

Answering Reviewers

Reviewer #1: Congratulations for the quality of yours work. I want make a personal comment that i think relevant. After any hemorrhagic event. We must make a contrasted esophagus-gastro-duodenal X-Ray seriogrphy since endoscopy dosen't allow to kniw the ulver depth.

Response:

In this study, an ulcer was defined as a mucosal defect 3 to 5 mm, or slightly more, in diameter on endoscopy. In Japan, X-rays are not commonly used to determine ulcer depth in patients with gastroduodenal ulcers. Therefore, X-rays were not used for ulcer depth measurement in this study.

Reviewer #2: In this retrospective study the authors examined the clinical characteristics of gastroduodenal ulcer bleeding in on low-dose aspirin (LDA) therapy with focus on age and LDA vs LDH plus other antiplatelet treatment. A total of 1105 patients with bleeding gastroduodenal ulcers were grouped by age and drugs used, and these groups were compared in several factors including length of hospital stay, hemoglobin (Hb) decrease, blood transfusion, Forrest I, Hp infection, presence or absence of underlying

disease, and percentage of severe cases. This study is important since it highlights aging-related upper GI injury in patients taking low dose of aspirin for cardiovascular prophylaxis. Overall, the paper is well conceived, but in my opinion requires several revisions, outlined below.

1) Title: Hemorrhagic gastroduodenal ulcer in elderly patients on LDA therapy. I would suggest changing it to Gastroduodenal ulcer bleeding in elderly patients on low dose aspirin therapy.

Response:

We agree with the reviewer's suggestion and changed the title to "Gastroduodenal ulcer bleeding in elderly patients on low dose aspirin therapy." (Page 1, Lines 5, of the revised manuscript)

2) The authors should define what low dose aspirin therapy is – 75 mg, 100 mg per day, etc. They should also define in the introduction combination therapy.

Response:

LDA, administered at doses of 70–330 mg/day, reportedly provides an antiplatelet effect [6,11]. In Japan, LDA is usually prescribed at a dose ≤ 162 mg/day. This also applies to our present study; that is, all patients in this study received ≤ 162 mg/day. We stated this

in the section providing definitions in the manuscript. (Page 12, Lines 178-180, of the revised manuscript)

6) Hiraishi H, Oki R, Tsuchida K, et al. Frequency of nonsteroidal anti-inflammatory drug-associated ulcers. *Clin J Gastroenterol*. 2012;5:171-176.

11) Lanas A, Scheiman J. Low-dose aspirin and upper gastrointestinal damage: epidemiology, prevention and treatment. *Curr Med Res Opin*. 2007;23:163-173.

3) If they have the data, they should spellout how many were gastric and how many duodenal ulcers.

Response:

The numbers and percentages of patients with gastric ulcer and with duodenal ulcer are shown in the Results section. (Page 13, Lines 207-208, of the revised manuscript)

4) There are 2 figures 1a but no Figure 1b. In Figure 3 blood transfusion requirements were higher in elderly patient on LDA vs. non-elderly patients on LDA.

Response:

We apologize for presenting two Figures labeled 1a. We corrected the second 1a to 1b.

In Figure 3, blood transfusion requirements were lower in non-elderly patients on LDA, although the decreases in Hb did not differ significantly between elderly and non-elderly patients. This was probably due to the transfusion having been given earlier in elderly patients.

5) The age difference is low 54.9 vs 78.5 years. This should be pointed out in the study limitation.

Response:

We compared results between patients ≥ 70 years of age and those < 70 years of age, which revealed a small difference in age. We added this observation to the section describing limitations. (Page 24, Lines 374-375, of the revised manuscript)

6) The papers requires linguistic revisions, e.g. “All authors helped to perform the research” should be changed to all authors contributed to this research study, “Japan’s population has recently entered an aged society” should be changed to Japan’s population is aging, etc. The authors should cite and discuss some references: Serebruany VL et al. Analysis of Risk of Bleeding Complications After Different Doses

of Aspirin in 192,036 Patients Enrolled in 31 Randomized Controlled Trials. Am J.
2005; 95; 1218-1222. García Rodríguez LA1, et al. Risk of upper gastrointestinal
bleeding with low-dose acetylsalicylic acid alone and in combination with clopidogrel
and other medications. Circulation. 2011 Mar 15;123(10):1108-15

Response:

In accordance with the reviewer's comment, we corrected the manuscript. (Page 1,
Lines 22, and Page 7, Lines 98, of the revised manuscript)

The other parts of the manuscript were checked by a native speaker of English. We are
again submitting a certificate of English editing with this resubmission. In addition, we
added the references suggested by the reviewer and described their findings in the
Discussion section. (Page 20, Lines 309-310, of the revised manuscript)

Reviewer #3: Congratulations for this interesting study that contains a very useful and
practical clinical information

Response:

Thank you.