

July 7, 2014

Dear Editor,

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

Title: Preventing and Localizing Anastomosis Leakage by Sleeve-Wrapping of the Pedicled Omentum

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Name of Journal: *World Journal of Gastroenterology*

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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 01047430:** Why do you not have a comparative control arm of patients who have undergone the conventional anastomotic technique? In its absence it is difficult to categorically conclude that the good results obtained are purely because of this innovation. what is the reason for using the anterior mediastinal route for gastric transposition? Lastly it well known that use of a circular stapler is associated with high anastomotic stricture rate; hence why this choice?

Answer: We thank the reviewer for this valuable suggestion. This really does need some explanation. The type of this article is a prospective single-center study. We made this study in order to describe the preliminary results of our new technique in preventing and localizing anastomosis leakage after

oesophagectomy. Such type of article was very popular in introducing a new technique, such as the following published article: *Endoscopy*. 2013;45(3):161-6. doi: 0.1055/s-0032-1326203. Epub 2013 Feb 6. In order to further clarify our good results of this technique, we have provided the outcomes of patients who have undergone the conventional anastomotic technique after oesophagectomy as the comparative control arm from precious published articles. Such content have added to the first paragraph of discussion section. In addition, a randomized controlled trail for this anastomosis method is undergoing and the trial registry number is ChiCTR-TRC-13003817 in the Chinese Clinical Trial Registry. The route for gastric transposition described in our manuscript may be misunderstood by reviews, which was considered as conventional. Such description can be also found in the published article (*Ann Thorac Surg*. 2006 Nov;82(5):1857-62.)“The newly constructed gastric tube was then carefully guided through the posterior mediastinum to the cervical area (or chest) for anastomosis”. Really, currently, it well known that use of a circular stapler is associated with high anastomotic stricture rate, and the hand-sewn method may be associated with lower anastomotic stricture rate. However compared with hand-sewn the circular stapler contributed to reducing the rate of anastomotic leakage which was more life-threatening in the latest decade. We have performed a meta-analysis including 10 RCTs published between 2003 to 2013; and the result is (RR: 0.66, 95% CI: 0.45-0.96, P=0.03); which identify the superior of circular stapler

method in reducing anastomotic leakage.

(2) **Reviewed by 02546377:** I have three comments/questions: 1、 There is a lack in the definition in complications. 2、 The mean operation time of this method should be offered.

3、 There are some spelling and grammatical errors. 4、 Several editing errors exists for many adjacent words were linked which should be corrected. 5、 There is no clarity as to when the anastomoses were constructed via the thoracotomy or a separate neck incision and in the latter cases how exactly the stapler was used.

Answer: Thank you for your kind comments for our manuscript to *World Journal of Gastroenterology*. We appreciate your valuable comments and suggestions to improve it. With regard to your comments and suggestions, we wish to reply with the following responses: 1、 We have clearly identified the main complications in results section and the diagnose method in method section. 2、 We have offered the operation time in the first paragraph of result section. 3、 Thank you for your valuable suggestion. We have reedited the manuscript for proper English. 4、 Thank you for your conscientious work. We have reedited the manuscript based on your valuable suggestions. 5、 I am really sorry for the misunderstanding caused by my poor description and we thank the reviewer for this valuable suggestion. In this study the anastomoses site was determined by the tumor size and the tumor site. In our

surgical procedure for both hand-sewn and stapled groups, the esophagus is circumferentially mobilized and tumor was dissected at the appropriate level, with both the proximal and distal margin were more than 5-8 cm through a right thoracotomy. Thus, all patients with tumor in the upper thoracic and a part of patients with tumor in the middle site were anastomosed in neck. In the neck incision for stapled anastomosis, CDH (Ethicon; Johnson & Johnson, Mexico) circular staplers were used and the doughnuts were verified routinely.

(3) **Reviewed by 02554808:** The English language used in this article proff is very poor. It can not be published in this form. Wrapping of the anastomosis does not necesarily prevent the development of a anastomotic fistula, but it can help block the fistula from the very beginning and thus lessen the clinical consequences of the fistula. It is debatable if the presence of the omentum brings enough growth factors and nutrients in the first 5-7 days after the operationt to really prevent development of a fistula. Wrapping the anastomosis with omentum is not really a new anastomotic technique, is just a supplimentary measure taken for a conventional technique. Surgical technique: description of dissection of the esophagus is very poor, unintelegible while the use of English language is extremely innacurate. The gastric tube with a diameter of 3 cm predisposes to anastomotic fistula because a very narrow tube has difficulties in supplying good blood flow to

the upper pole. Diameters of 4-6 cm are more likely to be associated with a lesser incidence in anastomotic fistula. The authors do not explain why do they bring the gastric tube in the chest using a route through the anterior mediastinum and not the orthotopic route. It is a rather unusual approach. The esogastric anastomosis was performed in an end-to-end fashion using a circular stapler. How did the authors introduce the shaft of the circular stapler in the gastric tube to perform the T-T anastomosis? It very unclear how have they done that. How did the authors survey patients in the postoperative period for development of a anastomotic fistula. There is no regular investigation for this purpose in a study that has concentrated on prevention of anastomotic fistula. Were there any patients which had subclinical fistulas? In the only patient reported to have a fistula was there any clinical sign? Did the authors perform regular upper GI contrast studies to evaluate the anastomosis? How was the patient with fistula managed conservatively with enteral nutrition since there was no feeding jejunostomy placed at the end of the operation? The authors state that: *"In our series of patients who are performed by the new technique after oesophagectomy, a lower leakage rate and quick recovery postoperatively were facilitated"* but they do not explain which is their group of reference which had a higher anastomotic insufficiency rate. The three measures the authors describe as innovative approach to the anastomosis are just examples of good surgical practice that should be employed in carefully done surgery. In esophageal cancers, the required margins are in the range of

10 cm due to the very rich submucosal vascular and lymphatic network, 5 cm may sometimes be too little and requires a frozen section.

Answer: Thank you for your conscientious comments for our manuscript to *World Journal of Gastroenterology*. We appreciate your valuable comments and suggestions to improve it. There really does need some explanation. The type of this article is a prospective single-center study. We made this study in order to describe the preliminary results of our new technique in preventing and localizing anastomosis leakage after oesophagectomy. Such type of article was very popular in introducing a new technique, such as the following published article: *Endoscopy*. 2013;45(3):161-6. doi: 0.1055/s-0032-1326203. Epub 2013 Feb 6. In order to further clarify our good results of this technique, we have provided the outcomes of patients who have undergone the conventional anastomotic technique after oesophagectomy as the comparative control arm from previous published articles. Such content have added to the first paragraph of discussion section. In addition a randomized controlled trial for this method is undergoing and the trial registry number is ChiCTR-TRC-13003817 in the Chinese Clinical Trial Registry. In many published articles (Haverkamp L, *Ann Surg*. 2014 Jan ; Bhat MA, *Ann Thorac Surg*. 2006; Zheng QF, *Eur J Cardiothorac Surg*. 2013) the diameter of the gastric tube performed was described as 3cm and we performed it as so. I'm sorry for our false description that "The esophagogastric anastomoses was performed in an end-to-end fashion". In fact, the esophagogastric anastomosis

was performed end-to-side on the anterior wall of stomach after closure of resection line of the stomach. We have corrected it in the method section. We have further clarified the postoperative follow-up in the method section. Both kinds of diagnostic methods (i.e., clinical findings and radiological diagnosis) were all applied. Clinical findings were used for the patients with obvious leaks that were easily judged. Radiological diagnosis was used for those who had small leaks that were difficult to find with the naked eye. That is correct, at the end of the operation a nasogastric tube was inserted into the duodenum under the assistance of the endoscope. The main clinical symptom in the only patient reported to have a fistula was as follows: fever up to 38.7°C and sudden chest pain. The patient with fistula managed conservatively with enteral nutrition through a nose-jejunum nutrition tube which doesn't need feeding jejunostomy. The proximal and distal margin were more than 5 cm after oesophagectomy and a frozen section was also performed for the residual proximal and distal margin.

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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