Do we need to conduct full-thickness closure after endoscopic full-thickness resection of gastric submucosal tumors?

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ABSTRACT

Background/Aims: *Successful closure of gastric wall defects is a pivotal step for endoscopic full-thickness resection (EFTR). Our study indicates that for submucosal tumors (SMTs) smaller than 2.5 cm, closing the mucosal layer is safe and feasible when the modified method, ZIP, is used.*

Materials and Methods: *We retrospectively analyzed 37 patients with gastric SMTs arising from the muscularis propria (MP) who underwent EFTR with defect closure of the mucosal layer. The main procedure involved: (1) making a longitudinal incision of the mucosal and submucosal layers above the lesion, (2) fully exposing the lesion and symmetrically punching holes on both sides of the incision into the submucosal layer, (3) en bloc resection of the lesion using an electrosurgical snare or knife, (4) hooking of metallic clips into the holes and clipping of the mucosal layer successively to close the gastric wall defect. This modified method was named ZIP.*

Results: *Successful complete resection by EFTR was achieved in 37 cases (100%). The median procedure time was 60 min (range: 30-120 min), whereas the closure procedure took a median of 8 min (range: 5-20 min). The median lesion size was 1.0 cm (range: 0.5-2.5 cm). No patients had severe complications. No residual lesions or tumor recurrence were found during the follow-up period.*

Conclusion: *Closing the mucosal layer of gastric wall defects after EFTR by ZIP is feasible and effective.*

Keywords: *Endoscopic full-thickness resection, gastric submucosal tumors, gastric perforation, esophagogastroduodenoscopy*

INTRODUCTION

With the application of endoscopic ultrasonography (EUS) and new endoscopic techniques, the detection rate of submucosal tumors (SMTs) has significantly increased (1). Endoscopic full-thickness resection (EFTR) provides a definitive diagnosis and potentially curative treatment of lesions involving any layer of the gastrointestinal (GI) wall (2, 3). A key step in the success of EFTR without the help of laparoscopy is whether it can successfully repair the wound defect after resection; thus, avoiding serious complications, such as peritonitis and pneumoperitoneum. Several methods and devices have been invented to close gastric wall defects, including purse string suture, suturing devices such as Apollo OverStitch, and over-the-scope clips (OTSCs) (4-8). However, most technologies choose to clamp the full layer of the stomach wall, after which the metallic clips may not fall off spontaneously (4, 5) and require complex or special instruments and complicated operations. Our method uses only a single-clamp endoscope and metallic clips, which are inserted into the submucosal layer by punching grooves on both sides of the incision. The mucous layer is closed sequentially like a garment zipper; thus, we named this modified method "ZIP." The advantages of our method include its simplicity and low cost and the fact that the metallic clip falls off easily after the operation. The purpose of this study is to evaluate the efficacy and safety of this method.

MATERIALS AND METHODS

Patients and Preoperative Preparation

In this study, we retrospectively analyzed 37 patients with gastric SMTs between August 2017 and December 2018. The inclusion criteria for this study were as follows: (1) The patients' age ranged from 18 to 75 years; (2) The lesion was located in the stomach and confirmed to originate from the muscularis propria (MP), which was assessed by EUS; (3) The tumor size was measured to be less than 2.5 cm; (4) The tumor had no malignant features (ulceration, rich vasculature, irregular borders, heterogeneity, or enlargement of regional lymph nodes) by EUS. The exclusion criteria were: (1) Patients with serious comorbidities diseases,

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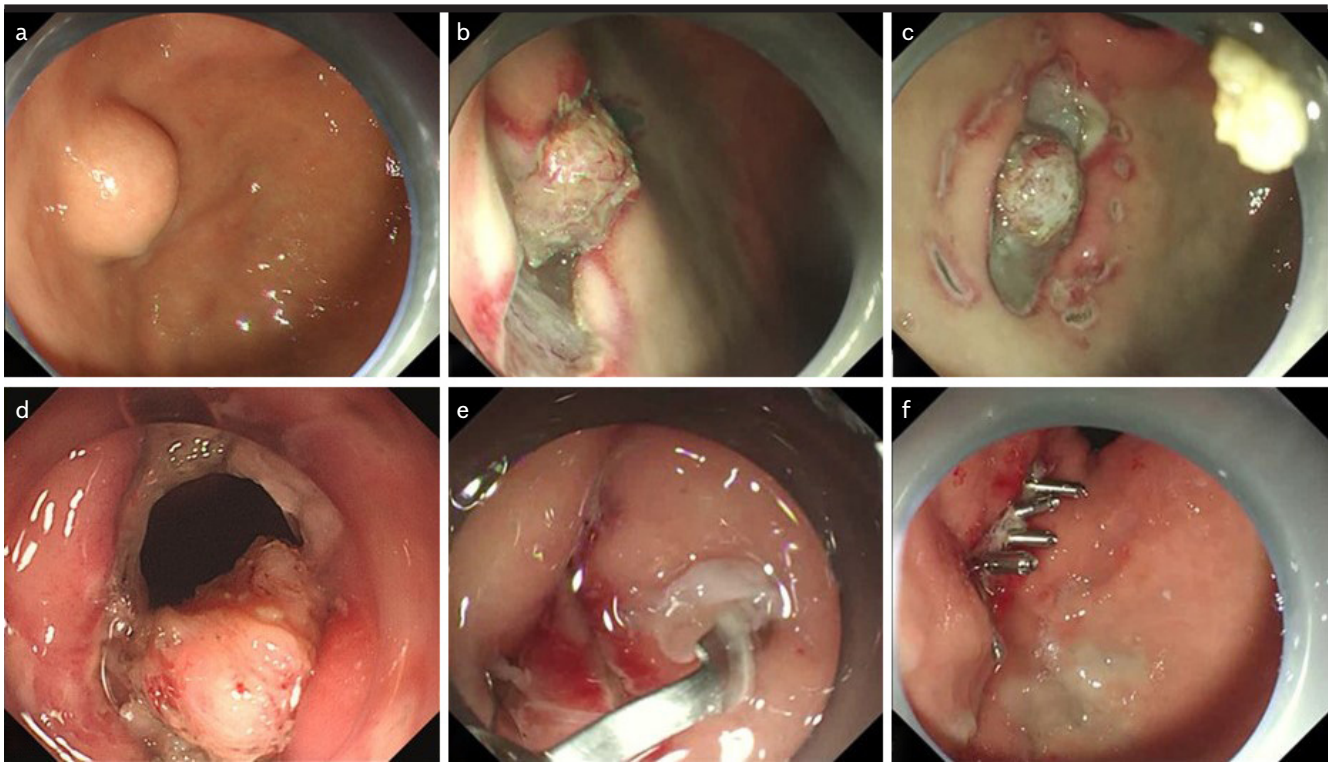

Figure 1. a-f. EFTR and defect closure of an SMT. (a) An SMT was located in the gastric fundus. (b) A longitudinal incision was made above the lesion, and the lesion was fully exposed. (c) Holes were punched on both sides of the incision into the submucosal layer. (d) En bloc resection of the lesion and visible perforation. (e) Metallic clips were hooked into the holes, and the mucosal layer was clipped. (f) The defect was closed with 5 metallic clips.

such as advanced malignant tumor or organ failure and (2) Patient could not tolerant general anesthesia with tracheal intubation. All operations were performed by the same operator in the same endoscopy center. Informed consent forms were signed before the operation, including secondary infection, intraoperative or postoperative bleeding, postoperative gastrointestinal tract leakage, and possible secondary surgery. The study was approved by the ethics committee of Zhejiang Cancer Hopital.

Endoscopic Equipment and Accessories

The following equipment and accessories were used: single-channel gastroscope (GIF-H260J; Olympus, Tokyo, Japan), high-frequency generator electronic cutting device (VIO 200D; ERBE, Tübingen, Germany), transparent cap (D-201-11802; Olympus, Tokyo, Japan), dual knife (KD-650L; Olympus, Tokyo, Japan), hook knife (KD-620LR; Olympus, Tokyo, Japan), injection needles (0910518211; MTW Endoscopie Manufaktur, Büderich, Germany), snares (SD-T-2423-15; KANGJIN, Changzhou, China), hot biopsy forceps (FD-410LR; Olympus, Tokyo, Japan), metallic clips (AG-5106-1950-135-9; AGS MedTech, Hangzhou, China), and carbon dioxide insufflator (CR4500; AGS MedTech, Hangzhou, China).

Procedures and Follow-up

Before the procedure, Iodophor diluent was used to wash the stomach. The EFTR technique and the endoscopic closure of the wall defect are shown in Figures 1-3. The major procedure was as follows: (1) The mucosal and submucosal layers were precut longitudinally above the lesion. The length of the incision was approximately 3 times that of the tumor, (2) The tumor was exposed by the tension of the gastric mucosa. Symmetrical punching to the submucosal layer was performed using a dual knife on both sides of the

MAIN POINTS

- *Closing the mucosal layer for gastric wall defects after EFTR is feasible in patients with SMTs less than 2.5 cm using method ZIP.*
- *ZIP does not require specialized or complex equipment when performing EFTR.*
- *The metallic clips are easy to fall off and the retained mucosa may benefit wound repair after operation.*

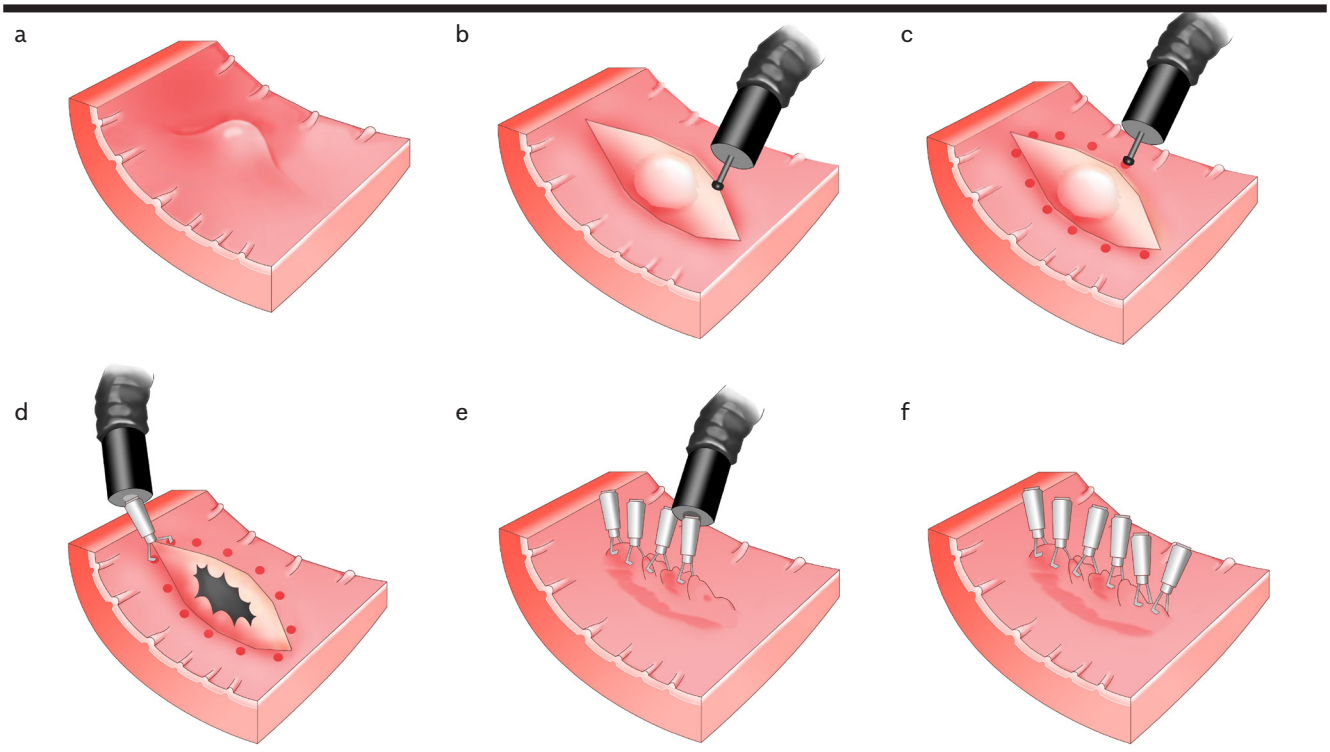

Figure 2. a-f. Schematic of an endoscopic closure technique, ZIP, for EFTR defects by punching holes and clipping the mucosal layer. (a) and (b) A longitudinal incision of the mucosal and submucosal layers is made above the lesion. (c) Holes are symmetrically punched on both sides of the incision into the submucosal layer after complete exposure of the lesion. (d) and (e) The metallic clips are hooked into the holes, and the mucosal layer is clipped in the proper sequence. (f) The gastric defect is closed with metallic clips.

linear incision, (3) En bloc resection of the lesion was performed as previously described (3, 9), and (4) The metallic clip was placed in the symmetrical grooves on both sides by dragging the mucosal layer and eventually clutching the incision. Three to six metallic clips were clamped sequentially according to the length of the incision. In addition, endoscopic carbon dioxide insufflation was used during the operation. Sufficient expansion of the stomach confirmed successful defect closure post operation.

Any adverse events during the procedure were recorded. Surveillance endoscopy was performed at 3, 6, and 12 months after the procedure and then annually thereafter.

RESULTS

A total of 39 patients (12 men and 25 women) successfully underwent EFTR. Mean age of the patients was 55.4 years (range: 34-71 years). The en bloc resection rate was 100%, and the median size of the lesions was 1.0 cm (range: 0.5-2.5 cm). The gastric wall defects were closed to the mucosal layer by ZIP (success rate: 100%). The median operation time was 60 min (30-120 min). The median time spent in gastric wall defect closure was 8 min (5-20 min).

The pathological diagnoses were as follows: gastrointestinal stromal tumor (GIST) (30/37), leiomyoma (4/37), heterotopic pancreas (2/37), and schwannoma (1/37). Only one patient had localized peritonitis after the procedure and recovered after conservative treatment. No patients required surgical intervention. A few patients had varying degrees of abdominal pain and fever after surgery and recovered with conventional therapy.

All wounds had healed by 3 months after the operation, and all metallic clips fell off spontaneously in patients who were followed up for more than 6 months. The median follow-up period was 12 months (range: 6-22 months), and no residual tumor or recurrence was found in any patient. The characteristics of the patients are shown in Table 1.

DISCUSSION

With the progress of endoscopic technology, endoscopic treatment of submucosal tumors of the digestive tract

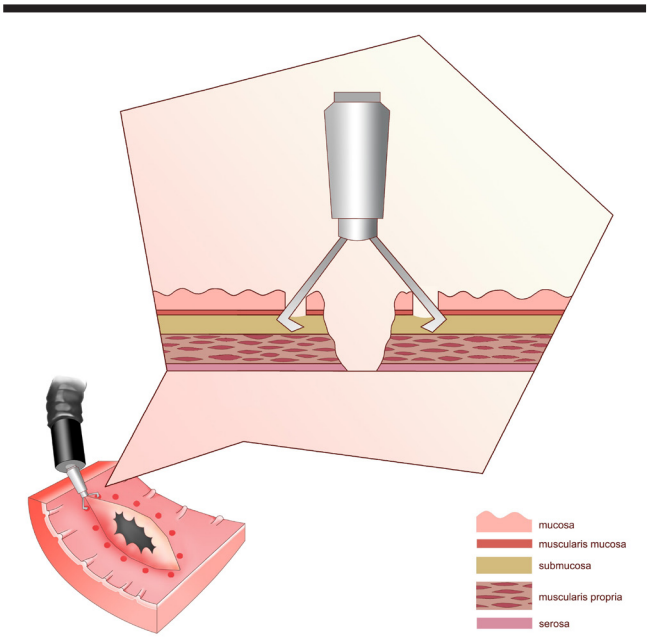

Figure 3. The metallic clip firmly clamped onto the submucosal layer by punching holes into the submucosal layer on both sides of the incision.

is being widely used in clinical practice. Many studies on SMTs originating from the MP have confirmed that EFTR can completely remove the tumor (2, 3, 10). One of the critical steps in EFTR is to completely close the resection defect and avoid laparoscopic intervention. Secure incision closure is of paramount importance. Therefore, exploring a secure, simple, effective, and inexpensive method to close the defect has been a topic of interest in recent years.

Recently, various techniques and devices have been applied to complete the closure of gastric wall defects after EFTR, such as purse string suture (4, 5, 11), Apollo OverStitch (6), new endoscopic suturing or sewing devices (7), T-tags (12), and OTSCs (8). Although the techniques above seem to be reliable, operational difficulties, equipment limitations, and high costs have hindered the promotion of these technologies. In China, Apollo OverStitch is not yet available, and OTSCs are too expensive for patients to afford. We reduce the procedure cost and equipment requirements by using only metal clips to close the defect.

Use of metallic clips to repair perforated stomach walls is a conventional approach and is mainly used for defects smaller than 1 cm (13). For defects larger than 1 cm, it is difficult to operate when the diameter of the defect is larger than the width of the open clip. We were able to close a larger defect with ZIP than with conventional clip suturing because the punching grooves provided a better grip for metallic clips, which then facilitated dragging the retracted mucosa across the defect without slipping. In this study, the maximum size of the lesions was 2.5 cm.

With conventional clip suture or other methods requiring clip assistance, such as purse string suture, metallic clip

Table 1. Clinical characteristics and surgical outcomes of gastric submucosal tumors treated by endoscopic full-thickness resection (EFTR).

Patients, n	37
Age, mean (range), y	55.4 (34-71)
Sex, male/female, n	12/25
Tumor size, median (range), cm	1.0 (0.5-2.5)
Tumor location, n	
· Gastric fundus	22
· Gastric body	13
· Gastric angle	2
Operating time, median (range), min	60 (30-120)
Closure procedure time, median (range), min	8 (5-20)
Postoperative complications, n	
· Abdominal pain	19
· Fever	16
· Delayed bleeding	0
· Delayed perforation	0
· Peritonitis	1
Pathological result, n	
· GIST	30
· Leiomyoma	4
· Heterotopic pancreas	2
· Schwannoma	1
Follow-up period, median (range), m	12 (6-22)
Tumor recurrence during follow-up, n	0
Patient survival, %	100

EFTR: Endoscopic full-thickness resection.

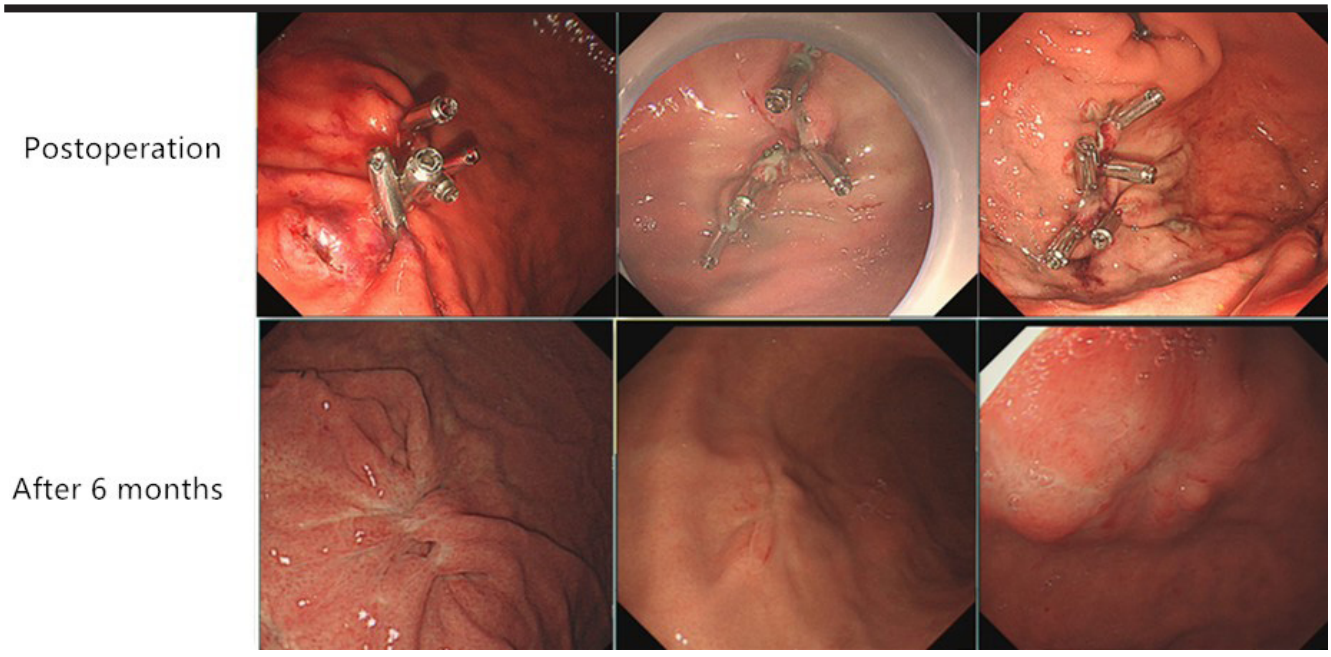

Figure 4. The wound post operation and 6 months later.

clamping at the mucosal layer makes it easy for clips to slip down, and therefore, these methods fail to close the defect tightly; in contrast, clamping at the MP layer may make it difficult for the clips to fall off (4, 5). In our method, the metallic clip was firmly clamped onto the submucosal layer by punching grooves into the submucosal layer on both sides of the incision (shown in Figure. 3). The clamping was firm due to the tenacity of the muscularis mucosae. The gastric wall defects were closed successfully in all 37 patients. There were some minor complications such as abdominal pain and fever. However, these only occurred in the first day after operation. We believe this was a normal postoperative physical response, and only 2 patients had a fever of more than 38.5°C. One patient had localized peritonitis after the procedure. This may be attributed to the relatively long time of operation and the small amount of gastric juice that leaked to the abdominal cavity. This patient recovered within 3 days after conservative treatment. No patients had severe complications or required surgical intervention. No residual tumor or recurrence was found in the follow-up period. It was preliminarily proved that closing the mucosal layer by ZIP is safe and effective for SMTs less than 2.5 cm. Furthermore, in patients who were followed up for more than 6 months, all metallic clips fell off spontaneously (shown in Figure 4).

In addition, ZIP has the following advantages: First, it does not require specialized or complex equipment, and most endoscopy centers are equipped with the required equipment, including single-channel endoscopes, electric knifes, and metallic clips; consequently, ZIP costs less. Second, the procedure is simple and easy to master; therefore, the average time spent closing the gastric wall defects is reduced. Third, the mucosal reserve benefits wound repair after surgery.

Based on our experience, we have some recommendations regarding the procedure. To ensure the integrity of the mucosa as much as possible, the mucosa above the tumor should be cut longitudinally, which is different from the previous trap resection of the mucosa and submucosa above the tumor. The mucosal and submucosal layers should be precut above the lesion, after which submucosal injection is performed before extending the incision to prevent the tumor from sliding too far under the mucosa. The length of the linear incision is approximately 3 times or slightly more than that of the tumor to ensure that the tumor can be fully exposed by the tension of the gastric mucosa. The distance between the punching hole and the incision is approximately 0.5-1 cm. If the distance is too far, it will create operational difficulty. If the distance is too small, there will be a risk of mucosal tearing. It is true that supplying air is difficult when EFTR is performed. In order to reduce the time of defect closure, we usually punch holes after fully exposing the lesion and before en bloc resection of the lesion with active

perforation. When the inflation is insufficient, we usually use the front end of the gastroscope and transparent cap to squeeze out the space for operation. According to our experience, because of the encirclement of the lesser omentum, it is relatively easy to supply air when the lesion is located in the lesser curvature and posterior wall. No matter where the lesion is located, we should make sure that the stomach cavity is filled properly and should not supply too much air. After the operation, we will have an abdominal percussion. If necessary, an injection needle is used to relieve the pneumoperitoneum.

Otake et al. (14) has reported using clips and punching holes to deal with colonic ESD wounds. As the muscular layer of gastric wall is much thicker, there is greater tension in closing gastric ESD wound in this way. In contrast to when gastric EFTR is completed by ZIP, we keep the mucous layer as much as possible, and the muscle layer is missing to make the operation easier to complete

In conclusion, closing the mucosal layer is effective, feasible, and safe for gastric wall defects after EFTR in patients with SMTs less than 2.5 cm. To ensure definite closure of the whole mucosal layer deeper than the muscularis mucosa, the ZIP method, which makes a linear incision and uses metallic clips to clamp into the punching grooves, is required. However, large-scale multicenter prospective studies and long follow-up periods are needed to evaluate the effectiveness of ZIP and to determine whether larger defects can be safely closed by this approach.

Ethics Committee Approval: The study was approved by the ethics committee of Zhejiang Cancer Hopital (Approval Date: 01 August 2018, Approval Number: IRB-[2018]313).

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

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Conflict of Interest: The authors have no conflict of interest to declare.

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