

Format for ANSWERING REVIEWERS

Sep, 30, 2014

Dear Editor,



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

Title: Hand-sewn versus linearly stapled esophagogastric anastomosis for esophageal cancer: A meta-analysis

Author: Xu-Feng Deng, Quan-Xing Liu, Dong Zhou, Jia-Xin Min, and Ji-Gang Dai

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 12782

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

- (1) **Reviewed by 02546377:** This meta-analysis addresses an important question for oesophago-gastric surgeons. This is a nicely written manuscript and the analyses seem to be well performed. The topic of the esophagogastric anastomosis is not really new, but it is still one of the mainly important problems in esophageal surgery.

Answer: Thank you for your kind comments for our manuscript to World Journal of Gastroenterology. We appreciate your valuable comments.

- (2) **Reviewed by 02554808:** The authors have found that there is not a significant difference in the rate of anastomotic leakage for intrathoracic anastomosis while this parameter showed significant improvement in favour of the LS group in the case of cervical anastomosis. This finding should trigger a detailed discussion about the differences in the quality of tissues and tension for the intrathoracic and cervical anastomosis and also into the differences between the LS and HS anastomosis and their consequences on the perfusion of the anastomosed tissues. The differences are not limited to the fact that LS has three rows and is more water-tight, as described by the authors; probably LS stapling, being less ischemic, is more likely to avoid necrosis in poorly vascularized tissues, such as the long gastric tube brought up in the neck. This necessary discussion is too vague in the present form of the paper. Reduction of anastomotic stricture is only explained in the present study by the difference in intraluminal width of the anastomosis. A comparison of LS with the circular stapled anastomosis should be made in this respect. However, there should also be a comment over the effect of anastomotic fistula on the risk of postoperative anastomotic stricture, maybe a subgroup analysis of the rate of anastomotic stenosis in the non-fistulized LS vs HS anastomosis would be very helpful in this respect and would better explain why the largest advantage of LS was found for the cervical anastomoses. Most of the papers analyzed were comparative trials and the only 3 RCT's included in the study did not show any difference between LS and HS concerning the rate of anastomotic fistula. The small number of RCT's represent a weak point of the study and should be addressed when conclusions are drawn.

Answer: We very much appreciate your careful review, constructive comments, and suggested corrections to our manuscript. Thank you for your suggestions and comments addressing the inadequacies of the manuscript. We have revised the manuscript according to your comments and have incorporated all of the corrections. This article is a meta-analysis. Before beginning this study, a rigorous protocol was established according to the recommendations of the Cochrane Collaboration. Databases and references were searched for all RCTs and comparative clinical studies that compared LS with HS esophagogastric anastomosis for esophageal cancer. The mechanism of anastomotic leakage and anastomotic stricture in the discussion was cited from studies which were included in our meta-analysis, e.g. J Thorac Cardiovasc surg 2000;119:277-288, World J Surg (2013) 37:1043–1050. This study aims to provide a pooled analysis of current trials comparing linearly stapled with hand-sewn esophagogastric anastomosis for esophageal cancer. Although most of the papers analyzed were comparative trials and the only 3 RCT's included in the study. The rigorous study protocol was established according to the recommendations of the Cochrane Collaboration before the analyses, to ensure the highest quality for this meta-analysis; all of the objective, inclusion and exclusion criteria, primary and secondary outcomes, and methods of synthesis were prespecified.

- (3) **Reviewed by 00057983:** 1. The authors collected a large number of patients in this meta-analysis. However, the design and analysis of this study is not strict. Thus, the conclusion seems not very reliable. 2. There are many risk factors of anastomosis leakage, e.g. patient underlying disease and nutrition status, American Society of Anesthesiology status, surgeon or hospital volume. Besides, the definition of leakage, method of discovery should also be mentioned. So, the authors should carefully discuss and compare the difference of these studies. 3. Is there any limitation of this study should be mentioned in this DISCUSSION part?

Answer: We very much appreciate your careful review, constructive comments, and suggested corrections to our manuscript. We have revised the manuscript according to your comments and have incorporated all of the corrections. 1. Fifteen studies were included in our meta-analysis. Although three randomized trial literatures included in our analysis, they all met our prespecified inclusion criteria. We are strictly apply flow chart of the literature search according to PRISMA statement. To make sure the high quality for this meta-analysis, a rigorous study protocol was prespecified and several electronic databases, references, and international conference abstracts for relevant trials, were searched without restrictions on language. 2. This is a very important problem. Firstly, this is a meta-analysis. Secondly, it's true that there are many risk factors of anastomosis leakage, e.g. patient underlying disease and nutrition status, American Society of Anesthesiology status, surgeon or hospital volume. But these risk factors were discussed too vague in the present form our included literatures. Further research will be performed in our next work; Secondly, for the purposes of this study, we considered patients to have experienced an anastomotic leak when the following were indicated:(i) positive contrast study with or without clinical signs; and (ii) clinical signs alone requiring a subsequent alteration in clinical care (e.g. wound drainage and packing, or re-operation). Similarly, patients were considered to have postoperative strictures, and a need for postoperative dilatation, if they experienced any dysphagia and required more than one dilatation in the first 6 months after surgery. In support of the diagnosis, anastomotic narrowing was noted at the time of endoscopy and dysphagia was typically relieved after dilatation. According to your suggestion, we have mentioned the definition of leakage, method of discovery in more detail in the *Study design* part in the revised manuscript with a red color. Finally, according to your comments we have revised the manuscript. We hope

that the revised manuscript will leave you with a good impression. **3.** PRISMA stands for Preferred Reporting Items for Systematic Reviews and Meta-Analyses. It is an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses. The PRISMA Statement consists of a 27-item checklist and a four-phase flow diagram. In DISCUSSION part of the PRISMA checklist includes three parts **Summary of evidence, Limitations, Conclusions.** According to PRISMA checklist we mentioned any limitation of this study.

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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