Endoscopic FullThickness Resection: A Systematic Review

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Abstract

Background Endoscopic full thickness resection (EFTR) is an emerging therapeutic option for resecting subepithelial lesions (SELs) and epithelial neoplasms. We aimed to systematically review the techniques, applications, outcomes, and complications of EFTR.

Methods A systematic literature search was performed using PubMed. All relevant original research articles involving EFTR were included for the review along with case report/series describing novel/rare techniques from 2001 to February 2022.

Results After screening 7,739 citations, finally 141 references were included. Non-exposed EFTR has lower probability of peritoneal contamination or tumor seeding compared with exposed EFTR. Among exposed EFTR, tunneled variety is associated with lower risk of peritoneal seeding or contamination compared with non-tunneled approach. Closure techniques involve though the scope (TTS) clips, loop and clips, over the scope clips (OTSC), full thickness resection device (FTRD), and endoscopic suturing/plicating/stapling devices. The indications of EFTR range from esophagus to rectum and include SELs arising from muscularis propria (MP), non-lifting adenoma, recurrent adenoma, and even early gastric cancer (EGC) or superficial colorectal carcinoma. Other indications include difficult locations (involving appendicular oriﬁce or diverticulum) and full thickness biopsy for motility disorders. The main limitation of FTRD is feasibility in smaller lesions (<20–25 mm), which can be circumvented by hybrid EFTR techniques. Oncologic resection with lymphadenectomy for superficial GI malignancy can be accomplished by hybrid natural orifice transluminal endoscopic surgery (NOTES) combining EFTR and NOTES. Bleeding, perforation, appendicitis, enterocolonic ﬁstula, FTRD malfunction, peritoneal tumor seeding, and contamination are among various adverse events. Post OTSC artifacts need to be differentiated from recurrent/residual lesions to avoid re-FTRD/surgery.

Conclusion EFTR is safe and effective therapeutic option for SELs, recurrent and non-lifting adenomas, tumors in difﬁcult locations and selected cases of superficial GI carcinoma.


ISSN 0976-5042.

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Introduction

Endoscopic resection has evolved from simple polypectomy to endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) for en-bloc removal of large tumors. ESD for non-lifting lesions arising from MP (e.g., gastrointestinal stromal tumor [GIST]) carries high risk of perforation and subsequently closure can be difficult in collapsed lumen. Hence, laparoscopic endoscopic cooperative surgery (LECS) was introduced to maintain continuity of the gastrointestinal (GI) tract and to allow traction during dissection. More recently, non-exposed technique of EFTR by “close first and cut later” strategy can help mitigate the challenges of exposed EFTR (cut first and close later strategy). This can be achieved by endoscopic suturing, full thickness resection device (FTRD) or novel robotic endoscopic platform.

Search Strategy

For the purpose of the review, we searched the PubMed using keywords “EFTR” or “FTRD.” We screened total 7,740 citations and 350 were identified. Finally 144 citations were included for our review excluding case reports/series/original articles with small sample size (other than describing novel technique or a unique complication)/letter to editor/editorials (► Fig. 1) and including relevant articles with specific searches and selected cross references.

Details of Technique

History of EFTR: Experimental Studies on Animal Model

Both ex-vivo and in-vivo (live) models showing feasibility of en-bloc/R0 resection in stomach/colon form the basis of current EFTR techniques. First prototype and the modern FTRD device for colorectal EFTR were developed in 2001 and 2015, respectively by Schurr et al. Among several techniques performed in animal models (► Table 1), some made it to clinical practice.

Techniques of EFTR

EFTR techniques can be divided into exposed and non-exposed EFTR. In exposed EFTR, resection is followed by defect closure (peritoneum exposed). In non-exposed EFTR, the lesion is invaginated into the lumen to allow serosa-to-serosa apposition followed by resection. Exposed EFTR can be further divided into non-tunneled and tunneled EFTR. In the former, the lesion is dissected through the MP like ESD using soft translucent cap and various knives (Flush knife, Dual knife and hybrid knife allow simultaneous injection and cutting). After dissection, EFTR is performed.

Tunneled exposed EFTR is similar to submucosal tunnel endoscopic resection (STER) in which mucosal incision is made followed by dissection through MP to create a tunnel through which the enucleated lesion is brought out. Tunneled EFTR does not warrant full thickness closure as only mucosal closure ensures wall integrity. It is applicable only for subepithelial lesions (SELS) and hence it is better with respect to infection control compared with other exposed EFTR techniques. This is feasible for lesions <4 cm particularly in the distal esophagus and gastric cardia.

Closure Techniques

Though the Scope Clip Closure

Though the scope (TTS) clips (designed for hemostasis) achieve only mucosal and submucosal apposition. However, post

Fig. 1 Search strategy for systematic review.
EFTR defect closure has been reported successfully with TTS clips. Peristalsis and radial force of large defects can compromise the integrity of gut wall apposition achieved with TTS clips leading to delayed perforation and bleeding. A “side to center” method is preferred when the diameter of the defect is less than the clip. For defects larger than TTS clip, a "suction-clip suture" technique or "omentumal patch closure" (e.g., sucking the omentum into the defect) can be done.

Endoloop Clip-Assisted Closure Method
Endoloop-assisted closure of post EFTR defects has been described which reinforces TTS clip closure. However, it cannot achieve closure of muscularis/serosa. Currently, endoscopic purse-string suture (EPSS) technique is most popular for endoloop clip closure, in which the defect is closed by tightening of endoloop after application of TTS clips circumferentially along defect margins anchoring the endoloop. This requires a double-channel scope, however, the use of a novel endoloop has enabled closure by single channel endoscope. The peritoneal exposure can be reduced by pre-EPSS method, in which one endoloop is applied distal to resection margin and another around lesion to make the lesion intraluminal following which the lesion is resected with immediate closure.

Cap Mounted Clip Closure
Unlike TTS clips, cap mounted clips like over the scope clips (OTSC) and Padlock clip are designed for full thickness closure. The edges of the defect are drawn into transparent cap by help of twin graspers following which OTSC is released to achieve full thickness closure. OTSC can close only defects <2 to 2.5 cm (due to small internal diameter).
and cannot be repositioned once deployed.\textsuperscript{30} After incomplete EFTR, OTSC removal by dedicated bipolar device is required before re-intervention. Though expensive (c.f. TTS clips), OTSC clips can significantly reduce hospital stay and procedure time.\textsuperscript{22}

**Combined Full Thickness Resection and Closure**

FTRD (Ovesco Endoscopy) (\textsuperscript{-Fig. 2}) has an integrated closure and resection device and consists of a transparent cap (outer diameter 21 mm) with modified OTSC (14 mm) (which can be mounted over colonoscope/endoscope 11.5–13.2 mm diameter and a working channel diameter of ≥3.2 mm), a tissue grasper and a 13-mm monofilament hot snare pre-loaded in the tip of the cap running on outer surface of the scope under a transparent plastic sheath (\textsuperscript{-Fig. 2}).\textsuperscript{2} The depth of the FTRD cap is 23 mm compared with 6 mm in conventional OTSC system to accommodate more tissue. It can be used in upper GI tract after bougie or balloon dilation of the lower esophageal sphincter (LES) up to 20 mm.\textsuperscript{31} After marking the lesion with integrated electrocautery, OTSC is applied after pulling the lesion with tissue grasper followed by resection with snare. The entire procedure is complete using a single device.

**Endoscopic Suturing System**

The limitation of OTSC in closing larger defects is overcome by dedicated flexible endoscopic suturing device (OverStitch endoscopic suturing system, Apollo Endosurgery, Austin, Texas, United States) or endoscopic puncture suture device using T-tags. Although technically demanding and costly, ESS can achieve full thickness “surgical closure” in a cost which is much lesser than conventional surgery.\textsuperscript{22} Preliminary reports have shown its safety and efficacy.\textsuperscript{13,32}

**Endoscopic Plicating Devices**

The full thickness plicator device (NDO Surgical Inc., Mansfield, Massachusetts, United States) with polytetrafluoroethylene-pledgeted sutures originally designed for anti-reflux therapy has been used for EFTR of gastric SELs.\textsuperscript{33} As this is currently unavailable, another anti-reflux device with a hydraulic closure mechanism: GERDX (G-Surg, Seeon, Germany) is being used for gastric SELs.\textsuperscript{34} The large diameter and limited manipulation have restricted its use to gastric lesions only.

**Endoscopic Stapling Devices**

SurgASSIST system (Power Medical Interventions Deutschland GmbH, Hamburg, Germany) with 20-mm linear stapling device can be passed co-axially along with endoscope and has been used to resect gastric SELs and superficial carcinoma. The large size and limited manipulative capacity increases risk of perforation with device passage.

The initial prototype FTRD had a semicircular stapler along with tissue grasper and a scalpel. The use was limited to the left colon due to its large size and currently no longer manufactured.\textsuperscript{4}

**Traction**

The use of distal transparent cap to expose the incision level during ESD may not be feasible in positions like fundus of stomach. Dental floss-assisted or metallic clip and rubber band-assisted pulley traction has been used to promote dissection for large mucosal lesions/SELs in different locations.\textsuperscript{35} The advantages are reduced operative time, better tumor/vessels exposure with prevention of tumor falling into the abdominal cavity.\textsuperscript{35}

**Comparison between Post EFTR Closure Techniques**

There is scarcity of comparative literature among post EFTR closure techniques with regard to complications except for animal studies. However, TTS or clip and loop cannot achieve full thickness closure in true sense. OTSC and suturing/plicating devices can achieve full thickness closure and hence can prevent delayed bleeding and perforation better than clips/clip loops. A limitation of OTSC is its limited internal diameter. However the cost effectiveness of these newer closure techniques needs to be studied in future.

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\textbf{Fig. 2} The full thickness resection device (FTRD). (A) The FTRD assembly: over the scope clip (OTSC) over transparent cap loaded on the tip of therapeutic endoscope, monofilament hot snare preloaded in the tip of the cap running on outer surface of the scope under a transparent plastic sheath. (B) Parts of FTRD during full thickness resection (▲ transparent cap, ▲ tissue grasper, ◆ OTSC).
Current Status of EFTR: Various Applications with Outcomes

EFTR in the Esophagus
Esophageal SELs originating from the MP can be resected using EFTR. Clinical cases are limited to case reports. A case of recurrent esophageal leiomyoma originating from MP which was operated twice, was treated with STER and muscle excision preserving adventitia followed by clip closure. ESD with closure of ulcer floor with clips has been described. Endoscopic submucosal excision (ESE) with LeCamp endoloop closure with single channel endoscope has been described.

EFTR Stomach
EFTR of stomach is done for gastric GIST, other SELs, adenomas, and early carcinoma. The latter could be restricted to only small (<2 cm) adenocarcinoma with mucosal/limited submucosal involvement (<0.5 mm) without high-risk features (lymphovascular invasion/intestinal subtype). EFTR of gastric metastasis from malignant melanoma has also been described. Although FTRD insertion needs prior dilation of LES for gastro-duodenal lesions, it can be technically successful in 93% cases with up to 68% R0 resection rates and minimal recurrence (3%) on short term follow-up (median 3 months).

EFTR Duodenum
Earlier reports of duodenal EFTR were on conventional EMR with laparoscopic closure of defect and inadvertent EFTR after EMR closed by hemoclips. We have summarized studies specifically evaluating duodenal EFTR in (Figs. 4 and 5). Duodenal EFTR was described with colonic FTRD device, modified FTRD loaded on endoscope (14 mm OTSC), OTSC-based multistep EFTR, flat-based OTSC (Padlock clips) and ESD with clip/loop/Overstitch closure. Indications included SELs and adenomas (non-lifting, recurrent, and residual lesion after failed ESD). Technical success ranged from 85 to 100%, R0 resection rates were 63.2 to 100%. Adverse events were minor bleeding (most common), followed by perforation and peritonitis. FTRD in duodenum was particularly effective for lesions <20 mm.

EFTR in Small Bowel (Other Than Duodenum)
Single and double balloon enteroscopy-guided EFTR of mid ileal endometriosis and Meckel’s diverticulum, respectively with conventional loop and snares have been described. Resection of non-lifting adenoma with FTRD device has been described in ileal pouch in a postoperative case of familial adenomatous polyposis.

EFTR Colorectum
Traditional methods of colorectal tumor resection have limitations like steep learning curve (ESD) and high recurrence rate (up to 15% for EMR). SELs, recurrent/non-lifting adenomas with scarring, deep invading lesions, and adenomas near appendix/diverticulum not amenable to EMR/ESD can be candidates for EFTR (Table 3). Dedicated FTRD device enables one step resection after pre-closure with OTSC. It has shorter learning curve although larger lesions may not be amenable which warrant hybrid techniques. Pooled technical success, R0 resection rate, adverse events, and recurrence are 87.6, 78.8, 12.2, and 12.6%, respectively according to recent meta-analysis of colorectal EFTR (total 1,936 patients). Lesions >2 cm have lower R0 resection and adverse event rates. R0 resection did not differ based on indication (difficult adenoma, early carcinoma, and SELs) or location (proximal, distal colon, and rectum). Two meta-analyses evaluating only FTRD have shown that success of insertion to target lesion, technical success, R0 resection, total complication rates were 96.1%, 89 to 90, 78 to 82, and 8 to 10%, respectively. Major bleeding, perforation, and need for emergent surgery occurred in roughly 1% cases whereas post-polypectomy syndrome was noted in 2%.

EFTR for Early Colorectal Cancer (CRC)
EFTR using FTRD device or EFTR with endoscopic lymphadenectomy has been described for superficial CRC. While many techniques are limited to case reports/series, 156 cases of adenocarcinoma detected incidentally on histology after resection using EFTR were described by Kuellmer et al. The R0 resection rate was lower in non-lifting lesion (61%) as compared with polypoidal lesion (87.5%). Given the suboptimal rate of R0 resection for lesions ≥20 mm with FTRD, the role is limited given the fact that submucosal invasive cancer (SMIC, <1,000 μm submucosal invasion) in <20 mm lesion is less common. So, ESD could still be preferable for lesions >20 mm if deep SMIC (>1,000 μm) is not likely based on image-enhanced endoscopic characterization. However, FTRD can have a role in non-surgical candidates. Retrospective analyses of Dutch EFTR registry have shown a curative resection rate of 23.7% in T1 CRC and 60.8% excluding high risk features (deep SMIC). Full thickness histological assessment after EFTR with FTRD can help in avoiding oncologic resection in low risk patients.
## Table 2 Endoscopic full thickness resection (EFTR) for duodenal lesions

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Location in duodenum</th>
<th>N</th>
<th>Indication</th>
<th>Technique</th>
<th>Max Diameter (mm)</th>
<th>Operative time (average, Range)</th>
<th>Hospital stay</th>
<th>Technical success</th>
<th>R0 resection</th>
<th>Adverse events</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schmidt et al</td>
<td>2015</td>
<td>First to third part</td>
<td>20</td>
<td>Non-lifting adenoma, Sub-epithelial lesions (SEL) including neuroendocrine tumor (NET)</td>
<td>Modified FTRD device loaded on endoscope</td>
<td>22–40</td>
<td>50–85</td>
<td>4–6</td>
<td>100%</td>
<td>75%</td>
<td>50% minor bleeding</td>
<td>None at 3 mo follow-up</td>
</tr>
<tr>
<td>Bauder et al</td>
<td>2018</td>
<td>Entire duodenum</td>
<td>20</td>
<td>Adenoma, non-lifting adenoma, SEL, adenocarcinoma</td>
<td>Colonic FTRD device after esophageal and pyloric CRE dilatation (20 mm)</td>
<td>5–35</td>
<td>61 (25–130 min)</td>
<td></td>
<td>85%</td>
<td>63.2%</td>
<td>15.8% minor bleeding</td>
<td>n = 2, re-EFTR</td>
</tr>
<tr>
<td>Ren et al</td>
<td>2019</td>
<td>First and second part</td>
<td>32</td>
<td>Non-ampullary duodenal SEL (GIST-14, NET-4, Pancreatic rest-11, Leiomyoma-2, Lipoma-1)</td>
<td>ESD followed by clip and/or loop or Overstitch closure</td>
<td>5–30</td>
<td>68 (17–186 min)</td>
<td>6.2 (2–10)</td>
<td>100%</td>
<td>100%</td>
<td>Perforation closed by Laparoscopy, Peritonitis, Fall in saturation</td>
<td>None, at 38 mo</td>
</tr>
<tr>
<td>Kappelle et al</td>
<td>2018</td>
<td>Proximal to ampulla</td>
<td>6</td>
<td>SELs</td>
<td>Flat-based OTSC (Padlock clip)</td>
<td>5–13</td>
<td>35 ± 10</td>
<td>7 (2–14)</td>
<td>100%</td>
<td>83%</td>
<td>Perforation, micro-perforation, hemorrhage</td>
<td>None</td>
</tr>
<tr>
<td>Wei et al</td>
<td>2021</td>
<td>Not specified</td>
<td>13</td>
<td>Adenomas, SELs</td>
<td>OTSC assisted multistep EFTR</td>
<td>10–32</td>
<td>38.7 ± 14.6</td>
<td>2–3 d post-operative</td>
<td>100%</td>
<td>92.3%</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

Abbreviations: FTRD, full thickness resection device; GIST, gastrointestinal stromal tumor; NET, neuroendocrine tumor.
However, recurrence can occur even up to 54 months post-resection.\textsuperscript{55} Current studies have evaluated recurrence (0.5–6\%) only in short term (3 months).\textsuperscript{54,56} Delayed perforation in this settings can significantly increase morbidity and decrease chance of cure after FTRD.\textsuperscript{55}

**EFTR near Appendicular Orifice**

Studies on EFTR using dedicated FTRD device has been summarized in \textsuperscript{Table 4.}\textsuperscript{57–59} Technical success was 89 to 100\%. R0 resection ranged from 64 to 93\%.\textsuperscript{57–59} Recurrence was nearly 12\%.\textsuperscript{59} Most of the resected lesions are
Table 3: Studies on endoscopic full thickness resection (EFTR) in the colorectum

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>Technique</th>
<th>Diameter (mm)</th>
<th>Time</th>
<th>Target lesion reached</th>
<th>En bloc resection</th>
<th>Pathology</th>
<th>R0 resection</th>
<th>Length hospital stay</th>
<th>Adverse events</th>
<th>Time to follow-up</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andrisani et al.</td>
<td>2019</td>
<td>20</td>
<td>FTRD</td>
<td>20 (6–42)</td>
<td>50 min</td>
<td>100%</td>
<td>91%</td>
<td>Adenoma, SEL, T1 carcinoma</td>
<td>90%</td>
<td>–</td>
<td>10%</td>
<td>3 mo</td>
<td>6.4%</td>
</tr>
<tr>
<td>Aepli et al.</td>
<td>2018</td>
<td>33 (62, C21)</td>
<td>FTRD</td>
<td>27 (11–42)</td>
<td>63 (26–190)</td>
<td>97%</td>
<td>88%</td>
<td>Adenoma, carcinoma, Polyp, NET</td>
<td>88%</td>
<td>3.1 (2–6) mo</td>
<td>13%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Albrecht et al.</td>
<td>2019</td>
<td>70 (8-19, C48)</td>
<td>FTRD</td>
<td>19 (5–37)</td>
<td>95.5 (48–143)</td>
<td>100%</td>
<td>97%</td>
<td>Adenoma, SEL, T1 carcinoma</td>
<td>90.8%</td>
<td>12.9%</td>
<td>3 mo</td>
<td>6% for adenoma</td>
<td></td>
</tr>
<tr>
<td>Andrisani et al.</td>
<td>2017</td>
<td>20</td>
<td>FTRD</td>
<td>26 (10–42 mm)</td>
<td>–</td>
<td>100%</td>
<td>100%</td>
<td>Superficial colorectal neoplasms (T1 carcinoma, HGD)</td>
<td>100%</td>
<td>–</td>
<td>5%</td>
<td>3 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Bauermeister et al.</td>
<td>2022</td>
<td>17</td>
<td>Hybrid EMR+FTRD</td>
<td>30 (18–50 mm)</td>
<td>35–160 min</td>
<td>100%</td>
<td>94.1%</td>
<td>Large colorectal adenomas</td>
<td>76.4%</td>
<td>–</td>
<td>23.5% minor; no perforation/major bleeding</td>
<td>–</td>
<td>16.6%</td>
</tr>
<tr>
<td>Bulut et al.</td>
<td>2022</td>
<td>26</td>
<td>FTRD</td>
<td>23 (10–35 mm)</td>
<td>69 (30–162) min</td>
<td>89%</td>
<td>81%</td>
<td>Adenoma and adenocarcinoma</td>
<td>86%</td>
<td>–</td>
<td>11.5%</td>
<td>3–12 mo</td>
<td>10%</td>
</tr>
<tr>
<td>Xu et al.</td>
<td>2013</td>
<td>19</td>
<td>FTRD</td>
<td>18 (12–30 mm)</td>
<td>67 (45–130) min</td>
<td>100%</td>
<td>94%</td>
<td>Laparoscopic closure in 2/18</td>
<td>94%</td>
<td>–</td>
<td>16.7%</td>
<td>18 (6–36) mo</td>
<td>0%</td>
</tr>
<tr>
<td>Fähndrich et al.</td>
<td>2015</td>
<td>17</td>
<td>Inoue Cap and OTSC (n = 16), FTRD (n = 1)</td>
<td>10–25 mm</td>
<td>100%</td>
<td>94%</td>
<td>Adenoma, carcinoma, NET</td>
<td>100%</td>
<td>–</td>
<td>0%</td>
<td>–</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Falt et al.</td>
<td>2021</td>
<td>52</td>
<td>FTRD</td>
<td>8–30 mm</td>
<td>16–65 min</td>
<td>100%</td>
<td>92%</td>
<td>Colorectal lesions ≤ 30 mm (adenoma, SET)</td>
<td>85%</td>
<td>1–7 d</td>
<td>13%</td>
<td>–</td>
<td>12%</td>
</tr>
<tr>
<td>Ichkanian et al.</td>
<td>2021</td>
<td>95</td>
<td>FTRD</td>
<td>15.5 ± 6.4 mm</td>
<td>59.7 ± 3.18 mm</td>
<td>98%</td>
<td>84.2%</td>
<td>Adenoma, carcinoma, SELs</td>
<td>82.7%</td>
<td>Mean 1.3 d</td>
<td>5.3%</td>
<td>61.7 ± 82.3 d</td>
<td>2.5%</td>
</tr>
<tr>
<td>Mbo de-frevo et al.</td>
<td>2019</td>
<td>9</td>
<td>FTRD</td>
<td>14–28 mm</td>
<td>Mean 55 min</td>
<td>100%</td>
<td>100%</td>
<td>Adenoma, NET</td>
<td>100%</td>
<td>1–2 d</td>
<td>0% major complications</td>
<td>6–12 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Meier et al.</td>
<td>2017</td>
<td>10</td>
<td>EMR + FTRD</td>
<td>30–50 mm</td>
<td>65–140 min</td>
<td>100%</td>
<td>100%</td>
<td>Adenoma</td>
<td>100%</td>
<td>–</td>
<td>0%</td>
<td>3 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Rushfeldt et al.</td>
<td>2021</td>
<td>10, all rectum</td>
<td>ESD + TTS/OTSC closure</td>
<td>30 (9–35 mm)</td>
<td>65–191 min</td>
<td>100%</td>
<td>100%</td>
<td>Adenoma, carcinoma, Polyp, NET</td>
<td>60%</td>
<td>1–3 d</td>
<td>20% delayed bleed</td>
<td>3–29 mo</td>
<td>20%</td>
</tr>
<tr>
<td>Schmidt et al.</td>
<td>2015</td>
<td>24</td>
<td>FTRD</td>
<td>24 (12–40 mm)</td>
<td>50 (10–177) min</td>
<td>95.8%</td>
<td>83.3%</td>
<td>Adenoma, adenocarcinoma, SET, suspected Hirschsprung’s disease</td>
<td>75%</td>
<td>4 (1–12 d)</td>
<td>4% minor bleed, 8% postpolypectomy syndrome</td>
<td>1.5–12 mo</td>
<td>20%</td>
</tr>
<tr>
<td>Schmidt et al.</td>
<td>2018</td>
<td>181</td>
<td>FTRD</td>
<td>15 (2–30 mm)</td>
<td>50 (3–190) min</td>
<td>100%</td>
<td>89.5%</td>
<td>Difficult adenoma, adenocarcinoma, SELs</td>
<td>76.9%</td>
<td>–</td>
<td>9.9%</td>
<td>3 mo</td>
<td>15.35%</td>
</tr>
<tr>
<td>Valli et al.</td>
<td>2018</td>
<td>60</td>
<td>FTRD</td>
<td>24 (10–35 mm)</td>
<td>60 (15–177) min</td>
<td>97%</td>
<td>91.4%</td>
<td>Adenoma, carcinoma, SELs</td>
<td>79%</td>
<td>–</td>
<td>7%</td>
<td>15 (2–54) mo</td>
<td>0% for R0 resection</td>
</tr>
<tr>
<td>Van der Spek et al.</td>
<td>2018</td>
<td>51</td>
<td>FTRD (n = 48), EMR + FTRD (n = 2)</td>
<td>12.2 (2–30 mm)</td>
<td>–</td>
<td>88%</td>
<td>86%</td>
<td>Adenoma, carcinoma, NET</td>
<td>80%</td>
<td>–</td>
<td>13%</td>
<td>4 mo</td>
<td>10%</td>
</tr>
<tr>
<td>Velegraki et al.</td>
<td>2019</td>
<td>17</td>
<td>FTRD</td>
<td>12.7 (5–30 mm)</td>
<td>30 (10–90) min</td>
<td>100%</td>
<td>82.3%</td>
<td>Adenoma, carcinoma, SELs</td>
<td>82.3%</td>
<td>1–3 d</td>
<td>17.6%</td>
<td>3 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Vital et al.</td>
<td>2018</td>
<td>13</td>
<td>FTRD</td>
<td>1 (4 mm)</td>
<td>68 ± 35 min</td>
<td>100%</td>
<td>100%</td>
<td>Adenoma and adenocarcinoma</td>
<td>83.3%</td>
<td>2.5 ± 12 d</td>
<td>15.4%, postpolypectomy syndrome</td>
<td>Up to 12 mo</td>
<td>27%</td>
</tr>
<tr>
<td>Von Helden et al.</td>
<td>2019</td>
<td>30</td>
<td>FTRD</td>
<td>25 (14–33 mm)</td>
<td>34.5 (11–120) min</td>
<td>93.3%</td>
<td>80%</td>
<td>Adenoma and adenocarcinoma</td>
<td>80%</td>
<td>–</td>
<td>19%, 6% serious delayed perforation</td>
<td>Not mentioned</td>
<td>8% with R0 resection</td>
</tr>
</tbody>
</table>

Abbreviations: EMR, endoscopic mucosal resection; FTRD, full thickness resection device; HGD, high grade dysplasia; MP, muscularis propria; NET, neuroendocrine tumor; OTSC, over the scope clips; SELs, subepithelial lesions.
<20 mm. For larger laterally spreading tumor (LST) (≤4 cm), ESD followed by EFTR with FTRD has been shown to be successful. The main complication is appendicitis (14–17%). Lesions involving >75% of the circumference have lower risk of appendicitis post-EFTR due to chronic obstruction. Enterocolonic fistula due to small bowel entrapment has been reported. Translation of adenoma tissue extramurally is reported in only an isolated case. EFTR of intussuscepted appendix resected with conventional snare and clip has been described.

### EFTR for NET

EFTR of rectal and duodenal NETs is described mostly in case reports. Earlier reports described laparoscopy-assisted EFTR using EMR/ESD or inadvertent EFTR after duodenal EMR. Resection of incompletely resected rectal NETs with OTSC-based EFTR and ESD followed by Overstitch was described later. Use of FTRD device for rectal NETs was first reported in 2016. A novel band ligation-assisted EFTR using the OTSC device has been described in animal model which could be helpful if FTRD device is unavailable. Padlock clip-assisted resection of duodenal NET has been reported. A study comparing transanal endoscopic microsurgery (TEM) with FTRD found that FTRD was equally effective with similar R0 resection rates with less operative time (19 minutes vs. 49 minutes) for small rectal NETs.

### FTRD for GIST and Other Subepithelial Lesions

Most of the earlier reports described endoscopic resection and laparoscopic defect closure. Robotic laparoscopy-assisted EFTR was described recently. EFTR has similar operating time and R0 resection rates compared with laparoscopy and was shown to be equivalent for GIST <2 cm. A 100% R0 resection rate without any recurrence was shown in a series of 69 patients with GIST originating from MP resected with ESD and loop-clip closure. Clip in line traction method, cap-assisted technique (in small GIST <1.5 cm) and direct EFTR (for gastric fundal SELs with intra-luminal growth pattern) can reduce the operating time. Snare-assisted EFTR was shown to be cost effective compared with band ligation-assisted or ESD-assisted EFTR with similar efficacy and complication rates. Omental patch, suturing device, or endoscopic loop ligation can be used for defect closure.

EFTR was shown to be equally effective as STER for gastric GISTs. Pre-closure techniques help maintain luminal insufflation during EFTR. Non-exposed EFTR for gastric GIST can be performed with full thickness plicator device or suturing platform. EFTR of colonic GIST with FTRD device was also reported. Technical difficulty of FTRD insertion into stomach can be overcome by prior use of sizing cap.

Apart from stomach, there are reports for EFTR for SELs in esophagus, duodenum, and colon. EFTR of inverted diverticulum can be resected using OTSC-assisted EFTR with or without dedicated FTRD device. Lesions >35 mm, large extramural component, systemic spread, GI surgery or stenosis impeding insertion of EFTR device are contra-indications of non-exposed EFTR for SELs.

### EFTR of Adenomas Arising at Diverticulum

Endoscopy resection of adenoma arising at diverticulum carries the high risk of perforation due to lack of muscle layer in diverticulum. EFTR of inverted diverticulum can be done with “ligate and let go” technique whereas adenomas arising at diverticulum can be resected using OTSC-assisted EFTR with or without dedicated FTRD device.

### Diagnosis of Gastrointestinal Motility Disorders

Surgical full-thickness biopsy is essential to diagnose motility disorders such as Hirschsprung’s disease and chronic intestinal pseudo-obstruction. A case series including four patients and a case report have shown the feasibility and safety of EFTR using FTRD. The technical success was achieved in all patients with mean diameter of specimen and mean procedure time being 20 mm and 21 minutes, respectively.

### Hybrid EFTR

The limitations of various techniques of EFTR can be circumvented by combining two methods of EFTR. The major limitation of FTRD is inability to perform EFTR in large lesions (≥20–25 mm). Hence, initially snare polypectomy/EMR/ESD/endoscopic variceal ligation (EVL) to reduce the size of the lesion for completion of EFTR by FTRD/endooscopic suturing has been described.

### Hybrid NOTES

NOTES is usually performed through natural orifice like mouth or anus, however, combining percutaneous laparoscopy with...
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>Dissection technique</th>
<th>Closure technique</th>
<th>Diameter (mm)</th>
<th>Time</th>
<th>En bloc resection</th>
<th>Pathology</th>
<th>R0 resection</th>
<th>Length hospital stay</th>
<th>Adverse events</th>
<th>Time to follow-up</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhou et al</td>
<td>2011</td>
<td>26</td>
<td>ESD</td>
<td>TTS Clips</td>
<td>28 mm (12–45 mm)</td>
<td>105 min (60–145)</td>
<td>100%</td>
<td>All SELs (GIST, glomus, schwannoma, leiomyoma)</td>
<td>85.7%</td>
<td>5.5 d (3–8)</td>
<td>None</td>
<td>8 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Ye et al</td>
<td>2014</td>
<td>51</td>
<td>ESD</td>
<td>TTS Clip and endoap</td>
<td>24 mm (13–35 mm)</td>
<td>52 (30–125 min)</td>
<td>98%</td>
<td>SELs arising from MP (leiomyoma, GIST)</td>
<td>–</td>
<td>3.9 d (3–9)</td>
<td>None</td>
<td>22.4 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Shi et al</td>
<td>2013</td>
<td>20</td>
<td>ESD</td>
<td>Endoloop and TTS clips</td>
<td>0.4–3 cm</td>
<td>100 min</td>
<td>8–20 min</td>
<td>100%</td>
<td>SELs arising from MP (GIST, leiomyoma, schwannoma, leiomyoma, GCT, pancreatic rest)</td>
<td>–</td>
<td>1–7 d</td>
<td>5 had fever and pain abdomen</td>
<td>2–13 mo</td>
</tr>
<tr>
<td>Wang et al</td>
<td>2022</td>
<td>21</td>
<td>ESD</td>
<td>Endoscopic Nylon loop ligation</td>
<td>23 mm (19–25 mm)</td>
<td>Closure time</td>
<td>Suture time</td>
<td>8–20 min</td>
<td>100%</td>
<td>SELs from MP (leiomyoma)</td>
<td>–</td>
<td>5 d (3–6)</td>
<td>1 with peritonism, treated conservatively</td>
</tr>
<tr>
<td>Tang et al</td>
<td>2016</td>
<td>34</td>
<td>ESD</td>
<td>TTS Clips</td>
<td>1–5 cm</td>
<td>50–100 min</td>
<td>100%</td>
<td>SELs from MP (Mainly spindle cell tumors)</td>
<td>–</td>
<td>3–5 d</td>
<td>1 pneumoperitoneum</td>
<td>5–23 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Jung et al</td>
<td>2021</td>
<td>8</td>
<td>ESD</td>
<td>TTS Clips</td>
<td>1–2.7 cm</td>
<td>25–96 min</td>
<td>100%</td>
<td>GIST</td>
<td>50%</td>
<td>5–18</td>
<td>1 bleeding</td>
<td>5–50 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Huang et al</td>
<td>2018</td>
<td>46</td>
<td>ESD</td>
<td>TTS Clips</td>
<td>1.2–4.5 cm</td>
<td>56–188 min</td>
<td>100%</td>
<td>GIST from MP, leiomyoma</td>
<td>100%</td>
<td>4–11</td>
<td>None</td>
<td>Mean 6 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Huang et al</td>
<td>2014</td>
<td>35</td>
<td>ESD</td>
<td>TTS Clips</td>
<td>2–4.5 cm</td>
<td>60–155 min</td>
<td>100%</td>
<td>GIST, leiomyoma, schwannoma</td>
<td>100%</td>
<td>4–10</td>
<td>None</td>
<td>Mean 6 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Guo et al</td>
<td>2015</td>
<td>23</td>
<td>ESD</td>
<td>OTSC</td>
<td>0.6–2 cm</td>
<td>16–104 min; closure time 2–12 min</td>
<td>100%</td>
<td>SELs from MP &lt;2 cm (GIST, leiomyoma)</td>
<td>100%</td>
<td>2–5</td>
<td>Post-operative fever 3, Localized peritonitis in 5</td>
<td>1–6 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Feng et al</td>
<td>2014</td>
<td>52</td>
<td>ESD</td>
<td>TTS Clips</td>
<td>0.5–4.8 cm</td>
<td>30–270 min</td>
<td>100%</td>
<td>GIST, leiomyoma, schwannoma</td>
<td>100%</td>
<td>4–7</td>
<td>No severe complication, distention in 5</td>
<td>2–24 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Li et al</td>
<td>2021</td>
<td>20</td>
<td>ESD</td>
<td>TTS Clips (ZIP technique)</td>
<td>0.5–2.5 cm</td>
<td>30–120 min; closure time 5–20 min</td>
<td>100%</td>
<td>GIST, leiomyoma, schwannoma</td>
<td>–</td>
<td>–</td>
<td>Peritonitis 1, pain and fever in nearly half</td>
<td>6–22 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Moer et al</td>
<td>2020</td>
<td>29</td>
<td>Gastric FTRD</td>
<td>Dedicated FTRD-OTSC</td>
<td>0.5–1.5 cm</td>
<td>24–90 min</td>
<td>89.7%</td>
<td>SELs &lt;2 cm (GIST, leiomyoma, schwannoma, Pancreatic rest)</td>
<td>76%</td>
<td>–</td>
<td>31% minor bleed</td>
<td>3 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Schlag et al</td>
<td>2013</td>
<td>20</td>
<td>Twin grasper and snare</td>
<td>OTSC or laparoscopic</td>
<td>0.7–3 cm</td>
<td>19–95 min</td>
<td>100%</td>
<td>SELs &lt;3 cm</td>
<td>85%</td>
<td>–</td>
<td>None</td>
<td>3 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Shichijo et al</td>
<td>2019</td>
<td>8</td>
<td>ESD</td>
<td>TTS cup and endoloop/ TTS only/ OTSC only</td>
<td>1–3.5 cm</td>
<td>50–166 min</td>
<td>100%</td>
<td>GIST with intraluminal growth pattern</td>
<td>37.5%, rest were indeterminate</td>
<td>4–11 d</td>
<td>No serious adverse events</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Sun et al</td>
<td>2018</td>
<td>69</td>
<td>ESD</td>
<td>TTS Clip and endoloop</td>
<td>0.6–6 cm</td>
<td>17–600 min; mean 128 min</td>
<td>100%</td>
<td>SELs (GIST, leiomyoma, hemangioma, and schwannoma)</td>
<td>100%</td>
<td>–</td>
<td>7.25%</td>
<td>7–84 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Yang et al</td>
<td>2015</td>
<td>41</td>
<td>ESD</td>
<td>TTS clips (86%) and OTSC (14%)</td>
<td>16.3 ± 5.89</td>
<td>78.82 ± 46.44 min (higher with more size and greater curvature)</td>
<td>100%</td>
<td>SELs</td>
<td>100%</td>
<td>5.39 ± 1.14</td>
<td>22%</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Abbreviations: ESD, endoscopic submucosal dissection; FTRD, full thickness resection device; GCT, granulose cell tumor; GIST, gastrointestinal stromal tumor; MP, muscularis propria; OTSC, over the scope clips; SELs, sub-epithelial lesions; TTS, through the scope.
EFTR is known as hybrid NOTES. These include: LAEFR—laparoscopy-assisted endoscopic full thickness resection (EFTR), NEWS—non-exposed endoscopic wall-inversion surgery, NESS-EFTR: non-exposure simple suturing EFTR with or without lymphadenectomy in gastric SELs/EGC/dueodenal NET, etc. (Table 6). Modified laparoscopic intragastric surgery in which resection is performed under endoscopic vision by laparoscopic instruments has been described for gastric GIST. NESS-EFTR has the advantage of preventing peritoneal seeding in EGC. Sentinel lymph node dissection under laparoscopic guidance using Tc-99m-phosphate and indocyanine green is feasible as shown in SENORITA 3 pilot study. Direct endoscopic visualization can reduce excessive gastric resection and can avoid gastrectomy in majority. Manual suture or linear stapler is used for suturing. Postoperative leak and stasis are the adverse events.

Competing Technologies
EFTR can be performed by ESD, FTRD, Hybrid NOTES, hybrid EFTR, and transanal endoscopic microsurgery (TEMS) for rectal tumors. The major limitation of FTRD is the maximum size of the lesion that can be treated. This can be overcome by hybrid EFTR. Hybrid NOTES techniques could be useful for oncologic resection of EGC and for SELs. For small SELs, EFTR is a better option than hybrid NOTES. Large rectal tumors can be resected in full thickness by TEMS as a primary therapy after FTRD failure.

Comparative Studies between Different Techniques of EFTR
Studies have compared EFTR modalities with different levels of invasiveness: surgery, laparoscopy-assisted EFTR, TEMS, ESD, STER, and FTRD, etc. Laparoscopic resection and EFTR showed comparable en bloc resection rates, operating time, hospital stay and complications. For GIST <2 cm, EFTR was associated with lower complication rates with comparable R0 resection rates compared with LECS. For gastric SELs with MP involvement, EFTR was associated with lower cost, faster postoperative recovery compared with surgery with higher en bloc resection rates with surgery for tumors >3 cm. Recent studies comparing non-exposed EFTR and laparoscopy-assisted EFTR showed higher procedure time (110 vs. 189 minutes; p < 0.0001) with the lower rate of tumor seeding with the former.

EFTR was shown to be equally effective compared with TEMS for rectal NETs with shorter operating time. Cap-assisted EFTR was shown to be particularly helpful for small GIST (<1.5 m) shorter operating time with lower complication rates. Dental floss traction can reduce the operating time with lower incidence of electrocoagulation syndrome for gastric fundal SELs originating from MP. A study comparing STER with EFTR for gastric GIST showed similar R0 resection rates, operating time, and complication rates whereas suture time and clip requirement were lower with STER. However, STER can be technically difficult in areas like stomach and rectum where tunnelling can be challenging. Another study comparing ESD and EFTR for colonic neoplasia <3 cm showed higher technical success.

Table 6 Summary of studies evaluating hybrid endoscopic full thickness resection (EFTR) and hybrid natural orifice trans-luminal endoscopic surgery (NOTES)

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Diagnosis</th>
<th>Method</th>
<th>Number</th>
<th>Tumor size (mean, mm)</th>
<th>Complete reaction rate (%)</th>
<th>Closure method</th>
<th>Conversion to gastrectomy</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abe et al</td>
<td>2009</td>
<td>Early gastric cancer (EGC)</td>
<td>LAEFR</td>
<td>1</td>
<td>30</td>
<td>100</td>
<td>Manual suture</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>Abe et al</td>
<td>2009</td>
<td>Gastric SET</td>
<td>LAEFR</td>
<td>4</td>
<td>37</td>
<td>100</td>
<td>Manual suture</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>Cho et al</td>
<td>2011</td>
<td>EGC</td>
<td>Hybrid NOTES</td>
<td>14</td>
<td>26</td>
<td>100</td>
<td>Linear stapler plus manual suture</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>Mori et al</td>
<td>2015</td>
<td>Gastric GIST</td>
<td>Hybrid EFTR</td>
<td>16</td>
<td>28.3</td>
<td>100%</td>
<td>Suture</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Kwon et al</td>
<td>2015</td>
<td>SET</td>
<td>Hybrid EFTR</td>
<td>6</td>
<td>31</td>
<td>100%</td>
<td>Manual suture</td>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Eom et al</td>
<td>2020</td>
<td>EGC</td>
<td>NESS-EFTR</td>
<td>18</td>
<td>16.5</td>
<td>83.3%</td>
<td>Laparoscopic suturing with endo-loops</td>
<td>Sentinel lymph node</td>
<td>None</td>
</tr>
<tr>
<td>Mahawongkajit et al</td>
<td>2020</td>
<td>Upper GI SETs</td>
<td>LAEFR</td>
<td>16</td>
<td>56 (LECS), 21 (NEWS)</td>
<td>100%</td>
<td>Staple or suture</td>
<td>No</td>
<td>None</td>
</tr>
</tbody>
</table>
Fig. 6  Schematic representation of different hybrid natural orifice transluminal endoscopic surgery (NOTES) techniques, their specific indications, and classification of gastric subepithelial tumors (SETs). CLEAN-NET, combination of laparoscopic and endoscopic approaches for treatment of neoplasia with a non-exposure technique; EGJ: esophagogastric junction; ESD, endoscopic submucosal dissection; LAEFR, laparoscopy-assisted endoscopic full thickness resection; NEWS, non-exposed endoscopic wall-inversion surgery; LECS, laparoscopic endoscopic co-operative surgery; LTGS, laparoscopic transgastric surgery; MLIGS, modified laparoscopic intra-gastric surgery; NESS-EFTR, non-exposure simple suturing EFTR.

Table 7 Advantages and limitations of various endoscopic full thickness resection (EFTR) techniques

<table>
<thead>
<tr>
<th>Method</th>
<th>Dissection technique</th>
<th>Closure technique</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposed EFTR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-tunneling techniques</td>
<td>ESD</td>
<td>Loop and clip, OTSC, endoscopic suturing device</td>
<td>Higher technical success and R0 resection</td>
<td>High risk of perforation, peritoneal seeding and technically challenging closure in collapsed stomach</td>
</tr>
<tr>
<td>Tunneling technique</td>
<td>STER: Submucosal tunnelling and tumor dissection</td>
<td>Mucosal closure</td>
<td>Low risk of peritoneal contamination and tumor seeding</td>
<td>Feasible for lesions &lt; 4 cm and mainly distal esophageal and gastric cardia lesions, may not be feasible to create tunnel in all anatomical locations</td>
</tr>
<tr>
<td>Non-exposed EFTR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FTRD</td>
<td>Snare fitted with FTRD device</td>
<td>OTSC clip</td>
<td>High technical and en bloc resection rates, enables full thickness biopsy, useful for recurrent and non-lifting lesions and difficult locations; shorter procedure time</td>
<td>Not feasible for large tumors (&gt; 25 mm), risk of appendicitis, small bowel entrapment and resultant enterocolonic fistula</td>
</tr>
<tr>
<td>Non-exposed endoscopic wall-inversion surgery (NEWS)</td>
<td>Excision using ESD technique after tumor inversion into lumen using laparoscopic guidance</td>
<td>Laparoscopic suturing prior to resection followed by endoscopic suturing after resection</td>
<td>Low risk of peritoneal contamination and tumor seeding</td>
<td>Applicable for small lesions as tumor is retrieved endoscopically</td>
</tr>
<tr>
<td>Hybrid NOTES</td>
<td>Dissection using endoscopic and laparoscopic stapling device</td>
<td>Laparoscopic stapling device</td>
<td>Anatomic and functional preservation of gut by precise definition of tumor boundary, can allow oncologic resection with lymphadenectomy for superficial GI carcinoma</td>
<td>Risk of peritoneal contamination and tumor seeding</td>
</tr>
<tr>
<td>Hybrid EFTR</td>
<td>EMR/ESD/Band ligation followed by OTSC and final resection</td>
<td>OTSC closure with or without additional TTS clip closure</td>
<td>Complete endoscopic full thickness resection can be performed for large lesions</td>
<td>May not be technically feasible for all lesions, tumor removed piecemeal, cannot exclude possibility of lymph nodal dissemination</td>
</tr>
</tbody>
</table>

Abbreviations: ESD, endoscopic submucosal dissection; FTRD, full thickness resection device; OTSC, over the scope clips; STER, submucosal tunnelling and endoscopic resection; TTS, through the scope.
and R0 resection with lower complications and operating time with EFTR although risk of residual neoplasia is higher.\textsuperscript{125} Pre-resection closure with OTSC followed by snare was shown to be faster with lower complications compared with ESD followed by post-resection OTSC closure.\textsuperscript{126}

A recent cost-effectiveness analysis showed that EFTR is cost effective not only with respect to surgery but also other minimally invasive endoscopic techniques for complex colorectal lesions.\textsuperscript{127}

**Limitations and Other Potential**
Advantages and limitations of various EFTR techniques have been described in \textsuperscript{–}Table 7.

EFTR has been used in other settings as anecdotal reports as in endoscopic transgastric fenestration for pancreatic walled off necrosis, EFTR of ectopic splenic nodules, EFTR of Dieulafoy’s lesion and in special situations (post liver transplant scenario and on anticoagulation).\textsuperscript{128–132}

**Complications**
Apart from well-known complications of EFTR like perforation and bleeding (immediate or delayed), post-polypectomy syndrome, appendicitis (occlusion of appendicular orifice),\textsuperscript{133} other unique adverse events have been described with EFTR. Overall complications occur in 12% of the patients.\textsuperscript{51} Colonic obstruction by OTSC clip and delayed perforation post-EFTR in suspected gastroparesis due to over-distension have been reported.\textsuperscript{134,135} Fracture of FTRD device snare wire warranting additional snare resection and/or TEMS are among other adverse events.\textsuperscript{118,136} The risk of tumor seeding during EFTR of EGC can be minimized by non-exposure technique.\textsuperscript{137} Enterocolonic fistula with small bowel intussusception causing peritonitis and mortality have been described following OTSC closure after resection of rectal LST.\textsuperscript{138}

**Contraindications**
Contraindications to EFTR include locally (nodal or extraluminal vascular invasion) or systematically advanced tumor and tumors with malignant potential (e.g., GIST) larger than 5 cm. Tumors greater than 3 to 4 cm in shortest diameter are often difficult to extract per orally without piecemeal removal.\textsuperscript{139}

**Learning Curve**
EFTR being a relatively new modality, there are no validated objective tool to assess competency in EFTR. Moreover, the learning curve and style may vary with each trainee. Hence specific feedback from the mentor is essential at least in the initial phase. It is important to recognize that device-assisted EFTR (e.g., FTRD) has shorter learning curve compared with conventional EFTR.\textsuperscript{140}

**Post OTSC Clip Artifact**
It is important to recognize different forms of post clipping artifact post-OTSC which can range from central depression, central erosion, semi pedunculated polypoid lesions, and even leiomyoma like mesenteric cell proliferation due to its bear claw configuration and transmural tissue capture.\textsuperscript{141–144} Examination of the surface pattern on white light/narrow band imaging is thus important to differentiate artifacts from recurrent/residual lesion which may warrant aggressive procedures like re-FTRD or surgery.\textsuperscript{143}

**Conclusion**
Exposed and non-exposed EFTRs are emerging techniques for the resection of non-lifting or recurrent adenoma associated with fibrosis, SELs with deeper invasion, and superficial GI neoplasia. Newer dissection, traction, and closure devices have revolutionized the techniques of EFTR. Novel methods like hybrid EFTR, hybrid NOTES, and novel robotic EFTR have the potential of expanding the indications of EFTR in future and enable even oncologic resection. Technological technical advances can further improve clinical outcomes in EFTR.

**Authors’ Contribution**

**Funding**
None.

**Conflict of Interest**
None declared.

**Acknowledgment**
None.

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