

## ANSWERING REVIEWERS



July 9, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: \_\_.doc).

**Title:** Submucosal tunneling and endoscopic resection of submucosal tumors at the esophagogastric junction

**Author:** De-Jun Zhou, Zhen-Bo Dai, Malcolm M. Wells, Dan-Lei Yu, Jing Zhang, Lei Zhang

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 11357

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 No.1

(1) In Abstract the author mentioned 'RESULTS:..... Full-thickness MP resection was performed in 9 of 21 patients (42.9%). Mediastinal and subcutaneous emphysema was observed in all 21 patients. At the time of the initial procedure, all patients received closure of the incision with hemoclips. One patient required subcutaneous puncture. The remaining 20 patients required no further endoscopic or surgical intervention.' However, in the RESULTS of the text, the authors described 'Full-thickness MP resection was performed in 9 of 21 patients (42.9%), with mediastinal and subcutaneous emphysema occurring in all nine. Eight of nine patients had successful closure with hemoclips and required no further treatment. One patient required subcutaneous puncture.' It really makes me confused and a table with details may help a lot.

Reply:

Owing to the differences between Chinese and English expressions, the translator encounters misunderstanding.

(2) I think the author should mention the background of these patients. Are these patients consecutive in your series? Are there any selection biases for Submucosal tunneling and endoscopic resection?

Reply:

According to your suggestion, supplementary table has been added to the manuscript, including the conditions of all patients.

Reviewer No.2

(1) I suggest the authors present a table regarding the clinicopathological features of included patients in the manuscript.

Reply:

According to your suggestion, supplementary table has been added to the manuscript, including the conditions of all patients.

(2) As the authors described "SET at the EGJ are often irregular and lobulated". Intriguingly, a very recent study by Sun et al. (J Laparoendosc Adv Surg Tech A, 2013 Jul;23) has demonstrated that tumor irregularity was an independent factor associated with incomplete resection for SET at the EGJ. How about the authors' situation? Please discuss about this point according to the authors' experience as compared to the study of Sun et al.

Reply:

Although conventional Endoscopic Submucosal Excavation (ESE), and Endoscopic full-thickness resection (EFR) are very effective methods for the removal of esophageal or cardiac SETs originating from the MP, they are found to have difficulty in closing the mucosal incision site and preventing leakage of the GI contents, owing to larger mucosal defects and irregular incision. In contrast, there is a certain distance between incision site and tumor after STER, with regular incision, which contributes to the closure of mucosa. It's concluded that mucosa has a closure easier after STER, preventing leakage of the GI contents effectively and resection could be performed completely by both ESD and STER.

(3) Nine patients experienced full-thickness resection, so were there any other peri-operative complications except for emphysema, such as fever, mediastinal infection or dyspnea? Did these patients undergo prolonged hospitalization? In addition, the authors have selected full-thickness for these patients. What was the circumstance, the tumor size was too large? With wide base? Or presented with tight connection to serosa?

Reply:

Mediastinal effusions were found in one patient, with obvious fever occurring. After treated with anti-inflammatory therapy as well as percutaneous drainage, the patient was discharged 7 days later with normal temperature. The reasons why we select full-thickness for these patients are as follows. First, when it comes to endoscopic full-thickness resection (EFR), there is a close relationship between submucosal tumors and deep longitudinal muscle during stripping process, which makes it difficult to remove tumors. Second, the wider base also limits the application of conventional Endoscopic Submucosal Excavation (ESE), and Endoscopic full-thickness resection (EFR).

(4) The follow-up period was relatively short in current study. It is difficult to draw a definite conclusion with respect to oncological feasibility, the authors are supposed to discuss about this limitation.

Reply:

Nowadays, considering that STER has not been widely applied to submucous tumor resection, long term effects of excision still require further clinical observation. Especially for invasive GIST, large quantities of long-term observation are still in need to study the possibility of tumor deposit. What's more, due to the limits of the development level of STER technique, it's difficult to deal with some problems, such as the pollution control in tunnel.

(5) The authors described "Moreover, SETs at the esophagogastric junction originating from the MP layer always grow annularly." Can the authors provide relevant references?

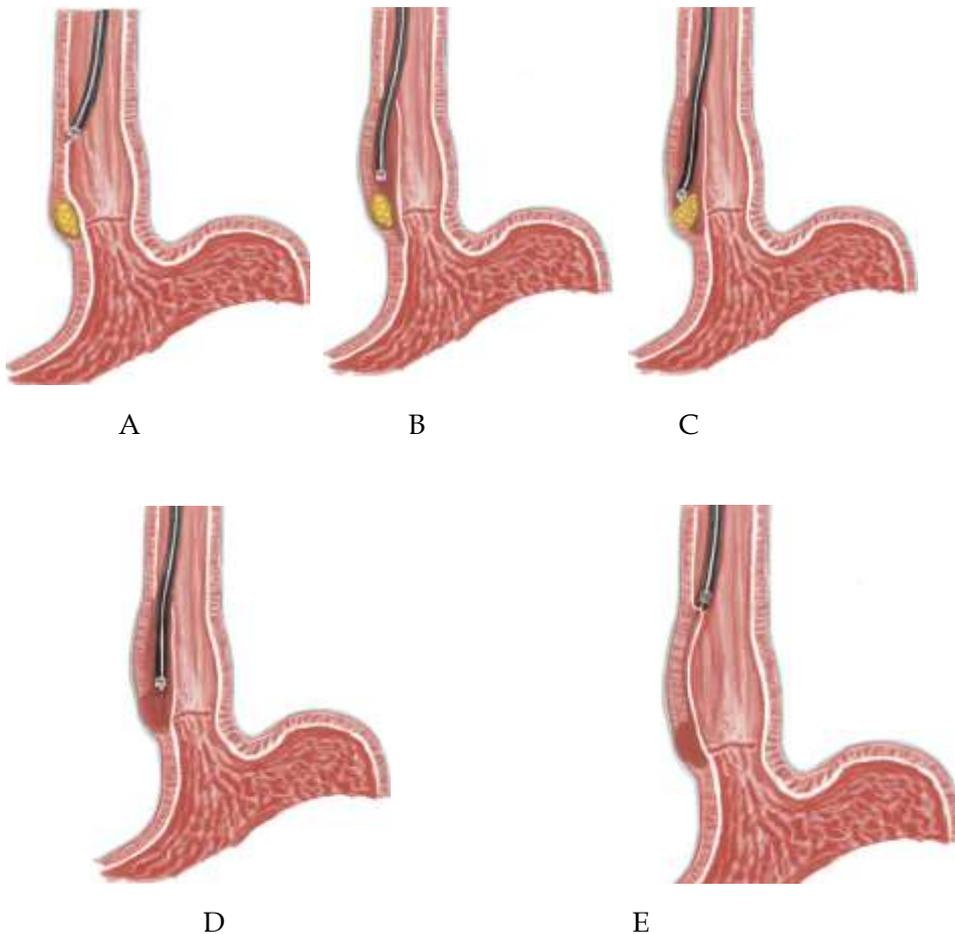
Reply:

On the basis of the extensive literature, references about morphological characteristics of SET at the EGJ are not available. However, clinical observation shows that of subepithelial tumors originating from the muscularis propria layer, the shape is often irregular and lobulated and they always grow annularly. To express it in English more accurately, changes have been made in the manuscript.

Reviewer No.3

(1) In the session on STER Procedure: the authors explained STEP procedure using endoscopic imaging. However, this figure is difficult to understand. Please show the schema for STEP Procedure in detail.

Reply:



A Mucosal incision

B Submucosal tunnel

C Endoscopic resection

D The lesion was completely resected and removed

E The mucosal incision site was closed with hemoclips

The figure comes from Xu M D, Cai M Y, Zhou P H, et al. Submucosal tunneling endoscopic resection: a new technique for treating upper GI submucosal tumors originating from the muscularis propria layer (with videos)[J]. *Gastrointest Endosc*,2012,75(1):195~199.

(2) In the session on Results: the authors mentioned, "One patient required subcutaneous puncture". The authors should show postoperative for this patient.

Reply:

After treated with anti-inflammatory therapy as well as percutaneous drainage, the patient was discharged 7 days later with normal temperature.

(3) If the patients after STER have stenosis in ECJ, how do the authors deal with stenosis? The authors should show the answer in the discussion part.

Reply:

When SETs originating from the muscularis propria layer are successfully removed, part of muscularis propria layer is resected at the same time without harming mucosa at the lesion, which prevents post-procedure stricture in theory. During the follow-up period, no patients were found to have post-procedure stricture.

(4) In the session on discussion, the authors should discuss the limitation for STER.

Reply:

The shortcomings and limitations of STER are as follows. First, the STER procedure aims to maintain the integrity of the digestive tract mucosa. The STER procedure will make no sense, when damaging the mucosa in submucosal tunnel. Second, when it comes to large tumors, they have to be divided into pieces before resection, making it difficult to perform STER.

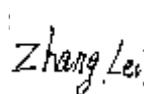
(5) In the session on Innovations and breakthroughs: the authors mentioned, "This new endoscopic technique has advantages over endoscopic submucosal dissection (ESD) in terms of maintaining the integrity of the digestive tract mucosa and submucosa, promoting rapid wound healing, and reducing the risk of pleural/abdominal infection". Is ESD useful for resection of submucosal tumors?

Reply:

In terms of submucosal tumors originating from the muscularis propria layer at the esophagogastric junction, tumors can be smoothly removed by STER. However, ESD is found to have difficulty in closing the mucosal incision site and preventing leakage of the GI contents, owing to larger mucosal defects and irregular incision. In contrast, there is a certain distance between incision site and tumor after STER, with regular incision, which contributes to the closure of mucosa. It's concluded that mucosa has a closure easier after STER, preventing leakage of the GI contents effectively and resection could be performed completely by both ESD and STER.

3 References and typesetting were corrected

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

Yours,  


Lei Zhang, MD  
Tianjin Medical University Cancer Institute and Hospital  
National Clinical Research Center for Cancer  
Key Laboratory of Cancer Prevention and Therapy  
Tianjin Lung Cancer Center  
Department of Thoracic Surgery  
Tianjin 300060, China  
Fax: +86-22-23359984  
E-mail: chinaray728@gmail.com