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Clinical Updates in Colorectal Endoscopic Submucosal Dissection

Dennis Yang and Peter V. Draganov

Division of Gastroenterology, Hepatology and Nutrition, University of Florida, Gainesville, Florida

Laterally spreading tumors (LSTs) are increasingly encountered with the uptake of colorectal cancer screening programs. The approach to LSTs is determined by the risk of submucosal invasive cancer (SMIC), because this dictates the most appropriate endoscopic or surgical intervention. In the West, endoscopic mucosal resection (EMR) is the first-line treatment for LSTs without SMIC, given its cost-effectiveness, superior safety profile, and patient quality of life when compared with surgery. Conversely, LSTs with SMIC have been traditionally referred for surgery. More recently, colorectal endoscopic submucosal dissection (ESD), has emerged as a minimally invasive alternative to surgery for LSTs with superficial SMIC. ESD enables the en bloc resection of lesions irrespective of size, which confers 2 distinct advantages: an ideal specimen for accurate histologic assessment and low risk for recurrence.

The Challenge of Classifying Laterally Spreading Tumors and the Risk of Submucosal Invasive Cancer

Polyp morphology can help predict the risk of SMIC. Several validated classification systems, including the Kudo and the Japanese NBI Expert Team (JNET) classification systems, are routinely used in Japan for lesion assessment before resection. Despite their accuracy in predicting SMIC, implementation in the West has been limited by their complexity and the need of high-level magnification endoscopy, which is not widely available. The NBI international colorectal endoscopic (NICE) classification system was introduced as a potentially more pragmatic approach for polyp categorization that does not require either magnification or dye spray. Nonetheless, the NICE classification has not been widely adopted in Western everyday routine clinical practice. The fact that multiple biopsies or even partial resection of LSTs for histologic diagnosis remain a common practice in the West suggests that we have yet to embrace real-time optical diagnosis in the evaluation of colorectal lesions.

Irrespectively, the main limitation of all of these classification systems lies in their inability to reliably

distinguish benign neoplastic colorectal polyps containing high-grade dysplasia from superficial SMIC. This limitation is inherent to the NICE classification where high-grade dysplasia and superficial SMIC are grouped under the same category (NICE type 2).¹ Lesions with suspected superficial SMIC should be resected en bloc for precise histopathologic assessment for curative intent. Piecemeal EMR of lesions with suspected superficial SMIC leads to pathologic uncertainty and unnecessary surgery for otherwise endoscopically curable lesions. This can be devastating for patients, particularly in the rectum, where postendoscopic surgery is associated with poor quality of life.

Colorectal Endoscopic Submucosal Dissection

Colorectal ESD has long supplanted EMR as the preferred endoscopic resection strategy in Japan for various factors, including the well-recognized inability to reliably identify superficial SMIC, the widely available ESD expertise, and other inherent advantages of ESD (accurate histopathology, low recurrence, and ability to provide cure for selected SMICs).

In the West, proponents of EMR over ESD argue that most LSTs are benign, can be adequately removed with piecemeal resection, and that the subset that contain SMIC that require ESD is low. However, the risk of covert SMIC among LSTs has been increasingly recognized in the West, being reported in 10% to as high as 32% of mixed-granular LST-Gs and LST-NGs, respectively.² It should also be noted that the true prevalence of SMIC in many of these studies may be underrepresented, because final histologic diagnoses were primarily based on specimens obtained by piecemeal EMR rather than ESD or surgery. Therefore, it is conceivable that the subset of LSTs for which ESD offers a reasonable higher chance of avoiding surgery may be higher than anticipated.

Recent advances in EMR have aimed to reduce the risk of recurrence. Notably among these, thermal

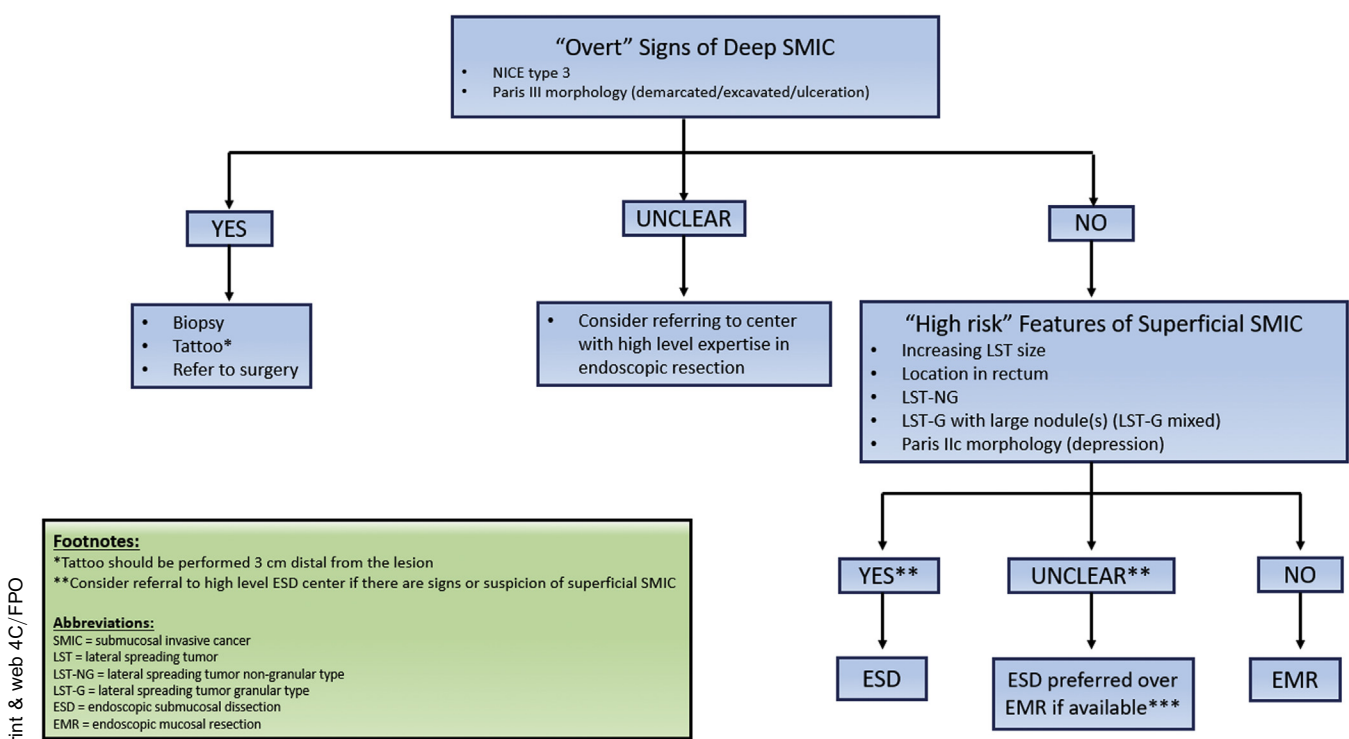


Figure 1. Clinical decision tree algorithm illustrating the role of endoscopic submucosal dissection in the management of colorectal lateral spreading tumors based on the risk of submucosal invasive cancer.

treatment of EMR defect margins seems to be a promising strategy.³ Nonetheless, early results are yet to be widely corroborated and recurrence after EMR remains a clinical concern in clinical practice. Incomplete EMR often entails more frequent colonoscopies, inconvenient bowel preparation, and time off work for patients, all with clearly adverse financial and psychosocial implications. Apart from these issues, although most benign recurrences can be adequately managed endoscopically, a small subset of patients may still end up requiring surgery for either benign recurrences no longer amenable to endoscopic treatment or even more concerning, for invasive and metastatic recurrence. Long-term surveillance is critical given the risk of recurrence and cancer, yet this is undermined by loss to follow-up partly caused by the need for frequent short-interval colonoscopies after piecemeal resection. In this setting, ESD, a more definitive procedure than EMR, may be better suited for patients who might be lost to follow-up.

Despite advances in colorectal EMR and evidence-based guidelines endorsing endoscopy as first-line treatment for most colorectal polyps, surgical referral remains exceedingly common in the United States.⁴ Multiple factors, including perceived medical-legal risks of incomplete EMR and recurrence, may contribute to this disconcerting trend. The incorporation of ESD into Western clinical practice may help curtail unnecessary

surgery for endoscopically removable LSTs. In fact, before the introduction of ESD at the National Cancer Center Hospital in Tokyo, surgery was commonly performed in approximately 20% of LSTs without evidence of SMIC. After the introduction of ESD, this number decreased to 1%, thus dramatically decreasing the need for surgery.⁵

Considering the ongoing struggles to accurately and reliably distinguish benign from superficial or even deep SMIC, should ESD be the preferred initial approach for selected lesions, particularly for rectal LSTs with risk for SMIC? The clinical algorithm in [Figure 1](#) illustrates the role of ESD for colorectal LSTs stratified based on risk of SMIC. This seems like a reasonable strategy, given the lower costs, morbidity, and mortality in comparison with surgery. This approach is further supported by mounting evidence indicating that ESD does not adversely affect long-term oncologic outcomes following secondary surgery for noncurative resection.⁶ Importantly, it should be emphasized that not all patients with endoscopic R1 resection of T1 colorectal cancer require secondary surgery. As a matter of fact, this “ESD for all LSTs devoid of overt signs of deep SMIC” is the current approach in Japan. Although we are clearly not there yet, strides have been made over recent years that have slowly narrowed the gap between ESD in the East versus the West.

The Current Status of Colorectal Endoscopic Submucosal Dissection in North America

Acquiring competency in ESD to ensure effective and safe outcomes has been the main barrier to its widespread adoption in North America. In the past 2 decades, an expanding number of Western endoscopists have pursued first-hand experience by visiting and observing Japanese ESD masters, followed by complementary skill acquisition via self-directed didactics and training on animal models. Over the years, this pool of endoscopists have become “Western ESD” experts themselves and served as mentors for trainees in their respective institutions. This noticeable growth in local ESD expertise and educational resources, including dedicated live and hands-on courses, has been the foundation of ESD training in the West. The expanding array of traction devices available and the introduction of different colorectal ESD techniques (eg, submucosal tunneling, pocket-creation method, hybrid ESD) have helped flatten the learning curve of colorectal ESD.⁷ In all, these improvements in ESD technique and its adaptation to Western practice have translated into improved outcomes. Our group recently reported the largest multicenter prospective study on ESD across 10 centers in North America with a total of 692 cases, of which 399 were for colorectal lesions.⁸ Overall, colorectal ESD led to complete (R0) resection in 85% of the cases with a perforation rate of 5%. These results are similar to those from our Asian counterparts and superior to those reported in non-Asian countries from a 2017 systematic review and meta-analysis. Notably, these favorable outcomes were attained despite submucosal fibrosis being identified in nearly half of the lesions; something less frequently encountered in Asia because preprocedure tattooing, partial snare resections, and biopsies are seldom performed. Furthermore, our study demonstrated that most colorectal ESD cases (70%) can be safely performed in the outpatient setting, further attesting to its viability and cost-effectiveness when compared with surgery. Nonetheless, we should highlight that at this time, these results are primarily confined to large-volume tertiary care centers with expertise in ESD. However, we anticipate that with aggregating data supporting the efficacy and safety of colorectal ESD, the development of a dedicated current procedural terminology will help ensure proper reimbursement, currently a hurdle for ESD dissemination.

Take Home Message

Making the distinction between benign LSTs versus SMIC on real-time optical diagnosis remains a clinical challenge. Colorectal ESD may be a suitable initial approach for lesions with suspected SMIC, because it can

be curative for selected superficial cancers yet without compromising outcomes for those who may require secondary surgery for deep invasion. ESD also represents a viable alternative to lesions not amenable to EMR, which should help curtail the need for unnecessary surgery. Although technical demand and lack of proper reimbursement are current challenges to ESD in the West, the increasing availability of local ESD mentors, training pathways, and dedicated devices have led to its adoption in many tertiary centers and should continue to facilitate its ongoing incorporation into mainstream endoscopic practice.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at <https://doi.org/10.1016/j.cgh.2021.09.025>.

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Reprint requests

Address requests for reprints to: Peter V. Draganov, MD, 1329 SW 16th Street, Room #5254, Gainesville, Florida 32608. e-mail: peter.draganov@medicine.ufl.edu; fax: (352) 627-9002.

Conflicts of interest

The authors disclose the following: Dennis Yang is a consultant for Boston Scientific, Lumendi, and Steris Endoscopy. Peter V. Draganov is a consultant for Boston Scientific, Olympus America, Cook Medical, Microtech, Steris, Merit, Fujifilm, and Lumendi.