

## Response to reviewer's Comments

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Dear Prof. Dr. Jerzy Tadeusz Chudek, Prof. Dr. George Kontogeorgos, Prof. Dr. Ja Hyeon Ku, Prof. Dr. Bao-Gan Peng, Prof. Dr. Maurizio Serati

We would like to thank you and the reviewers of *World Journal of Clinical Cases* for taking the time to review our article. We have made some corrections and clarifications in the manuscript (Manuscript NO: 81748) after going through the reviewers' comments. The changes are summarized below:

**\* Reviewer #1**

Inserting a standard upper endoscope into the deeper part of the duodenum than the second part to find jejunal tumors are uncommon. The manuscript is interesting, however, some clarify are needed.

**Comment 1:**

Page 10(case 3) figures should according to order.

**Our response:** We apologize for any mistakes. We have made the required changes.

Figure 7 → Figure 5

Figure 5 → Figure 6

Figure 6 → Figure 7

**Comment 2:**

Reference 10 is a journal not a guideline.

**Our response:** We appreciate taking the time to review our work and respect your comments. We have carefully rechecked the reference. The information is the result of communication with the ASGE Standards of Practice Committee, and it has been reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy. We are concerned there may have been some misunderstanding that this reference is not a guideline as your comment points out that this is a journal. We would like to request another review of this reference.



## GUIDELINE



# The role of endoscopy in the management of suspected small-bowel bleeding



Prepared by: ASGE STANDARDS OF PRACTICE COMMITTEE

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This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy.

### Comment 3:

Figure 2, A and B is incorrect labeled

### Our response:

Thank you for pointing this out. We apologize for this mistake. We have made the required change.

[Before change]

**Figure 2.** Abdominal computed tomography with contrast enhancement. It shows an enhancing mass(arrow) with central depression and luminal narrowing at proximal jejunum (A: coronal view; B: axial view).

[After change]

**Figure 2.** Abdominal computed tomography with contrast enhancement findings. The scan shows an enhanced mass (arrow) with central depression and luminal narrowing at the proximal jejunum (A: axial view; B: coronal view).

**Comment 4:**

Figure 4 B, examination modality should clarify

**Our response:** A small bowel series is a diagnostic procedure, which uses a “contrast agent” called barium sulfate and x-rays to obtain clear images of the small bowel. Barium sulfate coats the walls of the small bowel, thereby casting shadows that can be recorded on x-ray film. The examination can detect problems within the small bowel. We performed the examination after the patient drank a barium suspension and took abdominal x-ray images at regular intervals.

Small bowel series is an officially used examination term, and we have not been able to find another alternative test name. We have added the word “barium” to the test name in the figure for clarity. We are a little concerned that we may have misunderstood your comment.

[Before change] Figure 4. Abdominal computed tomography and small bowel series. A: Abdominal computed tomography with contrast enhancement. It shows an enhancing mass(arrow) with luminal narrowing at the proximal jejunum; B: An intraluminal protruding mass is seen in the small bowel series.

[After change] Figure 4. Abdominal computed tomography and small bowel series with barium findings. A: Abdominal computed tomography with contrast enhancement. It shows an enhanced mass (arrow) with luminal narrowing at the proximal jejunum; B: An intraluminal protruding mass is seen in the small bowel series with barium.

**Comment 5:**

Figure 7 C, examination modality should clarify.

**Our response:** The examination in Figure 7C is the same as the examination in Figure 4B. We have added the term “barium” to the test name in the figure for clarity.

As mentioned above, we are concerned that we may have not understood your comment properly.

[Before change] Figure 7. Abdominal computed tomography and small bowel series. A, B: Abdominal computed tomography with contrast enhancement. They show a 3.8cm-sized dumbbell-shaped enhancing mass in proximal jejunum (arrow) (A: coronal view; B: axial view); C: A 2.0-sized filling defect lesion is seen in the small bowel series.

[After change] Figure 5. Abdominal computed tomography and small bowel series with barium findings. A, B: Abdominal computed tomography with contrast enhancement. They show a 3.8cm-sized dumbbell-shaped enhanced mass in the proximal jejunum (arrow) (A: coronal view; B: axial view); C: A 2.0cm-sized filling defect lesion is seen in the small bowel series with barium.

**Comment 6:**

The format of references is not meet the criterion of demand of WJCC

**Our response:** We apologize for the incorrect format of the references. According to your recommendation, we have checked the PMID and DOI, and have added them to the references.

For reference 25, PMID and DOI are not applicable.

**\* Reviewer #2**

The authors reported three cases of obscure gastrointestinal bleeding from gastrointestinal stromal tumors in jejunum diagnosed by standard upper gastrointestinal endoscopy. The subject matter of this work sounds to be laudable and of interest to all endoscopists. I consider that the paper is publishable with minor scientific revisions.

**Comment 1:**

It is recommended that the tumor size of GISTs be specified, because risk classification of GISTs is based on tumor size and mitotic count in 50 high power fields (HPF).

**Our response:** We completely agree with your comment. We have specified the tumor size and mitotic counts for each case in the final diagnosis section.

[Before change] Line 224-228

**Final diagnosis**

Immunohistochemical studies of all cases showed positive staining of the tumor cells for CD 117 (c-kit) (Figure 8). The mitotic count was rare (<1/50 high-power field) in all cases. These findings supported a diagnosis of a gastrointestinal stromal tumor (GIST).

[After change] Line 226-235

**Final diagnosis**

Case 1: The tumor measured 2.7 cm × 2 cm, and the mitotic count was low (<1/50 high-power fields).

Case 2: The tumor measured 3.9 cm × 2.2 cm, and the mitotic count was low (<1/50 high-power fields).

Case 3: The tumor measured 2.5 cm × 1.6 cm, and the mitotic count was low (<1/50 high-power fields).

Immunohistochemical studies of all cases showed positive staining for CD 117 (c-kit) in the tumor

cells (Figure 8). These findings supported a diagnosis of a gastrointestinal stromal tumor (GIST) having a low risk.

**\* Reviewer #3**

I would like to congratulate you on your management success. I have several questions and suggestions after reviewing the manuscript.

**Comment 1:**

Title: Three Cases of Jejunal Tumors Detected by Standard Upper Gastrointestinal Endoscopy: A Case Series --I think you have performed a non-standard procedure using a standard upper gastrointestinal endoscope. (A case series should have more than four patients while four patients or less should be reported individually as case reports. References: Clinical “case series”: a concept analysis, PMID: 23515566)

Title Suggestion: Jejunal Tumors Detected by Standard Upper Gastrointestinal Endoscope: A Report of Three Cases

**Comment 2:**

Keywords: “Case report” should be changed.

**Our response:**

Thank you for your important comment. “More than four patients” in [Clinical “case series”: a concept analysis] published in African Health Sciences 2012 by Abu-Zidan FM, et al., which was suggested as a reference, is also a suggestion.

Definitions based on the number of patients in a case series are controversial. A case report typically involves one or two cases. A case series or case series report typically involves three to 10 cases.

{Reference websites}

[https://en.wikipedia.org/wiki/Case\\_series](https://en.wikipedia.org/wiki/Case_series)

<https://pubrica.com/academy/case-study-or-series/how-many-patients-does-case-series-should-have-in-comparison-to-case-reports/>

<https://www.bumc.bu.edu/irb/submission-requirements/special-submission-requirements/case-reports-and-case-series/>

Moreover, the same publisher (Baishideng Publishing Group) has previously allowed three cases to be published as a “case series.”

{Reference}



Hirakawa M et al. Case series of three patients with hereditary diffuse gastric cancer in a single family: Three case reports and review of literature. World J Gastroenterol 2020; 26(42): 6689-6697 [PMID: 33268956 DOI: 10.3748/wjg.v26.i42.6689]

Considering the value of the report, we sincerely ask that the title we first presented be maintained.

If it is not possible, use the suggested title in respect of your opinion, but request permission to add the “Case series study” to the “Keywords” as in other studies in the same journal.

{Reference}

Liu XM et. al. Localized primary gastric amyloidosis: Three case reports. World J Clin Cases 2020; 8(19): 4667-4675 [PMID: 33083432 DOI: 10.12998/wjcc.v8.i19.4667]

Keywords: Localized gastric amyloidosis, Mucosa-associated lymphoid tissue lymphoma, Different outcomes, Rare disease, A case series study, Case report

[Before change]

Title : Three Cases of Jejunal Tumors Detected by Standard Upper Gastrointestinal Endoscopy: A Case Series

Keywords: Esophagogastroduodenoscopy, Obscure gastrointestinal bleeding, Jejunal Neoplasm, Case report

[After change]

Title : Jejunal Tumors Detected by Standard Upper Gastrointestinal Endoscopy: A Report of Three Cases

Keywords: Esophagogastroduodenoscopy, Obscure gastrointestinal bleeding, Jejunal neoplasm, A case series study, Case report

### **Comment 3:**

What would you say about the application of this procedure with a colonoscope? You could add this to the discussion section. (Peroral colonoscopy, especially with pediatric colonoscopes)

**Our response:** Thank you for this comment. If the possibility of a tumor in the jejunum is very high and a small intestine endoscope is not prepared, we try to enter the jejunum using a colonoscope. However, since the jejunum is generally prepared for evaluation through an enteroscope, a colono-

scope is not used in second-look endoscopy for upper gastrointestinal observation. We searched for related data and have added the information to the text.

[Before change] Line 316-319

Standard upper gastrointestinal endoscopy may not be needed in cases where enteroscopic procedures, such as push enteroscopy, are available immediately. However, meticulous re-examination by standard upper gastrointestinal endoscopy is usually recommended in patients with obscure gastrointestinal bleeding.

[After change] Line 324-335

Standard upper gastrointestinal endoscopy may not be needed in cases where enteroscopic procedures, such as push enteroscopy, are available immediately. In some reports, lesions of the small intestine have been diagnosed through an oral approach using a colonoscope or pediatric colonoscope(25, 26). However, pediatric colonoscopes are often not available in hospitals that do not perform endoscopy frequently for pediatric patients, and an oral approach using a conventional colonoscope can cause discomfort to patients. In a previous report, there were no adverse effects when the upper gastrointestinal endoscope was inserted deep into the duodenum to the fourth part compared with insertion to the second part, and in our case, there were no adverse effects related to deep insertion(27). Meticulous re-examination by standard upper gastrointestinal endoscopy is usually recommended in patients with obscure gastrointestinal bleeding.

#### **Comment 4:**

Is the procedure performed under general anesthesia or with sedation?

**Our response:** All patients underwent endoscopy in a nonsedated state. We have added the information to the text.

[Before change]

Line 161-162 We used a video Gastroscope GIF-Q260 (working distance, 103 cm; Olympus Corp., Tokyo, Japan).

Line 178-179 Before enteroscopy, upper gastrointestinal endoscopy was performed again.

Line 190-193 To check for active bleeding and perform biopsy, endoscopic examination was decided, and previously described (as in cases 1 and 2) standard upper gastrointestinal endoscopy was performed.

[After change]

Line 161-163 We used a video Gastroscope GIF-Q260 (working distance, 103 cm; Olympus Corp., Tokyo, Japan). Endoscopy was performed without sedation.

Line 179-181 Before enteroscopy, upper gastrointestinal endoscopy was performed again without sedation.

Line 192-195 To check for active bleeding and perform biopsy, endoscopic examination was decided, and previously described (as in cases 1 and 2) standard upper gastrointestinal endoscopy was performed without sedation.

#### **Comment 5:**

From the text: In some cases, re-examination by standard upper gastrointestinal endoscopy with maximal insertion may be safe and effective in the detection of lesions in the proximal part of the jejunum.

Are there any complications of this technique reported in the literature?

**Our response:** Thank you for commenting on an aspect we did not consider. We reviewed the relevant literature again. Although we were not able to confirm that the upper gastrointestinal endoscope was inserted up to the jejunum, there is a report that the upper gastrointestinal endoscope went up to the distal duodenum (fourth part) (reference 27: Qiao, Wei Guang, et al. "Role of esophagogastroduodenoscopy in detecting distal duodenal lesions: A single-center pilot study in Southern China." *Journal of Digestive Diseases* 18.11 (2017): 618-624).

In the case of an oral approach with a colonoscope, there are adverse events such as sore throat and nausea, but in the case of deep insertion using an esophagogastroduodenoscope, there are no adverse events compared to when the upper gastrointestinal endoscope is inserted up to the second part, which is the general reach. We have added this information to the text. (Line 330–333)

**Comment 6:**

What should be our limit when applying this process? What should we pay attention to during the procedure? (Be gentle when trying to pass standard instruments into the third part of the duodenum and beyond. Pushing will initially only form a loop in the stomach, and any further advance will come at the cost of considerable discomfort to the patient. Williams, C. B., & Cotton, P. B. (2009). Practical Gastrointestinal Endoscopy: The Fundamentals. John Wiley and Sons.)

**Our response:** When inserting an endoscope, slight abdominal compression may be required, as in colonoscopy. However, there have been many cases in which it was inserted without abdominal compression, and as in a previous report (reference 24), it reached the jejunum without much effort. The point of our report is not to force insertion in the jejunum, but rather to indicate the chance to detect lesions in the jejunum by trying to insert the endoscope deeper when performing second-look examination according to guidelines.

[Before change] Line 319-322

In some cases, re-examination by standard upper gastrointestinal endoscopy with maximal insertion may be safe and effective in the detection of lesions in the proximal part of the jejunum.

[After change] Line 335-337

In some cases, efforts to maximally insert an endoscope during re-examination by standard upper gastrointestinal endoscopy may be safe and effective for the detection of lesions in the proximal part of the jejunum.

We hope the revised manuscript meets the requirements of your journal for publication. We thank the editor and the reviewers of *World Journal of Clinical Cases* once again for their constructive review of our paper.

Sincerely yours,

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