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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Endoscopy*

Manuscript NO: 82359

Title: Relationships of Hospitalization Outcomes and Timing to Endoscopy in Non-Variceal Upper Gastrointestinal Bleeding: A Nationwide Analysis

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04970307
Position: Peer Reviewer
Academic degree: MMed

Professional title: Associate Chief Physician, Surgeon, Surgical Oncologist

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2022-12-16

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-12-19 10:35

Reviewer performed review: 2022-12-22 03:04

Review time: 2 Days and 16 Hours

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Based on a nationwide analysis, the authors concluded that early EGD in NVUGIB is associated with lower mortality and decreased healthcare usage, irrespective of AC status. Although numerous studies have investigated the optimal time of EGD in patients with upper gastrointestinal bleeding and consensus that early EGD is associated with better outcomes have been achieved, this study is still has the strength of large sample, providing solid evidence. The design, analysis and writing of this manuscript are well, only one comment will be listed below:

Re: Thank you very much for acknowledging the importance and relevance of our study.

The definition of hospital volume in this study is complex and strange, it varied according to regions and beds. Actually, the outcomes of patients with almost very disease were better in experienced and high-volume hospitals, resulting from various reasons, one of which are the number of patients the clinicians experienced. The number of patients will not be decreased for clinicians to obtain the same experience when they work in hospitals with less volumes or located in rural. It is better to category hospitals

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based on the number of patients admitted for NVUGIB per year.

Re: The definition of hospital size in our study was in accordance with the National Inpatient Sample database which is the largest inpatient database in the USA, and which is the database used in our study.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06198465
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: United States

Manuscript submission date: 2022-12-16

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2023-01-29 09:35

Reviewer performed review: 2023-02-02 13:47

Review time: 4 Days and 4 Hours

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[Y] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This is a fascinating study on non-variceal upper gastrointestinal bleeding. Regarding the need for emergency nighttime endoscopy, it would be interesting if the results of night and day endoscopies could be compared in each group.

Re: Thank you for recognizing the pertinence of our study. Unfortunately, given the granularity of the database, the information between the nighttime and day endoscopy was not available.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02936184
Position: Editorial Board
Academic degree: MBChB, MD, MRCP, MSc
Professional title: Consultant Physician-Scientist, Professor
Reviewer's Country/Territory: United Kingdom
Author's Country/Territory: United States

Manuscript submission date: 2022-12-16
Reviewer chosen by: Dong-Mei Wang
Reviewer accepted review: 2023-01-29 21:53
Reviewer performed review: 2023-02-07 00:29
Review time: 8 Days and 2 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [Y] Grade D: No novelty
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	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Dear Authors Thank you for your great effort and time to collect all these data and analyze the results. I have some comments:

- Regarding classification of patients in relation to timing of endoscopy, the calcification used in this study is unusual and there is no referrals supporting this classification. - Usually patients are divided into: a) Emergency endoscopy in less than 6 hours b) Urgent endoscopy 6-12 hours c) Early endoscopy more than 12 hours but less than 24 hours d) Elective/late endoscopy after 24 hours - It is really on clear why the patient will remain admitted because of upper GI bleeding for 48 or even 72 hours without endoscopy and why a patient will need endoscopy done after 48-72 hours????

Re: Point well taken, however, across the USA hospitals, a more conservative measure has been adopted to manage upper GI bleed. Many patients are observed with a trial of PPI. Some patients can remain in the hospital for up to 72 hours and get an endoscopy then if the bleed is not controlled with the trial of PPI.

- In table 1: What is the importance of dividing patients according to the payment

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method/insurance type?

Re: Insurance plays a key role in the USA healthcare system, and it's always important to see how the method of payment can affect care.

- During assessment of hospital stay: Do days spent in the hospital before performing the gastroscopy are counted? Or the hospital stay is calculated from the time of having endoscopy done?

Re: hospital stay refers to the time spent in the hospital, including the time prior to the EGD.

- The classification according to hospital bit size has been accepted planed in a very long way and too many unnecessarily details. It would be better if the hospital bits ice classification was just divided into: Small-sized hospital less than 50 beds, medium-sized hospital from 50 to 100 and large sized hospital more than 100 beds. Hospitals can be divided into teaching versus non teaching and Urban versus rural. –

Re: The definition of hospital size in our study was in accordance with the National Inpatient Sample database which is the largest inpatient database in the USA, and which is the database used in our study.

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Although the number of patients in rolled in such study was very huge, important analysis has not been performed; comparison between the endoscopic findings of patients wonder went endoscopy in the 1st 24 hours with dose who underwent endoscopy after 24 hours after receiving medical treatment in the form of intravenous PPI. Do the endoscopic findings differ between both groups?

Re: The primary outcome of this study was in-hospital all-cause mortality which was successfully carried out. Furthermore, in figure 2 you can find different etiologies of the GI bleed found during EGDs, with PUD being the most common.

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02535147
Position: Editorial Board
Academic degree: MD, PhD

Professional title: Associate Professor, Doctor, Lecturer

Reviewer's Country/Territory: Japan

Author's Country/Territory: United States

Manuscript submission date: 2022-12-16

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2023-01-29 12:26

Reviewer performed review: 2023-02-07 11:37

Review time: 8 Days and 23 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
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Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Weissman S, et al. have identified that early EGD (< 24 hours) is important to reduce mortality, ICU admission, hospital length of stay, and hospital charges using the National Inpatient Sample database. Other factors such as male sex, Hispanic or Asian race, CCI=4 could predict poor outcomes in patients with NVUGIB. It is a unique and interesting study.

Re: Thank you very much for your keen analysis and these kind words.

However, there are several serious problems in the study and the authors should address the comments below.

Major points:

1) The authors should clearly show the result of subgroup analysis to identify the anticoagulation use in Table that was mentioned in Page 7, Lines 3–4. The authors should also show the result of sensitivity analysis in Table that was mentioned in Page 7, Lines 6–7.

Re: The subgroup analysis for all causes of in-hospital mortality of patients on AC and without AC are clearly reported in the Results section, making the need for a separate

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table dispensable.

2) The authors should include information of H. pylori infection status, medications (e.g., antiplatelets and anticoagulants), and hemostasis (e.g., endoscopic hemostasis, IVR, and surgery) in Table 1. Moreover, comorbidities should be described in more detail in Table 1.

Re: Point well taken, however, it was clearly stated in the results section that information about antiplatelets was not available, and the anticoagulants used were listed as well. "Total all cause in-hospital mortality for patients on long-term AC (either warfarin, dabigatran, rivaroxaban, or apixaban) (of note, anti-platelet therapy use was unable to be determined) admitted with NVUGIB was 7.0% as compared to 5.1% [aOR 2.02, p=0.001] in patients that were not on AC". Furthermore, given the granularity of the database, the information about H. Pylori infection was not available. 30 comorbidities were taken into account among which: Congestive heart failure, Cardiac arrythmias, Valvular disease, Pulmonary circulation disorders, peripheral vascular disorders, Hypertension, paralysis, neurodegenerative disorders, uncomplicated diabetes, complicated diabetes, hypothyroidism, renal failure, liver disease, peptic ulcer disease excluding bleeding, AIDS/HIV, lymphoma, metastatic cancer, solid tumor without metastasis, rheumatoid arthritis/collagen vascular diseases, coagulopathy, obesity, weight loss, fluid and electrolyte disorders, blood loss anemia, deficiency anemia, alcohol abuse, drug abuse, Psychoses, and depression. The list of comorbidities was added in the methods section. Marked in red.

3) Although the authors described that "other factors such as–Male sex, Hispanic or Asian race, Medicaid insurance, age > 50, and those with more numerous comorbidities, all of which may help predict patients at high risk for adverse hospital outcomes in NVUGIB", the results of Medicaid insurance and age > 50 were not found in Table 2. The authors should show the data in Table 2. Moreover, the authors should state in the

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footnote by which factors aOR was adjusted in Table 2.

Re: Thank you for the great point raised, there was a typo in the results and conclusion. Only, Male sex, Hispanic or Asian race, and those with more numerous comorbidities. And this was changed in the manuscript. Marked in red. The multivariate regression analysis was performed to adjust for gender, race category, age category, insurance payer, hospital details (region, size, location, ownership), comorbidities and EGD within 1 day of admission. Regression models were then built by including all confounders that were found to be significant by univariate analysis, to calculate adjusted odds ratio.

Minor points:

1) It would be ideal to add information about the location of bleeding peptic ulcer in Figure 2.

Re: the information was provided in the figure, esophageal ulcers, Mallory Weiss (lower esophagus), peptic ulcer (stomach and duodenum), and Gastritis/duodenitis.

2) The relationship between left and right pie charts is unclear in Figure 1. Moreover, the caption is too small and hard to be read in Figure 1.

Re: the chart on the left differentiates patients that underwent EGD and those who did not, whereas the chart on the right addresses the timing of EGD for patients that underwent EGD. The quality of the figure will be improved when we submit the power point file of the figure prior to publication.

3) The description of lowercase and uppercase ("a" and "A", "b" and "B") should be unified in Figure 3–6.

Re: Point well taken. However, these are unified.