Clinical outcomes of gastroscopy in critically ill patients using high-dose proton pump inhibitor for suspected bleeding

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Research

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Abstract

Background: Gastroscopy is a useful procedure for gastrointestinal (GI) bleeding. No definite clinical guidelines recommend on the choice of gastroscopy implementation in the intensive care unit (ICU) patient with suspected GI bleeding. The objective of this retrospective study was to compare the clinical effectiveness of gastroscopy in critically ill patients using high-dose proton pump inhibitor for suspected bleeding.

Methods: ICU patients using a high-does proton pump inhibitor for suspected GI bleeding from January 2015 to February 2020 were retrospectively included. Massive GI bleeding, such as hematemesis and hematochezia, were excluded. After propensity score matching (PSM) between the gastroscopy and no gastroscopy groups, the change in hemoglobin level, requirement of RBC transfusion, length of ICU stay, and ICU mortality were compared.

Results: Of the 116 subjects included, 34 patients had gastroscopy during ICU stay. Among the gastroscopy group, 13 (38.2%) patients showed normal findings, and the most frequent abnormal finding was gastric ulcer (n = 9, 26.5%), and 12 patients (35.3%) had a hemostatic procedure. After PSM, the gastroscopy group needed more red blood cell transfusion than the no-gastroscopy group (P = 0.01). There was no significant difference in the change in hemoglobin level (P = 0.10), length of ICU stay (P = 0.64), and ICU mortality (P = 0.55).

Conclusion: This retrospective study showed that gastroscopy had no definite clinical benefit in ICU patients using high-dose proton pump inhibitor for suspected GI bleeding.

Background

Intensive care unit (ICU) patients admitted for various reasons have a complex, stressful environment and frequent upper gastrointestinal (GI) bleeding. Occult or overt bleeding (positive nasogastric blood, mild fall in hemoglobin over several days, melena) was observed in 5–25% of ICU patients and clinically significant bleeding in 1.5–2% [1, 2]. Significant upper GI bleeding was associated with increased mortality and excess duration of ICU stay [3]. Core management of these patients consists of resuscitation, proton pump inhibitor (PPI), and endoscopic therapy.

Gastric acid suppression has been recommended in all ICU patients with high-risk stress-related mucosal damage (SRMD) [4, 5]. Prophylactic PPIs have been shown to be more effective than histamine 2 receptor antagonists in preventing SRMD [6]. According to the 2019 multidisciplinary international consensus statement, high dose-PPI infusion (80 mg intravenous bolus followed by 72 hours of an 8 mg/h continuous intravenous Infusion) for patients with bleeding ulcers with high-risk stigmata after endoscopic therapy, is recommended [7]. A possible biological benefit of this high-dose regimen is to promote clot stability by sustaining the intragastric pH above 6.

Upper gastroscopy is a useful management option in both a diagnostic (macroscopic examination of the lesions and biopsy sampling) and therapeutic roles. However, procedure induced complications also exist, such as pulmonary aspiration and adverse reactions to medications used to achieve conscious sedation. In particular, complications occurred more often (21% versus 2%) in the critically ill patient (Apache II score > 16 or hypotension prior to endoscopy) [8]. The consensus groups suggest early endoscopy within 24 hours for patients with upper GI bleeding based on improved mortality [7]. However, endoscopy in hemodynamically unstable patients, especially ICU patients, has been debated because of insufficient data.

During critically ill patients care, when suspicious upper GI bleeding occurred, there were concerns about whether and when to perform a gastroscopy after high-dose PPI use. Therefore, this study evaluated the clinical impact of gastroscopy performed in ICU patients using a high- dose PPI for suspected GI bleeding.

Methods

A retrospective cohort study was conducted on patients with suspected GI bleeding admitted to a medical or surgical ICU in a tertiary academic hospital from January 2015 to February 2020. All patients who used a high-dose PPI (pantoprazole or esomeprazole, 80 mg intravenous bolus followed by 72 hours of an 8 mg/h continuous intravenous Infusion) for suspected upper GI bleeding were analyzed based on the electronic medical records. Patients admitted for patent digestive bleeding or those transported to gastroenterology for known GI lesions such as solid cancer and varices were excluded. Patients with massive hematemesis or hematochezia were also excluded. Suspected upper GI bleeding cases were diagnosed with the change in color of nasogastric tube drainage material to red or dark brown, or resembling coffee grounds in texture; melena; and decreased hemoglobin level (drop in hemoglobin up to 3 g/dL).

Data collected included age, sex, hypertension, diabetes, cerebral vascular disease, cardiovascular disease, chronic lung disease (chronic obstructive pulmonary disease, asthma, interstitial lung disease), chronic liver disease, chronic kidney disease, solid cancer, reason for ICU admission, Simplified Acute Physiology Score (SAPS) II at ICU admission, length of ICU stay before suspected GI bleeding, administration of mechanical ventilation, gastroscopy findings, laboratory findings on suspected GI bleeding, requirement of red blood cell (RBC) transfusion after one week from suspected GI bleeding, length of ICU stay, and ICU mortality.

Gastroscopies were performed by expert gastroenterologists (senior physicians and clinical instructors). Endoscopies were performed at the bedside or endoscopy room. A major lesion was defined as a lesion that required a hemostatic procedure, such as electrical coagulation, epinephrine injection, or clipping; and a minor lesion was a lesion that could be pharmacologically treated.

Continuous variables are expressed as means and standard errors. Categorical variables are expressed as numbers and percentages. Differences between the gastroscopy group and no gastroscopy group

were analyzed using the independent sample t-test for continuous variables, and chi-squared tests or Fisher exact tests for categorical variables, respectively. Statistical analyses were performed using SPSS version 23.0 for Windows (SPSS, Chicago, IL). Using the OneToManyMTCH of SAS macro (SAS Institute Inc., Cary, NC) in case-control matching on the propensity score, we performed the 1:1 propensity score matching (PSM) based on sex and SAPS II. *P* values of < 0.05 were considered statistically significant.

Results

During the study period, 464 patients in the ICU used a high-dose PPI for suspected GI bleeding. About 348 of them met the exclusion criteria, and 116 were finally enrolled. Among the enrolled patients, 34 patients had gastroscopy during ICU stay, and 33 patients from each group were selected for the 1:1 PSM (Fig. 1).

Without PSM, no significant difference was found for age, sex, and the number of medical patients between the gastroscopy and no-gastroscopy groups (age, 67.24 ± 2.38 vs. 67.32 ± 1.68; male, 47.1% vs. 61%; medical patients, 79.4% vs. 85.4%). The no-gastroscopy group presented a higher SAPS II score, but the difference was not statistically significant (40.35 ± 1.73 vs. 39.62 ± 2.36, *P* = 0.81). The mean of the length of ICU stays before suspected GI bleeding was 9.01 ± 1.00 days, and the most common cause of suspected GI bleeding was the color change of nasogastric tube drainage material (no gastroscopy vs. gastroscopy, 62.1% vs. 61.8%, *P* = 0.97) (Table 1).

Table 1
General characteristics of suspected upper GI bleeding according to undergoing a gastroscopy

Variables	No gastroscopy (n = 82)	Gastroscopy (n = 34)	*P* value
Age (year)	67.32 ± 1.68	67.24 ± 2.38	0.98
Male	50 (61)	16 (47.1)	0.17
Medical patients	70 (85.4)	27 (79.4)	0.43
Surgical patients	12 (14.6)	7 (20.6)	0.43
SAPS II score	40.35 ± 1.73	39.62 ± 2.36	0.81
Mechanical ventilation	46 (56.1)	15 (44.1)	0.24
Hypertension	43 (52.4)	22 (64.7)	0.23
Diabetes	31 (37.8)	9 (26.5)	0.24
Cerebral vascular disease	21 (25.6)	5 (14.7)	0.20
Cardiovascular	18 (22)	5 (14.7)	0.37
Chronic lung disease	6 (7.3)	2 (5.9)	1.00
Chronic kidney disease	7 (8.5)	5 (14.7)	0.32
Chronic liver disease	5 (6.1)	1 (2.9)	0.67
Solid cancer	4 (4.9)	2 (5.9)	1.00
Time of suspected GI bleeding (days, after admission)	8.56 ± 1.08	10.09 ± 2.22	0.49
Cause of suspected GI bleeding			
The change of nasogastric tube drainage material	51 (62.1)	21 (61.8)	0.97
Melena	5 (6.1)	7 (20.6)	0.04
Hemoglobin decrease	26 (31.7)	6 (17.6)	0.12
Values are presented as number (%) or mean ± standard error *GI* gastrointestinal, *SAPS* Simplified Acute Physiology Score			

In the gastroscopy group. 38.2% of gastroscopies showed normal findings. Among the abnormal results, gastric ulcer was most common (n = 9, 26.5%), esophagitis and gastritis occurred in 6 (17.6%), and nasogastric tube erosion was observed in 4 (11.8%) cases. Major lesions requiring hemostatic procedures were 12 (35.3%) (Table 2).

Table 2
Findings of the gastroscopy

Normal	**13 (38.2%)**
Esophagitis or gastritis	6 (17.6%)
Nasogastric tube erosion	4 (11.8%)
Gastric ulcer	9 (26.5)
Duodenal ulcer	1 (2.9%)
Mallory-weiss tear	1 (2.9)
Minor lesion	9 (26.5%)
Major lesion	12 (35.3%)
Values are presented as number (%)	

Without PSM, the gastroscopy group's hemoglobin level at the time of suspected GI bleeding was lower than that of the no-gastroscopy group (8.91 ± 0.38 vs. 9.83 ± 0.22, $P = 0.03$). Hemoglobin level after one week was not significantly different between the two groups (gastroscopy group vs. no-gastroscopy group, 9.43 ± 0.23 vs. 9.70 ± 0.16, $P = 0.27$). The requirement for RBC transfusion in the gastroscopy group was higher than that in the no- gastroscopy group ($P = 0.03$). The length of ICU stay and ICU mortality were similar in both groups ($P = 0.95$ and $P = 0.36$, respectively) (Table 3). After PSM, a comparison between gastroscopy and no-gastroscopy groups showed the same result with analysis without PSM: lower initial hemoglobin level, similar hemoglobin level after one week, and higher requirement of RBC transfusion in the gastroscopy group than in the no-gastroscopy group ($P = 0.01$, $P = 0.21$, and $P = 0.01$, respectively). There was no significant difference between the groups in terms of length of ICU stay and ICU mortality ($P = 0.64$, $P = 0.55$, respectively) (Table 4). Regarding the change in hemoglobin level after one week from suspected GI bleeding, the gastroscopy group showed increased hemoglobin level, and the no-gastroscopy group presented a decreased hemoglobin level. However, there was no statistically significant difference between the two groups in all patients (gastroscopy vs. no gastroscopy, 0.52 ± 0.47 vs. − 0.08 ± 0.20; $P = 0.24$) and PSM matched patients (gastroscopy vs. no gastroscopy, 0.62 ± 0.47 vs. − 0.29 ± 0.28; $P = 0.10$) (Fig. 2).

Table 3
Blood transfusion requirements and outcome according to undergoing a gastroscopy

Variables	No gastroscopy (n = 82)	Gastroscopy (n = 34)	*P* value
Initial hemoglobin, g/dL	9.83 ± 0.22	8.91 ± 0.38	0.03
Initial hematocrit, %	29.47 ± 0.65	25.04 ± 1.56	0.01
Initial platelet, 10^{*3}/μL	192.37 ± 11.94	205.74 ± 20.44	0.59
Hemoglobin (after one week), g/dL	9.70 ± 0.16	9.43 ± 0.23	0.27
Hematocrit (after one week), %	29.31 ± 0.50	28.02 ± 0.69	0.16
Platelet (after one week), 10^{*3}/μL	227.83 ± 17.98	200.38 ± 20.80	0.38
RBC transfusion (packs)	2.28 ± 3.06	3.70 ± 0. 61	0.03
ICU stay (days)	22.87 ± 2.15	23.15 ± 4.06	0.95
ICU mortality	21 (25.6)	6 (17.6)	0.36
Values are presented as number (%) or mean ± standard error *ICU* intensive care unit, *RBC* red blood cell			

Table 4
After PSM, blood transfusion requirements and outcome according to undergoing a gastroscopy

Variables	No gastroscopy (n = 33)	Gastroscopy (n = 33)	*P* value
Initial hemoglobin, g/dL	10.10 ± 0.32	8.76 ± 0.36	0.01
Initial hematocrit, %	30.33 ± 0.92	24.58 ± 1.54	0.01
Initial platelet, 10^{*3}/μL	191.33 ± 17.37	206.55 ± 21.05	0.58
Hemoglobin (after one week), g/dL	9.81 ± 0.24	9.38 ± 0.24	0.21
Hematocrit (after one week), %	29.53 ± 0.74	27.90 ± 0.70	0.12
Platelet (after one week), 10^{*3}/μL	232.91 ± 24.89	198.09 ± 21.31	0.29
RBC transfusion (packs)	1.55 ± 0.46	3.81 ± 0. 61	0.01
ICU stay (days)	21.27 ± 3.06	23.67 ± 4.15	0.64
ICU mortality	8 (24.2)	6 (18.2)	0.55
Values are presented as number (%) or mean ± standard error *ICU* intensive care unit, *PSM* propensity score matching, *RBC* red blood cell			

Discussion

Our results showed that in PSM matched patients, hemoglobin levels at the time of suspected GI bleeding were lower in the gastroscopy group than in the no-gastroscopy group and similar hemoglobin levels were observed after one week in both groups. The gastroscopy group required more RBC transfusion and there was no significant difference in the length of ICU stay and ICU mortality between the two groups.

Complicated risk factors in ICU patients were associated with SRMD including mechanical ventilation, trauma, surgery, sepsis or severe burns, related coagulopathy. Bleeding is associated with a 20–30% increase in absolute risk of mortality and extends the length of ICU stay by about 4–8 days [3]. After the introduction of omeprazole, PPI has been the most effective currently available medication and is widely used for acid-related diseases, including peptic ulcers. It is also used in prophylactic treatment for critically ill patients and upper active GI bleeding. In acute GI bleeding, PPI therapy showed reduced mortality and reduced rebleeding risk compared to control treatment (placebo or histamine 2 receptor antagonists) (odds ratio, 0.56 [confidence intervals, 0.34 to 0.94] and 0.43 [0.29 to 0.63], respectively) [7]. Although one meta-analysis did not show any differences in the risk for mortality or rebleeding between high-dose and non-high-dose PPIs, high-dose PPI treatment seems to be tolerable in critically ill patients, considering that an indirect comparison study yielded the superiority of high-dose PPI therapy; adverse

effects of high-dose PPI were poorly reported in most studies [9, 10]. In this study also, no critical adverse event, such as thrombophlebitis and discontinuous infusion was found.

Gastroscopy is a useful tool for controlling acute GI bleeding for diagnostic and therapeutic purposes. However, the morbidity of the procedure is higher in ICU patients than in non-ICU patients. Other studies reported that post-procedure cardiopulmonary complications, such as newly developed pulmonary infiltration and edema were 20–50% in critically ill patients [11, 12]. The consensus guideline suggests that early endoscopy (within 24 hours of GI bleeding) based on the endoscopy within 24 hours was associated with lower in-hospital mortality [13], but that could not provide recommendations for hemodynamically unstable patients because of lack of data and debated results [13, 14]. There is no randomized study on the profitability of immediate gastroscopy in critically ill patients without massive upper GI bleeding. When GI bleeding is suspected during the ICU treatment, it is always challenging to determine whether or not to perform an endoscopy by comparing the benefits and risks. In a previous study, which was not a comparative study, among the 84 patients who underwent gastroscopy during ICU stay, only 5.8% needed a hemostatic procedure during gastroscopy; the other 94.2% had normal findings, or the lesions required only pharmacologic treatment [15]. Another study on ICU patients with overt GI bleeding showed that hemostatic procedures were performed in 9 (15%) of the total 66 patients. In this study, the percentage of normal findings (38.2%) and peptic ulcer (29.4%) lesions were similar to those reported in previous studies [16, 17]. Although more hemostatic procedures were performed (35.3%) than previous studies, the gastroscopy group did not show decrease in the requirement of RBC transfusion, ICU mortality, and duration of stay. In addition, comparison between the gastroscopy group with the hemostatic procedures and no- gastroscopy group after PSM also did not show any benefit in RBC transfusion requirement, length of ICU stay, and ICU mortality (data was not shown). Considering the higher morbidity and workload of medical personnel during endoscopy examination in ICU cases, including the transport of equipment or patients, it is appropriate to prioritize high-dose PPI treatment and avoid forced gastroscopy in ICU patients with suspected GI bleeding.

Our study has several limitations. Gastroscopy and hemostatic procedures were performed by gastroenterologists. There may be other factors that influenced the decision, which were not fully investigated due to the study's retrospective nature. However, we analyzed PSM results and did exclude massive GI bleeding requiring endoscopic procedure such as hematemesis or hematochezia. Therefore, we believe that this study is meaningful in determining the value of gastroscopy in critically ill patients with suspected GI bleeding. Second, this study was conducted in single center. There may be different results in other medical centers with another population and treatment policy regarding PPI and gastroscopy. Hence, further studies with large populations and multiple centers are needed.

Conclusion

Gastroscopy in critically ill patients using high-dose PPI for suspected GI bleeding, except massive bleeding, has no definite benefit. An individualized approach based on a complete clinical picture should

be given priority. It is appropriate to consider deferring if there is a hesitation in conducting gastroscopy in ICU stay patients.

Abbreviations

GI, gastrointestinal; ICU, intensive care unit; PPI, proton pump inhibitor; PSM, propensity score matching; RBC, red blood cell; SAPS, Simplified Acute Physiology Score; SRMD, stress-related mucosal damage.

Declarations

Ethics approval and consent to participate

This retrospective cohort study was approved by The Institutional Review Board (IRB) of Kyung Hee University Hospital approved the study protocol (IRB no: 2020-10-006). The need for informed consent was waived due to the retrospective nature of the study involving chart review only. The study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Consent for publication

Not applicable.

Competing interests

The author declare that they have no competing interests.

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Authors' contributions

WG analyzed and interpreted the patient data, and wrote the manuscript.

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Figures

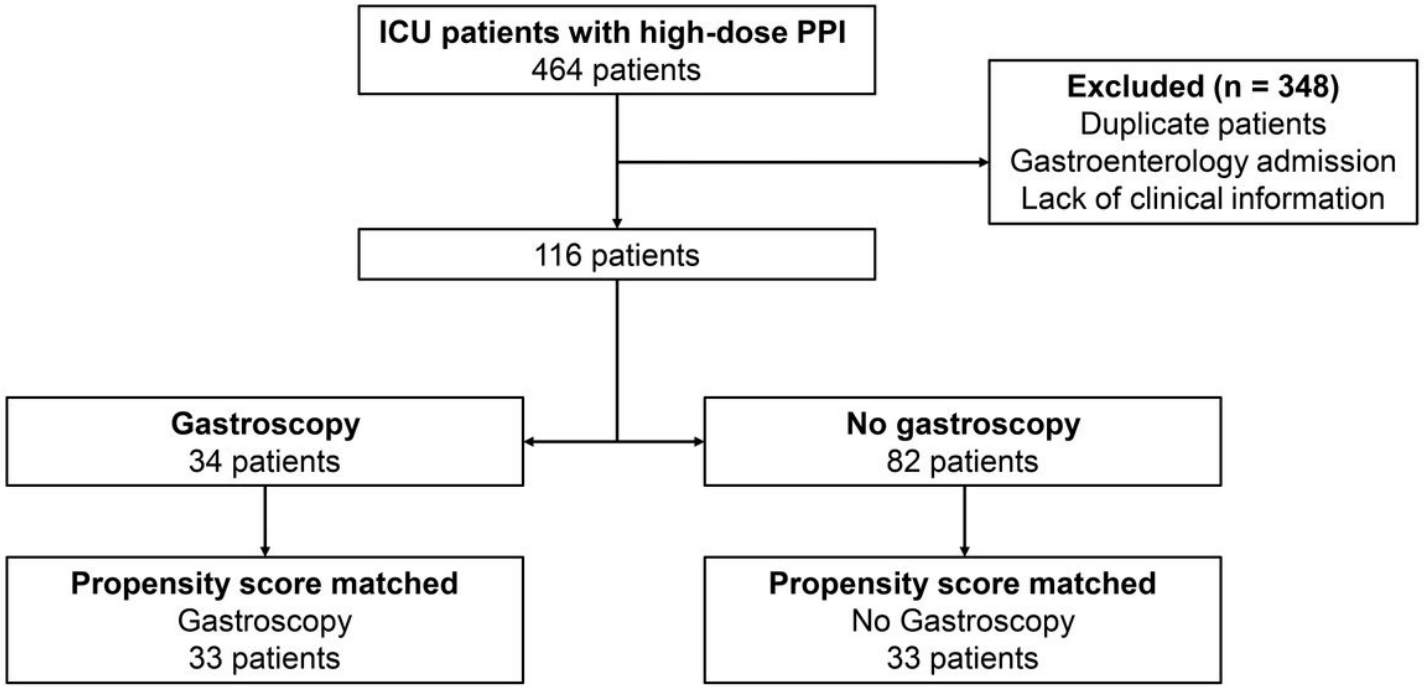
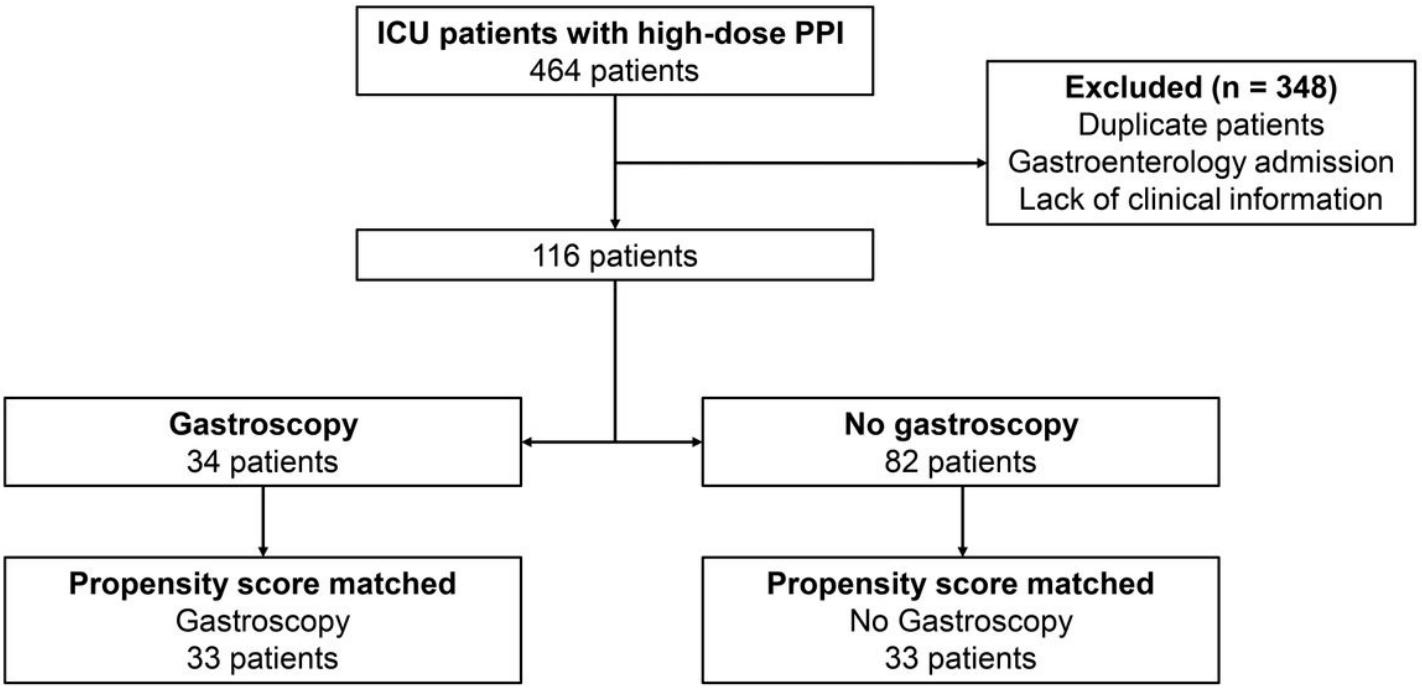


Figure 1

Diagram showing the flow of participants through each stage of the study. PPI: proton pump inhibitor.



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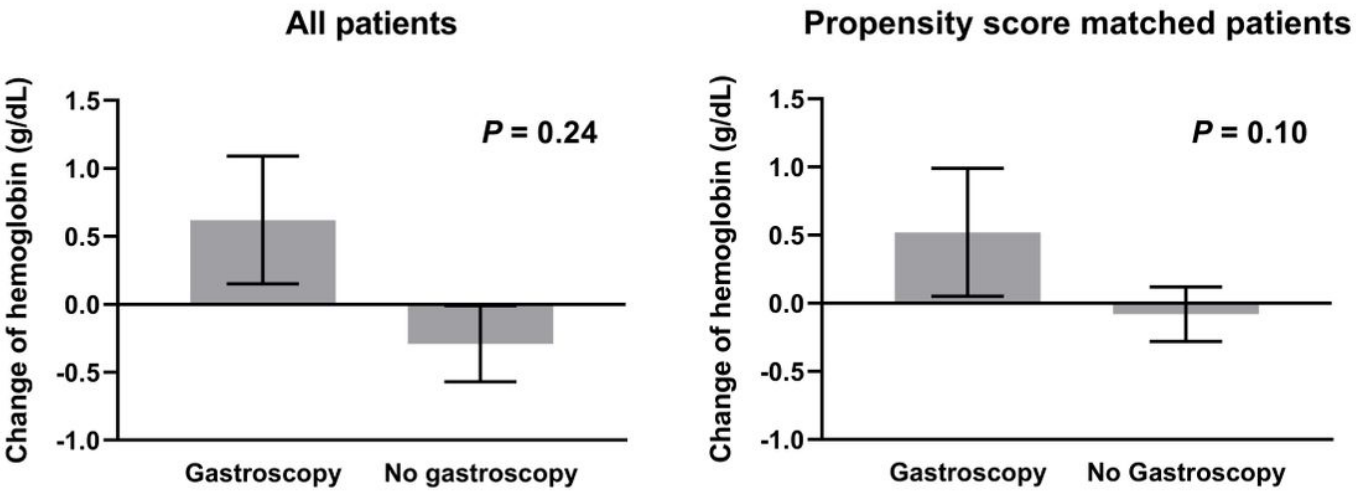
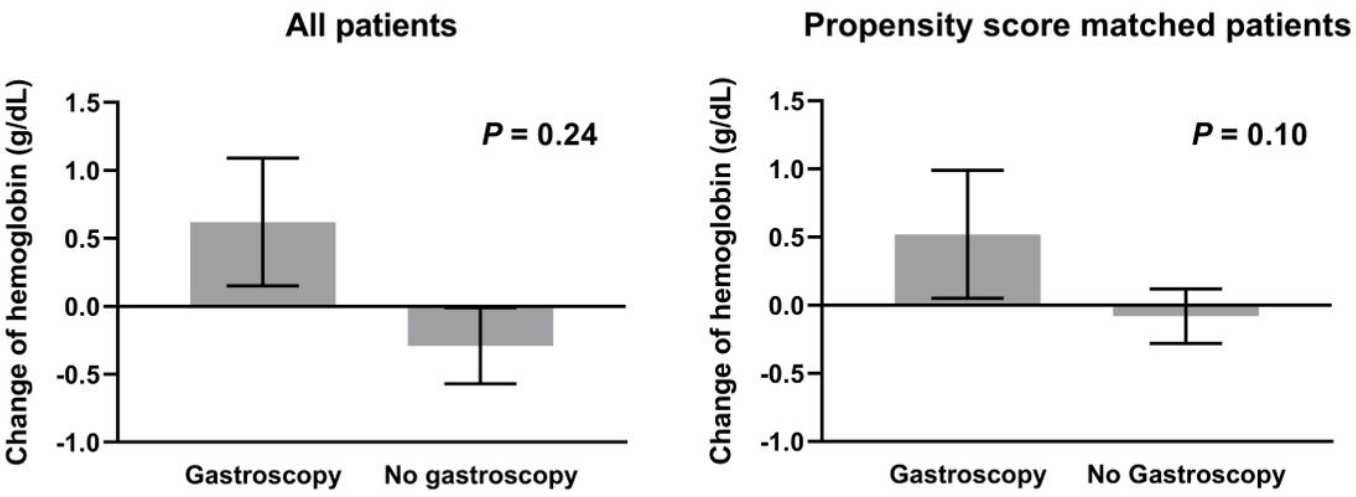


Figure 2

Comparison of the change of hemoglobin between the gastroscopy group and no gastroscopy group.



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