Discussion Summaries

Is Endoscopic Submucosal Dissection Ready for Primetime in North America?

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Discussion Summaries

Abstract

Endoscopic submucosal dissection (ESD) is a novel technique for endoscopic en bloc resection of neoplastic and dysplastic lesions in the gastrointestinal tract. Endoscopic Mucosal Resection (EMR) has been used historically; however, ESD carries the added advantage of providing an accurate histopathologic evaluation for resection margins, low recurrence rate, curative resection. Also compared to surgery it carries a lower risk of morbidity and mortality. ESD is well established in Asia however its adoption is lagging in North America.

We summarize the @GIJournal discussion held on March 10th, 2021 during which Draganov et al. "Endoscopic Submucosal Dissection (ESD) in North America: A Large Prospective Multicenter Study" was critically reviewed by our expert panel: Drs. Neil Sharma (NS), and Mohamed Othman (MO) and moderated by Dalbir Sandhu (DS).

Discussion Summaries

Introduction

Endoscopic Submucosal Dissection (ESD) has been established in Asian countries for a while for minimally invasive endoscopic resection of large premalignant lesions or early malignant lesions in the gastrointestinal tract, this has been gaining more popularity in Europe as well. Endoscopic Mucosal resection (EMR) is currently considered the first-line therapy for premalignant lesions in the US, but this is limited by the size of the snare and ability to safely remove large lesions en bloc. Therefore, most lesions larger than 2 cm end up being removed in a piecemeal fashion. (1)

ESD was introduced in mid 1990s and carries the advantage of being able to remove lesions with high en bloc, R0 resection rates and lower rate of residual neoplasia compared to EMR (2, 3). ESD has been adopted more widely in Japan and other Asian countries but despite its advantages it has not gained momentum in the United States yet. This delay has been due to many reasons including lack of ESD experts, lack of training centers, steep learning curve, lack of proper reimbursement, the procedure being time-consuming, and the bias of endoscopists towards EMR just to mention a few. (4)

The recent article "Endoscopic Submucosal Dissection (ESD) in North America: A Large Prospective Multicenter Study" By Draganov et al.(5) was designed to document the ESD experience in North America and reproduce the data from around the world. This was a prospective multicenter that included 10 centers in North America between 2016 and 2020. The primary outcome was the proportions of ESD cases with en Bloc resection, R0, and curative resection. 692 patients underwent ESD, the median lesion size was 40 mm. The most Common ESD site was the Colon (30.5%) followed by the rectum (27.2%), esophagus (26.2%), stomach (14.16%), and duodenum (1.6%). The median procedure time was 77.5 minutes.

Most of the cases were performed in the outpatient setting and patients were discharged on the same day of the procedure 66.9%, 33.1% of patients were admitted post-procedure and if admitted the mean hospital stay is 1.33 days. En bloc and R0 resection were achieved in 91.5% and 84.2% of the cases, respectively.

Adverse events were reported in 10.1%; of which most were either mild (50%) or moderate (40%) in severity. Delayed bleeding occurred in 2.3% of the patients. Perforation was reported in 2.9% (20/692) of the cases, all were successfully closed endoscopically except for one who needed right hemicolectomy. Lesion recurrence was identified in 5.8% of the cases: 8.9% in the esophagus, 11.1% in the stomach, 10% in the duodenum, and 2.7% in the colorectum. Predictors of failed en bloc resection included colorectal ESD compared to ESD in other locations, severe submucosal fibrosis, and ESD on lesions with depressed component on morphology.

Discussion Summaries

Discussion

GIJC Question #1: 91% of the lesions were manipulated prior to ESD (biopsy, EMR, Tattoo). How does that affect ESD?

MO: As demonstrated in our study, this was a predictor of failed en bloc resection. It also reflects that more education is needed among practicing endoscopists to avoid tattooing under the lesion, doing partial EMR or extensive biopsies for lesions which could be resected by ESD.

Many endoscopists initially think they can resect the lesions and they back off in the middle of the case due to time limitation. My advice is not to attempt EMR during screening colonoscopies if you don't have enough time to resect, or under pressure, reschedule with enough time to resect later on.

NS: Submucosal fibrosis can be a real challenge for EMR and ESD. It increases complication rates and time and complexity of technical completion.

Also, Gentle education of your referring physicians is key, this can help prevent repetitive lesion manipulation prior to referral. Tattoos should be placed on the opposite wall or > 3cm away from the lesion.

GIJC Question #2: Despite >90% biopsied or attempted EMR prior to ESD only 46.7% showed fibrosis. Do you think that these numbers do not match especially since tattoo and prior EMR attempt caused submucosal fibrosis, what are the strongest predictor for failed ESD?

MO: Fibrosis degree varies. Injecting tattoos peripherally may not affect the entire lesion. Also, acquiring biopsies causes less fibrosis compared to EMR or tattooing. It is possible that the endoscopists did not appreciate mild fibrosis since mild fibrosis is subjective.

NS: Fibrosis was measured as mild, moderate, and severe in our study. However, lesion manipulation is quite variable; multiple tunneled biopsies versus use of heart biopsies versus use of hot snare or cold snare all affect the degree of fibrosis differently. Also, the location of the lesion matters in terms of fibrotic response - colon and stomach are very different for example. I find the stomach to have less degree of fibrosis in general.

GIJC Question #3: The majority of the cases in this study (61.8%) Voluven (6% Hydroxyethyl Starch) was used for lifting, does choice of the lifting solution affect ESD?

MO: The degree of dark blue in the solution vary among ESD practitioners. I prefer very light blue to highlight blood vessels and avoid accidental bleeding. In Japan, some ESD are done

Discussion Summaries

with no Methylene Blue at all. Also, some of the commercially available lifting agent can cause bubbles. Voluven is widely available in hospital-based units and it is cheaper to use.

NS: We use Hetastarch, saline, and methylene blue. We have tried some other agents. The density and blue color vary. Anyone using EMR or ESD should be aware that lifting agents may cause artifact, in this article ORISE was shown to cause some histologic artifact (6)

GIJC Question #4: ESD resection bed closure was done in 24.4% of patients and 2.3% had delayed bleeding in this study. Was there any correlation between bed closure and delayed bleeding?

MO: Our study was not aimed to look for this association. I would guess that it decreases risk of -bleeding, but you have to power the study to look for that, also 50% of included lesions were colorectal lesions which tend to bleed less in comparison to esophageal and gastric lesions.

NS: I agree with Mohamed, that's not an endpoint designed to be measured in the study. I would say that I rarely close my ESD specimens (& never saw it done in Japan). Good dissection lowers delayed bleeding risk with ESD.

GIJC Question #5: How to select a lesion for ESD vs EMR as this study and other studies report that lesions removed by ESD could have been removed by EMR.

MO: ESD indications vary based on the region and expertise. To summarize ESD should be preferred for lesions 2 cm or larger for upper GI lesions and 3 cm or larger for lower GI lesions. The article cited here by Draganov et al. summarizes all the accepted indications in North America. Nodular Barrett's with early adeno carcinoma, localized squamous cell carcinoma of the esophagus, non-granular lateral spreading polyps of the colon and gastric dysplastic lesions are the most common indications for ESD. (4)

NS: Great question. There is a lot of differences between countries (west vs east, but even Europe vs Canada vs USA) even variance within the United States depending upon skill set, interest, and size/volume of the EMR practice in an interventional group.

-For Neuroendocrine tumors we have moved more to ESD >10mm. (7)

-We also prefer ESD for Paris or T1 SCC of the Esophagus. (8)

- For T1a adenocarcinoma of the Esophagus there is a lot of data around EMR effective for 15mm or less lesions. Data on >15mm sized cancers and even T1b will accumulate and support ESD with time.

GIJC Question #6: How was antiplatelet and anticoagulation managed in this group of patients undergoing ESD? Was it similar to EMR?

Discussion Summaries

MO: We have used the same recommendations as EMR. Surprisingly, bleeding control is more adequate with ESD in anticoagulated patients compared to EMR in the same patient population. This is due to the ability to meticulously coagulate the blood vessels seen during dissection.

NS: Many performing ESD use same antiplatelets and anticoagulation standards as EMR. We need more data to change our practice. Especially with the change in electrosurgery unit from Erbey (Vio3), the algorithms adjust power very effectively.

GIJC Question #7: Do you think ESD is ready for prime time? What are the biggest challenges for its widespread use in the western world?

MO: ESD is ready for prime time. Once CPT (Current Procedural Terminology) code is established for ESD (hopefully in 2023 or at max 2024) then ESD will become more popular. The most common pathway to adopt ESD in North American will be traction assisted ESD rather than pocket technique. I am confident that we will establish our style, technique and identity of performing ESD in North America. I am sure once ESD is widely adopted, we will take it to the next level.

NS: Clinically it's the right answer for select lesions in the right hands. I would say that anyone who is interested should do their best to: observe, attend ex vivo labs, assist, try en vivo labs, observe, and then be proctored. Many of us went to Japan for some period of time.

There's lots of opportunities however there's still many barriers. I would say Canada and USA are also very different. Single payer vs private. Cost reduction vs fee for service. Liability. More referral to less centers means more proficiency. (4)

GIJC Question #8: Is there a number that one needs to observe/assist before starting independent ESD practice?

NS: So much variability in the learning curves. As we all know from EUS/ERCP, we can set a minimum number needed to assess competency but even way above that number some individuals do not obtain competency. ESD is a different set of skills compared to ERCP/ EUS.

Discussion Summaries

Conclusion

Endoscopic Submucosal Dissection is being widely used in Japan and other parts of Asia, however, the adoption of this technique has lagged in the United States. In this prospective multicenter study of the North American experience, the safety, efficacy, and superior results were clearly demonstrated. The outcomes support the implementation of ESD in North America for early dysplastic and neoplastic gastrointestinal lesions.

Discussion Summaries

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