Author’s response to reviews

Title: Clinical impact of the perioperative management of oral anticoagulants in bleeding after colonic endoscopic mucosal resection

Authors:
Shoko Ono (onosho@med.hokudai.ac.jp)
Marin Ishikawa (marin.i.0719@gmail.com)
Kana Matsuda (kana.matsuda@true.ocn.ne.jp)
Momoko Tsuda (momoko0221tsuda@gmail.com)
Keiko Yamamoto (keiko_sannai@yahoo.co.jp)
Yuichi Shimizu (yshimizu@med.hokudai.ac.jp)
Naoya Sakamoto (sakamoto@med.hokudai.ac.jp)

Version: 2 Date: 24 Oct 2019

Author’s response to reviews:

BMGE-D-19-00579

Thank you for the thoughtful feedback you provided regarding our manuscript "Clinical impact of the perioperative management of oral anticoagulants in bleeding after colonic endoscopic mucosal resection". Point-by-point response to the reviewers' comments are as follows.

In reply to Reviewer 1 (Dr. Yosuke Tsuji)

1. Reviewer: Is the conclusion totally accepted by the authors? Certainly, there is no significant difference in bleeding rate between the HBT group and continuous warfarin or one-day skip of DOACs, but it does not directly mean that continuous anticoagulants without HBT did not prevent bleeding. Considering this conclusion, it seems that the perioperative management of anticoagulants should be reconsidered.

Authors: We would like to thank the reviewer for the comments. In the revised paper, we have changed to the following sentence:

(Abstract, in conclusion)
“perioperative management of oral anticoagulants based on the shortest cessation without HBT would be clinically acceptable.”

In reply to Reviewer 2 (Dr. JX Yu)

1. Reviewer: The authors should refer to their diagram of anticoagulation management schema (figure 3) in their methods section.

Authors: As the reviewer’s pointed out, we have referred figure 1(diagram of anticoagulation management schema) in the method section. (Figure 1 shows diagram of anticoagulation management schema.)

In the revised paper, we have added the following sentence:

(Methods section, line 43, page 6)

“Our management of anticoagulants is shown in figure 1.”

2. Reviewer: Please clarify in the methods section (statistical analysis, last sentence) if risk ratios or odds ratios were calculated. Do the authors mean: "the risk of bleeding were calculated by odds ratios". Also, was this a multivariate analysis?

Authors: We have revised the manuscript.

In the revised paper, we have revised the following sentence:

(Methods section, line11, page 9)

“Multivariate logistic regression analysis was performed for calculating odds ratios (ORs) of bleeding.”

3. Reviewer: The multivariate analyses presented in the third paragraph of the results section is confusing. They note there no patient factors associated with bleeding after EMR, yet they later discuss the increased rate of bleeding with HBT and anticoagulant use. Please reconcile this. I do not think this analysis adds to the study and the authors should consider removing this.

Authors: We would like to thank the reviewer for the comments. We have removed this paragraph.
4. Reviewer: It would be useful to present the actual bleeding rates and odds ratios of bleeding in the text of the results sections "bleeding according to antithrombotic agents" and "bleeding according to actual management of anticoagulants"

Authors: As the reviewer’s pointed out, we have added bleeding rates and odds ratios in the results section.

In the revised paper, we have added the following sentence:

(Results section, line 11 and 43, page 10)

“(Bleeding rates; 7.14%, 5.48% and 9.68%, Odds ratios 4.95, 3.67 and 6.88, respectively)”
“(Odds ratios 4.94, 3.29 and 4.94, respectively)”

5. Reviewer: What are the days to bleeding events for warfarin and HBT groups. It would be useful to see this along with the days to bleeding for the DOAC already presented in the 2nd to last paragraph of the results section.

Authors: As the reviewer’s pointed out, we have added comments in the results section.

In the revised paper, we have added the following sentence:

(Results section, line 53, page 10)

“On the other hand, bleeding occurred in the patient who continuously used warfarin on POD1 and in the patients who received HBT on POD1 and 5.”

6. Reviewer: In the discussion section, the authors discuss the high risk of bleeding with DOAC use. How do the authors interpret the equally high risk of bleeding with warfarin. Please also discuss the low risk of bleeding with antiplatelet use and the high risk of bleeding with HBT.

Authors: We would like to thank the reviewer for the comments. DOACs rapidly effects in 2-4 hours after taking drugs and show maximum effect. Therefore DOAC users are equally high risk of bleeding with the patients who continuously use warfarin. And, there have been some reports that antiplatelet agents have a lower risk of bleeding than anticoagulants.

In the revised paper, we have added the following sentence:

(Discussion section, line 11, page 13)
“DOACs have maximum effect in 2-4 hours after taking drugs, therefore DOAC users are equally high risk of bleeding with the patients who continuously use warfarin.”

7. Reviewer: It would be useful to have percentages in addition to proportions presented in the results tables.

Authors: As the reviewer’s pointed out, we have revised tables 1, 2 and 4.

Again, thank you for giving us the opportunity to strengthen our manuscript with your valuable comments and queries.

Shoko Ono

Department of Gastroenterology, Hokkaido University Hospital, Sapporo, Japan.
onosho@med.hokudai.ac.jp