

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The authors reported the outcome of ESD in elderly patients 80 years or older with gastric cancer. I have the following comments:

1、 On page 11, line 17-19, “However, some studies have reported that ESD carries a higher risk in elderly patients than in younger patients”, please elaborate on it, and discuss the reasons for the different results from the present study.

According to the reviewer’s comment, sentences as follow are added.

Toyokawa et al. reported that the bleeding rate was significantly higher in the elderly group (age ≥ 75 years) than in the non-elderly group (age < 75 years). However, in multivariate analysis, high age was not in itself an independent predictor of bleeding, and the reason why the bleeding rate was higher in the elderly group was unclear. It is also reported by Toyokawa et al. in another report that age ≥ 80 years was associated with a significantly higher risk of delayed bleeding after ESD, and they concluded that the use of antiplatelet agents or anticoagulants was not the reason for delayed bleeding in elderly patients. Also in this study, they could not specify the reason why delayed bleeding was predominant in elderly patients over non-elderly patients. In our institution, endoscopic examination on the next day of ESD was routinely performed, and coagulation of visible vessels at the ulcer floor was carried out. This endoscopic examination may contribute to low incidence of bleeding in our present study. In any case, attentive precautionary endoscopic hemostasis after dissection is crucial for aged patients, as they demonstrate age-related physiological decline with higher incidence of underlying diseases and worse overall condition^[16].

2、 On page 11, line 11-13, “the rates of bleeding and perforation among patients of all ages were reported to range from 3.7% to 15.6% and 1.2% to 6.7%, respectively”, but the results of this study was even lower, which are 3.4% and 1.1% respectively, please explain why.

Because the object lesions, patient characteristics, operators of ESD and protocol of ESD of each study were not identical to our study, we think it inadequate to say that the percentage of complications in our study is lower than previous reports of all ages.

Previous reports of all ages tended to have high incidence of complications.

The rates of bleeding and perforation reported are as follows:

• All age: 3.7-15.6%, 1.2-6.7%

•Elderly: 2.5-9.6%, 1.5-5.0%

•Non-elderly: 2.9%, 1.1%

These data above shows that the reported percentages of all ages were relatively high compared to the percentages of elderly and non-elderly. The reason is unclear, but we speculate that selection bias of recruited patients in each study may be one of the reasons.

According to the reviewer's comment, we added the following sentence, "*These previous reports and present study suggest that the rates of complications of ESD in elderly patients are not particularly higher than the rates in non-elderly or all ages.*"

3、It would be more persuasive to include the outcome of all ages or non-elderly patients during the same period, if available.

Sorry, unfortunately, we have no data concerning the outcomes of all ages or non-elderly patients during the same period.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This manuscript aims to define the safety and feasibility of ESD for EGC in the elderly. The study is well written and the statistical analysis appears proper. I only have few comments:

-please shorten the discussion section

This is a report concerning a topic which may strongly attract the readers. We believe that the discussion in great detail is helpful for the readers to understand the contents of our report and previous reports. Though we have considered and reconsidered carefully, the description written in the discussion section is indispensable. Therefore, we would like you to approve even if the section is slightly long.

-Table 1. Please specify U upper M medium L lower location of the lesion.

The abbreviations are now defined at the end of the figure legend to specify the meaning.

"Location, ESD quality (en-bolc or fractional dissection rate)". Please correct en.bloc

The spelling mistake is corrected.

-Table 4. Please correct the title "Details of patients who had complications of ESD"

The title is now corrected as "*Clinical characteristics of patients who had complications of ESD.*"

Reviewer #3:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: The authors retrospectively reviewed their ESDs performed in patients older than 80 years. They found ESD to be feasible, safe, and with good outcomes. The topic is very important. The paper is well written and conclusions are based on a good analysis of data.

Just a few questions:

- Do you perform biopsies around the lesion in a previous endoscopy to assess margins by protocol? Do you think that this is really necessary? What is the evidence that shows that horizontal margins will be free of lesion in a more percentage of cases, comparing with ESDs performed without that protocol?

Thank you for your comment.

We performed negative biopsies around the lesion if the margin was unclear, to assess margins precisely before the date of ESD, and avoid positive surgical margin as far as possible. These biopsies before endoscopic resection were not done by protocol, but done if the margin was unclear. Precise identification of horizontal margins before the treatment may shorten the dissection time, resulting in minimally invasiveness for aged patients. Histological assessment of outside-the-lesion biopsy specimens has been considered as a golden standard for identification of horizontal margin for lesions with unclear margin. However, after practical application of M-NBI (Magnifying Narrow-Band Imaging) recently, identification of horizontal margins due to demarcation line detected by M-NBI has been widely accepted in substitution for negative biopsies around the lesion, according to accumulation of reports about its usefulness.

The target of this study are aged patients treated from 2006 to 2014 in our institution. Magnifying endoscope and light source system with NBI (Narrow Band Imaging) function had been available in 2007 in Japan. At the time of enrolling period, the identification of horizontal margins due to demarcation line detected by M-NBI was still developing. Moreover, precise identification of horizontal margins by around-the-lesion biopsies are still now essential in some cases; (1)

undifferentiated type adenocarcinoma (por, sig) which may spread subepithelially, (2) gastric adenocarcinoma of fundic-gland type whose margin is often unclear, (3) lesions on severe atrophic area with marked intestinal metaplasia whose margin is unclear, (4) in case when M-NBI examination is difficult because of movement of the lesion according to heart beat or breathing, (5) in case when it is difficult to get close to the lesions by endoscope, and so on. Unfortunately, there is no detailed report about to what extent ESD with pretreatment around-the-lesion biopsy is superior to ESD without pretreatment around-the-lesion biopsy, concerning the incidence of negative surgical margins.

As the description of “*Around-the-lesion biopsy was performed beforehand to confirm the margin of the lesions*” may be misleading to readers, we added the term “*if necessary.*”

- What is the criteria for second-look endoscopy? In which patients? Do you perform some cases in an ambulatory setting?

Meaning of “second-look endoscopy” is a routine endoscopic exam “*which was basically performed on the day after ESD*”, as described in the manuscript. As the description was hardly conveyed to readers, we have revised the sentence as follows, “*endoscopic examination, which was basically performed routinely in all patients on the next day of ESD.*”

Usually, patients admitted on the date of ESD, and they were hospitalized for one week after ESD. Accordingly, none of the next-day endoscopic exam was performed in an ambulatory setting.

- What are the criteria for defining non-curative ESD? This must be clear in the methods

The criteria for defining non-curative ESD is described in the manuscript as follows; “*Curability was assessed according to the Japanese Gastric Cancer Treatment Guidelines 2010^[18]”. The Guidelines is widely accepted. To make it clear, the criteria for curability is now described in our manuscript as follows, “A curative resection was defined as satisfying all the following conditions: en bloc resection, negative horizontal and vertical margin, no lymphovascular infiltration, and absolute or expanded indication for endoscopic resection. Differentiated type intramucosal cancer ≤ 20 mm in size without ulceration was categorized as a lesion of absolute indication. A lesion of expanded indications was as follows: differentiated type intramucosal cancer >20 mm in size without ulceration, differentiated type intramucosal cancer ≤ 30 mm in size with ulceration, differentiated type submucosal superficial cancer ≤ 30 mm in size, and undifferentiated type intramucosal cancer ≤ 20 mm in size without ulceration.”*

- Authors said that "Many of the recruited patients had underlying diseases". **Data should be objective, not using "many"**

The description is revised as follows, "Of 124 recruited patients, 38 patients (30.6%) had circulatory underlying diseases, and 9 patients (7.3%) had respiratory underlying diseases."

- **Please revise tables legends.** Some tables are difficult to read

Tables are revised.

Science editor: 1 Scientific quality: The manuscript describes a Retrospective Study of the gastric endoscopic submucosal dissection in elderly patients. The topic is within the scope of the WJG. (1) Classification: Grade B, C and C; (2) Summary of the Peer-Review Report: The paper is well written and conclusions are based on a good analysis of data. Some sentences need to be explained. **Authors should rewrite Table illustration. The questions raised by the reviewers should be answered;** (3) Format: There are 7 tables and 2 figures; (4) References: A total of 36 references are cited; (5) Self-cited references: There is no self-cited reference. 2 Language evaluation: Classification: Grade B, B and B. The manuscript is reviewed by a native English speaker. 3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the Institutional Review Board Approval Form and Written informed consent. No academic misconduct was found in the Bing search. 4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJG.

5 Issues raised:

(1) **The "Author Contributions" section is missing. Please provide the author contributions;**

We have added the "Author Contributions" section in the manuscript.

(2) The authors did not provide original pictures. **Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;**

We uploaded the figures which could be reprocessed by the editor.

(3) PMID and DOI numbers are missing in the reference list. **Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references.** Please revise throughout;

We have provided the PMID, DOI numbers, and name of all authors of the references.

(4) The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text.

We have added the “Article Highlights” section at the end of the main text.

6 Recommendation: Conditional acceptance.