of 2021, the European Society of Gastrointestinal Endoscopy recommends considering high-

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Date of receipt: 12/8/2024
Date of scientific judgment: 16/9/2024
Reviewed date: 14/10/2024

dose PPI treatment for patients in the FIIB group without endoscopic hemostasis (strong recommendation, high level of evidence) [3].

Currently, at Can Tho Central General Hospital, hundreds of patients with GD-U bleeding are admitted annually, with a high proportion of FIIB lesions. However, the evaluation of short-term treatment outcomes with high-dose intravenous PPI without endoscopic hemostasis intervention has not been studied. Therefore, we conducted the study **"Short-term treatment outcomes of Forrest IIB gastric and duodenal ulcer bleeding using high-dose intravenous Nexium"** to analyze the mentioned issue.

II. MATERIALS AND METHOD

2.1. Study population

All patients with gastrointestinal bleeding due to FIIB GDU admitted to Can Tho Central General Hospital from June 2022 to May 2024.

Inclusion Criteria

Patients with upper GI bleeding due to FIIB GDU, diagnosed clinically with symptoms of hematemesis and/or melena, and confirmed by upper GI endoscopy.

Patients aged 18 years and above, regardless of gender.

Patients agreeing to participate in the study.

Exclusion Criteria

Patients with upper GI bleeding from causes other than GDU, such as esophageal variceal rupture, Mallory-Weiss syndrome, esophagitis, or esophageal cancer.

Patients with upper GI bleeding due to non-ulcerative causes like hemorrhagic GDU inflammation or hemorrhagic gastric cancer.

Patients with GI bleeding due to GDU with initially surgical complications (e.g., perforation).

Patients with upper GI bleeding due to GDU classified as FIA, FIB, FIIA, FIIC, or FIII.

2.2. Study method

Study design

Clinical trial without control group.

Sample size

Convenient sampling of eligible patients who meet inclusion criteria and do not fall under exclusion criteria during the study period. In practice, we selected 41 suitable subjects.

Study contents

General characteristics of study subjects: Age (<60 years, ≥60 years) and gender (male/female).

Clinical characteristics of study subjects: Hematemesis (yes/no), melena (yes/no), epigastric pain (yes/no), and hemodynamic instability symptoms including tachycardia at rest, hypotension, syncope, and altered mental status (normal, agitated/restless, confused, drowsy).

Description of Blatchford score and blood transfusion: Average Blatchford score, blood transfusion (yes/no), and average blood transfusion volume (units of 350 ml).

Laboratory characteristics of study subjects: Average red blood cell indices (million/mm^3), hematocrit (%), hemoglobin (g/dL), and blood urea (mmol/L).

Description of GDU bleeding location: Ulcer location in the stomach (antrum, pre-pyloric, body, angular notch), duodenal bulb, and duodenum (anterior wall, posterior wall, superior wall, D1-D2).

Evaluation of short-term treatment outcomes: Recurrent bleeding (yes/no), surgery (yes/no) and mortality (yes/no) in hospitalized time. Treatment failure was defined as having at least one aforementioned factor.

Analysis of cumulative probability of treatment failure and median survival time after 30 days.

Assessment on Blatchford's predictive value for short-term treatment failure.

Statistical analysis

Data were cleaned, coded using Microsoft Excel, and analyzed using R Statistical Environment. Qualitative variables were described by frequency and percentage, while quantitative variables were expressed as mean and standard deviation or median and interquartile range. The Kaplan-Meier method was used to estimate cumulative survival probability and median survival time at the evaluated time point. The receiver operating characteristic curve analysis and its corresponding area under the curve were used to assess the discriminative performance of Blatchford for predicting short-term treatment failure.

2.3. Ethics in research

The board of directors of Can Tho Central General Hospital and the ethics committee for biomedical research at Can Tho University of Medicine and Pharmacy approved this study (No. 22.384.HV/PCT-HĐĐĐ).

III. RESULTS

Our study on 41 patients with gastrointestinal bleeding due to FIIB peptic ulcers recorded a male-to-female ratio of approximately 3:1. Additionally, the majority of patients were aged ≥ 60 years (75.6%), with a mean age of 69.3 ± 14.3 years, ranging from a minimum of 30 years to a maximum of 93 years.

Table 1. Clinical characteristics

Clinical Symptoms			Frequency (n)	Percentage (%)
Hematemesis			13	31.7
Melena			36	87.8
Epigastric Pain			23	56.1
Average Blatchford score (points)			12 (10,5-13)	
Blood transfusion rate (%)			38	92.7
Average volume of blood transfused (350ml units)			3 (2-4)	
Hemodynamic instability symptoms	Tachycardia at rest		12	29.3
	Hypotension		4	9.8
	Syncope		3	7.3
	Consciousness	Normal	32	78.0
		Agitation/Restlessness	5	12.2
		Confusion	2	4.9
		Somnolence	2	4.9

The results showed that most patients with gastrointestinal bleeding due to FIIB peptic ulcers presented with melena (87.8%), more than half experienced epigastric pain (56.1%), and hematemesis occurred in 31.7% of cases. Regarding symptoms of hemodynamic instability, nearly one-third of the cases exhibited resting tachycardia (29.3%). The majority of patients had normal consciousness, while symptoms such as hypotension, syncope, agitation, restlessness, confusion, and drowsiness ranged from 2% to 13%. Our study results recorded an median Blatchford score of 12, with the interquartile ranged from 10.5 to 13 points. The blood transfusion rate was 92.7%, with a median transfusion volume of 3 units of 350 ml each and the interquartile ranged from 2 to 4 units.

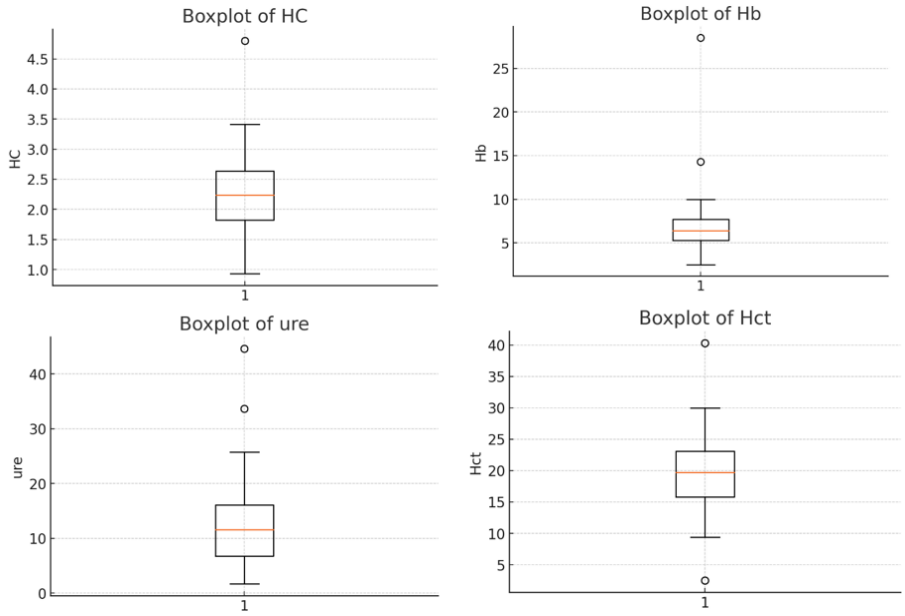
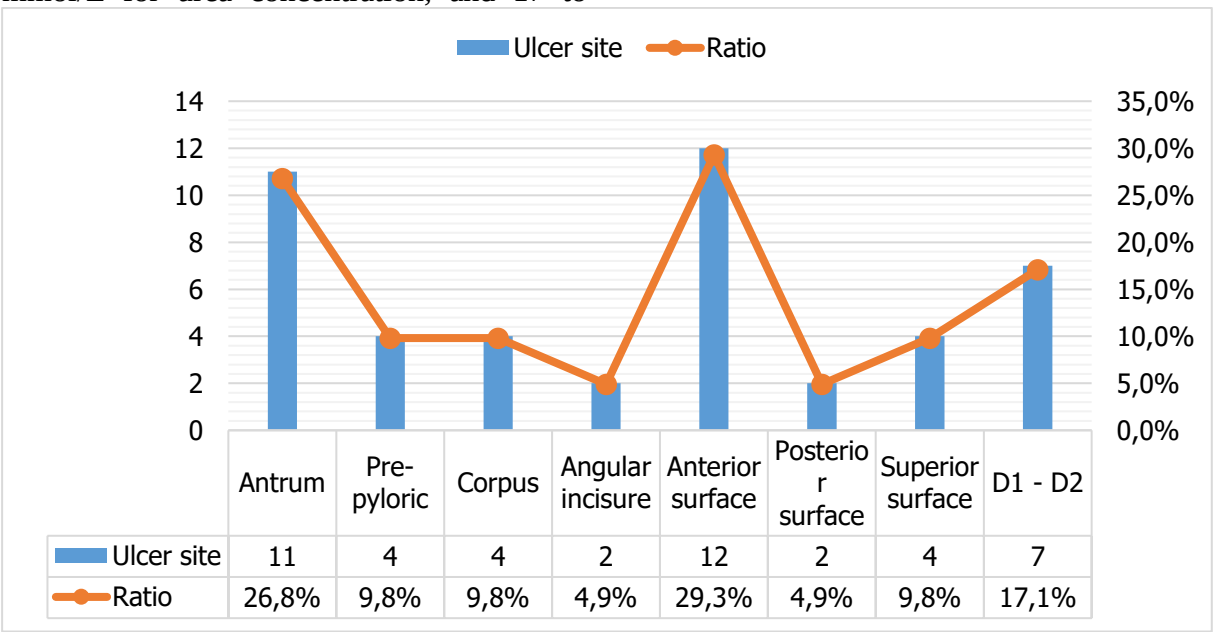


Figure 1. ***Boxplot of laboratory indices upon admission***

The study results show that the median values for hemocyte count, hemoglobin, urea concentration, and hematocrit are approximately 2.3 x 10^9 /L, 6.5 g/dL, 10 mmol/L, and 20%, respectively. Additionally, the interquartile ranges are from 1.8 to 2.7 x 10^9 /L for hemocyte count, 5.5 to 8 g/dL for hemoglobin, 6 to 16 mmol/L for urea concentration, and 17 to 22% for hematocrit. Among these, when evaluating hemocyte count, we observed one outlier above the threshold at approximately 4.5 x 10^9 /L, one outlier above the threshold at 25 g/dL for hemoglobin, two outliers near 35 and 40 mmol/L for Urea concentration, and one outlier above the upper threshold at approximately 37% for hematocrit.



	Antrum	Pre-pyloric	Corpus	Angular incisure	Anterior surface	Posterior surface	Superior surface	D1 - D2
Ulcer site	11	4	4	2	12	2	4	7
Ratio	26,8%	9,8%	9,8%	4,9%	29,3%	4,9%	9,8%	17,1%

Figure 2. ***Distribution ratio of GDU sites***

Regarding the distribution of GDU sites, results indicate that the antrum is the most common site of gastric ulcers (26.8%). Additionally, in the duodenum, the most frequent ulcer sites were observed on the anterior wall and in the D1 – D2 segments of the duodenum, accounting for 29.3% and 17.1% respectively. Furthermore, other ulcer sites such as the prepyloric region, corpus, angular incisure, posterior duodenum, and superior duodenum had prevalence rates ranging from 4% to 10%.

Table 2. ***Short-term treatment outcomes***

Treatment outcomes	Frequency (n)	Percentage (%)
Mortality	2	4.9
Recurrent bleeding	3	7.3
Surgery	1	2.4

A study conducted on 41 patients with gastrointestinal bleeding due to peptic ulcers (stomach and duodenal ulcers) of FIIB who were treated with high-dose Nexium showed that there were 2 cases of mortality, accounting for 4.9%, 3 cases of recurrent bleeding, accounting for 7.3%, and 1 case requiring surgery, accounting for 2.4%.

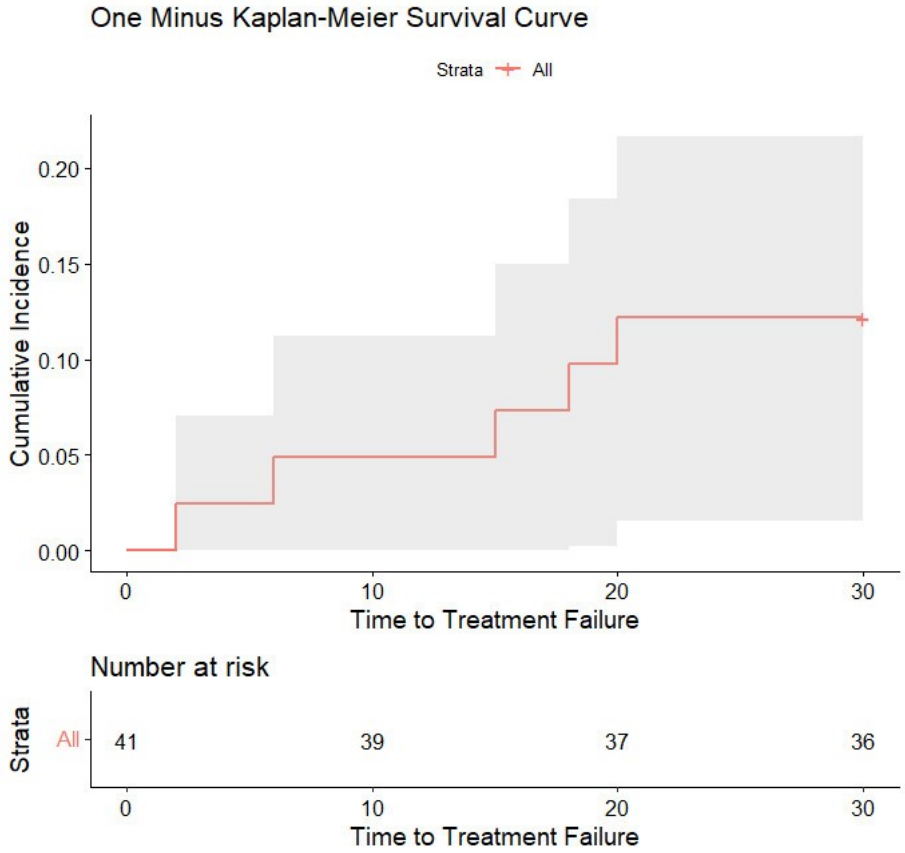


Figure 3. ***Cumulative One Minus Survival Function for patients with FIIB GDU bleeding using high-dose intravenous nexium***

Cumulative treatment failure risk was approximately 5% after 6 days of hospitalization and increased to 12.5% after 20 days of treatment. Two deaths occurred on days 6 and 15, respectively.

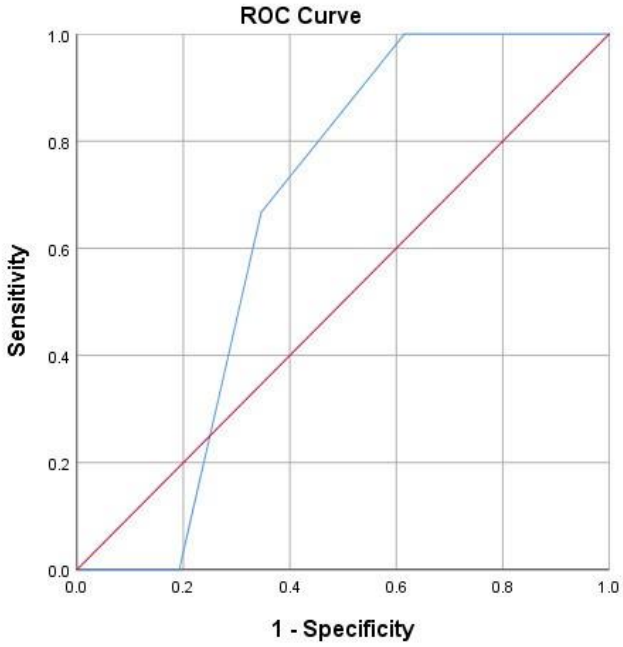


Figure 4. ***Predictive value of Blatchford score for short-term treatment failure***

ROC curve analysis demonstrated that a Blatchford score cut-off of ≥ 11.5 points effectively predicted treatment failure with high-dose intravenous Nexium in patients with FIIB upper gastrointestinal bleeding due to peptic ulcer disease. The area under the curve (AUC) was 0.66 (95% CI: 0.45-0.87).

IV. DISCUSSION

Our study was conducted on 41 patients diagnosed with gastrointestinal bleeding due to peptic ulcers classified as FIIB, treated with high-dose intravenous Nexium alone, without any intervention. The recorded male-to-female ratio was 3:1, with an average age of 69.3 ± 14.3 years, mostly concentrated in the age group of 60 and above. The in-hospital treatment outcomes recorded 2 cases of death and 3 cases of recurrent bleeding (one of which required surgery), corresponding to a treatment failure rate of 12.2%.

Regarding clinical characteristics, we noted that most study subjects had melena, over half experienced epigastric pain, and nearly one-third had hematemesis. These results are consistent with the study by author Huynh Hieu Tam, which found that epigastric pain, melena, and hematemesis were the most common symptoms in patients with gastrointestinal bleeding due to peptic ulcers [4]. This finding is appropriate because bleeding from peptic ulcers is typically a complication of pre-existing chronic peptic ulcer disease, making epigastric pain the most common symptom. Furthermore, FIIB peptic ulcer bleeding represents recent bleeding that has currently stopped due to clot formation, which usually occurs in small blood vessels or slow-bleeding ulcers, reducing the likelihood of rapid blood flow into the stomach causing hematemesis. Additionally, hematemesis usually requires a large amount of blood accumulation in the stomach to trigger the

vomiting reflex. Blood typically accumulates in the lower part of the stomach-duodenum, where it more easily moves into the intestines rather than upwards through the vomiting reflex. Therefore, bleeding from peptic ulcers, in general, and FIIB in particular, tends to present with melena rather than hematemesis. This is also reflected in the study of Huynh Hieu Tam, where the order of common symptoms remained the same even though the patient group included FIA, FIB, and FIIA, which are more severe than FIIB [4]. Additionally, hemodynamic disturbance symptoms such as resting tachycardia, orthostatic hypotension, syncope, and altered consciousness are evidence reflecting the patient's blood loss. Specifically, in theory, relatively speaking, resting tachycardia suggests blood loss of <15% [5], orthostatic hypotension suggests blood loss of over 40% [6], while syncope and altered consciousness tend to be more severe due to the extent of blood loss being so great that the body cannot compensate enough to maintain adequate blood and oxygen supply to the brain. Therefore, our study on Forrest IIB patients, with about one-third having resting tachycardia, one-tenth having orthostatic hypotension, and one-thirteenth having syncope and altered consciousness, is consistent.

Regarding the characteristics of the test indices, we observed a significant decrease in red blood cell count and hemoglobin levels, while urea levels and hematocrit were normal or increased. These results align with the condition of blood loss and are consistent with other studies on bleeding due to peptic ulcers [7]. Additionally, the average red blood cell and hemoglobin levels of the study subjects reflect severe anemia, which is the related reason why most patients required blood transfusions, with an average of 3 units. This result is also consistent with Wang J.'s study, which recorded the number of blood units needed for patients with FIIB peptic ulcer bleeding at 2.8 units [8]. The prolonged blood loss from the time the ulcer began to bleed until the patient presented with symptoms at the hospital led to a decrease in hemoglobin levels in most study subjects. Therefore, blood transfusion to raise hemoglobin levels according to major global recommendations is essential, not only to reduce anemia symptoms but also to improve patient prognosis. Additionally, the increase in blood urea levels is appropriate due to the increased absorption of urea in the intestines after blood proteins are broken down by the gut microbiota.

Regarding the location, we noted that antral ulcers, anterior wall ulcers, and D1-D2 duodenal ulcers were the most common lesions, consistent with global literature [9]. In practice, gastric ulcers are often found in the antrum and the angular incisure, while duodenal ulcers are mostly located in the first part of the duodenum (over 95%), with about 90% occurring within 3 cm of the pylorus. This can be explained by the fact that these areas are frequently exposed to gastric acid and pepsin. The antrum and the angular incisure of the stomach are regions with a high density of acid-secreting cells, increasing the risk of mucosal damage when the protective-destructive mechanisms are imbalanced. Additionally, the duodenum, especially its first part, receives gastric acid from the stomach, leading to a higher risk of damage.

In evaluating the short-term treatment outcomes of high-dose intravenous Nexium in patients with gastrointestinal bleeding due to peptic ulcers with FIIB lesions, we found

that the majority of patients responded well to treatment (85.4%). The risk of treatment failure was approximately 5% after 6 days of hospitalization and increased to 12.5% after 20 days of treatment. The rates of rebleeding, surgical intervention, and mortality were relatively low at 7.3%, 2.4%, and 4.9%, respectively. Notably, the two recorded deaths were in elderly patients with multiple severe comorbidities, and the cause of death was determined not to be due to rebleeding. This result is supported by the findings of Si Hye Kim et al., who noted that in patients with gastrointestinal bleeding due to FIIB peptic ulcers treated medically with high-dose intravenous PPIs without endoscopic intervention, the rates of rebleeding and mortality were relatively low, at 9.5% and 14.2%, respectively, with half of the mortality cases due to comorbid conditions. Moreover, when comparing treatment outcomes between the group receiving endoscopic hemostasis and the group receiving only medical treatment, the authors found no difference in rebleeding rates between the two groups (7.1% vs. 9.5%; p=0.641) [10]. More recently, a retrospective analysis by Wang J. over nearly 10 years from 2014 to 2023 on 605 patients with gastrointestinal bleeding due to FIIB peptic ulcers showed rebleeding rates in the high-dose PPI group on days 3, 7, 14, and 30 were 13.3%, 14.2%, 14.5%, and 14.5%, respectively. Furthermore, Wang J.'s study indicated rebleeding rates in the endoscopic hemostasis alone group were 17.4%, 20.8%, 20.8%, and 20.8%, respectively. However, there was no statistically significant difference on days 3, 7, and 14 [8]. Additionally, the potential benefits of endoscopic hemostasis techniques must be weighed against their risks, which are often not thoroughly considered. Unnecessary hemostasis efforts can lead to serious complications such as causing bleeding in non-bleeding lesions, sometimes resulting in more severe bleeding or even perforation. Moreover, endoscopic hemostasis tools are quite expensive, and the unnecessary use of clips, thermal therapy, injection therapy, or hemostatic sprays can significantly increase healthcare costs [11]. On the other hand, one of the reasons for recurrent bleeding in cases classified as Forrest IIB is the presence of an artery beneath the blood clot, which can be observed pulsating with the heartbeat. This poses a very high risk of recurrent bleeding if only medical treatment is administered without any intervention. Therefore, in cases where the risks of endoscopic hemostasis outweigh the benefits, high-dose intravenous Nexium treatment for this patient group, with its comparable effectiveness and high safety profile, is a reasonable option. Additionally, we noted the average Blatchford score of the study subjects was 12. This result is consistent with the findings of Si Hye Kim et al. in 126 patients with gastrointestinal bleeding due to FIIB peptic ulcers, who reported an average Blatchford score of 12-13 [10]. Assessing the predictive ability of the Blatchford score for short-term treatment failure risk, we propose a cutoff score of 11.5 to predict failure with high-dose intravenous Nexium treatment in patients with gastrointestinal bleeding due to FIIB peptic ulcers, with an AUROC of 0.66 (95% CI: 0.45-0.87).

Overall, the results of our study have contributed additional data demonstrating that in patients with gastrointestinal bleeding due to FIIB peptic ulcers, medical treatment with high-dose intravenous Nexium has a relatively high success rate. However, it must

be acknowledged that the major limitation of our study is the relatively modest sample size and the insufficient follow-up period. Additionally, this is an interventional study without a control group, making it impossible to directly compare the effectiveness of high-dose intravenous Nexium alone with either endoscopic hemostasis alone or a combination of endoscopic hemostasis and high-dose intravenous Nexium. We hope that in the future, the results of larger controlled clinical trials will provide further data clarifying the role of high-dose intravenous Nexium alone compared to other methods in patients with gastrointestinal bleeding due to FIIB peptic ulcers. This would aid clinicians in considering and selecting the appropriate, individualized treatment for each patient.

V. CONCLUSION

In patients with gastrointestinal bleeding due to FIIB peptic ulcers, treatment with high-dose intravenous Nexium has a relatively high success rate in short-term outcomes during hospitalization.

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