Author's response to reviews

Title: Postprandial fullness correlates with gastric barium excretion but not with chronic gastritis.

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Version: 2 Date: 29 August 2011

Author's response to reviews: see over
Dear Editor of *BMC Gastroenterology*

We enclose herewith our manuscript entitled “Postprandial fullness correlates with gastric barium excretion but not with chronic gastritis.” by Nobutake Yamamichi, Takeshi Shimamoto, Chihiro Minatsuki, Yoko Yoshida, Mitsuhiro Fujishiro, Shinya Kodashima, Osamu Goto, Jun Kato, Satoshi Ono, Keiko Niimi, Yu Takahashi, Maki Shimizu, Masao Ichinose, and Kazuhiko Koike. We would like to get it published in the *BMC Gastroenterology* (research article). We previously submitted this article in April 2011, and are now trying to resubmit this new article because we can address all the referees' concerns. We believe our finding would be of great interest to a broad section of the readership of your journal. Outlines of our work are as follows.

Among many symptoms of functional gastrointestinal disorders, our study focused on bothersome postprandial fullness. Postprandial fullness as well as early satiety is a major symptom of functional dyspepsia, but the underlying mechanisms remain unclear. In this study, we aimed to evaluate the correlation of postprandial fullness with chronic gastritis and gastric emptying, using the cohort of 253 healthy subjects who underwent gastrointestinal barium X-ray examination. Chronic gastritis was diagnosed by mucosal atrophy and/or hypertrophic thickened folds, both of them were frequently observed in subjects with chronic *Helicobacter pylori* infection (Sohn J et al., *Radiology* 1995, 195:763-767; Dheer S et al., *Br J Radiol* 2002,
On the contrary, there are no validated methods for measuring gastric emptying. In our study using the data from the upper gastrointestinal barium X-ray examination, therefore, we tried to evaluate it based on the gastric barium excretion and following inflow of barium into the duodenum. All subjects were divided into four categories based upon the tip of barium flow on a single-contrast frontal image of the stomach: V type (in the stomach), V-H type (in the proximal half of the duodenal bulb), H-V type (in the distal half of the duodenal bulb), and H type (in the descending part of the duodenum).

We could not detect any significant correlation between postprandial fullness and chronic (atrophic and/or hypertrophic) gastritis (p=0.973). On the contrary, there is a distinct correlation between postprandial fullness and gastric barium excretion based on barium X-ray imaging (p=0.002). We had speculated that subjects with slow gastric contents emptying such as those with gastroptosis (downward displacement of the stomach) would tend to have more gastric residue, and thereby be apt to cause the sensation of postprandial fullness. However, counter to our expectation, postprandial fullness tends to be present in situation where intragastric barium flow rapidly into the duodenum.

In conclusion, there is a distinct correlation between postprandial fullness and gastric barium excretion on barium X-ray imaging. That is, bothersome postprandial fullness is prone to be present in situations where intragastric contents rapidly flow into the duodenum. As for chronic gastritis, we could detect no correlation with postprandial fullness, judged from mucosal atrophy and/or
hypertrophic thickened folds on barium X-ray images.

According to the referees' comments, this resubmitted manuscript was revised as follows:

<The Comment from Referee A>

1. The authors need to provide details about the gastric emptying, such as whether the rate of barium emptying correlates with the gastric emptying under normal condition. The authors claimed that the result of gastric emptying by using noncaloric barium can explain the correlation between gastric contents emptying and postprandial fullness. However, the relative density of barium contrast medium is much heavier than normal food. The authors need to explain that the difference of relative density does not affect the gastric contents emptying. I think that the authors do not need to stick to “gastric emptying”. This study shows that rapid inflow of barium into the duodenum correlate with postprandial fullness.

The above comment from Referee A was also pointed out by Referee B (the comment 1 from Referee B). We tried to evaluate gastric emptying by “gastric barium excretion and following inflow of barium into the duodenum”, that is accurately and concisely measured with photos of upper gastrointestinal barium X-ray examination. However, it is certain that there is no validated method for measuring gastric emptying, and we agree that it is not enough to claim that our data from “gastric barium excretion and following inflow of barium into the duodenum” completely reflect the phenomenon of “gastric emptying”. Therefore,
following the comment of Referee A and Referee B, we have changed the phrase “gastric emptying” to “gastric barium excretion”. Consequently, we have also changed the manuscript title from “Postprandial fullness correlates with gastric emptying but not with chronic gastritis.” to “Postprandial fullness correlates with gastric barium excretion but not with chronic gastritis”.

<The Comments from Referee B>

1. **Non-validated method for measuring gastric emptying.**

   This is the same as the comment of Referee A. It is certain that there is no validated method for measuring gastric emptying, and we changed the phrase “gastric emptying” to “gastric barium excretion” in this resubmitted manuscript.

2. **Non-validated method for assessing gastric inflammation. No validation to histology.**

   In our study, we evaluated the chronic gastritis by double-contrast images of upper gastrointestinal barium X-ray examination. Chronic gastritis is mostly caused by *Helicobacter pylori* infection, and the evaluation of gastritis with double-contrast barium X-ray images has been validated with many previous studies. We already cited the report by Sohn J, et al. (*Radiology* 1995, 195:763-767). In this revised manuscript, we also newly cited the report by Dheer S. et al. (*Br J Radiol* 2002, 75:805-811). Both the reports clearly demonstrated the correlation between *Helicobacter pylori*-induced gastritis and double-contrast barium X-ray images of
stomach. In addition, we ourselves evaluated our chronic diagnoses of gastritis using another set of 30 subjects, which was described in the RESULTS section (Page 10, Line 10-16). In our study design, histological evaluation of gastritis could not be applied. However, based upon previous many studies and our validation trial from 30 subjects (Page 10, Line 10-16), we are convinced that histological analyses are not necessary in our study.

3. Non-validated symptom questionnaire.

For the evaluation of postprandial fullness, we used the question “Does your stomach feel heavy after meals?”, that is the 3rd question of “Frequency Scale for the Symptoms of GERD (FSSG)”. FSSG is the validated symptom assessment systems used worldwide for the evaluation of GERD and Functional Dyspepsia (Hepatogastroenterology 2010;57:1635-1638, J Gastroenterol. 2004;39:888-891, World J Gastroenterol 2007;13:4219-4223, J Gastroenterol Hepatol 2009;24:633-638, etc.). In this resubmitted manuscript, we clearly described an origin of the questionnaire in the METHODS section.

4. The radiation issue and ethics is not mentioned.

In the METHODS section of this resubmitted manuscript, we added the description about the radiation issue and ethics as follows: “This study was approved by the Working Group of Research Ethics, personnel and labor relations division of Nippon Steel Corporation. All the data were completely anonymized, and were
handled carefully according to the Declaration of Helsinki.” The proof of ethical approval is shown below (in Japanese).
5. The injection of spasmolytic agent and the use of barium make it difficult to assess normal gastric function.

   We agree that the use of heavy barium is not the best for evaluating the gastric content emptying. However, in return, the number of study subjects were considerably large (as mentioned by Referee B), because we used the data from yearly medical check-ups of the healthy people obtained at the clinic of one big company. The usage of spasmolytic agent certainly changed the normal gastric function by blocking the muscarinic acetylcholine receptors. However, it is no doubt that the repression of gastrointestinal peristalsis made the evaluation of barium flow tip easier and more accurate.

   As was described above, there is no validated method for estimating gastric emptying. Therefore, our trial and unexpected finding using the data from moderately large-scale cohort of healthy people should be considerable. We believe our surprising results using barium X-ray images should reflect the normal gastric function to some extent.

   This resubmitted manuscript has been carefully read and approved by all of the listed authors and consists of an original body of work which is not under consideration for publication elsewhere. For this work, we do not have non-preferred associate editors and non-preferred referees. Our suggested referees and associate editors are as follows:
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We have no suggested editors.

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We look forward to your reply. Please do not hesitate to contact me when you require anything further. Thank you for your consideration.

Yours sincerely,
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