Author's response to reviews

Title: Endoscopic resection of duodenal bulb neuroendocrine tumor larger than 10mm in diameter.

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Author's response to reviews: see over
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BioMed Central Editorial Team

MS: 7923410144762584
Dear BMC Gastroenterology Editorial;

Thank you for your mail of March 24, 2011. I really apologized for our delayed reply due to a trouble of our mailing system. Enclosed is a revised manuscript entitled, "Endoscopic resection of duodenal bulb neuroendocrine tumor larger than 10mm in diameter." by Yokoyama et al. for publication in *BMC Gastroenterology*. According to your valuable and considerable comments, we thoroughly revised our manuscript. Our manuscript has been looked over and corrected by Dr. Brian Quinn, Editor-in-chief, Japan Medical Communication. We sincerely hope that our manuscript meets with your approval and thank you for taking the trouble to review it.

Sincerely yours,

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Reply to the reviewer 1

Dear Dr. Hironori Tsujimoto,

Thank you for your review of our manuscript entitled, "Endoscopic resection of duodenal bulb neuroendocrine tumor larger than 10mm in diameter," by Yokoyama et al. for publication in BMC Gastroenterology. According to your valuable and considerable comments, we thoroughly revised our manuscript. We sincerely hope that our manuscript meets with your approval and thank you for taking the trouble to review it again.

1. If the authors want to emphasize the importance of this technique, the fruitful long-term outcome is very important. However, the follow up periods were only range 19 to 78 months. The author should address the limitation of this study.

We added the comment in Page 7, Line 4-5 as follows.

Further follow-up is required to address this technique is safely for long-term outcome of neuroendocrine tumors[16].

2. Several authors recommended that full-thickness resection of lesions in the gastrointestinal tract should be performed if the carcinoid tumor has extensively infiltrated the submucosal layer or involves the muscle layer, because conventional EMR does not eliminate the possibility of tumor seeding in the vertical margin due to the burning effect (Toyonaga et al. Surg Endosc, 1998, Tsujimoto et al. Surg Endosc 2009). The authors should comment this issue against these opinions.

This is a quite important point, and thank you so much for your valuable suggestion. We added the comment in Page 6, Line 11-14 as follows.

Meanwhile, it is recommended that full-thickness resection of lesions in the gastrointestinal tract should be performed if the neuroendocrine tumor has extensively infiltrated the submucosal layer or involves the muscle layer, because conventional EMR does not eliminate the possibility of tumor seeding in the vertical margin due to the burning effect[14, 15].

3. Because the duodenal wall is thinner than the gastric wall, EMR performed for duodenal lesions may be associated with a high risk of accidental perforation. In addition, because of the thinner wall of duodenum, the burning effects easily reach other organs such as transverse colon, gall bladder, and the pancreas. The author should state the merit of EMR in comparison to laparoscopic full thickness resection of the duodenum.

4. As mentioned above, can the EMR technique without laparoscopic observation perform the duodenal tumor especially located on the second portion? The authors
should state the successful and safe EMR technique for the duodenal carcinoid especially in the case the tumor other than duodenal bulb.

We added the following comment in Page 5, Line 12-16

EMR technique was successful and safe for most small duodenal bulb neuroendocrine tumor[1, 7-10]. Some report mentioned that EMR procedure is also useful for neuroendocrine tumor located on the second portion[11]. Although more case series for duodenal neuroendocrine tumor is needed, EMR technique is a safety procedure for small neuroendocrine tumors.

5. Regarding the drawback of this manuscript on small size (just 4 cases) of experience, the reviewer believes this is why the carcinoid tumor of the duodenum is quite rare. The authors should emphasize this issue in the discussion section.

We added the comment in Page 5, Line 2-7 as follows.

Duodenal neuroendocrine tumor, formerly termed as carcinoid tumor, is rare entity. The tumors is derived from enterochromaffin cells, and often occurred in gastrointestinal tract. Only 2.6% duodenal carcinoid tumors is reported of all carcinoid tumors in the United States(5). The rarity makes difficulty to address the feasibility of the endoscopic treatment for this tumor. Although larger study is needed to confirm the indication of endoscopic procedure for the tumor, small case series like our study is also important for uncommon tumor.
Reply to the reviewer 2

Dear Dr. Yoshinori Igarashi,

Thank you for your review of our manuscript entitled, "Endoscopic resection of duodenal bulb neuroendocrine tumor larger than 10mm in diameter," by Yokoyama et al. for publication in BMC Gastroenterology. According to your valuable and considerable comments, we thoroughly revised our manuscript. We sincerely hope that our manuscript meets with your approval and thank you for taking the trouble to review it again.

This is not indication of endoscopic treatments.

We changed the following sentence in Page 2, Line 2-3 as follows.

Endoscopic treatment for duodenal bulb neuroendocrine tumor larger than 10 mm is still controversial.

Carinoid tumors over 10mm have the high risk of metastasis.
Many reports wrote the metastasis of carcinoid over 10mm.
It is not the indication of endoscopic treatments.
Moreover the technique is not recommended.
Traditional EMR is sometime unclear of lateral margin.
Then EMR using EVL or ESD is usually performed.

The indication of endoscopic treatment for carcinoid tumor is still controversial as we mentioned on our manuscript in Page 3, Line 3-9 as follows.
This article showed the possibility of EMR for carcinoids over 10mm.

Most reports state that duodenal neuroendocrine tumor can be treated by endoscopic excision, when the diameter is less than 10mm and there is no invasion of the muscularis propria (1). On the other hand, others have shown that the features associated with metastatic risk are a diameter greater than 2 cm (2), and those with duodenal neuroendocrine tumor with a diameter larger than 10 mm can be successfully treated by endoscopic procedure (3, 4). Therefore, it is controversial whether endoscopic treatment is appropriate for duodenal neuroendocrine tumor larger than 10 mm in diameter.
Reply to the reviewer 3

Dear Dr. Stefan von Delius,

Thank you for your review of our manuscript entitled, "Endoscopic resection of duodenal bulb neuroendocrine tumor larger than 10mm in diameter," by Yokoyama et al. for publication in BMC Gastroenterology.

According to your valuable and considerable comments, we thoroughly revised our manuscript.
We sincerely hope that our manuscript meets with your approval and thank you for taking the trouble to review it again.

In general, the terminology should be “neuroendocrine tumors” not “carcinoid”

We changed “carcinoid” to “neuroendocrine tumors”.

Case presentation
To my opinion such a case presentation must include more details about the patients, i.e. age, sex, clinical presentation (especially in the light of the presence of a neuroendocrine tumor: diarrhea, ulcers,...?), comorbidities and the grading of the tumor. Moreover, details about pathology should be given: Grading? Immunohistochemistry?
Were the tumors endocrinologically active or inactive?

We added the comment in Page 3, Line 15, Page 4, Line 15-17 as follows.

All four cases had no symptoms for the tumor.

All four tumors were endocrinologically inactive, and diagnosed as carcinoids with positive immunohistochemical staining for chromogranin A.

Please improve grammar and English expression, e.g. replace “swollen” by “enlarged”.

We change “swollen” to “enlarged” in Page 4, Line 2.

Our manuscript has been looked over and corrected by Dr. Brian Quinn, Editor-in-chief, Japan Medical Communication.