Format for ANSWERING REVIEWERS

September 17, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 19725-Revised manuscript.doc).

Title: Technical feasibility of laparoscopic extended surgery beyond total mesorectal excision for primary or recurrent rectal cancer

Author: Takashi Akiyoshi

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 19725

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reviewer 1

(1) Very good review of the literature with conclusions according to actual evidence. Ready for publication.

Answer

Thank you for your favorable comments.

Reviewer 2

(1) MAJOR POINTS FOR GENERAL COMMENTS This invited review is a interesting topic, because of what is reported in the literature regarding this challenging pathology, both in terms of surgical and medical oncology, is still under discussion. It seems that the article is mainly focused on feasibility of the laparoscopic approach versus open surgery, especially in terms of some intraoperative and histopathologic features (in addition the attached images are of excellent quality and anatomically educational). If so, I think it is an article on technical feasibility and safety of a demanding miniinvasive surgical technique versus traditional approach. You do not make notes on post-operative specific complications (eg anastomotic fistula, intra-abdominal collections, changes in bowel or urinary or genital function): these features should be showed. In summary, it is not clear if this review is on technical aspects or a technical comparison between laparoscopic versus open surgery or a review of intraoperative and post-operative surgical outcomes.

Answer

Thank you for your valuable comments. As the reviewer pointed out, this topic highlight aimed to focus on the technical feasibility and safety of a demanding laparoscopic technique beyond total mesorectal excision (TME). To achieve this, I tried to introduce published studies about safety and feasibility of laparoscopic extended surgery beyond the TME. This paper did not aim to focus on a comparison between laparoscopic versus open surgery or a review of intraoperative and post-operative surgical outcomes, although intra- and post-operative complications are one of the important factors for safety and feasibility. However, at present, many studies regarding laparoscopic extended surgery beyond the TME did not have comparative open surgery groups, and therefore, there are no data on post-operative specific complications in laparoscopic extended surgery compared with those in open surgery. When the study had only the laparoscopic surgery group, I think postoperative complication rate itself would not be of great importance unless it is unexpectedly high. With regard to laparoscopic LPLD, there were no studies

comparing laparoscopic versus open LPLD, and therefore, I could not refer to specific morbidity, although I have shown overall morbidity of laparoscopic LPLD in table 1. With regard to laparoscopic surgery for rectal cancer invading adjacent organs, because three studies about this topic included not only rectal cancer but also colon cancer, there were no data on postoperative complications focusing on rectal cancer comparing laparoscopic versus open surgery. With regard to laparoscopic salvage surgery for locally recurrent rectal cancer, one paper (reference 45) compared laparoscopic versus open surgery. We have added the data on postoperative complications, as follows: "The percentage of postoperative complications was similar (30.8% *vs* 23.5%)" (revised manuscript, page 12). With regard to laparoscopic pelvic exenteration for primary or locally recurrent rectal cancer, only reference 48 compared laparoscopic and open approach. We already showed data on postoperative complications, as follows. "Importantly, overall rates of any complication (66.7% *vs* 89.7%) and major complications (0% *vs* 32.8%) were lower in the laparoscopic surgery group, although differences were not significant." (revised manuscript, page 13).

(2) SPECIFIC COMMENTS FOR ARTICLE SECTIONS TITLE The title should contain specific words as reported in the article "……excision for ADVANCED rectal cancer", or "…….excision for LOCALLY ADVANCED AND RECURRENT rectal cancer" A subtitle could be present specifying that it is a review on technical aspects or surgical outcomes, if this is the authors' core tip.

Answer

Thank you for your comments. I totally agree with the reviewer, and therefore, I changed the title to "Technical feasibility of laparoscopic extended surgery beyond total mesorectal excision for primary or recurrent rectal cancer", although this title exceeded the world limit.

(3) ABSTRACT Also here it seems that this review is focused mainly on technical aspect. May be useful to summarize also something about intraoperative and post-operative

complication during laparoscopic approach versus laparotomy Please provide clear delineation between background, objectives, material and methods, results and conclusions.

Answer

As I stated in the response to comment 1, at present, many studies regarding laparoscopic extended surgery beyond the TME did not have comparative open surgery groups, and therefore, there are very limited data on post-operative specific complications of laparoscopic extended surgery compared with open surgery. Therefore, it is difficult to summarize something about intraoperative and post-operative complication during laparoscopic approach versus laparotomy in the abstract. Furthermore, manuscript guideline of topic highlight requires an "unstructured" abstract no more than 200 words. Therefore, it is not suitable to delineate between background, objectives, material and methods, results and conclusions.

(4) MATERIAL AND METHODS AND RESULTS: Refine the structure of the material and methods and results, better specifying the medical databases employed (like PubMed, Medline, Embase, etc.) and which was the modality for articles' selection. For a review, a well organized material and method section and a brief chapter reporting results of articles selected and their main outcomes (also with tables) should be setted.

Answer

Thank you for your comments. I agree with the reviewer, but this paper is classified as a topic highlight. Guideline of manuscript preparation of topic highlight in *World J Gastroenterol* does not require material and methods and results section. In fact, previous papers in topic highlight did not have those sections.

(5) DISCUSSION: Structuring the discussion into chapters it's ok, but a clear division between outcomes (to report in the RESULT paragraph) and comment (in the DISCUSSION paragraph) is preferable. It is not clear if this is a revision based on technical

feasibility of LPLD + TME and / or a comparison between laparoscopy and laparotomy? Or a comparison on surgical intraoperative and postoperative autcomes? If the article is a review on intraoperative and short-term results after extended TME for advanced locally and recurrent rectal cancer, you should also report more results on them, in order to make this session more clearly readable as a review. In fact there is no mention on mortality, specific morbidity related to this demanding surgery; in addition the case studies reported in the literature and showed in this article are limited to a few cases, without follow-up cancer even in the medium-short term. Reporting in any chapters something about the rates of specific complications (fistula, pneumonia, postoperative ileus, acute urinary retention, etc .... typical of rectal surgery) – if published - would be useful to do; alternatively reporting that any result has not been described or only in summary. For example more data, may be with an additional more detailed table, regarding post-operative complications and their percentage in laparoscopy and in open surgery should be reported. If the article is focused only on technical and itraoperative aspects, it would be more useful that resulted more clear from the title and content; otherwise you have to add data and information mentioned above. Under the heading "laparoscopic lateral pelvich limph dissection" it was written that the LPLD is considered "futile" in Western countries. Perhaps it would be better to replace

Answer

Again, guideline of manuscript preparation and format of topic highlight in *World J Gastroenterol* does not require clear division of discussion into outcomes (to report in the RESULT paragraph) and comment (in the DISCUSSION paragraph). Repeatedly, with regard to laparoscopic LPLD, there were no studies comparing laparoscopic versus open LPLD, and therefore, I could not refer to specific morbidity of laparoscopic LPLD compared with open surgery, although I have shown overall morbidity of laparoscopic LPLD in table 1. As the reviewer suggested, it would be preferable to specify that this is a review on technical aspects. According to the reviewer's suggestion, I changed the title. Because studies about laparoscopic surgery for rectal cancer invading adjacent organs, laparoscopic salvage surgery for locally recurrent rectal cancer, and laparoscopic pelvic

exenteration for primary or locally recurrent rectal cancer are very limited with very small sample sizes, an additional more detailed table regarding post-operative complications and their percentage in laparoscopy and in open surgery is difficult, because most studies have no comparable open surgery groups. Although LPLD is frequently performed in Japan, it is regarded as futile in western countries because lateral pelvic lymph node metastasis is considered a systemic disease not amenable to surgical cure, with preoperative chemoradiotherapy considered the treatment of choice for western patients with lateral pelvic lymph node metastasis. However, recent studies have shown that preoperative chemoradiotherapy alone cannot eradicate lateral pelvic lymph node metastases, and therefore, LPLD is considered useful for selected patients with advanced low rectal cancer and clinically suspected lateral lymph node metastasis, even after preoperative chemoradiotherapy. Many Japanese surgeons consider that LPLD is “not” futile, and therefore, replacing the heading "laparoscopic lateral pelvic lymph dissection” is not suitable.

Reviewer 3

(1) No comments to the authors.

Answer

Thank you for your favorable comments.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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