

Round-1

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

**Manuscript NO: 65942**

Title: Effectiveness and safety of over-the-scope clip in closing perforations after duodenal surgery

**Responses for reviewer's comments**

**Reviewer's code: 05301514**

**Comment:**

This study focuses on the usefulness of OTSC in closing duodenal perforations after ESD for duodenal SEL. This paper details endoscopic treatment strategies for duodenal SEL, and coping with perforation using OTSC. This is an instructive and valuable paper for gastroenterologists. The manuscript is well written. I have several comments below:

1. Title: Effectiveness and safety of over-the-scope clip in closing perforations after duodenal surgery

Comment: The term "duodenal surgery" includes various surgeries such as open surgery, laparoscopic surgery and endoscopic surgery. The authors should clarify in the title which type of surgery is the main topic in this study. Please revise the title.

2. Short title: Effectiveness of OTSC in closing duodenum

Comment: "Closing duodenum" should be revised to "closing duodenal perforation" or "duodenal perforation closure" .

3. Abstract - RESULTS

"The rate of complete removal of duodenal SELs and successful closure was 100%."

Comment: “Successful closure” should be revised to “successful perforation closure” .

#### 4. INTRODUCTION

Comment: The authors described the disadvantage of surgery in the second paragraph. In the third paragraph, the authors should describe the advantage of OTSC to clarify why the authors focused on OTSC in this study.

#### 5. MATERIALS AND METHODS – Endoscopic procedures

Comment: Did the authors use Twin Grasper in the OTSC in this study? If the authors used Twin Grasper or any other accessory devices, please list them in the first paragraph. Also, please specify the size and type of OTSC used (e.g. 10 mm t-type). This is important information for readers who are planning to close the perforation using OTSC from now.

#### 6. DISCUSSION

Comment: Please briefly describe the results of this study in the first paragraph.

#### 7. DISCUSSION (the second paragraph)

“Endoscopy and endoscopic ultrasonography are of great value in the diagnosis of duodenal SELs which is sometimes difficult.”

Comment: The meaning of this sentence is unclear. What is "difficult"? Is it difficult to perform? or to learn? or to diagnose? Please clarify. Furthermore, “endoscopic ultrasonography” should be revised to “EUS” because the abbreviation “EUS” was already defined in the MATERIALS AND METHODS section.

### Author's response:

The authors appreciate for the comments from the reviewers and editors. The following are our responses for each question. We uploaded the file of the revised manuscript. Revisions in the text are shown in red for additions, and strikethrough font for deletions. The responses are presented as follows.

1. We have revised the title to “Effectiveness and safety of over-the-scope clip in closing perforations after endoscopic resection of duodenal subepithelial lesions” . The corresponding content has been revised in the manuscript.

- 1 **Name of Journal:** *World Journal of Gastroenterology*↵
- 2 **Manuscript Type:** ORIGINAL ARTICLE↵
- 3 ↵
- 4 **Retrospective Study**↵
- 5 **Effectiveness and safety of over-the-scope clip in closing perforations after**
- 6 ~~duodenal surgery~~ endoscopic resection of duodenal subepithelial lesions↵
- 7 ↵

2. The short title has revised to “ Effectiveness of OTSC in closing duodenal perforation” . The corresponding content has been revised in the manuscript.

- 9 Zhen W *et al.* Effectiveness of OTSC in closing ~~duodenum~~ duodenal perforation↵
- 10 ↵
- 11 Authors:↵
- 12 **Zhen-zhen Wang, Xian-bin Zhou, Yi Wang, Xin-li Mao, Li-ping Ye, Ya-qi**
- 13 **Song, Yue Cai, Shi-wen Xu, ling-ling Yan, Ya-hong Chen and Shao-wei Li\***↵

3. In the sentence “The rate of complete removal of duodenal SELs and successful closure was 100%.” (In Abstract – RESULTS), “Successful closure” has revised to “successful perforation closure” . The corresponding content has been revised in the manuscript.

69 RESULTS↵

70 The rate of complete removal of duodenal SELs and successful perforation  
71 closure was 100%. The median perforation size was 1 cm. No delayed bleeding  
72 or perforation occurred in any of the patients. Seven patients had postoperative  
73 infection, of which one patient developed septic shock and underwent surgery.  
74 All 18 patients recovered and were discharged. The mean postoperative  
75 hospital stay was 9.5 days. No residual or recurrent lesions were detected  
76 during the follow-up period (15-66 months).↵

4. We have added the advantage of OTSC in the third paragraph of INTRODUCTION. The corresponding content has been revised in the manuscript.

119 However, endoscopic resection of duodenal SELs is still regarded as a  
120 challenging procedure with a high risk of perforation. The incidence of  
121 perforations in duodenal ESD has been reported to range from 6.7-36.6%  
122 during the procedure and 0-14.3% during the post-operative period<sup>[1, 4-7]</sup>.  
123 Management of perforations after endoscopic removal of duodenal SELs is a  
124 great challenge. This may be achieved by using over-the-scope clip (OTSCs).  
125 OTSC was developed as an endoscopic full-thickness gastrointestinal closure  
126 device and has become one of the treatment options for gastrointestinal  
127 perforation because it is less invasive compared to conventional surgical  
128 closure. At present, there are few reports on endoscopic resection of duodenal  
129 SELs and endoscopic methods for management of perforations <sup>[1, 2, 8, 9]</sup>. This  
130 study aimed to assess the effectiveness and safety of OTSCs in the treatment of  
131 perforation after endoscopic resection of duodenal SELs. ↵

5. We have added accessory devices and the size and type of OTSC. The corresponding content has been revised in the manuscript.

159 *Endoscopic procedures*<sup>↵</sup>

160 The main equipment and accessories were as follows: a single-accessory  
161 channel endoscope (Q260J; Olympus) with a transparent cap (ND-201-11802;  
162 Olympus) attached to its tip, an argon plasma coagulation unit (APC 300;  
163 ERBE), a high-frequency electronic cutting device (ICC 200; ERBE), a hook knife  
164 (KD-620LR; Olympus), an insulated-tip knife (KD-611L, IT2; Olympus), hot  
165 biopsy forceps (FD-410LR; Olympus), foreign body forceps (FG-B-24, Kangjin,  
166 China), a snare (SD-230U-20; Olympus), a carbon dioxide insufflator  
167 (Olympus), **twin graspers (Ovesco Endoscopy AG, Tuebingen, Germany)**  
168 **OTSC (12/6 t-type, Ovesco Endoscopy AG, Tübingen, Germany),** and titanium  
169 clip (HX-600-135; Olympus and M00522600), **endoloop (Leo Medical Co., Ltd).**<sup>↵</sup>

6. We have briefly described the results of our study in the first paragraph of DISCUSSION. The corresponding content has been revised in the manuscript.

238 **DISCUSSION**<sup>↵</sup>

239 **Currently, endoscopic resection of duodenal SELs is a challenging procedure**  
240 **with a high risk of perforation. The published studies about endoscopic**  
241 **resection of duodenal SELs and endoscopic methods for management of**  
242 **perforations are few<sup>[1,2,8,9]</sup>. In this study, we use OTSC to close the perforations**  
243 **after endoscopic resection of duodenal SELs in 18 patients. The rate of complete**  
244 **removal of duodenal SELs and successful perforation closure was 100%. No**  
245 **delayed bleeding or perforation occurred in any of the patients. Thus, OTSC**  
246 **can effectively close the perforations after endoscopic resection of duodenal**  
247 **SELs by an experienced endoscopist.**<sup>↵</sup>

7. The sentence “Endoscopy and endoscopic ultrasonography are of great value in the diagnosis of duodenal SELs which is sometimes difficult.” has been revised as follows.

255     Though most duodenal SELs such as lipomas, Brunner's adenomas,  
256     heterotopic pancreas, and cysts, are benign, some including neuroendocrine  
257     tumors and GISTs, are potentially malignant<sup>[1-3]</sup>. Endoscopy and ~~endoscopic~~  
258     ~~ultrasonography~~ **EUS** are of great value in the diagnosis of duodenal SELs  
259     ~~which is sometimes difficult.~~ **However, sometimes it is still difficult to diagnose.**  
260     Patients with duodenal SELs can be monitored by endoscopy, especially for

**Reviewer's code: 03317016**

**Comment:**

This is a very interesting article about the possibility of closing of duodenal perforations by using OTSC. Data presented are important and encouraging.

There are some minor revisions:

1. Please present in detail in the Method section the technique of placing the OTSC, especially the steps of side anchoring. Also, offer details on the use of endoloops.
2. Discussion section is too large. the paragraph concerning the use of CO<sub>2</sub> insuflation is too large.
3. Please explain why the use of claw system of OTSC did not represent any problems for delayed perforations in your series.
4. A discussion about long-term outcome and when the OTSC should be removed it be very useful

**Author's response:**

The authors appreciate for the comments from the reviewers and editors. The following are our responses for each question. We uploaded the file of the revised manuscript. Revisions in the text are shown in red for additions, and strikethrough font for deletions. The responses are presented as follows.

1. We have added the procedure of placing the OTSC and endoloops. The corresponding content has been revised in the manuscript.

175 (4) A circumferential excavation was made as deep as the submucosa or  
176 muscularis propria layer around the lesion using an insulated-tip knife; (5) after  
177 the lesion was completely resected, it was removed using a snare or foreign  
178 body forceps, (6) ~~the wound was closed with an OTSC. Several clip and/or~~  
179 ~~endoloops, if needed.~~ **Duodenal** tissues adjacent to the perforation were  
180 **clamped with twin graspers and then drawn into the transparent cap of the**  
181 **OTSC device; then, they were fully inhaled into the transparent cap, and the**  
182 **OTSC closure system was released to close the wound. If defect closure was not**  
183 **complete, several clip and/or endoloops were used to close the remaining**  
184 **portions. When using endoloop, the mucosa defect was closed with several**  
185 **clips in a 'side to center' manner, and an endoloop was placed to trap all clips.**  
186 **Finally, the endoloop was slowly tightened, and all clips were tied together**  
187 **with the endoloop[8].**<sup>←</sup>

2. We have shortened the discussion about the use of CO2 insufflation. The corresponding content has been revised in the manuscript. The corresponding content has been revised in the manuscript.

331 **of delayed perforation.** A carbon dioxide pump is also recommended for  
332 endoscopic treatment, especially when perforation occurs. ~~Compared with air,~~  
333 ~~carbon dioxide is more easily absorbed, which can reduce the incidence of~~  
334 ~~pneumoperitoneum, pneumothorax, and subcutaneous emphysema.~~  
335 Moreover, the use of gastrointestinal decompression after endoscopic closure  
336 of perforation is helpful for the absorption of gas and liquid in the intestinal  
337 cavity; it also reduces tension in the wound, and promotes wound healing.

3. We have added the explanation why the use of claw system of OTSC did not represent any problems for delayed perforations in our study. The corresponding content has been revised in the manuscript.

325 Moreover, the duodenum is exposed to pancreatic juices and bile. Thus,  
326 delayed perforation is more likely to occur after endoscopic resection of  
327 duodenal lesions. Complete closure of the wound facilitates prevention of  
328 delayed perforation<sup>[6, 7, 17]</sup>. **With the strong tightening force and the gap**  
329 **between the teeth of OTSC, OTSC can manage full-thickness duodenal**  
330 **perforations and avoid tissue necrosis, which effectively reduce the occurrence**  
331 **of delayed perforation.** A carbon dioxide pump is also recommended for

4. We have added the discussion about long-term outcome and when the OTSC should be removed. The corresponding content has been revised in the manuscript.

351 resection, if resection is difficult, timely conversion to surgery or combination  
352 with laparoscopy may help to avoid greater harm to patients. ←

353 **For the strong holding strength, OTSC is more difficult to spontaneously**  
354 **detach from the mucosa than normal titanium clips. The OTSC is made of**  
355 **nitinol, which has favorable biocompatibility. Thus, this device is considered**  
356 **as a permanent implanted material for endoscopic treatment. However, OTSC**  
357 **should be removed in cases as follows: (1) poor healing, (2) OTSC misplacement,**  
358 **(3) repeat biopsy/therapy or further treatment, (4) adverse events after OTSC**  
359 **implantation, such as ulcers and stenosis of the digestive tract, (5) removal after**  
360 **recovery, and (6) patient wishes [20]. In our study, there were no such removal**  
361 **indications. During the follow-up period, OTSC detached spontaneously in**  
362 **most cases.** ←

Round-2

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

**Manuscript NO: 65942**

Title: Effectiveness and safety of over-the-scope clip in closing perforations after duodenal surgery

**Responses for reviewer's comments**

**Reviewer's code: 05301514**

**Comment:**

Almost all reviewer comments are properly addressed. However, no changes in the title and short title have been made to the revised manuscript although those titles have been revised in the Answering reviewer file. In the abstract, the first sentence of the RESULTS requires a space between "perforation" and "closure". And on the 4th line, the underline of "underwent" should be removed, and a space is required between "underwent" and "surgery".

**Author's response:**

According to the comment from Science Editor, we have edited manuscript to a professional English language editing company to polish the manuscript further. We have revised these sentences to "The rate of complete removal of duodenal SELs and successful closure of the perforation was 100%" and "Seven patients had postoperative abdominal infections, of which one patient developed an abscess in the right iliac fossa, another patient developed septic shock.". The corresponding contents have been revised in the latest version manuscript.

## before

### RESULTS

The rate of complete removal of duodenal SELs and successful perforation closure was 100%. The median perforation size was 1 cm. No delayed bleeding or perforation occurred in any of the patients. Seven patients had postoperative infection, of which one patient developed septic shock and underwent surgery. All 18 patients recovered and were discharged. The mean postoperative hospital stay was 9.5 days. No residual or recurrent lesions were detected during the follow-up period (15-66 mo).

## after

### RESULTS

The rate of complete removal of duodenal SELs and successful closure of the perforation was 100%. The median perforation size was 1 cm in diameter. Seventeen patients had minor intraoperative bleeding, while the remaining one patient had considerable amount of bleeding during the procedure. Seven patients had postoperative abdominal infections, of which one patient developed an abscess in the right iliac fossa, another patient developed septic shock. All 18 patients recovered and were discharged. No delayed bleeding or perforation were reported. The mean time taken to resume normal diet after the procedure was 6.5 days. The mean postoperative hospital stay was 9.5 days. No residual or recurrent lesions were detected during the follow-up period (15-66 months).