

Point-by-point responses

Name of Journal: *World Journal of Gastrointestinal Oncology*

Invited ID: 03475120

Manuscript ID: 41705 R1

Manuscript title: Laparoscopic and endoscopic cooperative surgery for gastric tumors: Perspective for actual practice and oncological benefits

Correspondence to: Tomohide Hori, PhD., MD., FACS.

Thank you for your valuable suggestions.

According to reviewers' comments, we revised our initial manuscript.

Please review our revised manuscript.

We prepared **Marked revised manuscript** and **Clear version**. In the marked version, additional mentions are **in Red**, and deleted sentences are shown **in Red with strikethrough**.

Also, this summary of responses (**Point-by-point responses**) was separately made.

English language: Manuscript (Main body and all Tables) was fully checked by English consultant (edanz editing, ordering ID: J1708-108313-Aisu). I attached a Certificate for English language, with the cover letter.

To Reviewer# 02534438

Thank you for your valuable suggestions.

According to your suggestions, we revised our initial manuscript as described below.

1. Feasibility and safety of LECS

‘The only thing I find missing are some numbers: do authors have any numbers to demonstrate feasibility and safety? Published as well as unpublished data on success rates (R0, R1...), mortality, morbidity and follow up should definitely accompany such a comprehensive review.’

Thank you for your valuable suggestion.

Success rates (resectability), mortality, morbidity and follow-up term are checked in previous important documents. We summarized these factors in added Table.

According to your suggestion, we made a new Table. As shown in added Table, no conversion to gastrectomy or laparotomy, no positive surgical margin, few postoperative complications, no mortality and no recurrence were documented in almost all previous reliable studies. Thus, LECS is considered as safe and feasible, including modified techniques such as Closed LECS, NEWS, Clean-NET and Lift-and-cut method.

We added the mention as ‘Previous important studies reported no recurrent cases (Table). (Page 21 line 4, in the Marked revised manuscript)’, ‘Clinical

outcomes (e.g., oncological resectability, mortality, morbidity and follow-up term) in previous important documents were summarized in Table. (Page 22 line 25-page 23 line 1, in the Marked revised manuscript)’ and ‘LECS has demonstrated no mortality and a low incidence of postoperative complications,^[48,81] and we speculate that strict performance of the leakage test may play an important role to avoid leakage. (Page 23 line 1-3, in the Marked revised manuscript)’.

To Reviewer# 02441737

Thank you for your valuable suggestions.

According to your suggestions, we revised our initial manuscript as below.

1. General characteristics of the methodology, in Abstract section

‘It would be recommendable for the authors to present some general characteristics of the methodology they follow to make this manuscript.’

Thank you for your valuable suggestion.

According to your suggestion, we added the mentions for some general characteristics of the methodology in the Abstract section, as ‘Interventional endoscopists and laparoscopic surgeons collaboratively explore curative resection. Simultaneous intraluminal approach with endoscopy allows surgeons

to optimizes the resection area. LECS, not simple wedge resection, achieves minimally invasive treatment and allows for oncologically precise resection.'

(Page 3 line 20-24, in the Marked revised manuscript).

2. The reason why LECS is only done in Asia and not in other parts of the world, in Introduction section

'The introduction is adequate and allows a proper understanding of the problem of study. It is recommended that the authors describe some reasons why novel cooperative laparoscopic and endoscopic techniques for gastric tumors, it is only done in Asia and not in other parts of the world?'

Thank you for your valuable suggestion.

The ESD has first developed in Asian countries, and the concept and procedures of LECS first reported from Japan. This may be a reason why LECS is spreading mainly in Asia at this time. However, LECS is a notable function-preserving surgery with oncological safety. So, we believe LECS spreads to all over the world.

According to your suggestion, we added the mention as 'Procedures of both ESD and LECS originate in Japan, and this may be the reason why LECS is mainly developed in Asian countries so far.' (Page 8 line 26-page 9 line 1, in the Marked revised manuscript).

3. Recommendable type of patients for LECS, in Methods section

'In the indications for the use of LECS, the authors could also mention some

recommendations regarding the type of patient. For example, age, sex, BMI, body composition, tumor extension, complications, comorbidity of the patient, among many other factors specific to patients that could be a limitation due to the use of the proposed technique.'

Thank you for your valuable suggestion.

As described in our manuscript, the indications for LECS should be considered based on the tumor's characteristics, institutional ability, and individual skills. We think no special consideration is needed for LECS adaptation except for these three factors. Other factors (e.g., age, sex, body mass index, comorbidity) don't affect the indication for LECS. The Indications and contraindications of LECS are the same as ordinary laparoscopic surgery.

However, based on important previous papers, we summarized these factors in added Table. We hope data in previous important papers will be informative for journal readers.

According to your suggestion, we added the mention, as 'Indication and contraindication for LECS are mainly considered based on three factors (i.e., the tumor's characteristics, institutional ability and individual skills). Other clinical factors (e.g., age, gender, body mass index and comorbidity) never affect the indication for LECS, and these factors in previous documents are summarized in **Table**. (Page 11 line 1-6, in the Marked revised manuscript)' and also added the new Table.

4. Statistics and characteristics of patients applied with LECS, in Discussion

section

'It is recommended that the authors present some statistics on the following points applying the novel LECS technique: a) The number of patients attended; b) The histological lineage of the tumor; c) Sex, age, and some clinical characteristics of the patients seen.; d) The number of recurrences; e) The type and number of adverse effects to the treatment; f) The number of deaths (if any).'

Thank you for your valuable suggestion.

We agree your suggestion that there should be some statistics and results of LECS so that it would be more convincing.

According to your suggestion, clinical factors (i.e., patient number, tumor diagnosis, age, gender, recurrence rate) in previous important are summarized in added new Table.

Moreover, as well as the comments from Reviewer# 02534438, other clinical factors (i.e., success rates, resectability, mortality, morbidity and follow-up term) are checked in previous important documents, and added new Table involves these data.

According to your suggestion, we added the mentions, as 'Previous important studies reported no recurrent cases (Table). (Page 21 line 4, in the Marked revised manuscript)', 'Clinical outcomes (e.g., oncological resectability, mortality, morbidity and follow-up term) in previous important documents were summarized in Table. (Page 22 line 25-page 23 line 1, in the Marked revised manuscript)' and 'LECS has demonstrated no mortality and a low incidence of postoperative complications,^[48,81] and we speculate that strict performance of the

leakage test may play an important role to avoid leakage. (Page 23 line 1-3, in the Marked revised manuscript)’.

5. More descriptive title in each figure

‘It is recommended to place a more descriptive title in all the figures.’

Thank you for your valuable suggestion.

According to your suggestion, we revised the figure titles. The modification points are shown, as ‘**Figure 1. Schema of LECS, and comparison of resection line between LECS and conventional wedge resection**’ (Page 41 line 3-4, in the Marked revised manuscript), ‘**Figure 2. Set-up of staffs and devices in the operation theater and port placement**’ (Page 42 line 1-2, in the Marked revised manuscript), ‘**Figure 3. Intraoperative laparoscopic view of LECS**’ (Page 43 line 1, in the Marked revised manuscript), ‘**Figure 4. Intraoperative endoscopic view of LECS**’ (Page 45 line 1, in the Marked revised manuscript), ‘**Figure 5. Importance of interventional endoscopist’s line of vision while cutting the proximal side**’ (Page 47 line 1-2, in the Marked revised manuscript), ‘**Figure 6. Options of Specimen specimen removal with plastic bag**’ (Page 48 line 1, in the Marked revised manuscript), ‘**Figure 7. Effective use of an overtube when removing the specimen**’ (Page 49 line 1, in the Marked revised manuscript), and ‘**Figure 8. Comparison of surgical specimens margins between LECS and conventional wedge resection**’ (Page 50 line 1-2, in the Marked revised manuscript).

6. The statistics of results using LECS in Asia. (Biostatistics)

'It would be interesting to present the results of the statistics of some results using the Laparoscopic and endoscopic cooperative surgery for gastric tumors in Asia.'

Thank you for your valuable suggestion.

As mentioned above, we also think there should be some statistics and results of LECS for this paper to be more persuasive.

In the revised manuscript, clinical factors and outcomes (i.e., tumor diagnosis, age, gender, success rates, resectability, mortality, morbidity and follow-up term) in previous important are summarized in added new Table.

According to your suggestion, we added the mentions, as 'Clinical outcomes (e.g., oncological resectability, mortality, morbidity and follow-up term) in previous important documents were summarized in Table. (Page 22 line 25-page 23 line 1, in the Marked revised manuscript)' and 'LECS has demonstrated no mortality and a low incidence of postoperative complications,^[48,81] and we speculate that strict performance of the leakage test may play an important role to avoid leakage. (Page 23 line 1-3, in the Marked revised manuscript)'.

To Science editor

According to your suggestions, we revised our initial manuscript as below.

1. SI units

Thank you for your valuable suggestion.

According to your suggestion, we added the mention as ‘Three additional ports (two ~~5-mm~~ 5- mm ports and one ~~12-mm~~ 12- mm port) are inserted into the left upper, left lower, and right upper quadrants, respectively, under pneumoperitoneum of 12 mmHg with a laparoscopic view. One additional ~~5-mm~~ 5- mm port in the right lower quadrant is acceptable, if necessary (**Figure 2B**).’ (Page 13 line 23-page 14 line 2, in the Marked revised manuscript).

2. English language

Manuscript have been already checked by English consultant (edanz editing, ordering ID: J1808-120277-Aisu). I attached a Certificate for English language, with this letter.

3. Shortened running title

We shortened the running title less than 6 words, in the revised manuscript (Page 2 line 2, in the Marked revised manuscript).

3. Postal code

We attached each postal code, in the revised manuscript (Page 1 line 13-22, in the Marked revised manuscript).

4. ORCID ID

We added each ORCID ID, in the revised manuscript (Page 1 line 24-26, in the Marked revised manuscript).

5. All authors abbreviation names and manuscript title under the CORE TIP section.

According to your suggestion, we added all authors abbreviation names and manuscript title (Page 4 line 4-6, in the Marked revised manuscript).

6. Deletion of 'COMMENT' paragraphs

We deleted 'COMMENT' section, in the revised manuscript (Page 25 line 21-page 26 line 19, in the Marked revised manuscript).

7. PMID and DOI, in References section

We added PMID and DOI, in each reference (Page 27-40, in the Marked revised manuscript).

8. Insert the figure legends right under the relate figure

We insert the figure legends under the related figure, in each figure (Page 41-50, in the Marked revised manuscript).