

Lian-Sheng Ma, President and Company Editor-in-Chief
“World Journal of Gastrointestinal Surgery”

October 3, 2017

Dear Prof. Lian-Sheng Ma

Thank you for your kind letter concerning our manuscript entitled “**Ectopic gastrointestinal variceal bleeding with portal hypertension**” by Minowa and Komatsu et al. We have revised the manuscript according to referees’ comments using a red color font and presented the outlining responses to your comments below.

We thank you for your kind comments and valuable suggestions for the manuscript. We have carefully revised it accordingly. Explanations have been provided point by point. We believe that our revised manuscript has been improved by these revisions, and satisfy your concerns. We cordially appreciate your work regarding our manuscript. We hope that the revised manuscript is now acceptable for publication in the “**World Journal of Gastrointestinal Surgery**”.

Sincerely yours

Shuhei Komatsu, M.D., Ph.D., FACS

Assistant Professor

Division of Digestive Surgery, Department of Surgery,

Kyoto Prefectural University of Medicine,

465 Kajii-cho, Kawaramachihirokoji, Kamigyo-ku, Kyoto 602-8566, Japan

Phone: +81-75-251-5527

Fax: +81-75-251-5522 E-mail: skomatsu@koto.kpu-m.ac.jp

Comments from editor-in-chief

First of all, thank you very much for your long-standing support and continued trust in the World Journal of Gastrointestinal Surgery!

The review of your manuscript, which you submitted to the World Journal of Gastrointestinal Surgery, is now completed and the first decision for publication is available. We request that you submit your revision in no more than 2 weeks.

Comments to editor-in-chef and senior editor:

We thank you for your kind comments and valuable suggestions for our manuscript. We have carefully revised it accordingly. Explanations have been provided point by point. We believe that our revised manuscript has been improved by these revisions, and satisfy your concerns.

We cordially appreciate your contribution regarding our manuscript. We hope that the revised manuscript is now acceptable for publication in the “**World Journal of Gastrointestinal Surgery**”.

1. Reviewer's code: 02569813

Reviewer's country: Spain

Conclusion: Major revision

Classification: Grade C (Good)

Language Evaluation: Grade

B: minor language polishing

Comments from reviewer 02569813:

The management strategy of a severe gastrointestinal bleeding from gastrointestinal varices in a patient with portal hypertension is a very interesting issue because this is one of the most serious complications in these patients. The manuscript is quite well written and easy to read. However, in my opinion, there are some issues that can be ameliorated.

Response to reviewer's comments

Thank you for your kind comments. We found the comments most helpful and have revised our manuscript accordingly. We hope that our manuscript has been improved by these revisions, and hope that we have adequately addressed your concern.

Query

1- The objective of the manuscript and the abstract must be more clearly described.

Reply: Thank you for your comment. As you indicated, we revised the abstract to clarify the objective of this manuscript as follows. Thank you for your helpful comments.

Revised

ABSTRACT

Massive gastrointestinal bleeding from gastrointestinal varices is one of the most serious complications in patients with portal hypertension. However, if no bleeding point can be detected by endoscopy in the predilection sites of gastrointestinal varices, such as the esophagus and stomach, ectopic gastrointestinal variceal bleeding should be considered as a differential diagnosis. Herein, we report a case of ectopic ileal variceal bleeding in a

57-year-old woman, which was successfully diagnosed by multi-detector row CT (MDCT) and angiography and treated by segmental ileum resection. To date, there have been no consensus for the treatment of ectopic ileal variceal bleeding. This review was designed to clarify the clinical characteristics of patients with ectopic ileal variceal and discuss possible treatment strategies. From the PubMed database and our own database, we reviewed 21 consecutive cases of ileal variceal bleeding diagnosed from 1982 to 2015. MDCT and angiography is useful for the rapid examination and surgical resection of an affected lesion and is a safe and effective treatment strategy to avoid further bleeding.

Query

2- Discussion section must be more structured, including more details of the advantages, pitfalls and results of all treatment options, especially about minimally invasive procedures, as embolization. The laparoscopic approach must be deeply discussed as well.

Reply: Thank you for your comment. As you indicated, we revised Discussion with special reference to advantage, pitfalls minimally invasive approach as follows. Thank you for your helpful comments.

Revised

..... portosystemic shunt (TIPS)^{[8]-[10]} and balloon-occluded retrograde transvenous obliteration (BRTO) ^{[11][12]}.

Possible treatment strategy for ectopic gastrointestinal variceal bleeding

There were no patients with re-bleeding in previous reports of ileal variceal bleeding. However, re-bleeding rates of 23–39% have been reported in TIPS and 5–16.6% in BRTO in all reports of ectopic gastrointestinal variceal bleeding^{[13]-[16]}. Although non-invasive treatment such as IVR may be desirable for ectopic gastrointestinal variceal bleeding in high-risk patients with co-morbidities, surgical resection of an affected intestine is currently a safe and effective treatment strategy to avoid further re-bleeding. Moreover, laparoscopic surgical resection of an affected intestine could be possible effective strategy as a minimally invasive procedure.

Query

3. I suggest to include a management algorithm could be of interest for the journal readers.

Reply: Thank you for your comment. As you suggested, we added the management algorithm in **Figure 2**. Thank you helpful comments.

Thank you for your expert comments. We cordially appreciate your contribution to our manuscript. If you have further queries, we are willing to reply them. Thank you so much for your helpful comments.

2. Reviewer's code: 03317059

Reviewer's country: Turkey

Classification: Grade C (Good)

Language Evaluation: Grade

B: minor language polishing

Comments from reviewer 03317059:

Interesting paper about ectopic variceal bleeding.

Response to reviewer's comments

Thank you for your kind comments. We cordially appreciate your contribution regarding our manuscript. We hope that the revised manuscript is now acceptable for publication in the "World Journal of Gastrointestinal Surgery".

3. Reviewer's code: 02544751

Jana Katuchova, MD, PhD. Professor of Surgery First Department of Surgery
University Hospital Košice Slovakia

Reviewer's country: Slovakia

Conclusion: Accept

Classification: Grade A (Excellent)

Language Evaluation: Grade

A: priority publishing

Comments from reviewer 02544751:

Recension of manuscript No. 36016 „Ectopic gastrointestinal varices bleeding with portal hypertension written by Keita Minowa, Shuhei Komatsu, Ken-ichiro Takashina, Sachie Tanaka, Tatsuya Kumano, Ken-ichiro Imura, Katsumi Shimomura, Jun Ikeda, Fumihiro Taniguchi, Yasuo Ueshima, Chol Joo Lee, Eito Ikeda, Eigo Otsuji and Yasuhiro Shioaki“, which will be published in World Journal of Gastrointestinal Surgery.

The structure of manuscript is in keeping with the common required criteria. The topic of the work is very actual. Massive gastrointestinal bleeding from gastrointestinal varices is one of the most serious complications in patients with portal hypertension. However, if no bleeding point can be detected by endoscopy in the predilection sites of gastrointestinal varices, such as the esophagus and stomach, ectopic gastrointestinal variceal bleeding should be considered as a differential diagnosis. The research work follows several aims and interesting parametric studies. Work is clearly legible, brings summarizes new knowledge. The citations are well-chosen and relevant and their format respects usual standards. The conclusion summarizes the author's results. Summarizing, I recommend that the manuscript can be published.

Comments from reviewer

Thank you for your kind and valuable comments. We cordially appreciate your contribution regarding our manuscript. We hope that the revised manuscript is now acceptable for publication in the “World Journal of Gastrointestinal Surgery”.

4. Reviewer's code: 03259574

Reviewer's country: Algeria

Comments from reviewer 03259574

In this present case report, authors described diagnosis and treatment strategy with literature review of complicated ectopic varices of the terminal ileum with portal hypertension secondary to liver cirrhosis .The article is an interesting and rare clinical situation, however the following concerns have been noted.

Response to referee's comments

Thank you for your kind comments. We found the comments most helpful and have revised our manuscript accordingly. We hope that our manuscript has been improved by these revisions, and hope that we have adequately addressed your concern.

Query

1-The article is not well drafted and language is poor.

Reply: Thank you for your comment. We revised our manuscript completely based on reviewers' comments. Thank you for your helpful comments.

Query

2-Abstract is unclear and not very concise.

Reply: Thank you for your comment. As you indicated, we revised the abstract to clarify the objective of this manuscript as follows. Thank you for your helpful comments.

Query

3-Discussion section is missed

Reply: Thank you for your comment. As you indicated, we revised Discussion with special reference to advantage, pitfalls minimally invasive approach as follows. Thank you for your helpful comments.

Revised

..... portosystemic shunt (TIPS)^{[8]-[10]} and balloon-occluded retrograde transvenous obliteration (BRTO)^{[11][12]}.

Possible treatment strategy for ectopic gastrointestinal variceal bleeding

There were no patients with re-bleeding in previous reports of ileal variceal bleeding. However, re-bleeding rates of 23–39% have been reported in TIPS and 5–16.6% in BRTO in all reports of ectopic gastrointestinal variceal bleeding^{[13]-[16]}. Although non-invasive treatment such as IVR may be desirable for ectopic gastrointestinal variceal bleeding in high-risk patients with co-morbidities, surgical resection of an affected intestine is currently a safe and effective treatment strategy to avoid further re-bleeding. Moreover, laparoscopic surgical resection of an affected intestine could be possible effective strategy as a minimally invasive procedure.

Query

4- More details are needed to be added regarding diagnosis and therapeutic strategies and results.

Reply: Thank you for your comment. As you indicated, we revised Discussion with special reference to advantage, pitfalls minimally invasive approach as follows. Thank you for your helpful comments. Moreover, we added the management algorithm in **Figure 2**. Thank you for your expert comment.

Thank you for your expert comments. We cordially appreciate your contribution to our manuscript. If you have further queries, we are willing to reply them. Thank you so much for your helpful comments.

5. Reviewer's code: 03317059

Reviewer's country: Slovenia

Science editor: Fang-Fang Ji

Conclusion: Accept

Classification: Grade C (Good)

Language Evaluation: Grade

B: minor language polishing

Comments from reviewer 03317059

Interesting paper about ectopic variceal bleeding.

Comments from reviewer

Thank you for your kind comments. We cordially appreciate your contribution regarding our manuscript. We hope that the revised manuscript is now acceptable for publication in the "World Journal of Gastrointestinal Surgery