Study on the preventive effect of intravenous esomeprazole in the management of nonvarices upper gastrointestinal bleeding

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Abstract
This retrospective study investigated the preventive effect of intravenous esomeprazole (IVEO) in the prevention of nonvarices upper gastrointestinal bleeding (NUGIB).

This study enrolled 130 patients with NUGIB and all of them underwent successful endoscopic hemostasis, of which 65 cases received routine management and IVEO (Group A) and the other 65 cases received routine management alone (Group B). The primary outcome (recurrent bleeding rate within 72-hour, 7-day, and 30-day), and secondary outcomes ((all-cause mortality, bleeding-related mortality, blood transfused, hospital stay (day), and incidence of adverse events)) were compared between 2 groups.

Patients in the group A showed lower recurrent bleeding rate within 72-hour (P < .05), 7-day (P < .05), and 30-day (P < .05), than that of patients in the group B. However, no significant differences were identified in all-cause mortality (P = .26), bleeding-related mortality (P = .57), blood transfused (P = .33), and hospital stay (P = .74) between 2 groups. In addition, both groups had similar safety profile.

This study found that routine management and IVEO was superior to the routine management alone for preventing the recurrent bleeding rate after successful endoscopic hemostasis in patients with NUGIB.

Abbreviations: AEs = adverse events, IVEO = intravenous esomeprazole, NUGIB = nonvarices upper gastrointestinal bleeding.

Keywords: adverse events, effect, esomeprazole, nonvarices upper gastrointestinal bleeding

1. Introduction
Nonvarices upper gastrointestinal bleeding (NUGIB) is one of the most common encountered emergency disorders in daily clinical practice worldwide. It is reported that its incidence varies between 50 and 150 cases per 100,000 adults annually. Although its therapeutic managements have developed, its morbidity and mortality rate remain substantial. It is reported that its 30-day mortality rate ranges from 5% to 10%. Thus, the current management of NUGIB aims to stabilize hemodynamic circulation, stop existing bleeding, and prevent its recurrence. Endoscopic hemostatic intervention is reported that it cannot only identify high-risk stigmata on ulcers, but also can help control gastrointestinal bleeding to prevent its rebleeding and to decrease its mortality and morbidity. However, there are still some patients who suffer from rebleeding accident. Thus, further medication is needed after successful endoscopic hemostasis.

Studies suggested that intravenous esomeprazole (IVEO) can help prevent NUGIB. But there is lacking of evidence to support it for the prevention of recurrent bleeding in Chinese patients with NUGIB. This retrospective study evaluated the preventive effect of IVEO for the prevention of recurrent bleeding in patients with NUGIB after successful endoscopic surgery.

2. Methods
2.1. Ethical approval
This retrospective study, based on the clinical data, was approved by the local ethics committee (Medical Ethical Committee of Shanghai Hospital Affiliated to Navy Medical University). This study waived the requirement of sign informed consent from patients, because it was not risky for the patients.

2.2. Patients and study design
We performed this study based on the relevant guidelines and regulations. In this retrospective study, 130 eligible patients with...
NUGIB treated at Changhai Hospital Affiliated to Navy Medical University in China from June 2016 to May 2018 were included. All those patients achieved successful endoscopic hemostasis and routine management. In addition, among all those patients, 65 cases received IVEO (Group A), while the other 65 cases did not receive it (Group B).

Patients aged between 18 and 75 years old and diagnosed with NUGIB were included in this retrospective study. Moreover, all patients received successful endoscopic hemostasis. Exclusion criteria mainly included the following criteria:

1. bleeding from multiple ulcers or concomitant upper gastrointestinal sources;
2. gastrointestinal cancers;
3. patients had taken IVEO;
4. active GI bleeding;
5. advanced renal and liver diseases;
6. allergy to NUGIB; and
7. incomplete patient case records.

2.3. Intervention schedule
All patients in both groups received successful endoscopic hemostasis and routine management. The routine treatment included monitoring vital signs and circulatory conditions, and replenishing body fluids (established venous channels to replenish blood volume, and applied vasodilatory drugs to improve blood perfusion). In addition, patients in the Group A also received IVEO 80 mg (AstraZeneca China, Shanghai, China) as a bolus infusion over 30 minutes. Then, it followed by a continuous intravenous infusion of 8 mg/h over 71.5 hours.

2.4. Outcome measurements
The primary outcome was recurrent bleeding rate within 72-hour, 7-day, and 30-day. The secondary outcomes were all-cause mortality, bleeding-related mortality, blood transfused, hospital stay (day), and adverse events (AEs).

2.5. Statistical analysis
In this study, we utilized SPSS software (SPSS V.19.0, IBM Corp., Armonk, NY) for statistical analysis. The continuous data was calculated as mean and standard deviation or number (%). The t test or Mann–Whitney U test was employed to compare continuous data, and the chi² test for Fisher exact test was placed to compare categorical data. For all statistical analysis, a 2-side P < 0.05 was defined statistically significant.

3. Results
3.1. Patient baseline features
A total of 130 eligible patients after successful endoscopic hemostasis were enrolled in this study. Of those, 65 patient cases received routine management and IVEO (Group A), and the other 65 patient cases underwent routine treatment only (Group B). The clinical baseline features of 130 patients in both groups are presented in Table 1. All features were balanced between 2 groups in statistics (P > 0.05, table 1).

### Table 1

| Characteristics                  | Group A (n = 65) | Group B (n = 65) | P value |
|----------------------------------|-----------------|-----------------|---------|
| Mean age (yr)                    | 54.4 (12.3)     | 53.9 (11.7)     | .81     |
| Gender                           |                 |                 |         |
| Male                             | 41 (63.1)       | 45 (69.2)       | .46     |
| Female                           | 24 (36.9)       | 20 (30.8)       |         |
| Race (Asian China)               | 65 (66.2)       | 65 (75.4)       |         |
| Body mass index (kg/m²)          | 22.9 (3.0)      | 23.1 (3.2)      | .71     |
| Current alcohol consumption      | 23 (35.4)       | 20 (30.8)       | .58     |
| Current smoking                  | 43 (66.2)       | 49 (75.4)       | .25     |
| Helicobacter pylori status       |                 |                 |         |
| Positive                         | 39 (60.0)       | 42 (64.6)       | .59     |
| Negative                         | 19 (29.2)       | 18 (27.7)       | .85     |
| Unclear                          | 7 (10.8)        | 5 (7.7)         | .55     |
| Previous ulcer disease           | 20 (30.8)       | 24 (36.9)       | .46     |
| History of peptic ulcer          |                 |                 |         |
| Duodenal ulcer                   | 15 (23.1)       | 19 (29.2)       | .43     |
| Gastric ulcer                    | 17 (26.2)       | 13 (20.0)       | .41     |
| Both ulcer                       | 3 (4.6)         | 4 (6.2)         | .70     |
| Bleeding ulcer location          |                 |                 |         |
| Stomach                          | 14 (21.5)       | 10 (15.4)       | .37     |
| Duodenum                         | 51 (78.5)       | 55 (84.6)       |         |

Data are presented as mean ± standard deviation or number (%).

3.2. Primary outcome in Group A and Group B
Results of recurrent bleeding rate are listed in Table 2. Patients in the Group A achieved better improvement of overall recurrent bleeding rate within 72-hour (P < 0.05, table 2), 7-day (P < 0.05, table 2) and 30-day (P < 0.05, table 2), than that of patients in Group B. However, there were not significant differences in results of recurrent bleeding rate at different time points when patients were grouped based on the type of age and sex (P > 0.05, table 2).

3.3. Secondary outcomes in Group A and Group B
There were not significant differences in secondary outcomes of all-cause mortality (Group A, 3.1% vs Group B, 7.7%; P = .26; Table 3), bleeding-related mortality (Group A, 1.5% vs Group B, 3.1%; P = .57; table 3), blood transfused (Group A, 1.57 (2.21) vs Group B, 1.57 (2.21) (P > 0.05, table 3).
Group B, 9.2%; Group B, 7.7%; 6.2%; P = .77; P = .57; P = .33; table 4). Its results partly are consistent with the findings suggest that high-dose IVEO after successful endoscopic treatment can benefit participants with high-risk peptic ulcer bleeding decreased recurrent bleeding within 72 hours and even lasts upon to 30 days. Its results partly are consistent with the present study. In this retrospective cohort study, we compared the preventive effect between Chinese NUGIB patients with IVEO combined routine treatment, and routine therapy alone. Our study reported that there were significant differences in preventing recurrent bleeding rate within 72-hour, 7-day, and 30-day between 2 groups. It indicates that IVEO may benefit in preventing recurrent bleeding rate within 30 days after successful endoscopic hemostasis.

On the other hand, we did not detect significant differences in all-cause mortality, bleeding-related mortality, blood transfused, and hospital stay between 2 groups. It suggests that IVEO may not prevent mortality and hospital stay in patients NUGIB. Moreover, no AEs (serious AEs, duodenal ulcer hemorrhage, gastric ulcer hemorrhage, vomiting, nausea, abdominal pain, constipation, and dyspepsia) differed significantly between 2 groups, which showed that treatments in both groups had similar safety profile.

There were several limitations in this retrospective study. The first limitation was its retrospective nature because of the purely observational features when compared with prospective studies. The second limitation was that its very finite sample size made the statistical results that may be inaccurate sufficiently to reach an undisputed conclusion. The third limitation was that a total of 30 days from baseline to the end of observation was quite short. Thus, longer term of preventive effect and safety of IVEO in the prevention of NUGIB should be explored in further studies. To address such limitation, studies should harvest complete data from multiple hospitals to increase its sample size and follow-up period.

5. Conclusion
The results of this study found that routine management and IVEO can decrease the recurrent bleeding rate after successful endoscopic hemostasis in patients with NUGIB.

Table 3

| Outcomes               | Group A (n=65) | Group B (n=65) | P value |
|------------------------|----------------|----------------|---------|
| All-cause mortality    | 2 (3.1)        | 5 (7.7)        | .26     |
| Bleeding-related mortality | 1 (1.5)    | 2 (3.1)        | .57     |
| Blood transfused (unit) | 1.57 (2.21)  | 1.96 (2.38)    | .33     |
| Hospital stay (d)      | 4.6 (5.0)      | 4.9 (5.3)      | .74     |

Data are present as mean±standard deviation or number (%).

3.4. AEs in Group A and Group B
There were not significant differences in AEs of serious AEs (Group A, 1.5% vs Group B, 3.1%; P = .57; Table 4), duodenal ulcer hemorrhage (Group A, 3.1% vs Group B, 10.8%; P = .10; table 4), gastric ulcer hemorrhage (Group A, 1.5% vs Group B, 7.7%; P = .13; table 4), vomiting (Group A, 1.5% vs Group B, 4.6%; P = .33; table 4), nausea (Group A, 3.1% vs Group B, 6.2%; P = .41; table 4), abdominal pain (Group A, 3.1% vs Group B, 7.7%; P = .26; table 4), constipation (Group A, 3.1% vs Group B, 9.2%; P = .16; table 4), and dyspepsia (Group A, 4.6% vs Group B, 7.7%; P = .47; table 4) between 2 groups.

4. Discussion
Previous study investigated the efficacy of IVEO prevents recurrent peptic ulcer bleeding in a multiethnic subject. Its findings suggest that high-dose IVEO after successful endoscopic treatment can benefit participants with high-risk peptic ulcer bleeding decreased recurrent bleeding within 72 hours and even lasts upon to 30 days. Its results partly are consistent with the present study. In this retrospective cohort study, we compared the preventive effect between Chinese NUGIB patients with IVEO combined routine treatment, and routine therapy alone. Our study reported that there were significant differences in preventing recurrent bleeding rate within 72-hour, 7-day, and 30-day between 2 groups. It indicates that IVEO may benefit in preventing recurrent bleeding rate within 30 days after successful endoscopic hemostasis.

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Table 4

| AEs                     | Group A (n=65) | Group B (n=65) | P value |
|-------------------------|----------------|----------------|---------|
| Serious AEs             | 1 (1.5)        | 2 (3.1)        | .57     |
| Duodenal ulcer hemorrhage | 2 (3.1)      | 7 (10.8)       | .10     |
| Gastric ulcer hemorrhage | 1 (1.5)       | 5 (7.7)        | .13     |
| Vomiting                | 1 (1.5)        | 3 (4.6)        | .33     |
| Nausea                  | 2 (3.1)        | 4 (6.2)        | .41     |
| Abdominal pain          | 2 (3.1)        | 6 (9.2)        | .16     |
| Constipation            | 2 (3.1)        | 5 (7.7)        | .26     |
| Dyspepsia               | 3 (4.6)        | 5 (7.7)        | .47     |

Data are present as number (%).

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