Journal of Translational Gastroenterology **2023** vol. 1(1) | 40–46
DOI: 10.14218/JTG.2023.00001

Review Article

Endoscopic Resection of Gastrointestinal Lesions: Preference and Feasibility of *En bloc* Resection Techniques

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Received: January 28, 2023 | **Revised:** March 21, 2023 | **Accepted:** April 20, 2023 | **Published online:** June 06, 2023

Abstract

Gastrointestinal (GI) malignancies account for over a quarter of all new cancer diagnoses worldwide, and pose a significant burden on public health. As endoscopes are improved over the years, upgraded high-definition cameras have allowed for better polyp detection. Due to the absence of symptoms in GI malignancy, lesions are often incidentally detected in various stages by endoscopists. Careful polyp morphology evaluation and classification is paramount when selecting the most appropriate endoscopic (or surgical) resection method. The technique that would allow for an *en bloc* or R0 resection is preferred (endoscopic submucosal dissection [ESD]), while those that present with lower risk features can be reasonably removed in a piecemeal fashion or hybrid fashion with care in ablating clean margins to decrease recurrence. Although Eastern and European endoscopists have more experience in ESD, this expertise is not widely available in North America. The present study aims to explore the following questions: (1) Is ESD always necessary? (2) In which scenarios are ESD always indicated? (3) Can endoscopic mucosal resection be used to achieve resection goals, since this expertise is more widely available and has an easier learning curve?

Introduction

Luminal gastrointestinal (GI) malignancies (esophageal, gastric and colorectal) account for over 20% of newly diagnosed cancers and related deaths worldwide.[1] Although various societies have provided guidance for population wide screening, its early detection, particularly in asymptomatic individuals, remains a difficult task, and at present, its diagnosis is primarily made based on endoscopic evaluation.[2] Endoscopists consequently encounter lesions that range from clearly amenable and endoscopic resections (i.e. small tubular adenomas and sessile serrated polyps), to malignant masses that are more suited for surgical resection (i.e. invasive carcinoma with local or regional metastasis). Differentiating lesions and predicting the depth of invasion based on endoscopic appearance is imperative, since surgery for non-malignant lesions carries significant morbidity and mortality, and healthcare cost burdens.[3–5] Over the years, endoscopic advancements have been developed, refined and validated as the preferred first-line method for appropriately selected lesions.[6–9]

Endoscopic resection methods have advanced over the last two decades, and these presently range from simple polypectomy to endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), and endoscopic full thickness resection (EFTR). Various techniques exist for EMR, including submucosal injection/lifting, cap assisted, band ligation technique, and underwater.[10] Although EMR has been well-described, *en bloc* resection remains limited due to the snare size, and piecemeal resections lead to recurrences, which have been reported in up to 20% for colonic lesions and 30% for esophageal dysplasia.[11,12] ESD was first described in Japan in 1988 for gastric neoplasia, and its indication has since expanded to other parts of the GI tract, emerging as the preferred method for complex lesion resection.[13,14] In ESD, the lesion is circumferentially marked with visible clear margins, followed by submucosal injection of the lifting agent, and dissection by an electrosurgical knife to allow for *en bloc* resection, regardless of the tumor size, and for lesions that are fibrotic and "non-lifting" for EMR.[15] EFTR was first described in Japan in 1998 for the full thickness excision of GI tract lesions. The lesion is circumferentially marked and gently suctioned, and an over the scope clip is deployed with the subsequent removal of the lesion with the serosa.[16] However, this method is generally limited to lesions of ≤2 cm due to the over the scope clip.[17] The challenge

Keywords: Endoscopic submucosal dissection; Endoscopic mucosal resection; Hybrid endoscopic submucosal dissection; Endoscopy.

Abbreviations: EFTR, endoscopic full thickness resection; EMR, endoscopic mucosal resection; ESCC, esophageal squamous cell cancer; ESD, endoscopic submucosal dissection; GI, gastrointestinal; H-ESD, hybrid endoscopic submucosal dissection; HGD, high grade dysplasia; JGES, Japanese Gastrointestinal Endoscopy Society; LST, lateral spreading tumor; NET, neuroendocrine tumor.

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How to cite this article: Weng E, Dharan M. Endoscopic Resection of Gastrointestinal Lesions: Preference and Feasibility of *En bloc* Resection Techniques. *J Transl Gastroenterol* 2023;1(1):40–46. doi: 10.14218/JTG.2023.00001.

remains in the recognition of lesions that are candidates for endoscopic resection, and the subsequent selection of the most suitable endoscopic technique.

Several methods of endoscopic lesion stratification based on gross morphology and polyp surface patterns have been proposed to predict the histology and depth of invasion.

The use of narrow-band imaging (NBI), which leads to the NBI international colorectal endoscopic (NICE) classification, has been studied to be applied without optical magnification.[18] The Japanese universal NBI magnifying endoscopic (JNET) classification was proposed, and this has been widely used to further differentiate low-grade from high-grade neoplasia, based on the surface and vessel patterns.[19] The Paris Classification developed in 2002, and the lateral spreading tumor (LST) subtypes are additional tools for lesion architectural assessment in risk of deep invasion and lymph node metastasis.[20] A number of endoscopic classifications exist to guide the endoscopic identification of lesions that can be candidates for endoscopic resection.

Is ESD always necessary?

ESD is a safe and validated endoscopic resection method for GI tract lesions, including carcinoma *in situ*, with the advantage of allowing *en bloc* resections, regardless of the lesion size. Although this has benefits, this approach is not always necessary or an available option, depending on the local endoscopy expertise, particularly in North America, when compared to its Asian counterparts. Although this is certainly the preferred and recommended method for lesions that require confirmation of the negative margins by pathologists (which cannot be determined when removed in a piecemeal fashion), not all GI tract lesions carry the same invasion risk, and need to be removed *en bloc*. Ultimately, endoscopic resection has been generally reserved for lesions confined to the lamina propria for curative intent, or alternatively for staging purposes.

The careful endoscopic examination of the lesion morphology (using the Paris and LST classification), surface pattern (utilizing the NICE, JNET and Kudo classifications, among others) and size can provide clues to the lesion invasion depth, and guide the resection approach. For example, esophageal squamous cell carcinomas (ESCCs) of ≤15 mm can be removed using EMR or ESD, given the similar *en bloc* resection rate and five-year local recurrence rate.[21] A 2021 meta-analysis also suggested that for ESCC, Barrett's esophagus-associated neoplasia, and esophageal adenocarcinoma (EAC), the choice of EMR vs. ESD can be risk stratified based on the lesion size. Thus, lesions of ≤10 mm would be appropriate for EMR, lesions of >20 mm should be resected with ESD, and either of these approaches would be acceptable for lesions within 11–20 mm.[22] For visible lesions, specifically in Barrett's esophagus, EMR should be preferred over ESD, unless the lesion is larger, does not lift, or has a risk of submucosal invasion.[7] Similarly, gastric tumors can be stratified based on size, although increasing evidence suggests higher rates of recurrences, showing that ESD is more preferred, particularly for lesions with ulceration, and located in more proximal locations, which are predictors of non-curative resection.[23] In the colon, LST granular type lesions have been shown to have the lowest rate of submucosal invasion, and these can be generally removed by piecemeal EMR with cauterization of the clean margins, in order to decrease the recurrence rate.[24] It was also advised that areas with ulceration (which would be a concern for carcinoma) should be removed in one piece, and not transected as part of a piecemeal resection. Similar to the other areas of the GI tract, larger lesions tend to have higher rates of T1 carcinoma, and EMR for these cases would be less ideal.[8]

In which scenarios are ESD always indicated?

The absolute indications of ESD varies, depending on the GI lesion location, and the endoscopy society guidelines (Table 1).[7–9,25,26] This is primarily due to the variance in metastasis risk with various tumor depth invasions to different parts of the GI tract due to the lymphatic drainage location.

In the esophagus, Barrett's esophagus-associated lesions can be typically removed *en bloc* by EMR. However, high-grade dysplasia to moderately differentiated adenocarcinoma T1a (m1-m3) lesions of >15 mm should be removed with ESD. Furthermore, ESCCs with moderate to well differentiated histology, m1-m2 involvement, Paris 0-II lesion morphology, and involving less than two-thirds of the esophageal circumference should undergo ESD. Expanded indication include lesions that are within 200 μm of the submucosal layer.[27] Lesions with m3 to sm1 can also be referred for ESD, *albeit* for staging purposes.[9] Overall, ESD should be attempted for superficial ESCCs (carcinoma limited to the mucosa or submucosa), given the less significant difference in recurrence and long-term outcomes, when compared to esophagectomy, and the significantly decreased risk of complication and all-cause mortality.[28]

For gastric lesions, the European Society of Gastrointestinal Endoscopy (ESGE) recommends ESD over EMR, unless the lesion is smaller than 10–15 mm, with low risk features (Paris 0-IIa).[7] The American Gastroenterology Association (AGA) elaborates on this, and ESD is absolutely indicated for mucosal adenocarcinomas and lesions with high grade dysplasia (HGD) that are well- or moderately differentiated (G1 or G2), have no ulceration, and are ≤2 cm in size. Expanded indications include well-differentiated adenocarcinomas (without ulceration of any size, submucosal invasive [<500 μm], or ≤3 cm with ulceration), or low or undifferentiated (G3, G4) diffuse type adenocarcinomas without ulceration of ≤2 cm in size.[9] The Japanese Gastric Cancer Association released guidelines in July 2021, and recommends the absolute indication for ESD as lesions that are differentiated-type adenocarcinomas without ulcerative findings (T1a and >2 cm in diameter), differentiated-type adenocarcinomas with ulcerative findings (T1a and ≤3 cm in diameter), or undifferentiated-type adenocarcinomas without ulcerative findings (T1a and ≤2 cm in diameter). Expanded indications include locally recurring lesions that are T1a.[25]

The duodenum is unique, because it is highly vascular with a thin muscularis propria, and exposed to various GI secretions. This makes ESD more technically difficult, given the high risk of adverse events, including bleeding and perforation.[9] Due to this, the ESGE previously recommended against ESD, but have since revised this in the 2021 guidelines to recommend ESD for duodenal adenomas. However, overall, this still maintains the safety that should be emphasized over R0 resection, with preference for EMR, in addition to prophylactic post-endoscopic resection closure.[29] In countries with more expert ESD experience, ESD in the duodenum has a higher R0 resection rate, with 0% recurrence rate cited.[30] In Japan, the general expert consensus is in favor of ESD for duodenal lesions of ≥20 mm, given that there is no significant difference in adverse events between ESD and non-ESD resection for lesions of >19 mm.[31]

In the colon, non-granular pseudo-depressed (NG-PD) colon LSTs were identified to have the highest risk (85.5%) of containing HGD or carcinoma, with a rate of 12.9% when invading the submucosa.[32] A study reported that nodular mixed-type LST has a higher risk of malignancy potential, with an odds ratio of 2.41.[33] Another independent risk factor is the lesion size, in which larger lesions have

Table 1. Absolute indications for ESD across Asia, Europe, and North America, adapted from Draganov, Ishihara, Pimentel-Nunes, Tanka, and Japanese Gastric Cancer Association[7–9,25,26]

	JGES	ESGE	AGA
Esophagus absolute indications	Non-circumferential ESCC, T1a- MM/T1b-SM1	Squamous cell: m1-m2 involvement; well-differentiated m3/sm1 tumor (≤200 μm) without lymphovascular invasion, and with low risk of metastasis. Barrett's esophagus: ≥15 mm; poor mucosal lift; risk of submucosal invasion.	Squamous cell: HGD to well (G1)- to moderately (G2)-differentiated; Paris 0-II lesions; m1-m2 involvement with ≤2/3 of esophageal circumference. Barret's esophagus: HGD to moderately (G1 or G2) differentiated T1a (m1-m3) lesions ≥15 mm; large or bulky area of nodularity; equivocal pre-procedure histology; lesions with a high likelihood of superficial submucosal invasion; intramucosal carcinoma; recurrent dysplasia; EMR with invasive carcinoma and positive margins.
Esophagus expanded indications	(weakly recommended) Circumferential ESCC with a major axis length of ≤50 mm		ESCC m3 or sm of <200 μm, clinically N0
Stomach absolute indications	Differentiated-type adenocarcinoma without ulceration, T1a, >20 mm; Differentiated-type adenocarcinoma with ulceration, T1a, ≤30 mm	Any lesion with very low possibility of lymph node metastasis	Nonulcerated mucosal lesions (adenocarcinoma, HGD), intestinal type, G1 or G2 differentiated that are ≤20 mm
Stomach expanded indications	Undifferentiated-type adenocarcinoma without ulceration, T1a, ≤20 mm		Adenocarcinoma, intestinal type, G1 or G2 differentiation, any size, without ulceration; Adenocarcinoma, intestinal type, G1 or G2 differentiation, sm-invasive (<500 μm); Adenocarcinoma, intestinal type, G1 or G2 differential, ≤30 mm with ulceration; Adenocarcinoma, diffuse type, G3 or G4 differentiation, ≤20 mm, without ulceration; Any size, without ulceration
Duodenum		"ESGE does not recommend the routine use of ESD for duodenal or small-bowel lesions"	Reserved for endoscopists with extensive ESD experience due to high risk of adverse events
Colon	Type V kudo pit pattern; Large depressed-type tumors; Large protruded-type lesions suspected to be carcinoma; Non-granular LST; Carcinoma with T1 (sm) invasion; Mucosal tumors with submucosal fibrosis ; Tumors in chronic inflammatory disease states; Residual or recurrent early carcinoma	Depressed morphology; Irregular or non-granular surface pattern; Lesions of ≥20 mm	Type V kudo pit pattern; Depressed component (Paris 0-IIc); Complex morphology (0-Is or 0-IIa+Is); Rectosigmoid location; Non-granular LST ≥20 mm; Granular LST ≥30 mm; Residual or recurrent colorectal adenomas

AGA, American Gastroenterological Association; EMR, European Society of Gastrointestinal Endoscopy; ESCC, Esophageal squamous cell cancer; HGD, high-grade dysplasia; JGES, Japanese Gastrointestinal Endoscopy Society; LST, lateral spreading tumor.

an increased risk of deeper submucosal invasion.[34] Subsequently, LST-NG should be particularly removed with ESD. In addition, lesions with a highly disorganized pit pattern (type V kudo pit pattern), carcinomas with shallow invasion, large depressed tumors (Paris 0-IIc), or those with protruding lesions suspicious for carcinoma should be removed with ESD.[35] The Japanese Gastroenterological Endoscopy Society (JGES) published guidelines for colorectal lesion resection, and recommended the ESD indication for lesions that cannot be otherwise removed *en bloc* with EMR, mucosal tumors with submucosal fibrosis, sporadic localized tumors in chronic inflammatory conditions (such as inflammatory bowel disease), and local residual or recurrence of previously resected early carcinomas.[8] The ESGE guidelines published in 2015 also had similar recommendations, with limitations placed on ESD for lesions with a histology of well-differentiated adenocarcinomas with ≤1 mm submucosal invasion and lymphatic involvement.[7] The American Gastroenterological Association (AGA) guidelines are similar to both the ESGE and JGES guidelines, which recommend ESD for lesions at risk of submucosal invasion, and in addition to disorganized pit patterns and depressed components, these guidelines also notes complex morphology (0-Is or 0-IIa+Is), rectosigmoid location, NG-LST of ≥20 mm, and granular LST of ≥30 mm as high-risk lesions.[9]

Can EMR be used to achieve resection goals, since this expertise is more widely available and has an easier learning curve?

The barrier to the wide-spread implementation of ESD in North America has been multifactorial, including its steep learning curve

and access to mentors. The difficulty of the procedure execution varies based on the lesion location, with the esophageal, colon and small bowel being more challenging than rectal and gastric lesions.[36] In the West, more colonic lesions are generally encountered, when compared to gastric lesions, during training, making ESD an even more difficult skill to learn. The number of cases required to achieve proficiency has been quoted to reach up to 250 cases in the colon to achieve 80% R0 resection more than 80% of the time, and up to 400 cases to achieve R0 resection more than 95% of the time.[37] Given these limitations, various endoscopic resection techniques have been described, including the development of the underwater, adjunctive therapy, and hybrid approach.[38]

The *en bloc* resection by conventional EMR remains limited due to the available snare size and polyp characteristics, such as prior manipulation and fibrosis. Piecemeal EMR has a higher recurrence (increases with the number of resected neoplasm specimens), which was cited to reach 20%, when compared to the 3% for *en bloc*, and this was mostly detected at six months after EMR.[39,40] The EMR of lesions of ≥4 cm and intraprocedural bleeding are additional risk factors for local recurrence.[41] Thus, present practice recommends a repeat endoscopic evaluation at 6–12 months after the piecemeal removal of the polyp.[9] In order to decrease the risk of recurrence, adjunctive techniques should be employed. The residual visible polyp should be removed by hot avulsion, which has been considered to be superior to argon plasma coagulation (APC), with a recurrence rate of 10.3% vs. 59.3%.[42] Hot avulsion can be performed by using (hot biopsy) forceps to grasp the residual polyp, applying traction, while applying low voltage cutting current to shear the remnant tissue.[43,44] Subsequent studies have revealed that EMR through the hot avulsion technique has a similar local recurrence rate, when compared to lesions resected by EMR that did not require hot avulsion.[43] After the piecemeal EMR with the complete removal of all residual polyps, the resection margin should undergo thermal treatment with APC or snare tip soft coagulation, in order to further reduce the risk of recurrence due to microscopic residual disease at the edges, from 20% to 5%.[41,45–47] Snare tip coagulation is performed by exposing 1–2 mm of the snare tip, and lightly touching it to the resection margin using a low voltage setting (i.e. soft coagulation) to create a circumferential 2–3 mm rim around the resection defect.[46] APC and snare tip coagulation were compared in a study, and there was no significant difference in adverse effects and recurrence rate after the resection of large LST lesions, while the snare-tip was a more cost efficient option.[48] Motchum *et al*. investigated the recurrence rate of large pedunculated colon polyps (average: 30 mm) with post polypectomy edges treated by hybrid APC, and they reported a recurrence rate of 2.2% on first follow-up colonoscopy.[49]

Underwater EMR is a technique described in 2012, in which instead of conventional EMR with submucosal injection to separate the lesion from deeper muscularis mucosa, water immersion is used to allow the lesion to "float" up.[50] Studies have also validated its use and safety, with a number of studies reporting a lower recurrence rate, and a higher *en bloc* and R0 resection, even for larger sized non-fibrotic lesions, when compared to conventional EMR and hybrid ESD (H-ESD).[51–54]

Hybrid ESD is a technique, in which EMR and ESD are combined to compound the benefits of each, such that larger lesions can be removed *en bloc*, with less procedure time and lower risk of adverse events.[55] The lesion is lifted with a submucosal injection, circumferentially marked, and partially dissected. Then, the remaining lesion is completely resected with a snare.[56] A study on small (≤20 mm) early gastric neoplasms revealed that the hybrid technique has a shorter procedure time (33 minutes vs. 62 minutes), with comparable curability and safety, when compared to ESD (possible lower thermal damage to the submucosal layer in H-ESD).[57] A shorter procedure time was observed for H-ESD, when compared to conventional ESD, for colonic lesions, with a lower *en bloc* and R0 resection rate.[56] H-ESD requires less time to complete, with lower risks of intraprocedural perforation, bleeding, and post-polypectomy syndrome.[58]

A recent meta-analysis compared the outcomes between hybrid ESD and conventional ESD for colorectal lesions that involved over 2,000 patients.[59] Hybrid ESD was associated with a shorter procedural time (mean difference: 18.5 minutes, $p = 0.003$). Furthermore, the rate of adverse events was lower for hybrid ESD, when compared to conventional ESD (odds ratio: 1.56, $p = 0.04$), but no difference was observed when these were stratified by perforation or delayed bleeding rates. Lower *en bloc* resection was noted with hybrid ESD, when compared to conventional ESD (odds ratio: 0.31, $p < 0.001$). However, several limitations were noted in this study. The majority of the studies included in the analysis were observational studies. Furthermore, important variables, such as lesion size, endoscopist experience, and type of snare, were not adjusted in most of the studies. In addition, in some of the included studies, hybrid ESD was used as a rescue therapy after failed conventional ESD. Moreover, merely a small sub-set of the included studies were conducted in Europe, while none of these studies were conducted in the US. In addition, the findings of the meta-analysis could not be extrapolated to the US population. Thus, high-quality studies that evaluate hybrid ESD for colorectal lesions in the Western population are needed.

A recently published Japanese multicenter 10-year study examined lesions of 20–30 mm in size, and concluded that H-ESD is safe. However, the data behind the *en bloc* resection rate and local recurrence remains conflicting, with some of the data suggesting an overall lower *en bloc* resection rate, and a subsequently higher local recurrence rate in H-ESD, while several Asian and European studies reported no statistically significant differences.[55,56,60–63] More generalized conclusions are difficult to draw due to the varied study designs (most of the studies were observational and retrospective), study size, lesion characteristics, such as the location, and level of endoscopic expertise. The current available evidence comparing hybrid ESD and conventional ESD is summarized in Table 2.[55–57,59–63]

Overall, H-ESD is a valuable technique, particularly for fibrotic lesions or lesions in challenging locations, and when employed in the right clinical setting, this proves to be useful, and perhaps just as effective as ESD.

EFTR is an endoscopic resection option, particularly for non-lifting lesions that are not amenable to EMR or ESD, such as subepithelial tumors or neoplasia, with extension to deeper tissue layers, or polyps with significant fibrosis. As described in the 2019 American Society for Gastrointestinal Endoscopy (ASGE) guidelines for endoscopic full thickness resection and submucosal tunnel endoscopic resection, full thickness resection can be achieved through "exposed" EFTR, in which the defect closure occurs after full thickness resection via submucosal tunneling or the non-tunneled technique (dissection around the lesion), or "non-exposed" EFTR, in which the closure occurs before resection by invaginating the bowel wall that contains the lesion.[17] Since EFTR devices are over the scope, this limits the lesion size that can be completely resected using this method, since the lesion needs to be retracted into the cap. However, novel advances in device design have allowed for the resection of lesions of up to 30 mm, and studies have reported lower R0 resections with lesions of >20 mm in size.[64,65] A Dutch registry reported a technical success rate for EFTR of

Table 2. Studies that compared conventional ESD (c-ESD) with hybrid ESD (h-ESD)

Study	Design	Pathology	Number of patients or lesions	Findings for h-ESD vs. c-ESD
Milano RV *et al*.[55]	Retrospective Study	Colorectal lesions	52 patients	Longer PT and lower bleeding with c-ESD; Similar R0 and *en bloc* resection rates
Wang XY *et al*.[56]	Retrospective Study	Cecal LST >2 cm	62 patients	Increased fibrosis in the h-ESD group; Reduced PT and R0 rates in h-ESD; AE similar in both groups
Esaki *et al*.[57]	Prospective RCT	Differentiated intramucosal early gastric neoplasia, no ulceration, <20 mm	79 patients	Lower PT in h-ESD; Other outcomes and AE similar
McCarty T *et al*.[59]	Meta-analysis	Colorectal lesions	2,000 patients	Shorter PT, lower R0 resection, fewer complications with h-ESD; Comparable recurrence rates
Yu QY *et al*.[60]	Retrospective study to analyze DPPB	Colorectal LST	665 patients	No difference in DPPB
Kang DU *et al*.[61]	Retrospective study to analyze long-term outcomes	Colorectal lesions	836 patients	Lower PT, lower *en bloc* resection, increased perforation rate, increased recurrence in h-ESD
Wang XY *et al*.[62]	Retrospective study to analyze the risk for incomplete resection	Rectal NET	272 patients	Lower PT in h-ESD with similar *en bloc* resection, R0 resection and bleed rates
Okamoto K *et al*.[63]	Retrospective study with rescue h-ESD for difficult c-ESD lesions	Colorectal lesions	137 c-ESD lesions; 27 h-ESD lesions	No local recurrences in the study; Shorter PT with lower *en bloc* resection in h-ESD; AE similar

AGA, adverse events; C-ESD, conventional endoscopic submucosal dissection; DPPB, delayed post polypectomy bleed; ESD, endoscopic submucosal dissection; H-ESD, hybrid endoscopic submucosal dissection; NET, neuroendocrine tumor; PT, procedure time.

83.9% and R0 resection of 82.4% (an average lesion size of 23 mm in the study), with a rate of 9.2% for device malfunction. Furthermore, that study acknowledged the additional limitations of EFTR, such as limited visibility, decreased endoscope tip flexibility with the required long cap, mobilization of the lesion into the cap, and other concerns, such as stenosis from the partial bowel wall resection, and perforation. However, EFTR has a shorter learning curve, when compared to ESD, and offers the additional benefit of full thickness specimen for pathology reviews. In general, this is a valuable endoscopic resection tool, although this has limited utility towards larger lesions and upper GI tract lesions, due to the proximity to adjacent structures and risk of inadvertent damage.

Conclusions

As endoscopic resection methods expand and techniques mature, more GI lesions are presently becoming potential candidates for endoscopic curative or staging resection, which may not need surgical intervention, and these are often associated with increased morbidity and mortality. The preferred method of resection is one that can offer an *en bloc* resection, in order to allow for the pathology evaluation of the margins, particularly when the polyp has a malignancy potential. For lower risk lesions, it remains permissible to employ piecemeal EMR with thermotherapy applied to the clear margins (i.e. APC and soft coagulation). ESD is a time-consuming procedure with a steep learning curve, limiting its widespread use, despite the guideline recommendations. Thus, an increasing number of studies have evaluated the safety and efficacy of the hybrid approach, which may serve as a compromise to the lack of ESD access.

Acknowledgments

None.

Funding

None.

Conflict of interest

The authors have no conflict of interests related to this publication

Author contributions

Contributed to the study concept and design (EW and MD); acquisition of data (EW and MD); data analysis (EW and MD); drafting of the manuscript (EW and MDL); critical revision of the manuscript (MD); supervision (MD).

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