

Dear Editor,

Thank you for your letter and comments concerning our manuscript (Manuscript NO.: 64137, Retrospective Study). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made a careful revision which we hope meet with approval. All revised portions are marked in red in the manuscript which we would like to submit for your kind consideration.

The responds to the reviewers' and editor's comments are as following (the replies are highlighted in blue).

Reviewer #1:

Specific Comments to Authors:

1- It is not clear why the authors choose the nonoperative treatment of patients with PPU? This should be clarified.

Author response: Thank you for your comments. The reasons of why we choose the nonoperative treatment of patients with PPU are: Nonoperative treatment should be considered in patients with uncomplicated PPU, which avoids surgery and its resultant morbidity. Moreover, several retrospective series have reported that success rates of nonoperative treatment is in the range of 40%-80% for patients with PPU, and overall morbidity and mortality are comparable to operative treatment. (Please see Introduction section)

2- It should be clarified on what bases the authors assigned patients for non-operative treatment and others for operative treatment

Author response: Thank you for your comments. Patients were assigned for non-operative treatment and operative treatment based on whether vital parameters are normal and the findings of peritonitis or septic shock. Non-operative management (NOM) could be considered in patients who have normal vital parameters and does not have signs of peritonitis or sepsis. Otherwise, patients with severe diffuse peritonitis or septic shock received direct surgery after fluid resuscitation. (Please see Study population section)

3- The authors did not mention if endoscopic closure of PPU was applied or not and why?

Author response: Thank you for your comments. According to WSES guidelines (doi.org/10.1186/s13017-019-0283-9), patients with perforated peptic ulcer were suggested to avoid endoscopic treatment such clipping, fibrin glue sealing, or stenting. This approach needs further validation, for it may not be effective in perforated ulcer cases due to fibrotic tissue with loss of compliance. (Please see Discussion section).

4- The base line patient characteristics should include other factors that affect the serum albumin specially Liver disease or Renal disease

Author response: We agree with editor that serum albumin was affected by liver disease and renal disease. All patients who enrolled in this study did not have severe

liver disease or renal disease. We have added that severe liver disease or renal disease as one of exclusion criteria. Thanks. (Please see Study population section)

5- What is the explanation of the authors that the proportion of patients with serum albumin <30 g/L was higher in the surgical group?

Author response: Accumulating evidence showed that serum albumin is not only a parameter of nutritional status, but also a marker of acute inflammation and is associated with disease severity. Patients in the surgery group represented a relatively serious infections. Therefore, the proportion of patients with serum albumin <30 g/L was higher in the surgical group. (Please see Discussion section).

Reviewer #2:

Specific Comments to Authors:

1. Is the infusion of somatostatin a regular therapy for ulcer patient?

Author response: In the perforation patients with conservative treatment, somatostatin is a regular therapy. Somatostatin can inhibit the secretion of gastric acid, obviously reduce the speed and total amount of gastric juice production, and reduce the pressure in the stomach. At the same time, somatostatin can inhibit the release of inflammatory mediators and cytokines, reduce the inflammatory response in the abdominal cavity, and can significantly reduce the incidence of complications. Therefore, the application of somatostatin can significantly increase the successful rate of non-surgical treatment.

2. What do the authors mean by improvement in patient clinical condition?

Author response: Thank you for your comments. Clinical improvement was defined as a composition of improvements in vital signs and abdominal signs. They were managed by the experienced surgeon. If patients were clinically stable and improving, surgery may not be warranted. (Please see Nonoperative management section).

3. Is CT of the abdomen standard procedure or is X-ray sufficient to confirm the perforation?

Author response: CT is one of the abdomen standard procedures. CT has numerous advantages compared with X-ray: abdominal CT scan is far more sensitive than X-ray for detecting small amounts of free air. Moreover, it can identifying the site and cause of perforation. This is important in the management of patients with gastrointestinal tract perforation.

4. Do the authors have some data regarding the outcome depending on waiting time to the surgery in patients with ulcer disease?

Author response: Patients who treated by non-surgical treatment were closely monitored in the first 12 hours after admission, and if clinical condition of patients deteriorate, they will promptly undergo emergency surgery. Although there are articles reporting that delayed surgery will increase the incidence of complications, this conclusion was not obtained in our study.

EDITORIAL OFFICE'S COMMENTS:

(1) The title is too long, and it should be no more than 18 words;

Author response: Thank you for your comment, we have rephrased the title as follows:
"Low serum albumin may predict poor efficacy in patients with perforated peptic ulcer treated nonoperatively"

(2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Author response: Thank you for your reminding. We have prepared and arranged the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

(3) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

Author response: We have provided the PubMed numbers and DOI citation numbers to the reference list and listed all authors of the references. Thanks.

(4) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text;

Author response: Thank you for your reminding, we have added the "Article Highlights" section at the end of the main text.

(5) The scientific quality can't meet the requirement of WJG.

Author response: We appreciate for transferring our paper to World Journal of Gastrointestinal Surgery by editors.

We greatly appreciate the efficient, professional and rapid processing of our paper by editors. If there is anything else we should do, please do not hesitate to let us know.

Thank you and best regards.

Yours sincerely,

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