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DYNAMIC MANUSCRIPT

Over-the-scope clip-assisted endoscopic full thickness resection: a video-based case series

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Abstract

Background In the management of mucosal neoplasm and early cancer, therapeutic gastrointestinal endoscopy evolved from simply polypectomy, endoscopic mucosal resection, endoscopic submucosal dissection (ESD), to endoscopic full thickness resection (EFTR). Full thickness clip closure followed by transmural resection mimics surgical principles. It is safe, effective, and technically less demanding compared to other techniques. Over-the-scope clip (OTSC)-assisted EFTR or OTSC-EFTR enables the endoscopists to manage difficult lesions.

Methods We video recorded and report our 1-year single center experience of 12 consecutive EFTR cases since the dedicated OTSC-EFTR device was approved in the USA.

Results We demonstrate that OTSC-EFTR can be very useful to manage residual neoplastic tissue that cannot be removed during conventional mucosal resection due to deeper invasion, submucosal fibrosis, scaring from prior intervention, and appendiceal involvement. Caution should be used for EFTR of the ileocecal valve lesions.

Conclusion We propose that layered or stacked biopsy of the appendiceal stump after EFTR should be performed to rule out a positive residual base. Due to the limited size of the FTRD resection hood (13 mm internal diameter × 23 mm depth), for larger sessile adenomas in the colon, we propose a hybrid approach for complete removal: piecemeal EMR for tumor debulking followed by OTSC-EFTR to achieve R0 resection. We believe OTSC-EFTR offers safety and efficiency with very high success rate.

Keywords Endoscopic mucosal resection · Endoscopic full thickness resection · Over-the-scope clip · Over-the-scope clip-assisted endoscopic full thickness resection · Endoscopy

In the management of mucosal neoplasm and early cancer, therapeutic gastrointestinal endoscopy evolved from simply polypectomy, endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), to endoscopic full thickness resection (EFTR) using tunneling techniques (tunneling-EFTR) or direct resection without closure first [1–8]. Recently, submucosal tunnel endoscopic resection for extraliminal tumors was also reported [8]. During EMR, thermal ablation or excisional biopsy can be utilized to manage residual neoplastic tissue [9]. However, this method potentially leave residual tissue and deeper tissue involvement is unknown. For ESD and EMR, limitations and higher risk of complication arise when there is significant submucosal fibrosis due to neoplasm or prior endoscopic inventions such as direct tattooing, biopsy, or partial EMR. When the pathology is peri-appendiceal or peri-diverticular location, involving muscular propria, advanced endoscopic skills and even higher complication risks have to be considered when managing such lesions.

Full thickness clip closure followed by transmural resection mimics surgical stapling resection principles [10–17]. It is safe, effective, technically less demanding compared to other techniques, and is less time consuming. Over-the-scope clip (OTSC)-assisted EFTR or OTSC-EFTR enables the endoscopists to manage difficult lesions such as

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peri-appendiceal or peri-diverticular adenomas, non-lifting neoplasms, scar around the neoplasm, and submucosal lesions involving muscularis propria. We video recorded and report our one-year single center experience of 12 consecutive EFTR cases since the dedicated OTSC-EFTR device was approved in the USA.

Materials and methods

This is a retrospective study at the University of Mississippi Medical Center between May, 2018 and July 2019. Institutional Review Board approval is not required for this review. We video recorded every case of EFTR since we adopted this method in May, 2018 after FTRD® (Full Thickness Resection Device; Ovesco Endoscopy, Tübingen, Germany) became available in the USA. FTRD is a modified OTSC system incorporated with an electrocautery snare [10, 11]. OTSC-EFTR was performed by a single endoscopist (Tang) in a standard endoscopy room. All patients underwent procedures under monitored anesthesia care. A pediatric colonoscope (PCF-Q180, Olympus America, Center Valley, PA) was used for all cases. The patients' characteristics, indications for endoscopy and EFTR, and endoscopic interventions prior to EFTR are listed in Table 1. Table 2 lists EFTR outcomes, complications, pathology, and learning points from each case. Selected images and all case videos are indexed in Table 2 as well. Our first 4 cases were included in a US multicenter retrospective study [18]: cases 2, 3, 4, and 7.

Results

OTSC-EFTR was technically successful in 11 out of 12 patients. In one patient (case 2) with a 20 × 16 mm gastrointestinal stromal tumor (GIST), the tumor could not be pulled into the FTRD plastic hood (13 mm internal diameter × 23 mm depth) due to its size and hard consistency. In all other cases, endoscopic examination showed serosal adipose tissue within the clipped area and full thickness resection was confirmed on pathology in all patients with successful EFTR. The mean size of colon resections was 17.7 × 12.3 mm. R0 resection was achieved in all patients except one with significant intra-appendiceal adenoma growth (case 7). The residual appendiceal adenoma was completely removed during a follow-up endoscopy and R0 resection was confirmed on layered biopsy of the appendiceal stump.

Table 1 Consecutive 12 cases of OTSC-EFTR

Case	Age/Sex	Indication for EFTR	Location	Prior endoscopic invention	Intervention prior to EFTR during the same session
1	73/M	20–30 mm adenoma, non-lifting due to prior tattoo	Mid gastric body	Direct tattoo, partial EMR	–
2	54/W	20 × 16 mm GIST, needing full thickness resection	Distal gastric body	–	–
3	67/M	12 × 12 mm bleeding submucosal vascular lesion	Duodenum	–	–
4	57/M	6 × 6 mm submucosal nodule, recurrent or residual gastrinoma	Duodenum	Surgical resection	–
5	56/W	40 mm ileocecal valve adenoma, residual polypoid tissue after EMR	Ileocecal valve	Partial EMR	Partial EMR
6	64/W	25 mm peri-appendiceal adenoma with intra-appendiceal growth	Appendix	–	EMR to remove the peri-appendiceal adenoma
7	75/W	25 mm peri-appendiceal adenoma with intra-appendiceal growth	Appendix	Partial EMR	–
8	78/M	30 mm malignant polyp with invasive cancer 8 mm residual cancer	Hepatic flexure	–	Partial EMR
9	75/M	22 mm adenoma with prior tattoo inside, residual polypoid tissue after EMR	Mid transverse colon	Tattoo	Partial EMR
10	69/M	25 mm adenoma with a residual 8 mm adenoma after EMR	Distal transverse colon	–	Partial EMR
11	70/M	30 mm malignant polyp with only 1 mm negative margin on pathology	Splenic flexure	EMR	–
12	59/M	Prior EMR scar and residual adenoma	Ascending colon	EMR	

M man, *W* woman, *EMR* endoscopic mucosal resection, *GIST* gastrointestinal stromal tumor

Table 2 OTSC-EFTR outcomes, pathology, and learning points

Case	Immediate outcomes	30 days Complications	Resection size & pathology (mm)	Full thickness specimen	Learning points	Images and videos
1	Successful resection	None	15 × 10 × 10 Adenoma, negative lateral and deep margins	Yes	Management of non-lifting mucosal neoplasm	Video 1, Fig. 1
2	Incomplete resection due to the hard consistence of the tumor and limited inner diameter of the EFTR hook (18 mm)	None	GIST, partial resection	No	If the tumor is hard and close to 2 cm in size, it cannot be retracted into the hook	Video 2, Fig. 2
3	Successful resection	Bleeding from the resection, treated endoscopically	15 × 10 × 7, lipoma	Yes	Risk of GI bleeding in duodenum, improved EFTR clip design since	Video 3
4	Successful resection	None	15 × 11 × 6, 6.5 gastrinoma	Yes	EUS localization of submucosal lesion	Video 4, Fig. 3
5	Successful resection	Small bowel obstruction or post-resection ileus	20 × 11 × 7 and 15 × 11 × 6, Foci of adenoma	Yes	Risk of small bowel obstruction or post-resection ileus after valve resection	Video 5, Figs. 4 and 5
6	Successful resection	None	19 × 16 × 12, adenoma, negative margins	Yes	Appendiceal adenoma resection, resection base layered biopsy to rule out a residual	Video 6
7	Successful resection	None	20 × 13 × 5, adenoma	Yes	Layered biopsy to rule out a residual	Video 7, Figs. 6 and 7
8	Successful resection	None	21 × 12 × 7, T2 cancer invasion to the muscularis propria, 3 mm negative margin on the serosal side	Yes	Patient referred back to surgery for potential nodal metastasis	Video 8, Figs. 8 and 9
9	Successful resection	None	19 × 8 × 2, focal HGD	Yes	Residual adenoma resection	Video 9
10	Successful resection	None	15 × 12 × 10, residual adenoma	Yes	Residual adenoma resection	Video 10
11	Successful resection	None	15 × 18 × 8, normal EMR scar	Yes	Malignant polyp management	Video 11
12	Successful resection	None	15 × 10 × 10, Scar and Indian ink	Yes	Prior EMR scar and residual adenoma management	Video 12

HGD high-grade dysplasia, *EMR* endoscopic mucosal resection

No patient developed perforation. Only one patient (case 3) developed delayed bleeding from the resection base in the duodenum on the medial wall. The bleeding was managed with conventional thermal coagulation of the base during repeat endoscopy. The bleeding is due to the rich vascular supply within the duodenum at this location and using an older generation of the FTRD device. Since then, the company has come out with a revised clipping device with narrowed space between the clip teeth. One patient (case 5) had a 40 mm adenoma involving the ileocecal valve and she had prior partial EMR. After adenoma and partial valve resection by using two FTRD devices, the valve opening became significantly narrowed. This patient developed small bowel obstruction or post-resection ileus. She did not develop peritoneal free air or leucocytosis. After admission, small bowel obstruction or post-resection ileus resolved a few days later without surgery or endoscopic removal of the clipping devices.

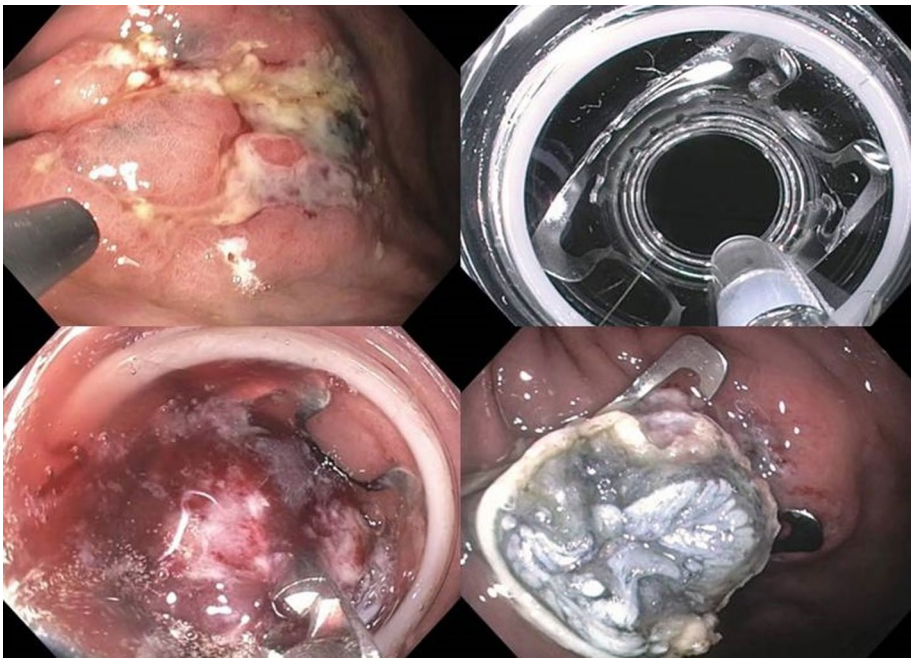

Fig. 1 Endoscopic images of case 1: a 20–30 mm gastric adenoma, non-lifting due to prior direct tattooing. This lesion was completely removed with OTSC-EFTR. The resection base shows serosal adipose tissue that is stained with Indian ink

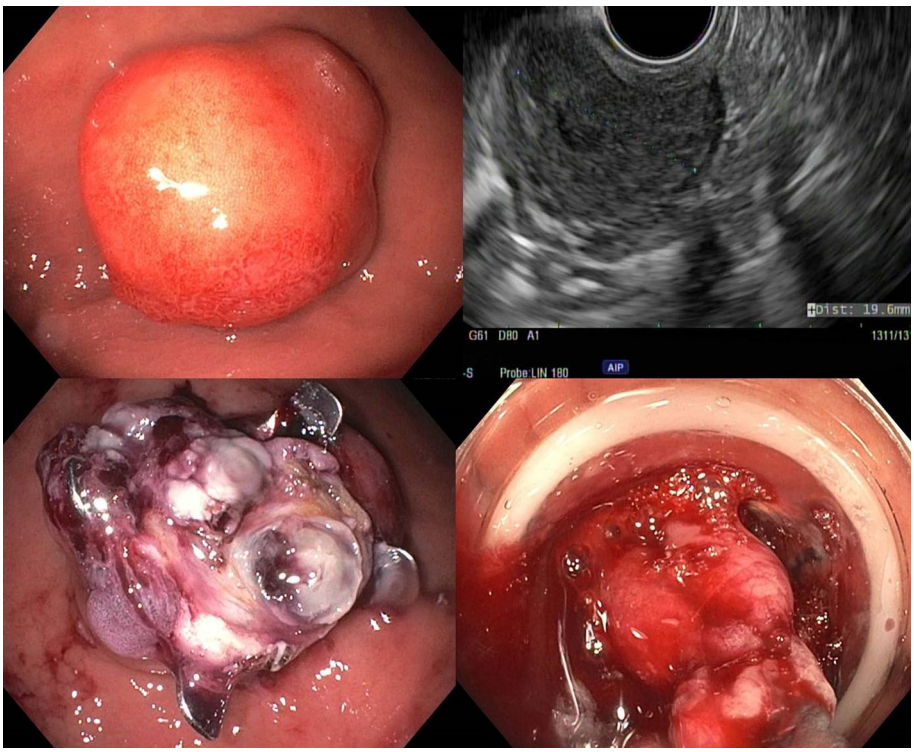

Fig. 2 Endoscopic images of case 2: a 20 × 16 mm GIST. This lesion could not be pulled into the FTRD plastic hood (13 mm) due to its size and hard consistency

Discussion

In the literature, reported indications for OTSC-EFTR include untreated, recurrent or incompletely resected adenoma with non-lifting sign, adenoma involving the appendix or diverticulum, diagnostic re-resection after incomplete resection of a T1 carcinoma, submucosal tumor, and diagnostic full thickness resection in patients with motility disorders such as Hirschsprung's disease [11–17]. In a porcine study, the average diameter of the tissue resected with the OTSC-EFTR was 31–54 mm and the serosa had primarily healed in all cases after 28 days [10]. In clinical cases, the reported en bloc resection rate was

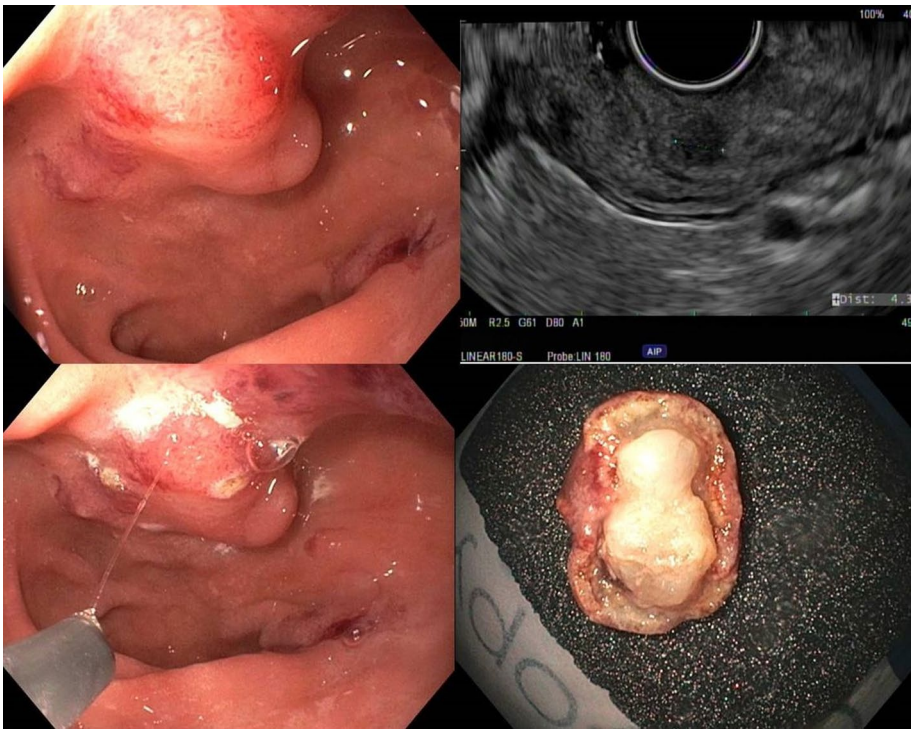

Fig. 3 Endoscopic images of case 4: a 6 × 6 mm submucosal nodule on endoscopic ultrasound and it was a recurrent or residual gastrinoma

83.3% and the mean diameter of the resection specimen was 24 mm (range 12–40 mm). The R0 resection rate was 75–87%. In a European multicenter study, OTSC-EFTR was technically successful in 89.5% cases, and R0 resection rate was 76.9%, and cases had deep submucosal infiltration > 1000 μm [12]. R0 resection rate was higher with lesions ≤ 2 cm vs. > 2 cm (81.2% vs. 58.1%, $P = 0.0038$). Adverse event rate was 9.9% with a 2.2% rate of emergency surgery. In another recent report of 156 patients underwent OTSC-EFTR with histologic evidence of colon adenocarcinoma, the technical success rate was 92.3%, and R0 resection rate was 71.8% [17]. Severe procedure-related adverse events were recorded in 3.9% of patients.

In our series, two patients had appendiceal adenoma that were successfully removed by using OTSC-EFTR method. We propose that layered or stacked biopsy of the appendiceal stump after EFTR should be performed to rule out a positive residual base. In one of these two patients, the stump was positive on layered biopsy for adenoma which was successfully removed during follow-up endoscopy and confirmed by layered biopsy of the base. Due to the limited size of the FTRD resection hood, for larger sessile adenomas in the colon, we propose a hybrid approach for complete removal: piecemeal EMR for neoplasm debulking follow by OTSC-EFTR to achieve R0 resection. As we demonstrated in this series, OTSC-EFTR can close and resects the entire colon EMR base even the lesion was larger than 20–30 mm in size. OTSC-EFTR mimics surgical principles. It is safer, utilizes less time, and technically and skill-wise less demanding compared to ESD and tunneling-EFTR. The learning curve of OTSC-EFTR is short. Most therapeutic endoscopists can master this technique after a one-day training course. We demonstrate that OTSC-EFTR can be very useful to manage residual neoplastic tissue that cannot be removed during conventional mucosal resection or submucosal dissection due to deeper invasion, submucosal fibrosis, and appendiceal involvement. We believe OTSC-EFTR offers safety and efficiency with very high success rate.

In our opinion, the limitations of OTSC-EFTR include: (1) patients with luminal narrowing or anastomotic stenosis downstream to the target lesion that make advancement of the device loaded endoscope very difficult, risky, or not possible; (2) Large bulky lesions without preceding debulking mucosal resection. Large tumors may not be pulled into the FTRD plastic hood (13 mm internal diameter × 23 mm depth) due to its size and hard consistency; The upper limit of the resectable size by EFTR is also important. If this technique is applied to T1 carcinoma and en bloc resection is not achieved without careful inspection and diagnosis before treatment, it might leads to another problem such as recurrence or incorrect pathological diagnosis. Although in a porcine study, the average diameter of the tissue resected with the OTSC-EFTR was 31–54 mm, there was no neoplastic pathology [10]. In this series, OTSC-EFTR can close and resects the entire colon EMR base even the lesion was larger than 20–30 mm in size. We propose that after diligent EMR and careful examination of the base, if the residual lesion is less than 20 mm at only one location and the surrounding

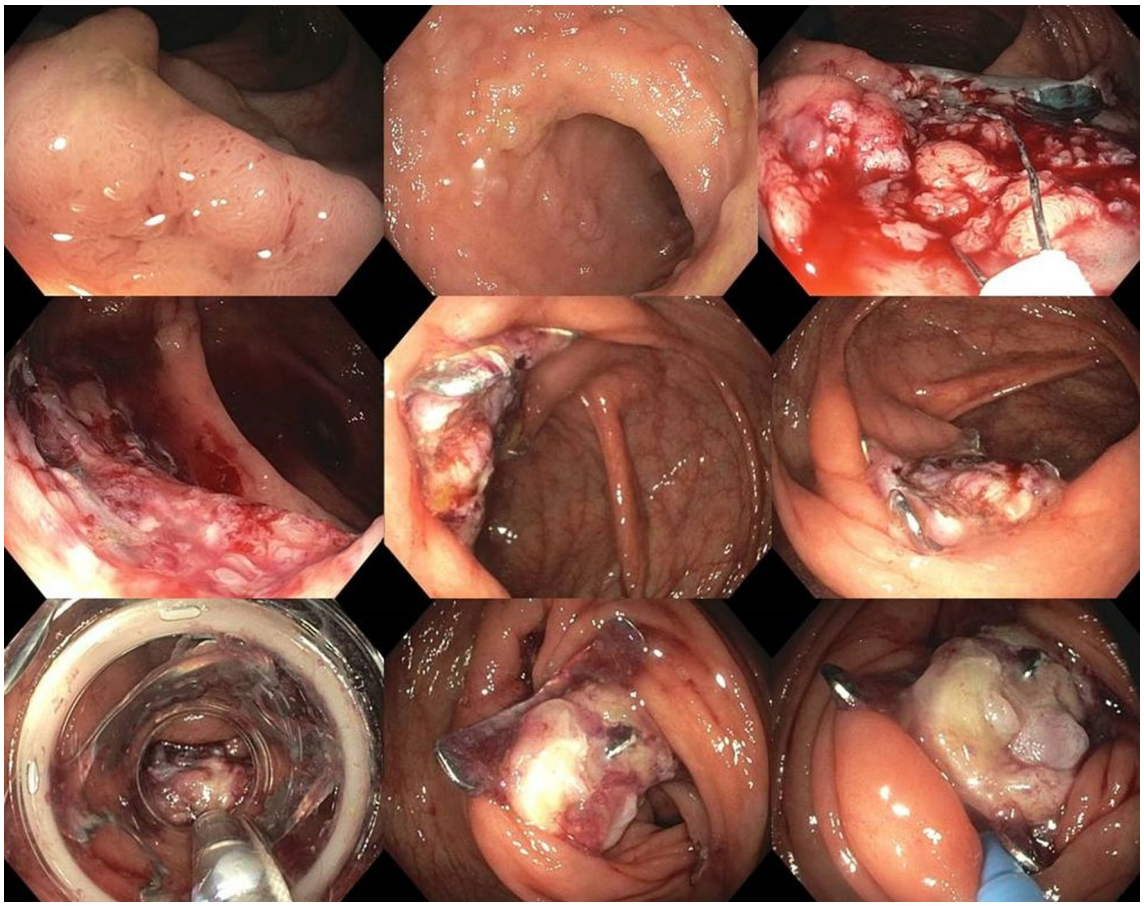

Fig. 4 Endoscopic images of case 5: a 40 mm ileocecal valve adenoma without terminal ileum involvement. There was residual polypoid tissue after EMR. After adenoma and partial valve resection by using two FTRD devices, the valvular opening became narrowed. This patient developed small bowel obstruction or post-resection ileus. She did not develop peritoneal free air or leucocytosis. After admission, small bowel obstruction or post-resection ileus resolved without surgery or endoscopic removal of the clipping devices

Fig. 5 Endoscopic images of case 5: this patient developed small bowel obstruction or post-resection ileus (left image). She did not develop peritoneal free air or leucocytosis. After admission, small bowel obstruction or post-resection ileus resolved (right image) without surgery or endoscopic removal of the clipping devices

areas demonstrate a clear submucosal plane, OTSC-EFTR can be performed. If there are multifocal residual neoplasm spanning greater than 20 mm, EFTR en bloc resection may not be achieved. (3) Target lesions involving the ileocecal valve. Extreme cautions should be used for EFTR of the ileocecal valve. We need to consider the possibility of small bowel obstruction or ileus due to post polypectomy syndrome [11]

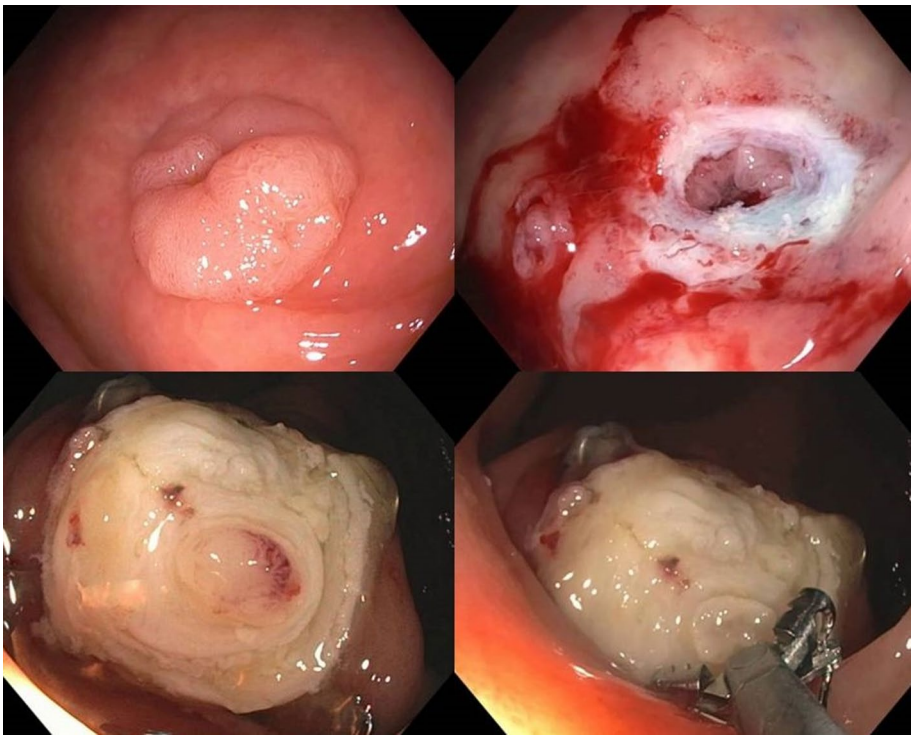

Fig. 6 Endoscopic images of case 7: significant intra-appendiceal adenoma growth. OTSC-EFTR did not achieve R0 resection. Residual adenoma was seen on layered appendiceal stump biopsy

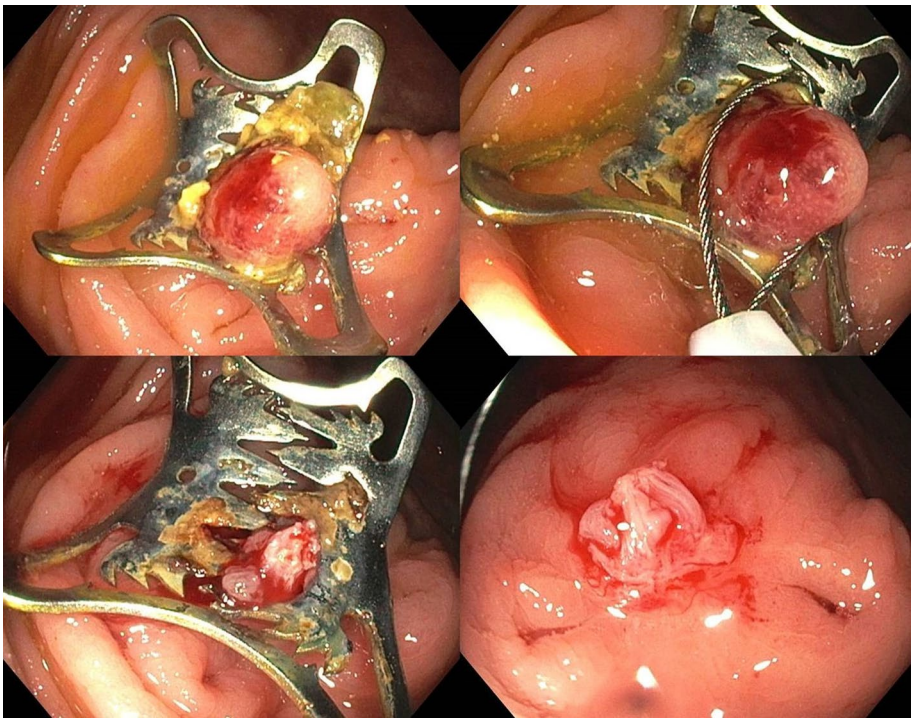

Fig. 7 Endoscopic images of case 7: The residual appendiceal adenoma was completely removed during a follow-up endoscopy and R0 resection was confirmed on layered biopsy of the appendiceal stump

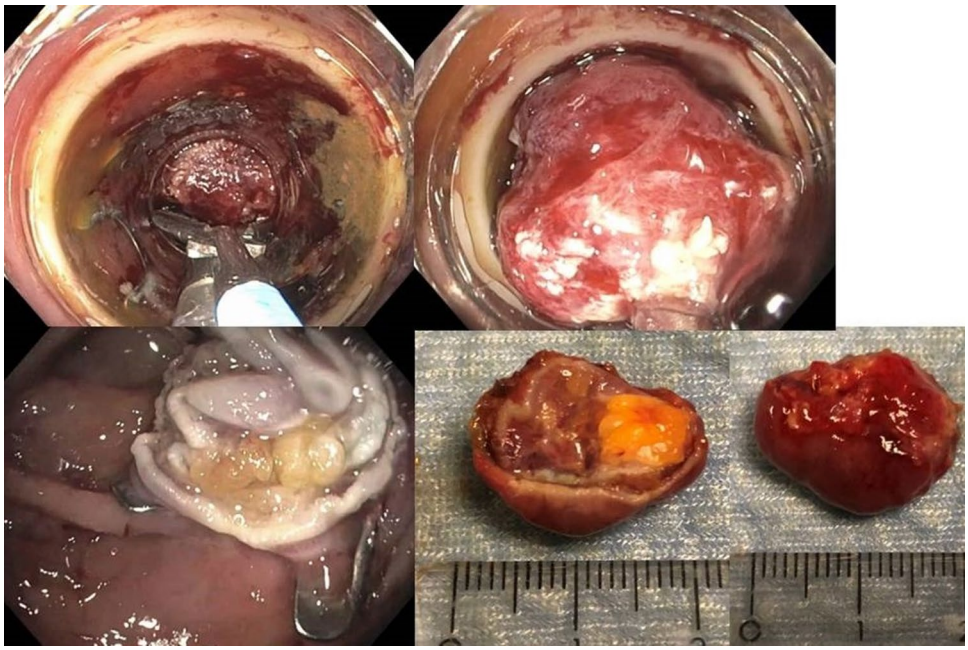

Fig. 8 Endoscopic images of case 8: a 30 mm malignant polyp with an 8 mm invasive cancer that could not be lifted and removed through EMR

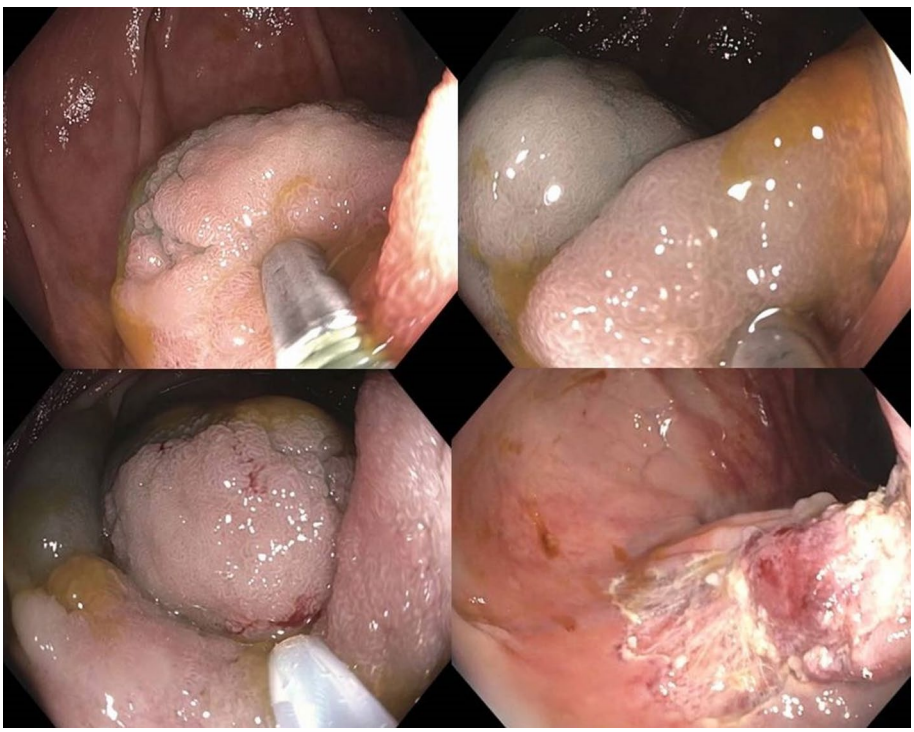

Fig. 9 Endoscopic images of case 8: the entire EMR base was removed through OTSC-EFTR. Pathology showed a T2 cancer invasion to the muscularis propria with a 3 mm negative margin on the serosal side. The patient was referred back to surgery for nodal status concern

Compliance with ethical standards

Disclosures Dr. Shou-jiang Tang, Dr. Yehia Naga, Ruonan Wu, Dr. Shengyu Zhang has no conflicts of interest or financial ties to disclose.

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