Techniques in Gastrointestinal Endoscopy 17 (2015) 108–111

Contents lists available at ScienceDirect

Techniques in Gastrointestinal Endoscopy

journal homepage: www.techgiendoscopy.com/locate/tgie

Identification and preparation of lesions suitable for endoscopic full-thickness resection

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ARTICLE INFO

Article history:
Received 30 January 2015
Accepted 20 June 2015

Keywords:
Endoscopic full-thickness resection
endoscopic mucosal resection
endoscopic submucosal dissection

ABSTRACT

Recent technological advances in the field of gastroenterology have revolutionized the way endoscopy is used to manage both premalignant and malignant lesions throughout the gastrointestinal tract. For many decades, endoscopic treatment was limited to superficial mucosal lesions. However, with the advent of endoscopic mucosal resection in 1992, the armamentarium of the endoscopist started to expand. More recently, endoscopic submucosal dissection and endoscopic muscularis dissection have emerged as therapeutic methods for overcoming the limitations of endoscopic mucosal resection. For deep submucosal lesions that may be challenging or technically impossible to remove with these latter methods, is there a role for taking dissection even 1 step (ie, layer) further? To help answer this question, we address the preparation and identification of lesions that may be suitable for endoscopic full-thickness resection.

1. Introduction

Recent technological advances in the field of gastroenterology have revolutionized the way endoscopy is used to manage both premalignant and malignant lesions throughout the gastrointestinal (GI) tract. For many decades, endoscopic treatment was limited to superficial mucosal lesions through polypectomy with the use of biopsy forceps or use of hot or cold snare. However, with the advent of endoscopic mucosal resection (EMR) described by Inoue et al [1] in 1992, the armamentarium of the endoscopist started to expand.

More recently, endoscopic submucosal dissection (ESD) has emerged as a therapeutic method for overcoming the limitations of EMR, namely allowing for greater success of en bloc resections, collection of intact specimens, and lower rates of local recurrence [2]. Standard ESD techniques have been applied for mucosa-based lesions as well as for lesions originating from the submucosal layer. In the latter case, this has been accomplished with dissection of the submucosa below the lesion under direct vision [3].

Standard and modified ESD techniques have since been applied to the management of lesions with involvement of the muscularis propria (MP) [4]. In some studies, these techniques have been labeled as endoscopic muscularis dissection (EMD). Initial trials involving subepithelial tumors of the gastric wall demonstrated success rates of en bloc resection of these deeper lesions in the range of 64%-75% [5-7]. Further investigation by Li et al [8] in 2012 demonstrated improved success of ESD or EMD in the management of gastroesophageal tumors arising from the MP. In this study, 94% of 143 tumors were completely resected en bloc, and follow-up over a mean of 21 months demonstrated no local recurrence of tumor or distant metastatic disease. Similarly, Liu et al [9] found EMD successful in achieving en bloc resection in 30 of 31 (96.8%) MP-based upper GI tract tumors.

With the rates of success demonstrated in these studies, is there a role for taking dissection even 1 step (ie, layer) further? To help answer this question, we address the preparation and identification of lesions that may be suitable for endoscopic full-thickness resection (EFTR). To help clinicians make appropriate referrals, we discuss the imaging of subepithelial lesions, the existing relevant guidelines from the GI and oncologic societies, the inclusion criteria used in previous studies of EFTR, and the results and experiences reported by the authors in the aforementioned studies.

2. EFTR—a brief history

A discussion of the indications for performing EFTR obviates a basic understanding of the involved technique and demonstrated success rates published in case series and clinical trials. Despite its relatively recent introduction into the endoscopic theater, EFTR

The author reports no direct financial interests that might pose a conflict of interest in connection with the submitted manuscript.

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http://dx.doi.org/10.1016/j.tgie.2015.06.002
0049-0172/

has already undergone several modifications and revisions of technique. In its very fundamental form, EFTR typically involves a submucosal dissection followed by an incision into the serosal layer around the tumor, a full-thickness resection of the tumor including the serosal layer, and closure of the GI tract wall defect [10]. Specific methods of EFTR are discussed in full detail in separate articles in this journal edition.

Reports of the use of EFTR in the literature are limited because of the recent introduction of this endoscopic method and the expertise required to perform such procedures. EFTR with a snaring technique was first reported by Suzuki and Ikeda [11], in which the authors described the successful removal of 1 duodenal carcinoid and 2 rectal carcinoid tumors. In 2011, Zhou et al [12] described the successful use of EFTR (without laparoscopic assistance) in 26 patients with gastric subepithelial tumors originating from the MP; no serious complications were reported and no evidence of tumor recurrence was noted in a follow-up period ranging from 6-24 months.

In a smaller case series, Bona et al [13] reported successful EFTR of 4 large leiomyomas involving the cardia. In 2013, Shi et al [14] reported a retrospective analysis of 20 patients with gastric tumors arising from the MP with a 100% en bloc resection rate. Also in 2013, Schlag et al [15] conducted a prospective study of 20 patients with gastric subepithelial tumors, where EFTR was successfully performed in 70% of cases. In 2014, in 2 separate publications, Huang et al [10,16] reported 100% success in complete resection of 67 gastric MP-based subepithelial tumors.

EFTR has also been reported in the treatment of gastric mucosal lesions involving high-grade dysplasia where repeated ESD failed due to diffuse edema and unclear margins [17]. Limited experiences have also reported on EFTR (with laparoscopic assistance including lymphadenectomy) as a treatment modality of gastric adenocarcinoma [18,19]. In one of these studies involving 14 patients, tumor-free margins were achieved in all patients, though 5 cases were converted to a gastrectomy.

EFTR has also not been limited to the stomach. In 2010, Tsujimoto et al [20] reported 2 cases in which EFTR was used in the resection of duodenal carcinoid tumors under laparoscopic observation. In 2013, Xu et al [21] conducted a prospective pilot study to evaluate the feasibility, safety, and efficacy of EFTR of colonic submucosal lesions. In this study, endoscopic resection of the entire intact tumor capsule was achieved in 18 of 19 patients; in 2 patients laparoscopic closure of the colonic wall defect was needed.

3. Identifying lesions suitable for EFTR

3.1. Initial workup

In terms of procedural workup before referral, it is now accepted that endoscopic ultrasonography (EUS) has become the gold standard in evaluating lesions to assess the depth of invasion or origin and help guide diagnostic maneuvers such as fine-needle aspiration or biopsy. However, endoscopists should be aware that EUS is not a perfect study, and occasionally a planned ESD needs to be converted or modified to allow for deeper dissection including EFTR [8]. Using ESD as the standard of reference, Bialek et al [6] found EUS to be only 73% accurate in determining the origin of gastric subepithelial tumors in a series of 37 patients. The authors attributed most errors in staging to the presence of thin muscular fibers or an unapparent stalk between the tumor and MP.

Chu et al [22] formally evaluated the use of EUS and computed tomography (CT) imaging in 72 patients with GI subepithelial tumors. These patients were planned to undergo endoscopic removal with either submucosal excavation, submucosal tunneling endoscopic resection, or EFTR. After randomization of 36 patients to receive EUS plus CT scan and 36 patients to receive EUS alone, the authors analyzed the concordance between the preplanned endoscopic procedure and the actual procedure performed. The concordance rate was higher in the group that received EUS and CT evaluation compared with the EUS group alone (83.3% vs 61.1%, $P < 0.05$), and furthermore procedure times were shorter and propofol doses were lower in those receiving EUS and CT by a significant degree. The authors postulated that CT imaging can often provide greater understanding of the entire tumor in question, helping define relationships to adjacent structures and clarifying depth of invasion when EUS is not entirely clear.

If a subepithelial lesion is identified to be a GI stromal tumor (GIST) based on biopsy results, CT of the abdomen and pelvis is preferred as the initial imaging study according to recent National Comprehensive Cancer Network (NCCN) guidelines [23]. This is owing to the fact that up to 47% of patients with malignant GISTs, depending on the size and mitotic activity of the primary tumor, have metastatic disease at the time of presentation [24]. For patients with primary rectal GISTs, magnetic resonance imaging (MRI) may offer improved anatomical detail. For submucosal lesions identified as carcinoid tumors, initial imaging with multiphase CT or MRI should be used to evaluate for metastatic disease involving the liver, and octreotide scans can be ordered as appropriate [25].

If a mucosal lesion in the stomach is biopsied and identified as a gastric cancer, the NCCN guidelines [26] similarly recommend imaging of the chest and abdomen with CT, as well as EUS if no evidence of metastatic disease is detected. Multidisciplinary review is advised to help guide further workup.

3.2. Review of existing treatment guidelines

Most studies employing EFTR have involved management of subepithelial tumors within the upper GI tract. These tumors may be benign, such as leiomyomas or lipomas. However, they can also be malignant, as seen with GISTs, lymphomas, and carcinoid tumors. In general, any lesion that is symptomatic (even if biopsied and found to be benign) or suspected or found to be malignant without evidence of metastasis should be considered for definitive treatment.

Optimal management of GISTs, the most commonly identified subepithelial mass encountered in the upper GI tract, remains controversial. All GISTs have malignant potential, but there is debate as to whether the risks of surgical resection are acceptable for dealing with small lesions (less than 2 cm) with a low potential for growth and spread. The American Gastroenterological Association suggests that treatment decisions for GISTs (ie, surveillance vs surgery vs endoscopic therapy) be made on an individual basis given the lack of sufficient evidence to guide management [27]. This review outlines different approaches reported in case studies for dealing with lesions arising in the MP layer, including removal with polypectomy snare [28], enucleation [29], band ligation [30], and insulated-tip electrosurgical knife [31]. However, given the early publication date, no mention is made of EFTR, and no definitive recommendations are made on endoscopic therapy for GISTs, citing the need for further clinical investigation.

In a recent review of the NCCN, Kneisl et al [23] note that, “despite advances in systemic therapy, surgery remains the only potentially curative therapy for GIST.” Although the authors state that GISTs 2 cm in size or greater should be resected, the guidelines recommend that smaller GISTs (less than 2 cm) may be observed endoscopically in the absence of high-risk EUS features. Similar to the American Gastroenterological Association review, it is noted that resection requires merely a negative margin, without need for wide margins as required by other sarcomas given a low