

Format for ANSWERING REVIEWERS

January 25, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 15898-edited.doc).

Title: Risk Factors for Small Bowel Angioectasia: the Impact of Visceral Fat Accumulation

Author: Atsuo Yamada, Ryota Niikura, Yuka Kobayashi, Hirobumi Suzuki, Shuntaro Yoshida, Hirotsugu Watabe, Yutaka Yamaji, Yoshihiro Hirata, and Kazuhiko Koike

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 15898

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer 1

The results of this study are interesting. There are comments:

1. ABSTRACT: In the results, you only mentioned the positive results (VFA, liver cirrhosis), but show not data about SFA and other indicates;

→We appreciate the reviewer's suggestion. We added the following sentences in abstract in results;

The proportion of patients with chronic renal failure was higher in patients with small bowel angioectasia(22% vs. 9%, P=0.11). There were no significant differences in the SFA or waist circumference.

2. "Visceral fat accumulation can be calculated using computer software based on CT images":please provide references;

→We appreciate the reviewer's suggestion. We added the reference on this sentence. Consequently, reference numbers were modified.

Visceral fat accumulation can be calculated using computer software based on CT images^[1]

3. The second inclusion criteria: why 3 month? CT is used to evaluate VFA/SFA, will not they change in 6 month?

→We appreciate the reviewer's suggestion. Plain or contrast-enhanced CT was performed on OGIB patients to investigate bleeding source as soon as possible after the diagnosis of OGIB in our institution. We selected OGIB patients who underwent CT within only 3 months before or after the CE, because they were elderly patients and were affected by their concomitant diseases and general condition^[2]. If

we selected patients within 6 month, the mean VFA was significantly higher in patients with (n=19) than without small bowel angioectasia in patients (n=189) (92.4 ± 75.5 vs 62.8 ± 51.1 cm², respectively; $P=0.023$), whereas there were no significant differences in the SFA (99.4 ± 68.5 vs 98.1 ± 69.7 cm², respectively; $P=0.94$).

4. There is no necessary to mention "There was no significant difference in patients' characteristics between CT group and non-CT group." Even the table1 is redundant.
→We appreciate the reviewer's suggestion. Table 1 was removed. Consequently, table numbers were modified. And Underlined parts were modified in Results 1st paragraph.

During the study period, 246 patients underwent CE after diagnosis of OGIB. Of these 246 patients, 198 underwent both CE and CT examinations and satisfied the inclusion criteria, whereas the remaining 48 did not undergo CT. A total of 198 patients, 117 males and 81 females, with the mean age 65.8 ± 12.8 were analyzed. The mean VFA and SFA were.....

Reviewer 2

The manuscript is well written. The authors clearly state the purpose of the manuscript. Ethics of the research was respected. The structure is good and concise. The statistical methods used are appropriate. The references are appropriate, and relevant.

→We appreciate the reviewer's comments.

Reviewer 3

Dear Editor, I reviewed the manuscript by Yamada et al., entitled " Risk Factors for Small Bowel Angioectasia: the Impact of Visceral Fat Accumulation" The finding of the study is interesting. However multivariate analysis suggesting that Visceral Fat Accumulation and liver cirrhosis are an independent risk factor for Small Bowel Angioectasia seems to be not clear. Also, it is known that adipose tissue expresses are characterized by their release of various secretory molecules, including leptin, tumor necrosis factor- α , plasminogen activator inhibitor-1, interleukin-6, and VEGF. Thus it is important to demonstrate the level of adipose tissue released factors in sera of patients diagnosed with small bowel angioectasia.

→We appreciate the reviewer's suggestion. We agree with the reviewer that it is important to demonstrate the level of adipose tissue released factors in sera of patients diagnosed with small bowel angioectasia. However, this study was a retrospective analysis and we had no data on cytokine levels. Although the relationship between cytokine levels and small bowel angioectasia was unclear, our results indicate that visceral fat accumulation may play a role in the pathogenesis of small bowel angioectasia. Thus, further research about the relationships between the level of adipose tissue released factors and small bowel angioectasia is required. Underlined parts were modified in Discussion, 4th paragraph and 6th paragraph.

Although we had no data on cytokine levels, and although the relationship between VEGF and small bowel angioectasia was unclear, our results indicate that visceral fat accumulation may play a role in the pathogenesis of small bowel angioectasia.

Therefore, a larger prospective study is needed to confirm the contribution of these risk factors to small bowel angioectasia and to investigate the relationships between cytokine levels and small bowel angioectasia.

1 Kvist H, Chowdhury B, Grangard U, Tylen U, Sjostrom L. TOTAL AND VISCERAL ADIPOSE-TISSUE VOLUMES DERIVED FROM MEASUREMENTS WITH COMPUTED-TOMOGRAPHY IN ADULT MEN AND WOMEN - PREDICTIVE EQUATIONS. *American Journal of Clinical Nutrition* 1988; **48**(6): 1351-1361 [PMID: WOS:A1988R380700001]

2 Neu B, Ell C, May A, Schmid E, Riemann JF, Hagenmuller F, Keuchel M, Soehendra N, Seitz U, Meining A, Rosch T. Capsule endoscopy versus standard tests in influencing management of obscure digestive bleeding: Results from a German multicenter trial. *American Journal of Gastroenterology* 2005; **100**(8): 1736-1742 [PMID: WOS:000230992100015 DOI: 10.1111/j.1572-0241.2005.41649.x]

3 References and typesetting were corrected

4 This manuscript was rechecked by native speaker. We attached a certificate.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in black ink, appearing to be 'Atsuo Yamada', written in a cursive style.

Atsuo YAMADA, MD, PhD
Department of Gastroenterology,
University of Tokyo
7-3-1 Hongo Bunkyo-ku,
Tokyo, Japan 113-855
Fax: +81-3-3814-0021
E-mail: yamada-a@umin.ac.jp