

August 26, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 4395-brief.doc).

**Title:** Characteristics and prognosis of synchronous multiple early gastric cancer

**Author:** Taro Isobe, Kousuke Hashimoto, Junya Kizaki, Naotaka Murakami, Keishiro Aoyagi, Kikuo Koufujii, Yoshito Akagi, Kazuo Shirouzu

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 4395

My colleagues and I wish to thank both the reviewers and yourself for your thoughtful consideration of our manuscript.

The manuscript has been improved according to the suggestions made by the reviewers.

1 The formatting has been updated.

2 The suggested revisions have been made, as follows:

(1) Reviewer 1 (No. 00036951)

Authors should improve some aspects of the paper: 1. the casistic should be expanded to have results more statistically significant

This was a retrospective study conducted over two decades. I agree with your comment, and I would ideally like to expand the casistic to give better statistical significance. However, medical progress has been remarkable, and I do not think that results could be compared over a period lasting more than 20 years. I have addressed this in the discussion of the study limitations, where I refer to the small number of patients.

2. the conclusions need to be expanded with a greater number of references

I have added some more references and I now compare my results with those of previous studies in the DISCUSSION section.

3. in some points of the manuscript, a revision of English language is need

I have used two English Language editing service and native check to correct these errors (Editage Cactus Communications: <http://editage.com>; American Journal Experts: <http://www.journalexperts.com>).

(2) Reviewer 2 (No. 00722706)

I'd like to congratulate because I think the article to be well written and quite clear also for not-specialists, with interesting considerations about risks factors of SMGCs.

Thank you so much.

(3) Reviewer 3 (No. 00069467)

### Major concerns

1. What the authors presented, concluded and discussed seem to be far away from the aim of authors as stated in the abstract. It would be suggested that either rephrase the aim or give more comments on the safety and efficacy of minimally invasive procedures for SMGCs.

I have rephrased the AIM section in the abstract stating, "To assess the clinicopathologic characteristics, risk factors, and prognosis for synchronous multiple early gastric cancer (SMGCs)."

2. There has been somewhat logical disfluency in the interpreting of the introduction. Specifically, according to the authors' logic, SMGCs should have been mentioned straightforwardly in the beginning, followed by raising the serious clinical issues to be addressed or readily overlooked (say, given the clinical nature of SMGCs that early staging and atypical histopathological characteristics, patients with potential SMGCs were understandably easy to get insufficient attentions and management, thus influencing the outcomes of patients.....however, there have been little published reports concerning the clinical characteristics of SMGCs.....). So, it would be nice to recast the introduction for the readers.

I have made a major revision to the INTRODUCTION section.

3. The authors fail to mention that the study presented was approved by the local medical ethics commission in the first paragraph of materials and methods section.

I have added a sentence in the first paragraph of the MATERIALS AND METHODS section starting that, "Our study was approved by The Ethical Committee of Kurume University (No. 13091)"

4. The authors mentioned Brinkman index but didn't relate where it from in the first sentence of the third paragraph in materials and methods section

I have added two references [9, 10] relating to the Brinkman index.

5. Last sentence of the third paragraph in discussion section, as overstated by the authors, seem not to be supported or documented by the data shown. The reviewer hasn't seen any genetic data provided regarding SMGCs in the text. Strictly, genetic instability and familial genetic are two different definitions. Judging from your data shown in table 2, it can be at best concluded that familial genetics may play a certain role in the pathogenesis of SMGC.

I have changed the text regarding familial history in the third paragraph of the DISCUSSION section.

6. There seems to be conflicting in regard to the role of family history in the pathogenesis of SMGCs, as listed in table 4 and as stated in the first sentence of the third paragraph in discussion section. Please check it.

In univariate analysis, the number of patients with a family history of gastric cancer in SMGCs was significantly higher than for those with a single gastric cancer. However, it was not an independent risk factor in multivariate analysis. I have changed the

sentences about familial history in the third paragraph in the DISCUSSION section and added "in multivariate analysis" to table 4.

7. The same holds true for the smoking and drinking habits shown in table 4, while claimed to be inconsistent with Morita et al.'s findings. Actually, the drinking and smoking weren't risk factors insofar as SMGCs in your current study. Please word carefully.

Smoking and drinking habits were significantly different in univariate analysis. However, these were not independent risk factors in multivariate analysis. I have changed the text referring to smoking and drinking habits in the fourth paragraph of the DISCUSSION section.

8. It is surprising that there were two p values appear meanwhile in the table 2 where statistical performance between synchronous and metachronous. Please check it

I have checked the statistical analysis in table 2, and it appears to be correct.

9. If possible, pointing out the limitations of your retrospective studies on your own.

I have added some text regarding the limitations of this study in the DISCUSSION section, immediately before the CONCLUSION.

10. The discussion part would benefit from shortening and instead, giving more comments on safety and efficacy of minimally invasive resections (EMR, ESD) on patients with SMGC.

I have added text regarding minimally invasive resections in the first and eighth paragraphs of the DISCUSSION section.

#### Minor concerns

1. Some grammar and syntax errors, making hard to read. Take, for instance, results section where lots of sentences should have been used passive voice not active. "Table 2 summarizes the clinical differences between the groups" should have been "summarized are the clinical differences between the groups in Table 2" for the sake of idiomatic; similarly, "Table 3 lists the pathological features of each group" would be more acceptable "listed are the pathological features of each group in Table 3".

I have used two English Language editing service and native check to correct these errors.

2. The second sentence in the first para of discussion part, "few investigations have reported" should have been "few investigations have been reported", and the like are frequent in other parts of manuscript. Please scrutinize prior to submission.

I have used an English Language editing service and native check to correct these errors.

3 The references and typesetting errors have been corrected.

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

Sincerely yours,

A handwritten signature in black ink, reading "Taro Isobe". The signature is written in a cursive, flowing style.

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