# EMR/ESD/STER: To the Third Space and Beyond the Mucosa

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# Financial Disclosures

- I, Nanlong Liu, Have no Financial Disclosures

# Learning Objectives

1. Identify the indications between EMR/ESD/STER
2. Discuss the differentiation between the need for Endoscopic vs Surgical Resection
3. Perform systematic lesion assessment to guide resection strategy
4. Identify Post Resection Pathology
5. Describe the Technical approaches EMR/ESD/STER

# Why do we care?

- Why not send large lesions and polyps to surgery?
- When is surgery truly indicated?
- How can we better identify early malignant features and refer appropriate patients to surgery and when to send for endoscopic resection
- When choosing endoscopic resection what is the best method for resection?

# Surgical Outcomes for Benign Colon Polyps Systematic Analysis

- Of the 4210 studies retrieved, 26 studies describing 139,897 patients were included
- Reasons for surgical referral for noncancerous polyps: polyp location (right side), median polyp size (3.0cm), sessile morphology (flat).
- Laparoscopic Surgery main surgical approach
- Pooled Complication Rate was **24%** with a surgical complication rate of 17% (within 30 days)
  - Anastomotic Bleeding, stricture, abdominal abscess, leakage, ileus, DVT,
  - 1 month mortality was 0.7%
  - Average hospital stay 5 days (median 4-11 days)
  - Readmission rates not reported in these studies
- Colon EMR 5-7% with bleeding, 1.4-1.5% perforation (EMR), 5% perforation (ESD), with polyp recurrence rate for EMR of 16-20%.
- Cost saving of 7602$ per patient (not including readmission post 30 days)

tot Babberich Outcomes of surgical resections for benign colon polyps: a systematic review. *Endoscopy*, *51*(10), 961-972.

# Outcomes of surgical resections for benign colon polyps: a systematic review

Michael P.M. de Neree tot Babberich‡ *, Maxime E.S. Bronzwaer‡ *, Jurr O. Andriessen , Barbara A. J. Bastiaansen , Nahid Mostafavi , Willem A. Bemelman , Paul Fockens , Pieter J. Tanis , Evelien Dekker

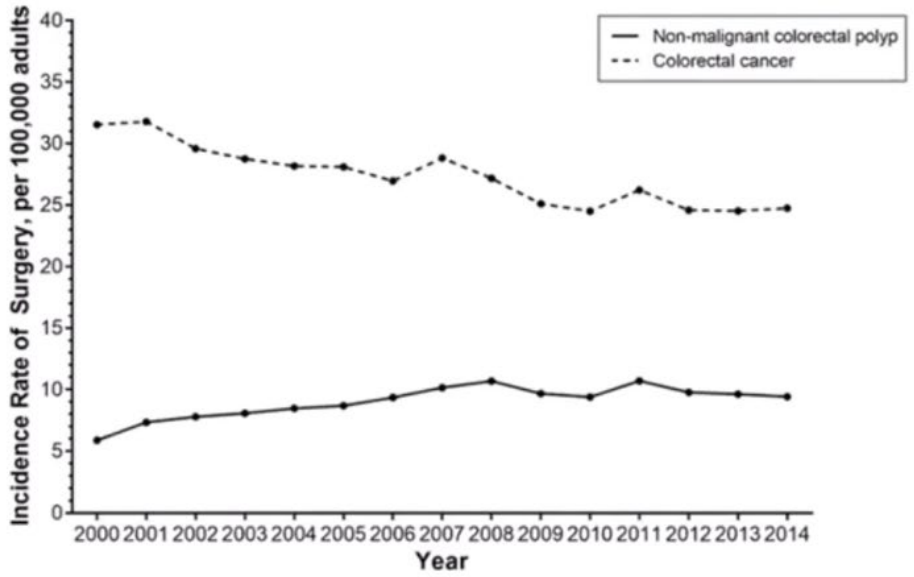
- Of the 4210 studies retrieved, 26 studies describing 139,897 patients were included

**Results** Of the 4210 studies retrieved, 26 studies describing 139897 patients were included. The most common indications for surgical resection were polyp location in the right-sided colon, non-pedunculated morphology, and large polyp size. The pooled 1-month complication and mortality rates of studies that included patients after the year 2000 were 24% (95% confidence interval [CI] 15%–36%) and 0.7% (95%CI 0.6%–0.8%), respectively.

**Conclusion** The postoperative morbidity and mortality after colonic resection for benign polyps are substantial. Referral to an advanced interventional endoscopist should be considered before referral for surgery to evaluate the possibilities for endoscopic treatment of large, non-pedunculated, and/or colonic polyps in difficult locations without suspicion of submucosal malignant invasion.

# Surgery for nonmalignant colorectal polyps

2000 to 2014: ~ 300,000 surgeries for non-malignant polyps.




| | % |
|---|---|
| Thirty-day mortality | 0.7 |
| Major post-op AE | 14 |
| 30-day readmission | 7.8 |
| Second major surgery | 3.6 |
| Colostomy | 1.8 |

Peery AF et al. Gastroenterology. 2018

# The Physiological & Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM)

## Endoscopic versus surgical mortality

Predicted surgical mortality >>>>
Actual endoscopic mortality rate

| Physiologic score | No. (%) | Endoscopic mortality | Surgical mortality % |
|---|---|---|---|
| 6 | 46 (11.8) | 0 (0.0) | 0.7 |
| 7 | 35 (9.0) | 0 (0.0) | 1.0 |
| 8 | 69 (17.7) | 0 (0.0) | 1.3 |
| 9 | 93 (23.8) | 0 (0.0) | 1.9 |
| 10 | 57 (14.6) | 0 (0.0) | 2.6 |
| 11 | 22 (5.6) | 0 (0.0) | 3.6 |
| 12 | 3 (0.8) | 0 (0.0) | 5.0 |
| 13 | 19 (4.9) | 0 (0.0) | 6.9 |
| 14 | 27 (6.9) | 0 (0.0) | 9.3 |
| 15 | 8 (2.1) | 0 (0.0) | 12.6 |
| 16 | 7 (1.8) | 0 (0.0) | 16.8 |
| 17 | 2 (0.5) | 0 (0.0) | 22.0 |
| 18 | 2 (0.5) | 0 (0.0) | 28.4 |

Ahlenstiel G al. GIE. 2014

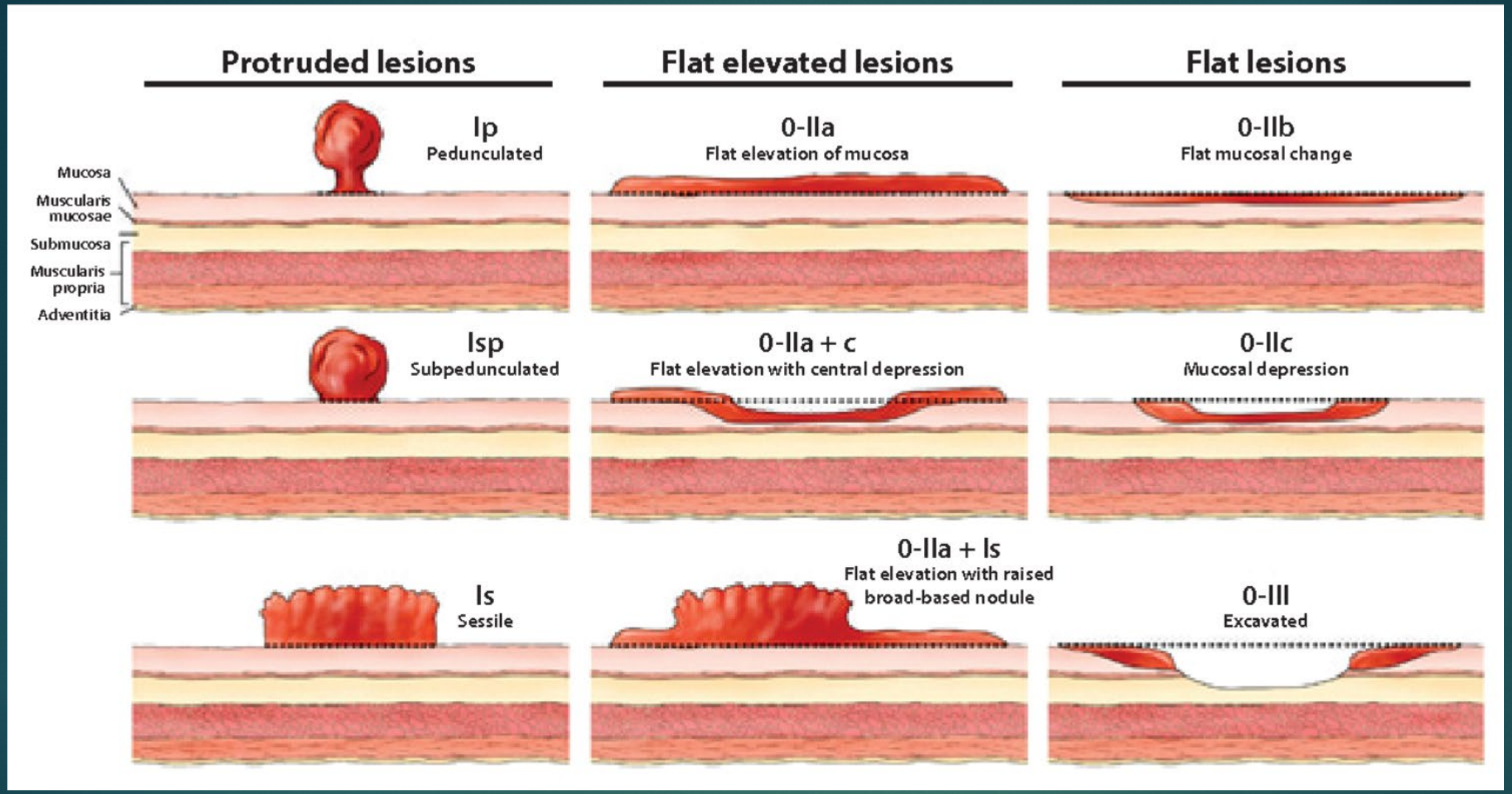
**Physiological (12):**
-Age,
-cardiac failure,
-BP,
-Pulse,
-hemoglobin,
-urea
**Operative (6):**
-Operative severity
-blood loss
-peritoneal soiling,

Actual endoscopic versus predicted surgical mortality for treatment of advanced mucosal neoplasia of the colon

Golo Ahlenstiel, MBBS, MD [1,7] · Luke F. Hourigan, MBBS, FRACP [2,3] · Gregor Brown, MBBS, FRACP, PhD [4,5] · Simon Zanati, MBBS, FRACP [4,6] · Stephen J. Williams, MBBS, FRACP, MD [1] · Rajvinder Singh, MBBS, FRACP, MRCP, FRCP [6,7] · Alan Moss, MBBS, FRACP, MD [1,6] · Rebecca Sonson, BNurs [1] · Michael J. Bourke, MBBS, FRACP [1,7] · The Australian Colonic Endoscopic Mucosal Resection (ACE) Study Group Show less

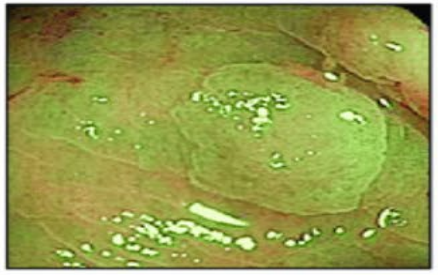
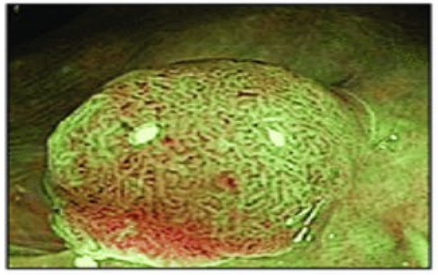
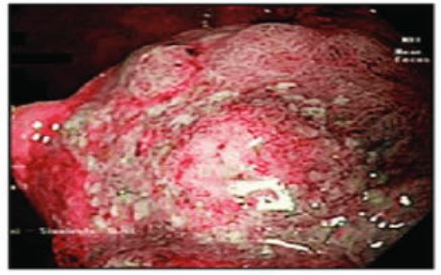
# Lesion Identification

- Size Not as Important as Morphology
- how can we predict lesions early rightcheck out
- Which lesions need to go to surgery
- logical features predict this



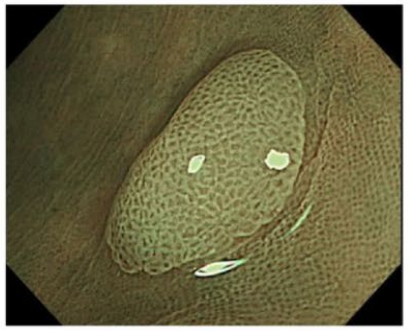
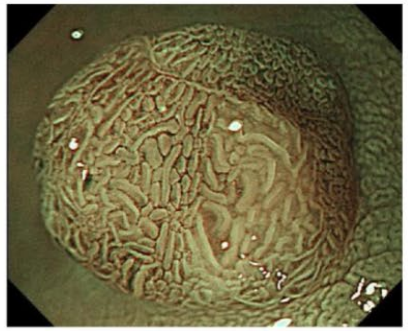
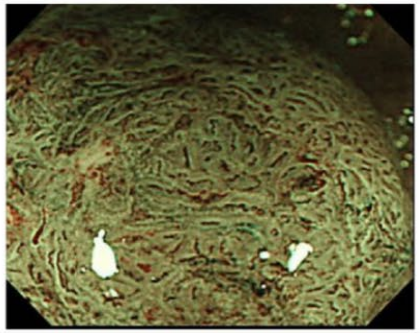
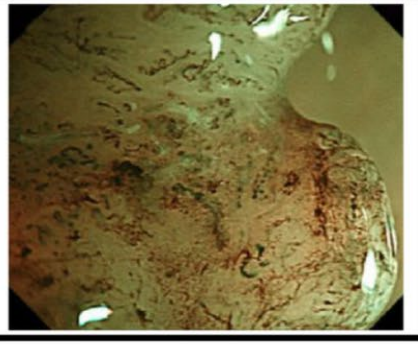

# Paris Classification

# Narrow-band imaging International Colorectal Endoscopic (NICE) classification

| | Type 1 | Type 2 | Type 3 |
|---|---|---|---|
| Color | Same or lighter than background | Browner relative to background (verify that color arises from vessels) | Brown to dark brown relative to background, sometimes patchy whiter areas |
| Vessels | None or isolated lacy vessels coursing across the lesion | Brown vessels surrounding white structures | Has area(s) with markedly distorted or missing vessels |
| Surface pattern | Dark or white spots of uniform size, or homogeneous absence of pattern | Oval, tubular, or branched white structures surrounded by brown vessels | Areas with distortion or absence of pattern |
| Most likely pathology | Hyperplastic | Adenoma | Deep submucosally invasive cancer |
| |  |  |  |

Narrow-band imaging International Colorectal Endoscopic (NICE) classification. Adapted from Hayashi N, et al. Gastrointest Endosc 2013;78:625-632. 7

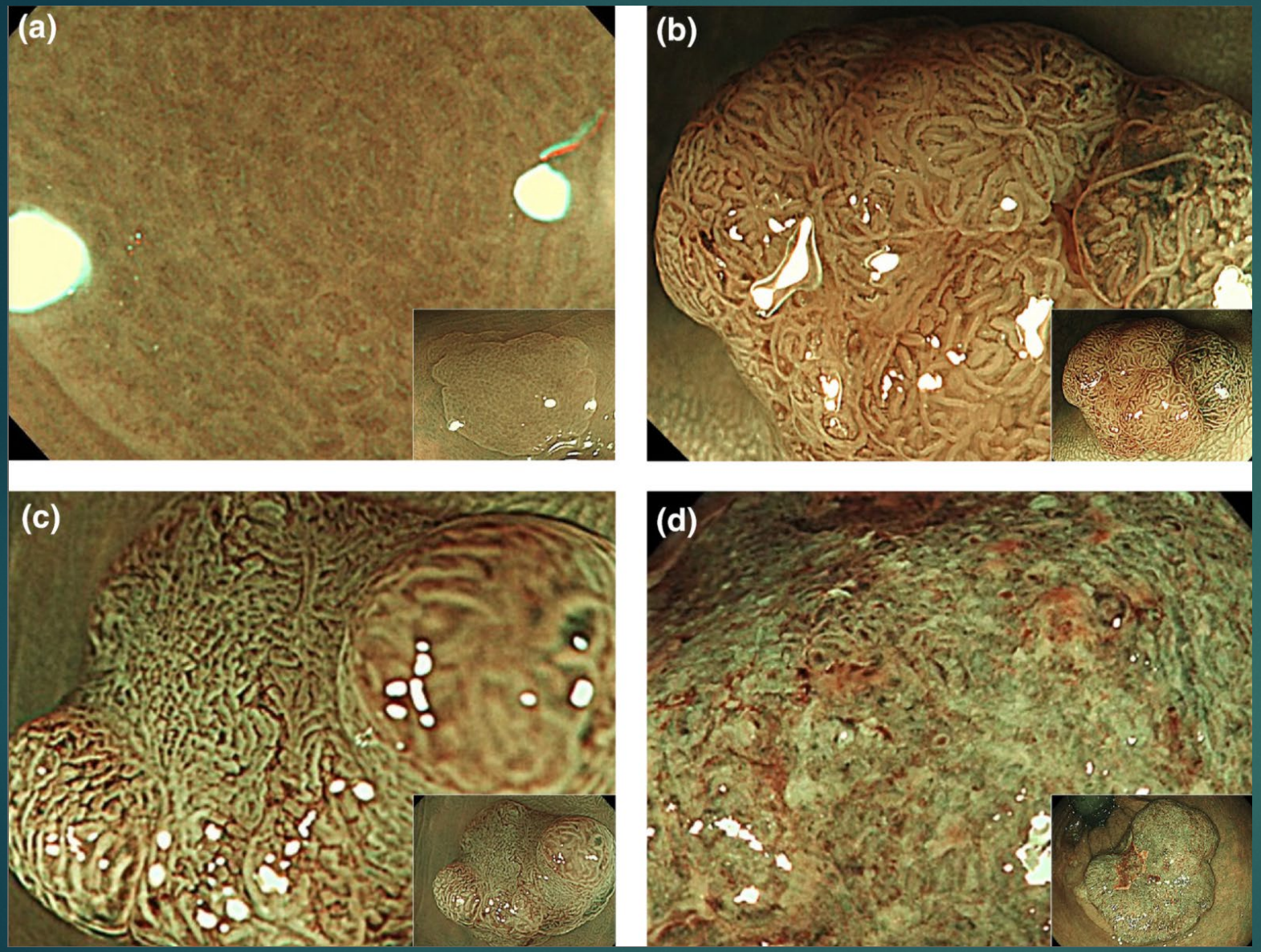
# Japanese NBI Expert Team (JNET) Classification

| | Type 1 | Type 2A | Type 2B | Type 3 |
|---|---|---|---|---|
| **Vessel pattern** | ・Invisible ※1 | ・Regular caliber<br>・Regular distribution (meshed/spiral pattern) ※2 | ・Variable caliber<br>・Irregular distribution | ・Loose vessel areas<br>・Interruption of thick vessels |
| **Surface pattern** | ・Regular dark or white spots<br>・Similar to surrounding normal mucosa | ・Regular (tubular/branched/papillary) | ・Irregular or obscure | ・Amorphous areas |
| **Most likely histology** | Hyperplastic polyp/ Sessile serrated polyp | Low grade intramucosal neoplasia | High grade intramucosal neoplasia/ Shallow submucosal invasive cancer ※3 | Deep submucosal invasive cancer |
| **Endoscopic image** |  |  |  |  |

*1. If visible, the caliber in the lesion is similar to surrounding normal mucosa.

*2. Microvessels are often distributed in a punctate pattern and well-ordered reticular or spiral vessels may not be observed in depressed lesions.

*3. Deep submucosal invasive cancer may be included.




(a) Japan NBI Expert Team (JNET) type 1. (b) JNET type 2A. (c) JNET type 2B. (d) JNET type 3.

Sano, Y., Hirata, D., & Saito, Y. (2018). Japan NBI Expert Team classification: Narrow-band imaging magnifying endoscopic classification of colorectal tumors. *Digestive Endoscopy*, *30*(4), 543-545.

# Kudo Classification

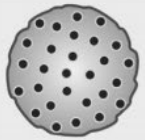
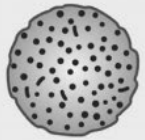
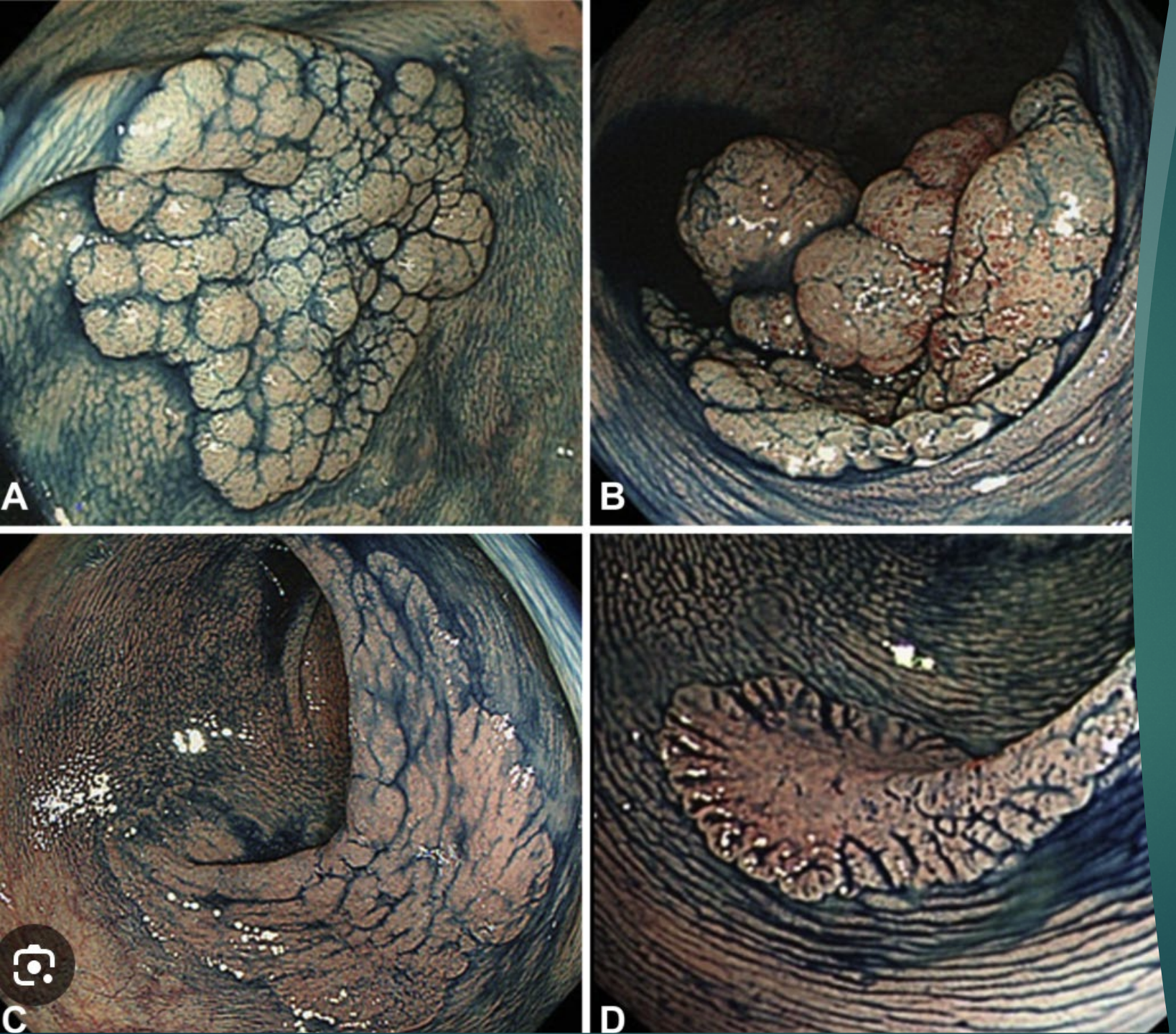
| TYPE | | CHARACTERISTICS | INTERPRETATION |
|---|---|---|---|
| I |  | Round, normal | Normal |
| II |  | Asteroid | Hyperplastic |
| $III_S$ |  | Tubular or round pit smaller than normal pit (type I) | Neoplastic<br>Tubular Adenoma |
| $III_L$ |  | Tubular or round pit larger than normal pit (type I) | Neoplastic<br>Tubular Adenoma |
| IV |  | Dendritic/gyrus brain-like | Neoplastic<br>Tubulovillous or villous |
| Vi |  | Irregular arrangement (sizes of $III_S$, $III_L$, IV type pits) | Neoplastic<br>High grade or invasive |
| Vn |  | Loss or decrease of pits with amorphous structure (non-structural) | |

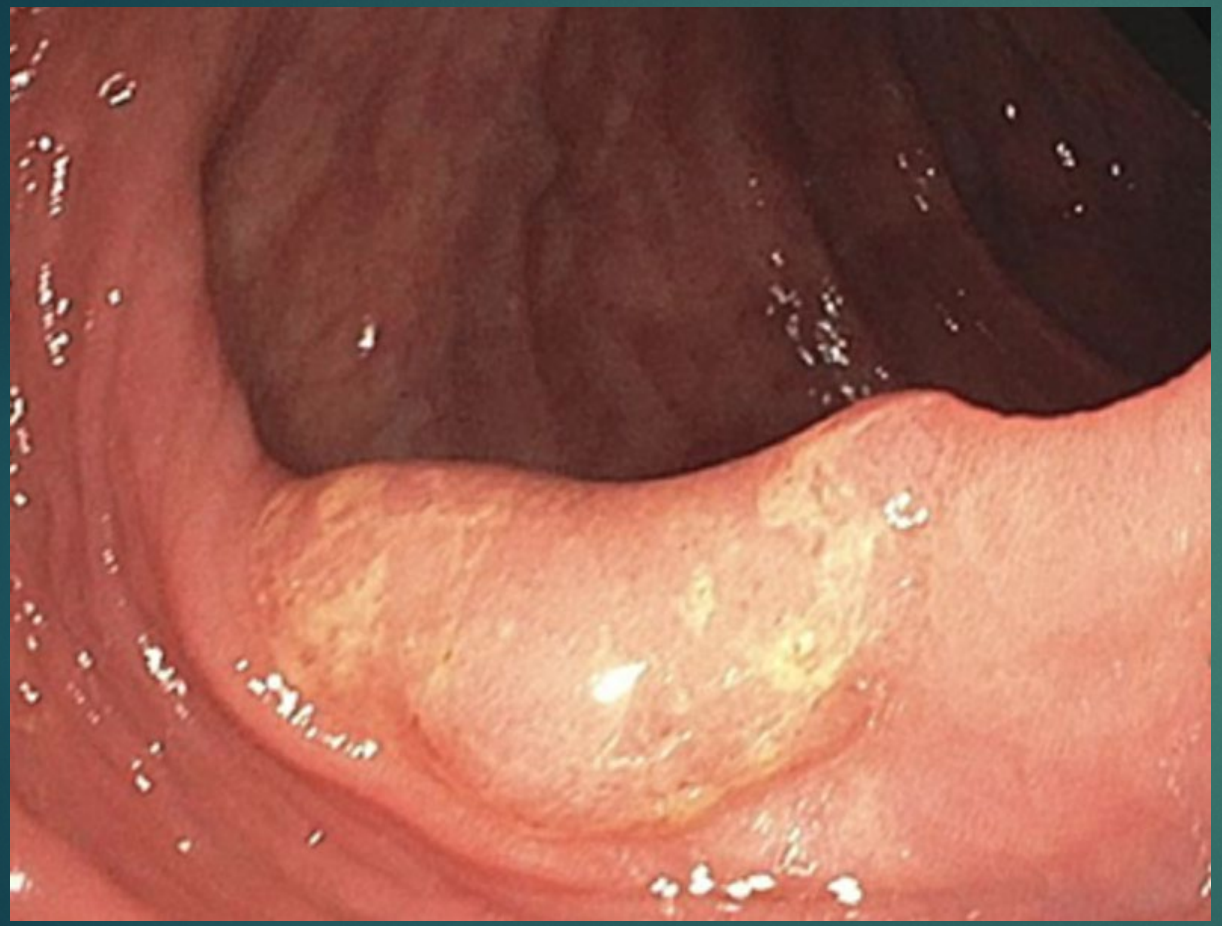
**Figure 2.** The Kudo classification for prediction of histology of colorectal lesions by pit structure analysis.

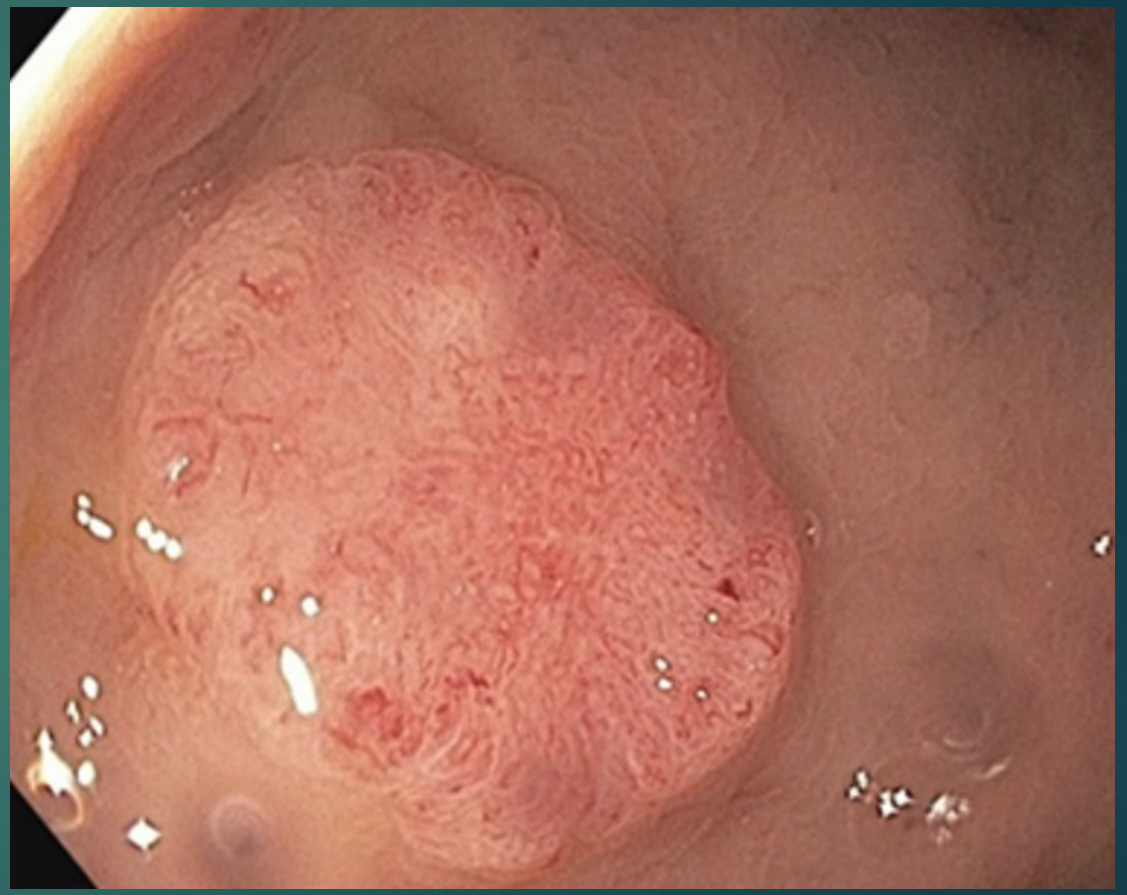
▸Rex, D. K., Shaukat, A., & Wallace, M. B. (2019). Optimal management of malignant polyps, from endoscopic assessment and resection to decisions about surgery. Clinical Gastroenterology and Hepatology, 17(8), 1428-1437.




# Granular Lesion (LSL-GT)

# Non-Granular LSL





# Risk of Occult Submucosal Invasive Cancer (SMIC) According to Gross Morphology and Location
n = 1712

A typical proximally located 0-IIa Granular Lesion.
Overall risk of SMIC 0.7%.

## 0-IIa G

SMIC risk by Paris Type Alone 2.1%
SMIC risk by Surface Morphology Alone 3.5%

**SMIC Risk 0.8%**

Proximal 0.7% Very Low Risk
Distal 1.2% Low Risk

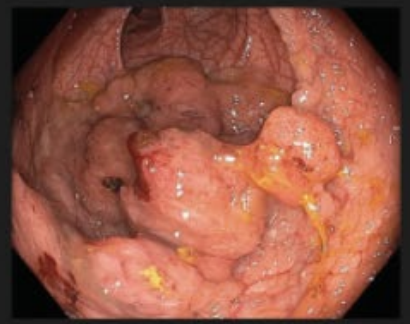
## 0-IIa NG

SMIC risk by Paris Type Alone 2.1%
SMIC risk by Surface Morphology Alone 8.1%

**SMIC Risk 4.2%**

Proximal 3.8%
Distal 6.4%

A proximal 0-IIa Non-Granular Lesion.
Overall risk of SMIC 3.8%



A rectal (distal) 0-IIa+Is Granular Lesion.
Overall risk of SMIC 10.1%.

## 0-IIa+Is G

SMIC risk by Paris Type Alone 8.4%
SMIC risk by Surface Morphology Alone 3.5%

**SMIC Risk 7.1%**

Proximal 4.2%
Distal 10.1%

## 0-IIa+Is NG

SMIC risk by Paris Type Alone 8.4%
SMIC risk by Surface Morphology Alone 8.1%

**SMIC Risk 14.1%**

Proximal 12.7% High Risk
Distal 15.9% High Risk

A transverse colon (proximal) 0-IIa+Is Non-Granular Lesion.
Overall risk of SMIC 12.7%.

A sigmoid colon (distal) 0-IsGranular Lesion.
Overall risk of SMIC 5.7%.

## 0-Is G

SMIC risk by Paris Type Alone 6.0%
SMIC risk by Surface Morphology Alone 3.5%

**SMIC Risk 3.7%**

Proximal 2.3% Low Risk
Distal 5.7%

## 0-Is NG

SMIC risk by Paris Type Alone 6.0%
SMIC risk by Surface Morphology Alone 8.1%

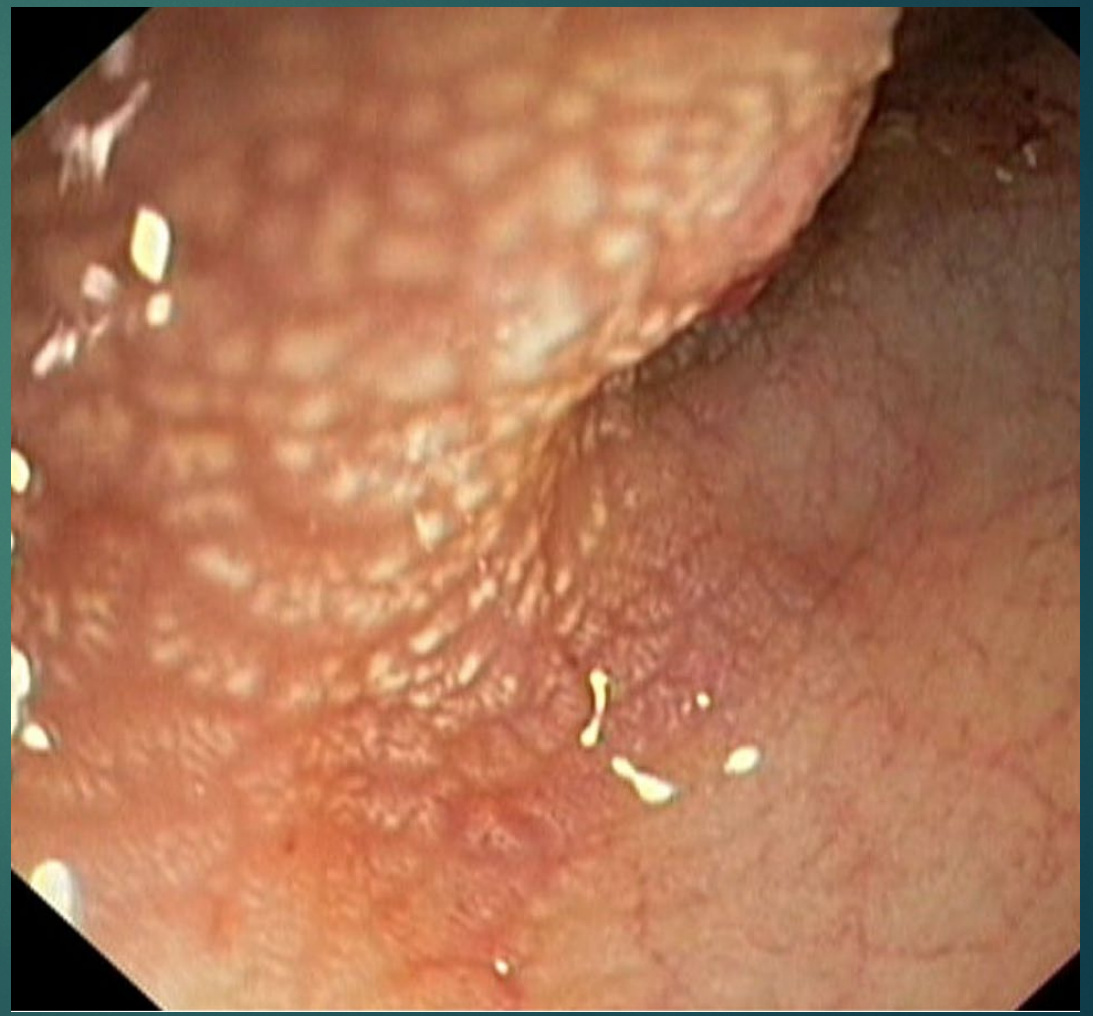
**SMIC Risk 15.3%**

Proximal 12.3% High Risk
Distal 21.4% Very High Risk

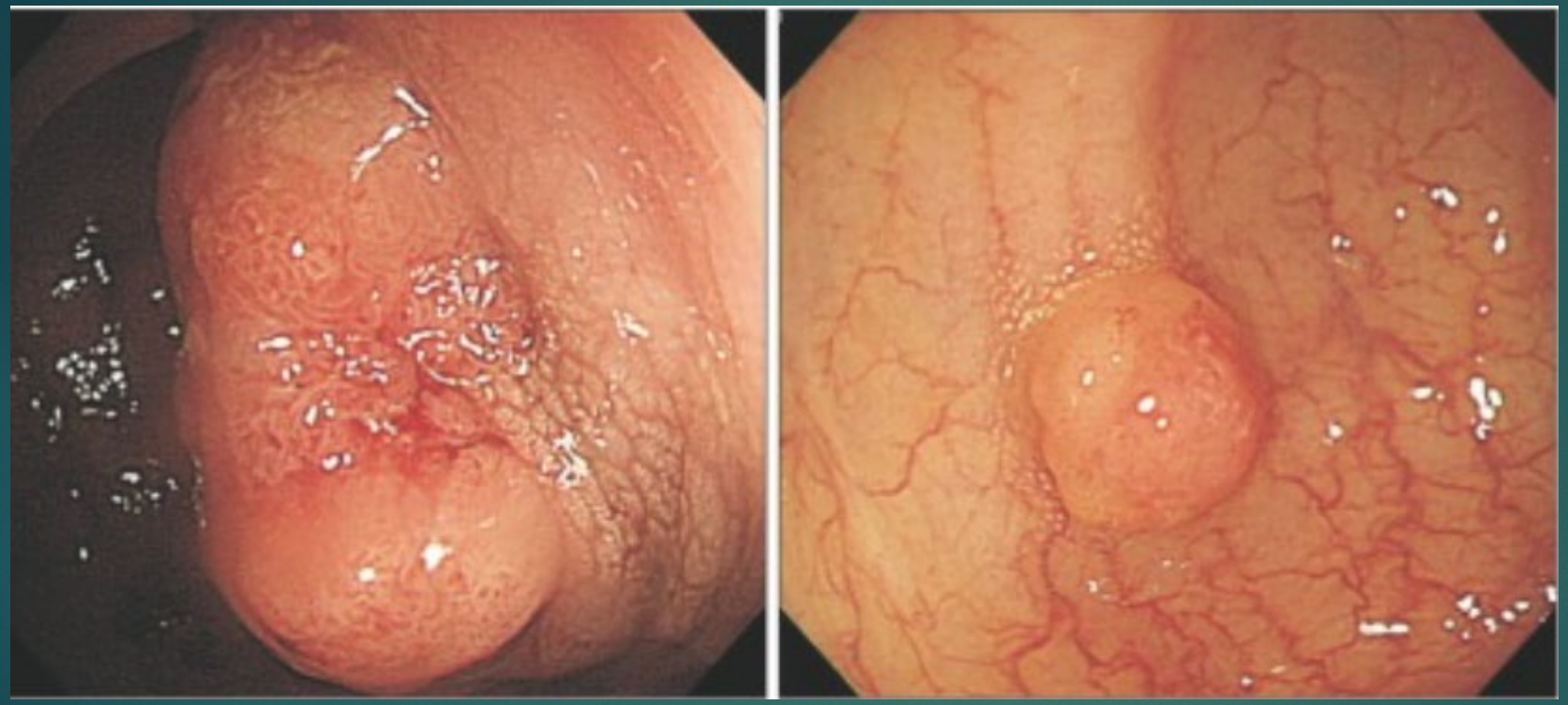
An ascending colon (proximal) 0-IsNon-Granular Lesion.
Overall risk of SMIC 12.3%.

Adapted from Burgess et al. *Gastroenterology* 153(3), 2017; 732–742.e1

# Chicken Skin Pattern



# Chicken Skin Pattern



-Aggregation of lipid laden macrophages
-Possible advanced adenoma
-Make sure to tattoo location after removal

# Risk of Cancer: Granular Vs Non Granular

| Lesion class | Risk of cancer |
|---|---|
| Granular LST - homogeneous | 1-2% |
| Granular LST- mixed nodular | 5-10% |
| Non-granular flat elevated | 5% |
| Non-granular – pseudodepression | 30-50% |
| Large sessile (1s) | 10-20% |

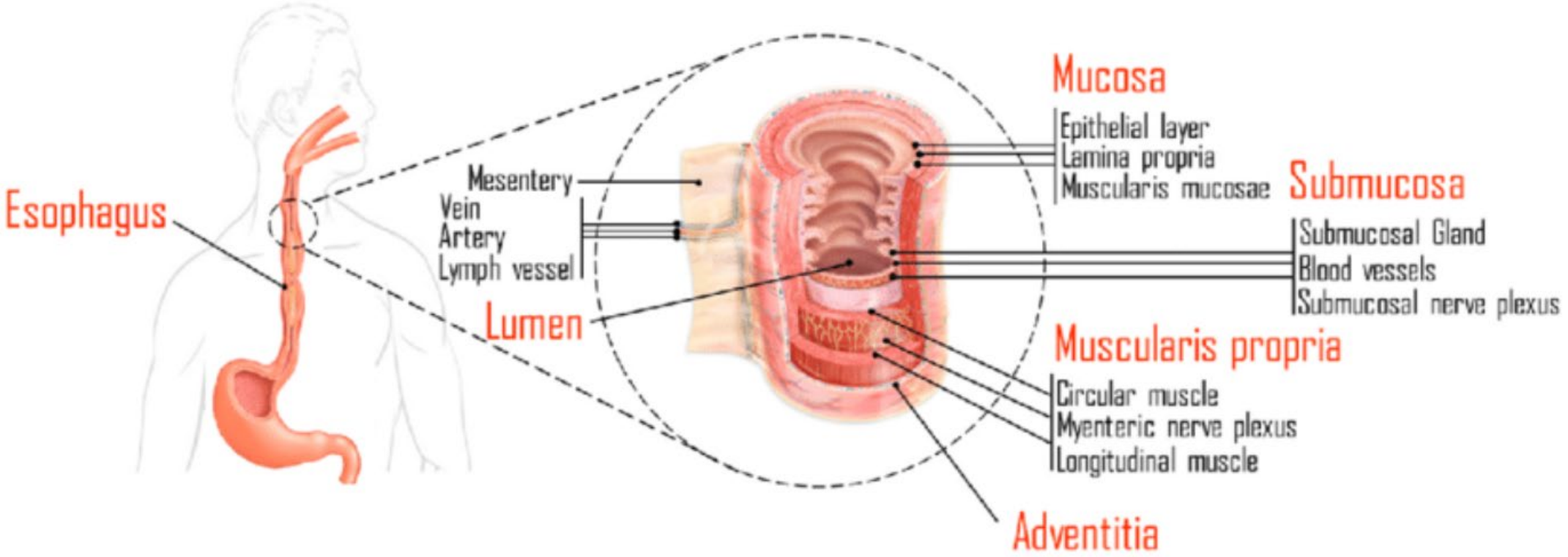
# Cold Snare Resection

## Cold Snare Polypectomy Assessment Tool (CSPAT)

- Put the lesion at 5-6 o'clock*
- Keep a good working distance*
- Place the snare accurately (margin of normal tissue)*
- Retrieve the specimen
- Inspect the site

# Surgical Oncology Terms

- En-Bloc Resection- Single piece removal of a tumor with normal margin of tissue
- R0-Microscopic margin negative resection
- R1-Macroscopic removal but microscopic margins positive
- R2-Gross residual disease with gross tumor not removed




# Esophageal Layers

**American Joint Committee on Cancer (AJCC)**
**TNM Staging Classification for Carcinoma of the Esophagus and Esophagogastric Junction (8th ed., 2017)**
**Squamous Cell Carcinoma and Adenocarcinoma**

***Table 1.*** **Definitions for T, N, M**

| T | Primary Tumor |
|---|---|
| TX | Primary tumor cannot be assessed |
| T0 | No evidence of primary tumor |
| Tis | High-grade dysplasia, defined as malignant cells confined to the epithelium by the basement membrane |
| T1 | Tumor invades the lamina propria, muscularis mucosae, or submucosa |
| T1a | Tumor invades the lamina propria or muscularis mucosae |
| T1b | Tumor invades the submucosa |
| T2 | Tumor invades the muscularis propria |
| T3 | Tumor invades adventitia |
| T4 | Tumor invades adjacent structures |
| T4a | Tumor invades the pleura, pericardium, azygos vein, diaphragm, or peritoneum |
| T4b | Tumor invades other adjacent structures, such as the aorta, vertebral body, or airway |

| N | Regional Lymph Nodes |
|---|---|
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastasis |
| N1 | Metastasis in one or two regional lymph nodes |
| N2 | Metastasis in three to six regional lymph nodes |
| N3 | Metastasis in seven or more regional lymph nodes |

| M | Distant Metastasis |
|---|---|
| M0 | No distant metastasis |
| M1 | Distant metastasis |

| G | Histologic Grade |
|---|---|
| GX | Grade cannot be assessed |
| G1 | Well differentiated |
| G2 | Moderately differentiated |
| G3 | Poorly differentiated, undifferentiated |

**Squamous Cell Carcinoma**

| Location | Location Criteria |
|---|---|
| X | Location unknown |
| Upper | Cervical esophagus to lower border of azygos vein |
| Middle | Lower border of azygos vein to lower border of inferior pulmonary vein |
| Lower | Lower border of inferior pulmonary vein to stomach, including gastroesophageal junction |

*Note*: Location is defined by the position of the epicenter of the tumor in the esophagus.

## PRINCIPLES OF ENDOSCOPIC STAGING AND THERAPY

**Primary Treatment**

- The goal of endoscopic therapy [by endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), and/or ablation] is the complete removal or eradication of early-stage disease (pTis, pT1a, selected superficial pT1b without LVI) and pre-neoplastic tissue (Barrett esophagus).
- Early-stage disease, Tis, also known as HGD, needs to be fully characterized, including evaluating presence of nodularity, lateral spread, and ruling out multifocal disease, as well as ruling out lymph node metastases by EUS in select higher risk cases. This is important to permit decisions on endoscopic therapy with ablative methods such as radiofrequency ablation (RFA), cryoablation, photodynamic therapy (PDT), and/or ER.[12-15] Areas of nodularity or ulceration should be resected rather than ablated. Completely flat, small lesions (≤2 cm) of squamous cell HGD/Tis (carcinoma in situ) and Barrett esophagus associated with flat HGD should be treated by ER as it provides more accurate histologic assessment of the lesion. Larger flat lesions (>2 cm) can be treated effectively by ER, but this is associated with greater risk of complications. Such lesions can be effectively treated by ablation alone, but there are very limited data on treating squamous cell HGD by ablation alone.[12,13,16-19]
- Lesions that are found to be pathologically limited to the lamina propria or muscularis mucosae (pT1a), or the superficial submucosa (pT1b), in the absence of evidence of lymph node metastases, LVI, or poor differentiation grade can be treated with full ER.[20-22] However, a thorough and detailed discussion regarding comparative risk of esophagectomy versus potential for concurrent nodal disease should be undertaken, preferably between patient and surgeon, especially in cases with larger tumors or deeper invasion. Ablative therapy of residual Barrett esophagus should be performed following ER.[17] Complete eradication of Barrett esophagus can also be performed with more aggressive application of EMR (widefield EMR) or ESD at the initial intervention, if necessary to completely resect an area of superficial tumor or mucosal nodularity ≤2 cm in maximal dimension.[23]
- The level of evidence for ablation of squamous cell carcinoma (SCC) after ER is low. However, additional ablation may be needed if there is multifocal HGD/carcinoma in situ elsewhere in the esophagus. Ablation may not be needed for lesions that are completely excised.[16,24,25]
- Endoscopic therapy is considered "preferred" for patients with limited early-stage disease (Tis and T1a, ≤2 cm, and well or moderately differentiated carcinoma), because the risk of harboring lymph node metastases, local or distant recurrence, and death from esophageal cancer is low following endoscopic therapy.[17]

# ESD Specimen BE with multifocal T1a nodularity

# Favorable Margins

- Synoptic Report Details
  - Margin assessment
  - Depth of invasion
  - Lymphovascular Invasion
  - Tumor Size
  - Tumor Budding
  - >2cm size
  - Differentiation (well/moderate/poor)

# Risk of LN Metastasis In T1a Disease BE

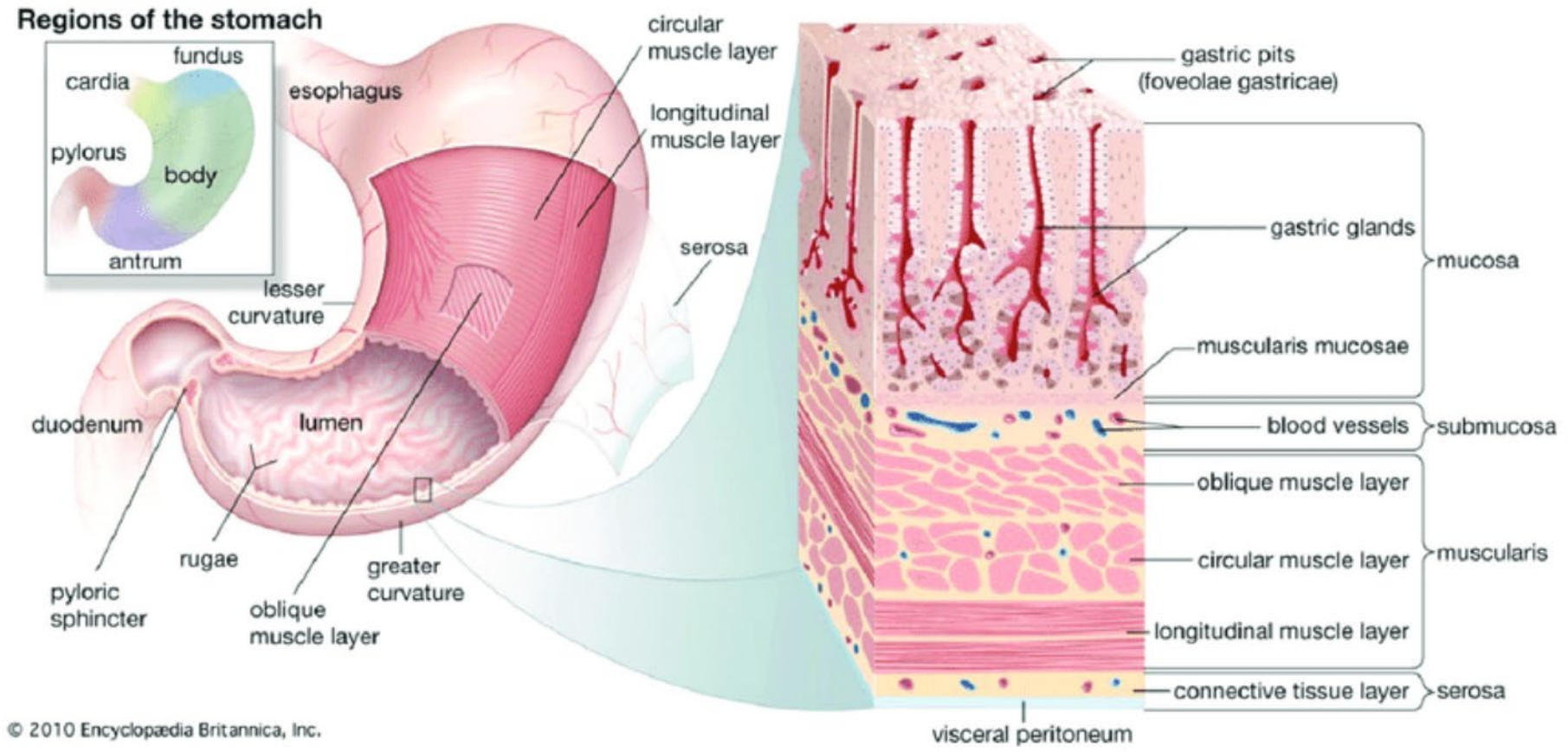
- T1a with favorable margins and pathology
  - 0-2% risk
  - Consider age, comorbidities, and differentiation as well
  - Endoscopy can be considered a definitive treatment pending favorable features
  - ESD Specimen Below

```
Tumor Extent: Invades lamina propria
Treatment Effect: No known presurgical therapy
Lymphovascular Invasion: Not identified
Perineural Invasion: Not identified
Margin Status for Invasive Carcinoma: All margins negative for intramucosal adenocarcinoma
Closest Margin(s) to Intramucosal adenocarcinoma: Deep
Distance from intramucosal adenocarcinoma to Closest Margin: 1.36 mm
Margin Status for High-Grade Glandular Dysplasia: All margins negative for high grade dysplasia
Margin Status for Low-Grade Glandular Dysplasia: All margins negative for low grade dysplasia
Margin(s) Involved by Intestinal Metaplasia: Mucosal
Regional Lymph Node Status: Not applicable (no regional lymph nodes submitted or found)
Distant Site(s) Involved, if applicable: Not applicable
PATHOLOGIC STAGE CLASSIFICATION (pTNM, AJCC 8th Edition): pT1a
```

# T1B Submucosal Invasion

- SM1 <500 µm (micrometers)=(0.5mm)
  - 5-10% overall LN metastasis risk
  - 2-5% if no LVI, tumor <2cm, well/moderately differentiated
  - Multi-disciplinary discussion
- SM2 500-1000 µm (0.5mm to 1mm)
  - 15-25% LN Risk
  - Endoscopy not curative
- SM3 >1000 µm (1mm)
  - 25-40% LN risk
  - Surgery highly recommended
  - ESD is only for diagnosis

# Gastric walls



**American Joint Committee on Cancer (AJCC)**
**TNM Staging Classification for Carcinoma of the Stomach (8th ed., 2017)**

***Table 1.*** **Definitions for T, N, M**

| | **Primary Tumor** |
|---|---|
| **TX** | Primary tumor cannot be assessed |
| **T0** | No evidence of primary tumor |
| **Tis** | Carcinoma *in situ*: intraepithelial tumor without invasion of the lamina propria, high-grade dysplasia |
| **T1** | Tumor invades the lamina propria, muscularis mucosae, or submucosa |
| T1a | Tumor invades the lamina propria or muscularis mucosae |
| T1b | Tumor invades the submucosa |
| **T2** | Tumor invades the muscularis propria* |
| **T3** | Tumor penetrates the subserosal connective tissue without invasion of the visceral peritoneum or adjacent structures**,*** |
| **T4** | Tumor invades the serosa (visceral peritoneum) or adjacent structures**,*** |
| T4a | Tumor invades the serosa (visceral peritoneum) |
| T4b | Tumor invades adjacent structures/organs |

*A tumor may penetrate the muscularis propria with extension into the gastrocolic or gastrohepatic ligaments, or into the greater or lesser omentum, without perforation of the visceral peritoneum covering these structures. In this case, the tumor is classified as T3. If there is perforation of the visceral peritoneum covering the gastric ligaments or the omentum, the tumor should be classified as T4.

**The adjacent structures of the stomach include the spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal gland, kidney, small intestine, and retroperitoneum.

***Intramural extension to the duodenum or esophagus is not considered invasion of an adjacent structure, but is classifi ed using the depth of the greatest invasion in any of these sites.

| | **Regional Lymph Nodes** |
|---|---|
| **NX** | Regional lymph node(s) cannot be assessed |
| **N0** | No regional lymph node metastasis |
| **N1** | Metastasis in one or two regional lymph nodes |
| **N2** | Metastasis in three to six regional lymph nodes |
| **N3** | Metastasis in seven or more regional lymph nodes |
| N3a | Metastasis in seven to 15 regional lymph nodes |
| N3b | Metastasis in 16 or more regional lymph nodes |

| | **Distant Metastasis** |
|---|---|
| **M0** | No distant metastasis |
| **M1** | Distant metastasis |

| | **Histologic Grade** |
|---|---|
| **GX** | Grade cannot be assessed |
| **G1** | Well differentiated |
| **G2** | Moderately differentiated |
| **G3** | Poorly differentiated, undifferentiated |

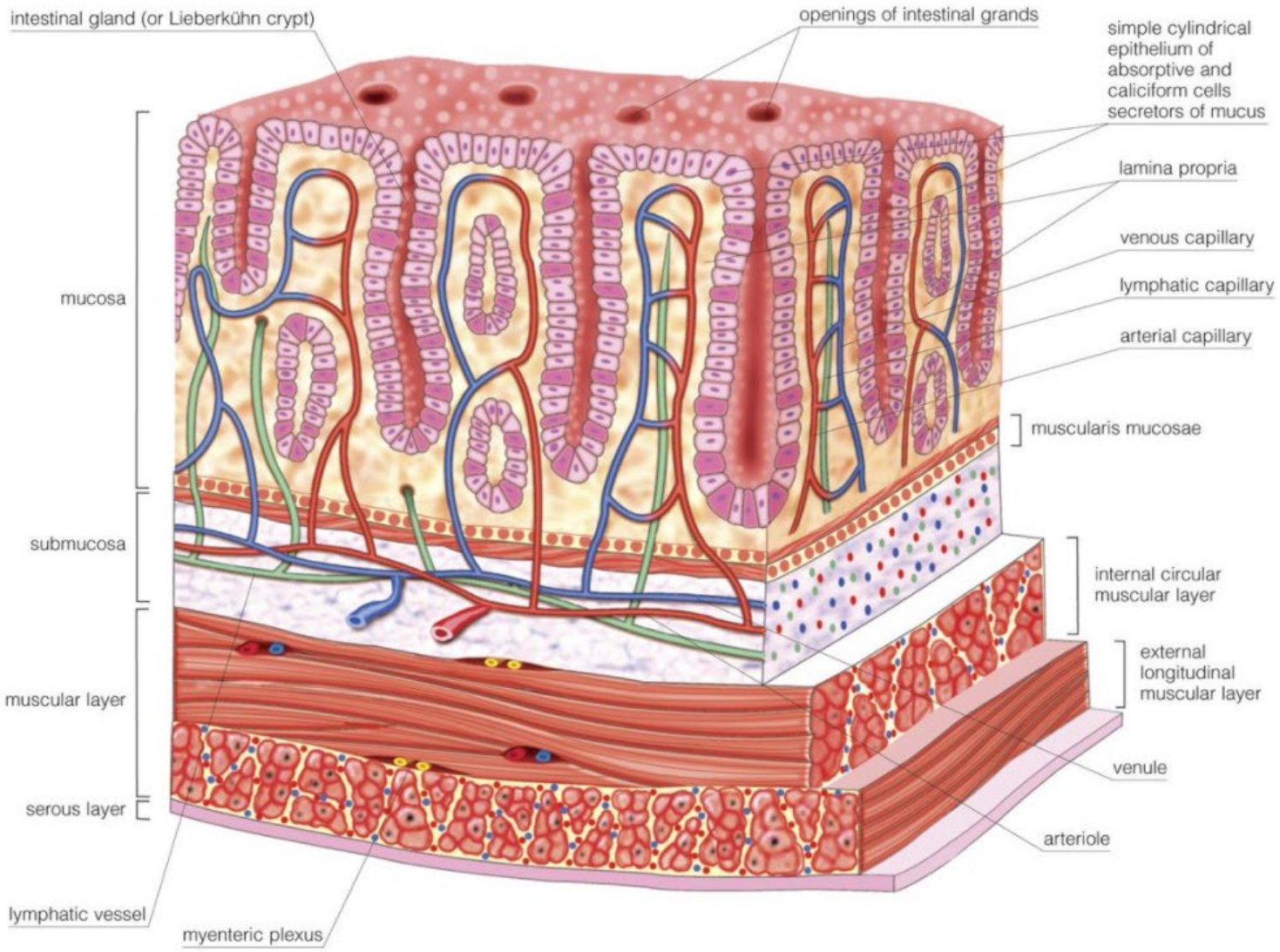
## PRINCIPLES OF ENDOSCOPIC STAGING AND THERAPY

**Treatment**

- EMR or ESD of early-stage gastric cancer can be considered adequate therapy when the lesion is ≤2 cm in diameter, is shown on histopathology to be well or moderately well differentiated, does not penetrate beyond the superficial submucosa, does not exhibit LVI, and has clear lateral and deep margins. En-bloc excision of small gastric lesions by ESD has been shown to be more effective than EMR in curing *small* early-stage gastric cancer, but requires greater skills and instrumentation to perform and has a significant risk of complications including perforation.[9]
- Japanese Gastric Cancer guidelines recommend that EMR or ESD should be considered for early-stage gastric cancer lesions ≤2 cm in diameter without associated ulcer formation.[3]
- EMR or ESD of gastric cancers that are poorly differentiated, harbor evidence of LVI, invade into the deep submucosa, or have positive lateral or deep margins or lymph node metastases, should be considered to be incomplete. Additional therapy by gastrectomy with lymphadenectomy should be considered.[10]
- EUS performed after chemotherapy or radiation therapy has a reduced ability to accurately determine the post-treatment stage of disease.[11] Similarly, biopsies performed after chemotherapy or radiation therapy may not accurately diagnose the presence of residual disease but still provide useful information.[12]
- Endoscopic tumor ablation can be performed for the short-term control of bleeding. Endoscopic insertion of expandable metal stents is effective in long-term relief of tumor obstruction at the EGJ or the gastric outlet, though surgical gastrojejunostomy may be more efficacious for those with longer-term survival (see Principles of Palliative Care/Best Supportive Care [GAST-J]).[13,14]
- Long-term palliation of anorexia, dysphagia, or malnutrition may be achieved with endoscopic- or radiographic-assisted placement of a feeding gastrostomy tube in carefully selected cases where the distal stomach is uninvolved by tumor, or the placement of a feeding jejunostomy tube (J-tube).[15]

**Post-Treatment Surveillance**

- Endoscopic surveillance following definitive treatment of gastric cancer requires careful attention to detail for mucosal surface changes, and multiple (4–6) biopsies of any visualized abnormalities. Strictures should be biopsied to rule out neoplastic cause. EUS performed in conjunction with endoscopy exams has a high sensitivity for detecting recurrent disease.[16] EUS-guided FNA should be performed if suspicious lymph nodes or areas of wall thickening are seen.




# Colonic Walls

## American Joint Committee on Cancer (AJCC) TNM Staging Classification for Colon Cancer 8th ed., 2017

***Table 1.*** **Definitions for T, N, M**

| | |
|---|---|
| **T** | **Primary Tumor** |
| **TX** | Primary tumor cannot be assessed |
| **T0** | No evidence of primary tumor |
| **Tis** | Carcinoma *in situ*, intramucosal carcinoma (involvement of lamina propria with no extension through muscularis mucosae) |
| **T1** | Tumor invades the submucosa (through the muscularis mucosa but not into the muscularis propria) |
| **T2** | Tumor invades the muscularis propria |
| **T3** | Tumor invades through the muscularis propria into pericolorectal tissues |
| **T4** | Tumor invades* the visceral peritoneum or invades or adheres** to adjacent organ or structure |
| T4a | Tumor invades* through the visceral peritoneum (including gross perforation of the bowel through tumor and continuous invasion of tumor through areas of inflammation to the surface of the visceral peritoneum) |
| T4b | Tumor directly invades* or adheres** to adjacent organs or structures |

| | |
|---|---|
| **N** | **Regional Lymph Nodes** |
| **NX** | Regional lymph nodes cannot be assessed |
| **N0** | No regional lymph node metastasis |
| **N1** | One to three regional lymph nodes are positive (tumor in lymph nodes measuring ≥0.2 mm), or any number of tumor deposits are present and all identifiable lymph nodes are negative |
| N1a | One regional lymph node is positive |
| N1b | Two or three regional lymph nodes are positive |
| N1c | No regional lymph nodes are positive, but there are tumor deposits in the subserosa, mesentery, or nonperitonealized pericolic, or perirectal/mesorectal tissues |
| **N2** | Four or more regional lymph nodes are positive |
| N2a | Four to six regional lymph nodes are positive |
| N2b | Seven or more regional lymph nodes are positive |

| | |
|---|---|
| **M** | **Distant Metastasis** |
| **M0** | No distant metastasis by imaging, etc.; no evidence of tumor in distant sites or organs. (This category is not assigned by pathologists) |
| **M1** | Metastasis to one or more distant sites or organs or peritoneal metastasis is identified |
| M1a | Metastasis to one site or organ is identified without peritoneal metastasis |
| M1b | Metastasis to two or more sites or organs is identified without peritoneal metastasis |
| M1c | Metastasis to the peritoneal surface is identified alone or with other site or organ metastases |

# NCCN Guidelines Colon Cancer



National Comprehensive Cancer Network®

## NCCN Guidelines Version 5.2025
## Colon Cancer

NCCN Guidelines Index
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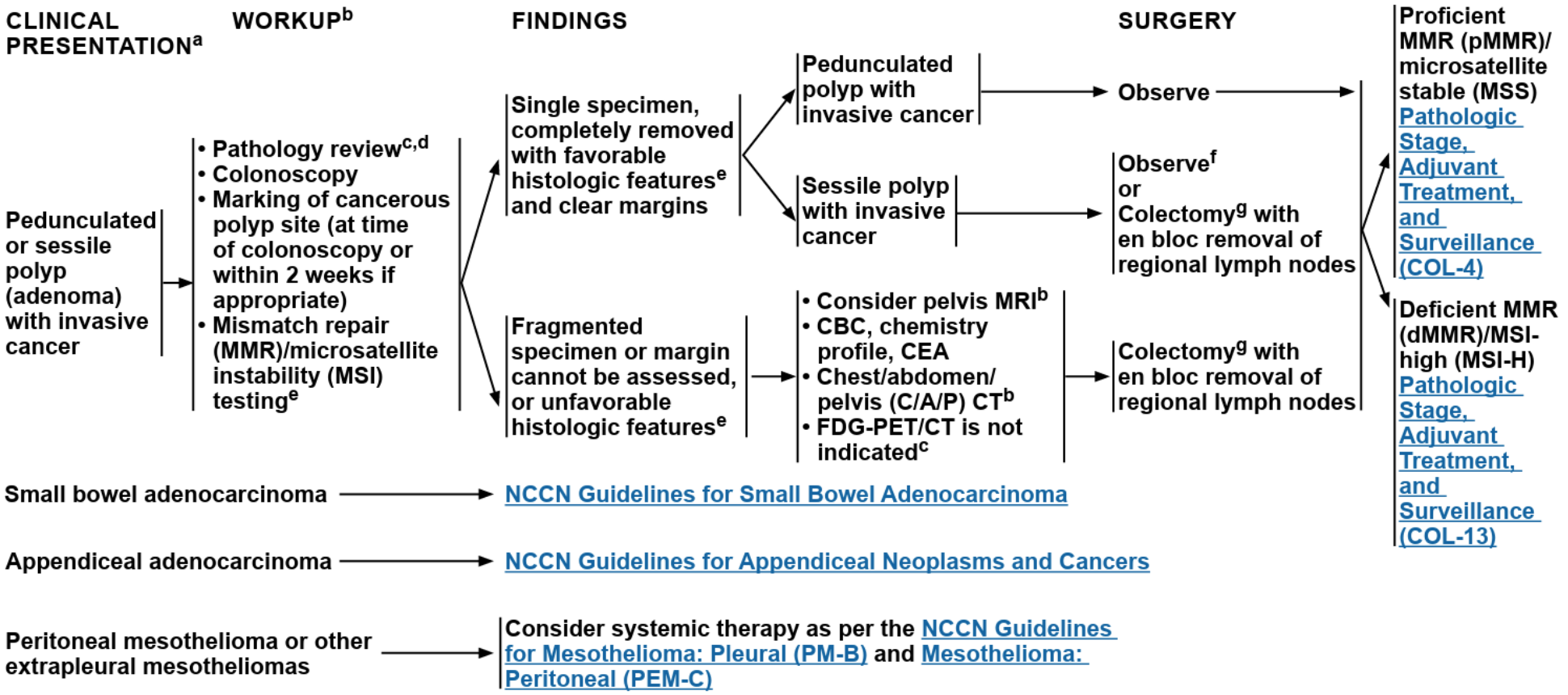
Discussion



# Margins and Histologically Favorable Conditions for Endoscopic Resection

## PRINCIPLES OF PATHOLOGIC AND MOLECULAR REVIEW

**Endoscopically Removed Malignant Polyps**

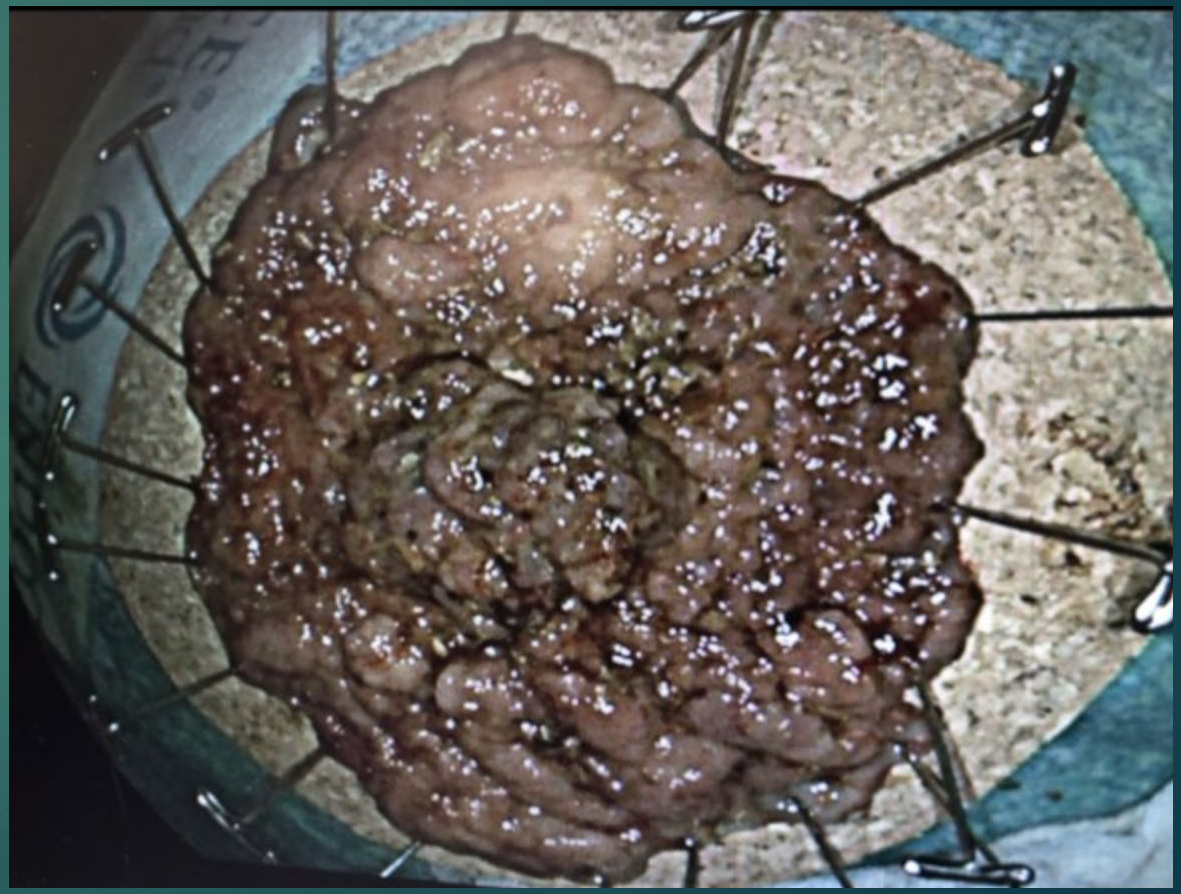
- A malignant polyp is defined as one with cancer invading through the muscularis mucosa and into the submucosa (pT1). pTis is not considered a "malignant polyp."
- Favorable histologic features: grade 1 or 2 (low-grade histology according to WHO 2019), no angiolymphatic invasion, and negative margin of resection. There is no consensus as to the definition of what constitutes a positive margin of resection. A positive margin has been defined as: 1) tumor <1 mm from the transected margin; 2) tumor <2 mm from the transected margin; and 3) tumor cells present within the diathermy of the transected margin.[1-4]
- Unfavorable histologic features: grade 3 or 4 (high-grade histology according to WHO 2019), angiolymphatic invasion, or a "positive margin." See the positive margin definition above. In several studies, high tumor budding has been shown to be an adverse histologic feature associated with adverse outcome and may preclude polypectomy as an adequate treatment of endoscopically removed malignant polyps.
- There is controversy as to whether malignant colorectal polyps with a sessile configuration can be successfully treated by endoscopic removal. The literature seems to indicate that endoscopically removed sessile malignant polyps have a significantly greater incidence of adverse outcomes (residual disease, recurrent disease, mortality, and hematogenous metastasis, but not lymph node metastasis) than do pedunculated malignant polyps. However, when one looks closely at the data, configuration by itself is not a significant variable for adverse outcome, and endoscopically removed malignant sessile polyps with grade I or II histology, negative margins, and no lymphovascular invasion can be successfully treated with endoscopic polypectomy.[3-7]

**Colon Cancer Appropriate for Resection**

- Histologic confirmation of primary colonic malignant neoplasm

**Pathologic Stage**

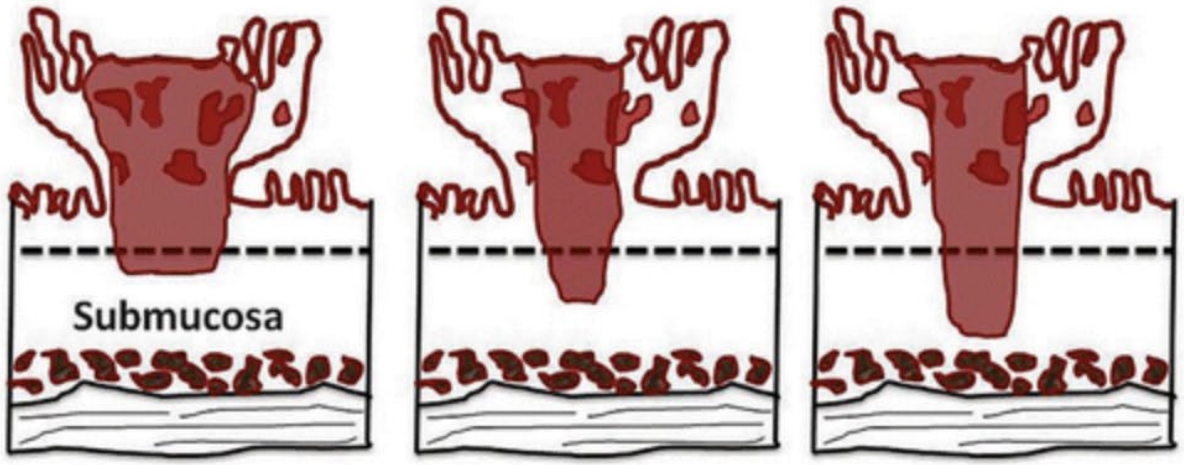
- The following parameters should be reported:
  - Grade of the cancer
  - Depth of penetration (T)
  - Number of lymph nodes evaluated and number positive (N)
  - Status of proximal, distal, radial, and mesenteric margins[8,9]; see Staging (ST-1)
  - Lymphovascular invasion[10,11]
  - Perineural invasion (PNI)[12-14]
  - Tumor deposits[15-18]



# Colo-rectal SM invasion

**Kikuchi Classification (for T1): Based on Extent of Submucosal Invasion**

- Sm 1 = upper third of submucosa
- Sm 2 = middle third of submucosa
- Sm 3 = lower third of submucosa




| | Sm 1 | Sm 2 | Sm 3 |
|---|---|---|---|
| Rate of LN Involvement | 1-3% | 8% | 23% |

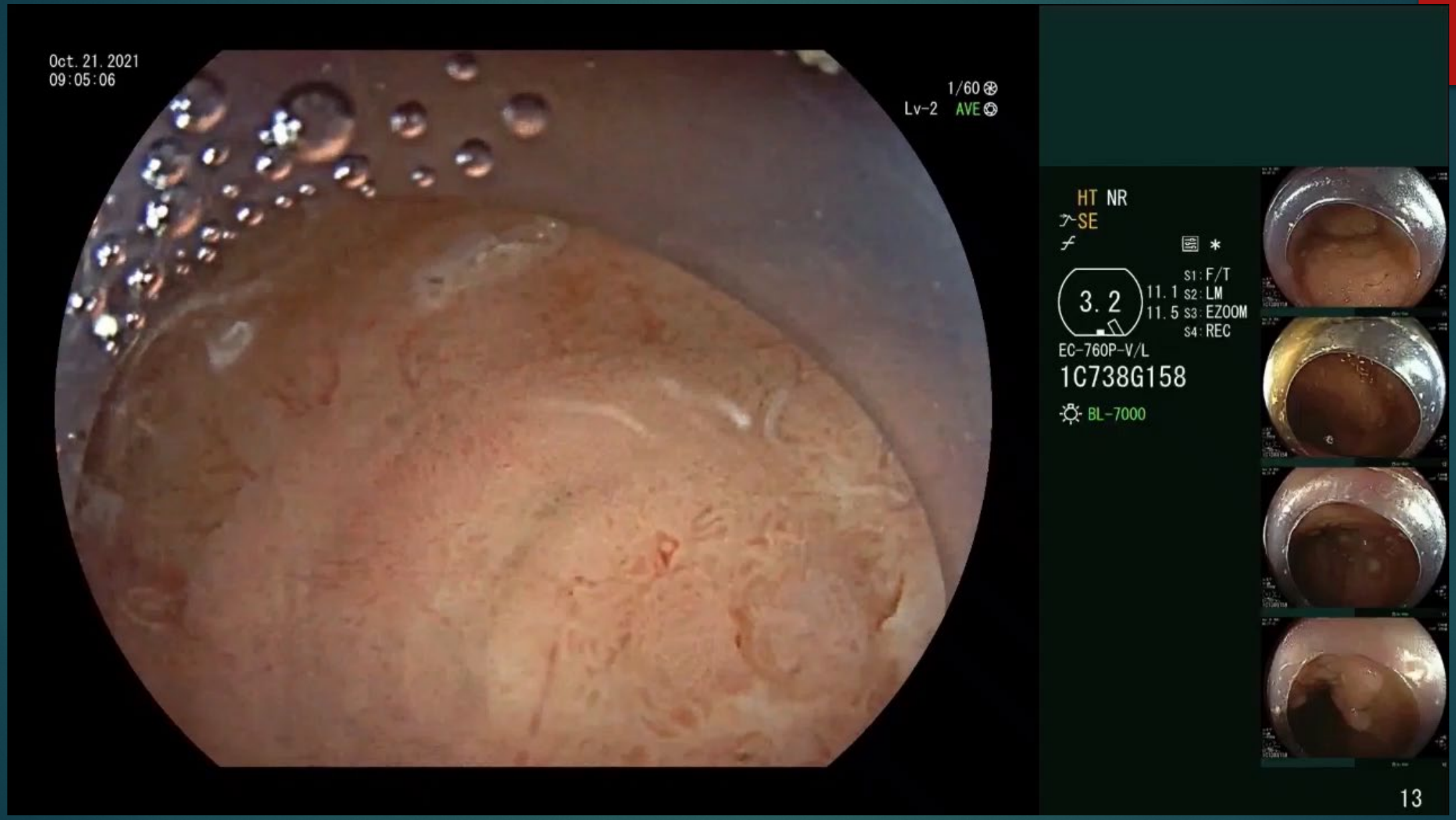
Not recommended for local excision

# Resection Techniques

- EMR
  - Standard Submucosal Lift and Hot snare
  - Underwater Approach
  - Band Assistance and Snare
- ESD (Third Space Convention)
  - Conventional ESD
  - Hybrid ESD
  - Pocket
  - Underwater ESD
  - Traction Assisted ESD
  - STER

- Unconventional
  - FTRD
  - 2T Scope Resection with Tissue Helix
  - Endoloop Resection
  - Band without resection
  - Full-Thickness Resection

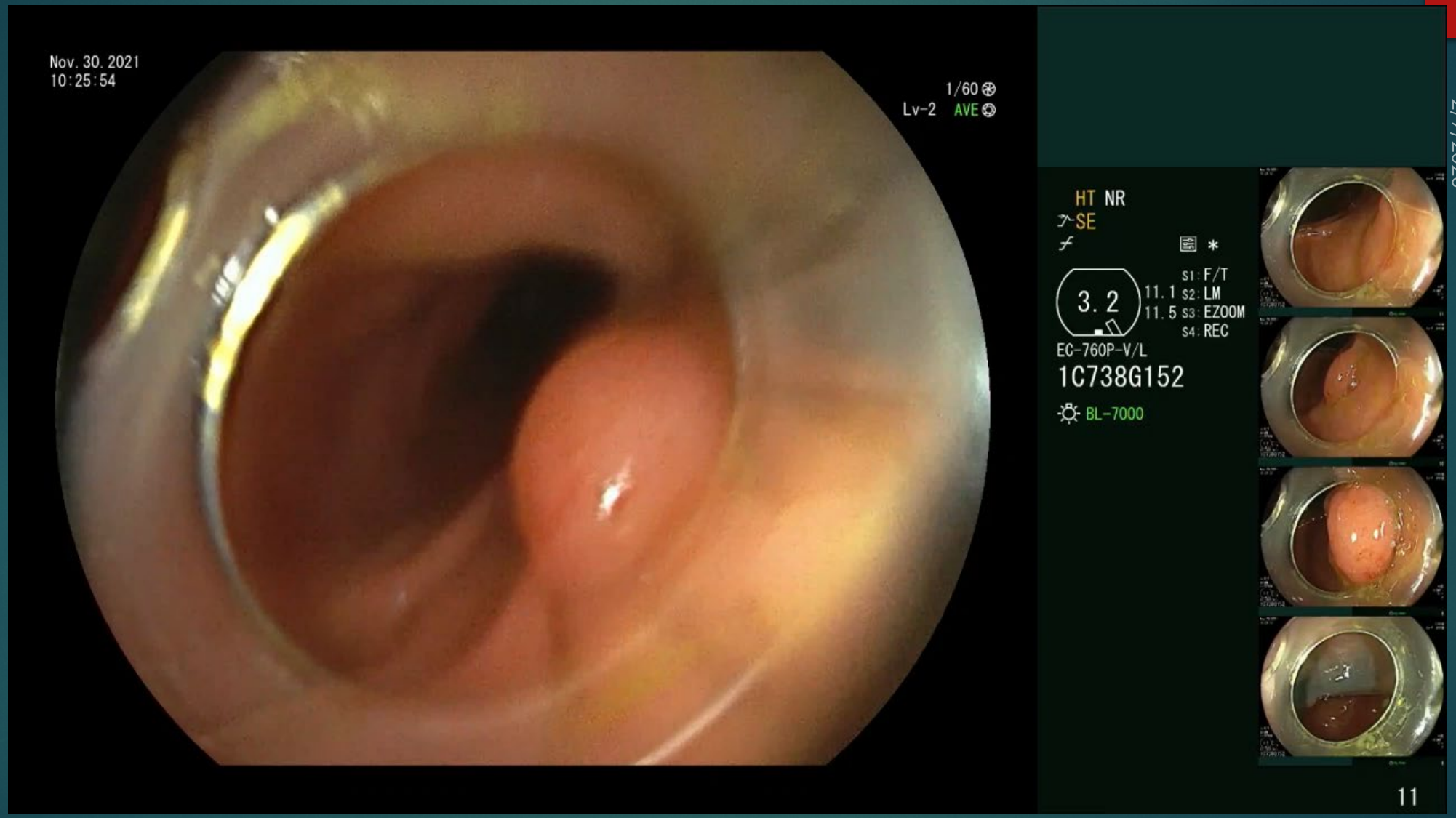
# Conventional standard lift EMR



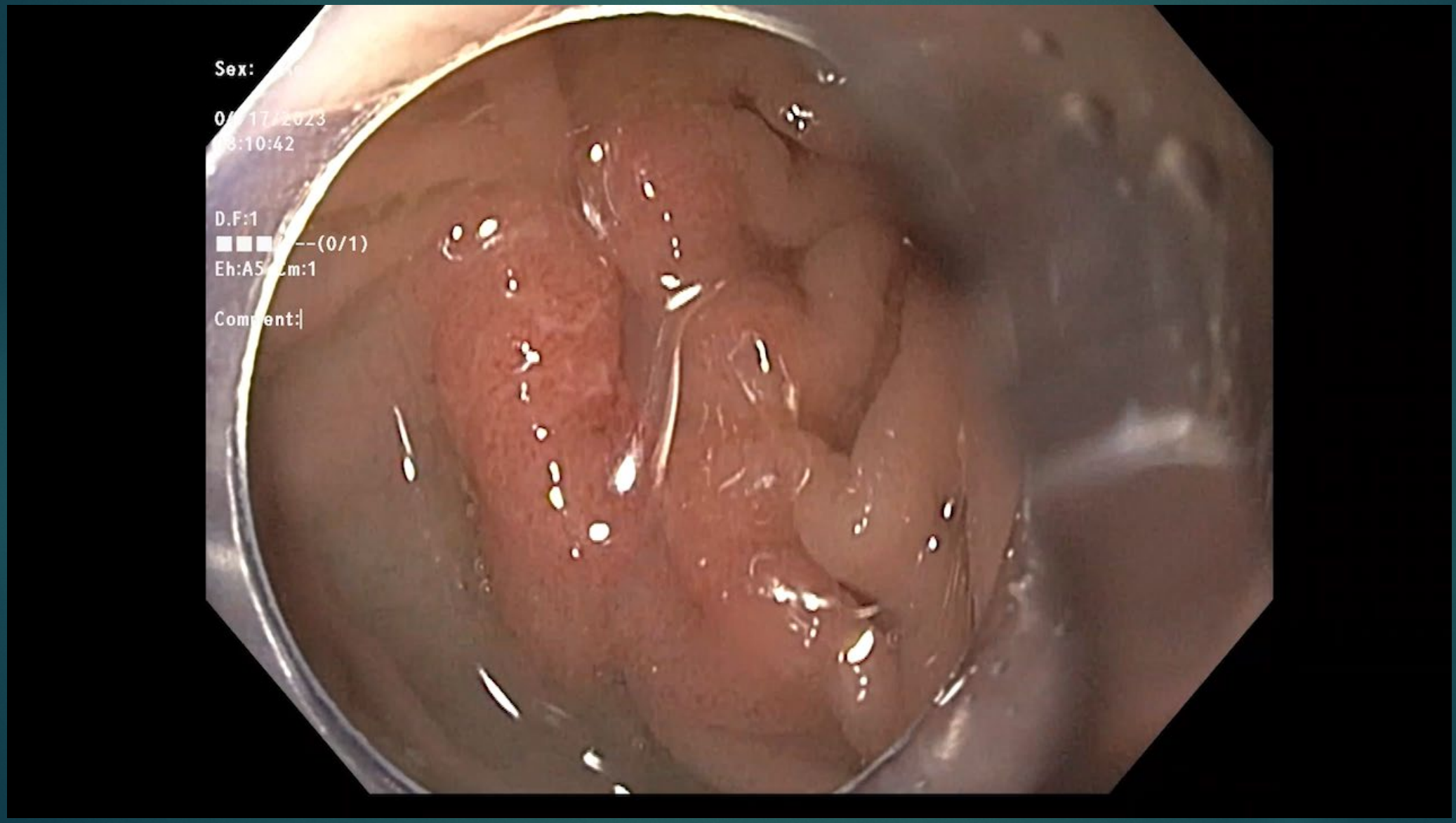
# Underwater EUS

# Underwater EMR

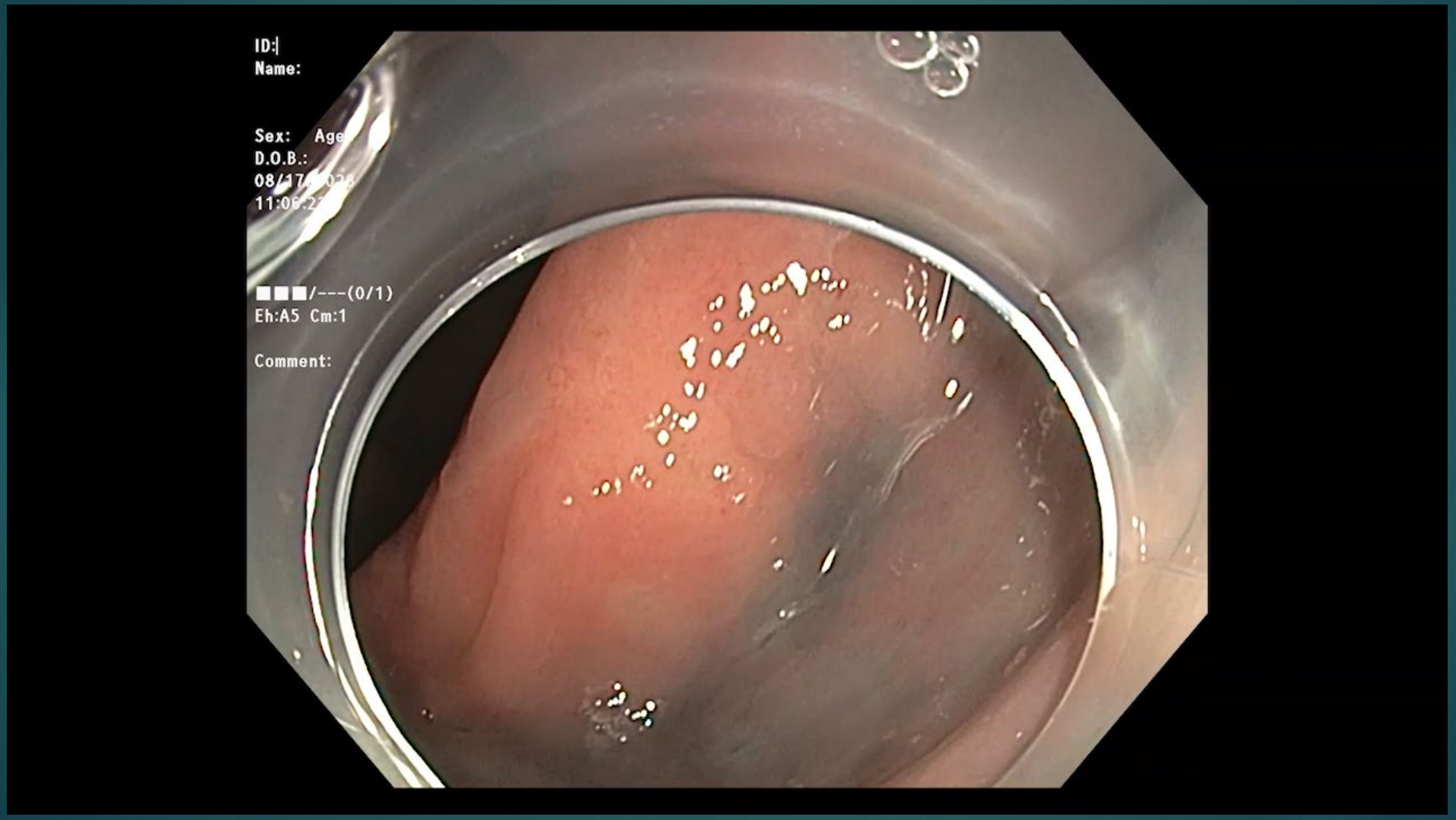




# Underwater EMR En-bloc



# Piecemeal Underwater EMR



# Limitations of Traditional Lift EMR

- EMR limited by lifting, scar tissue and wall tension (snare slips)
- Surgery required for deeper or fibrotic disease
- Time-consuming

# Endoscopic Submucosal Dissection (ESD)

- ESD Definition: Use of the endoscope to expose the submucosal plane to allow for controlled dissection to help achieve margin assessment
- Piecemeal Resection precludes Margin assessement

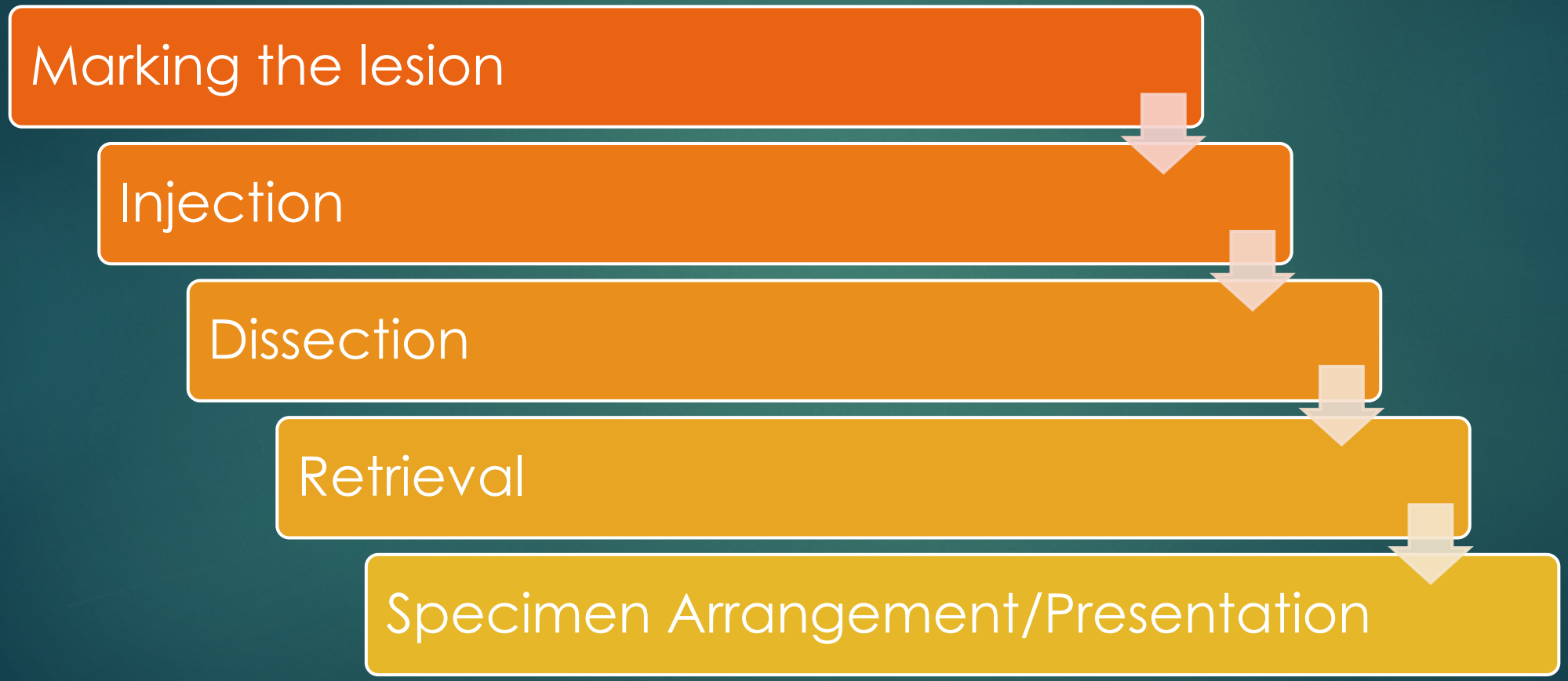
# ESD Benefits

- EMR piece-meal resection sacrifices histologic certainty in early invasive disease
- ESD enables en bloc, margin-negative resection
- Potentially curative without surgery

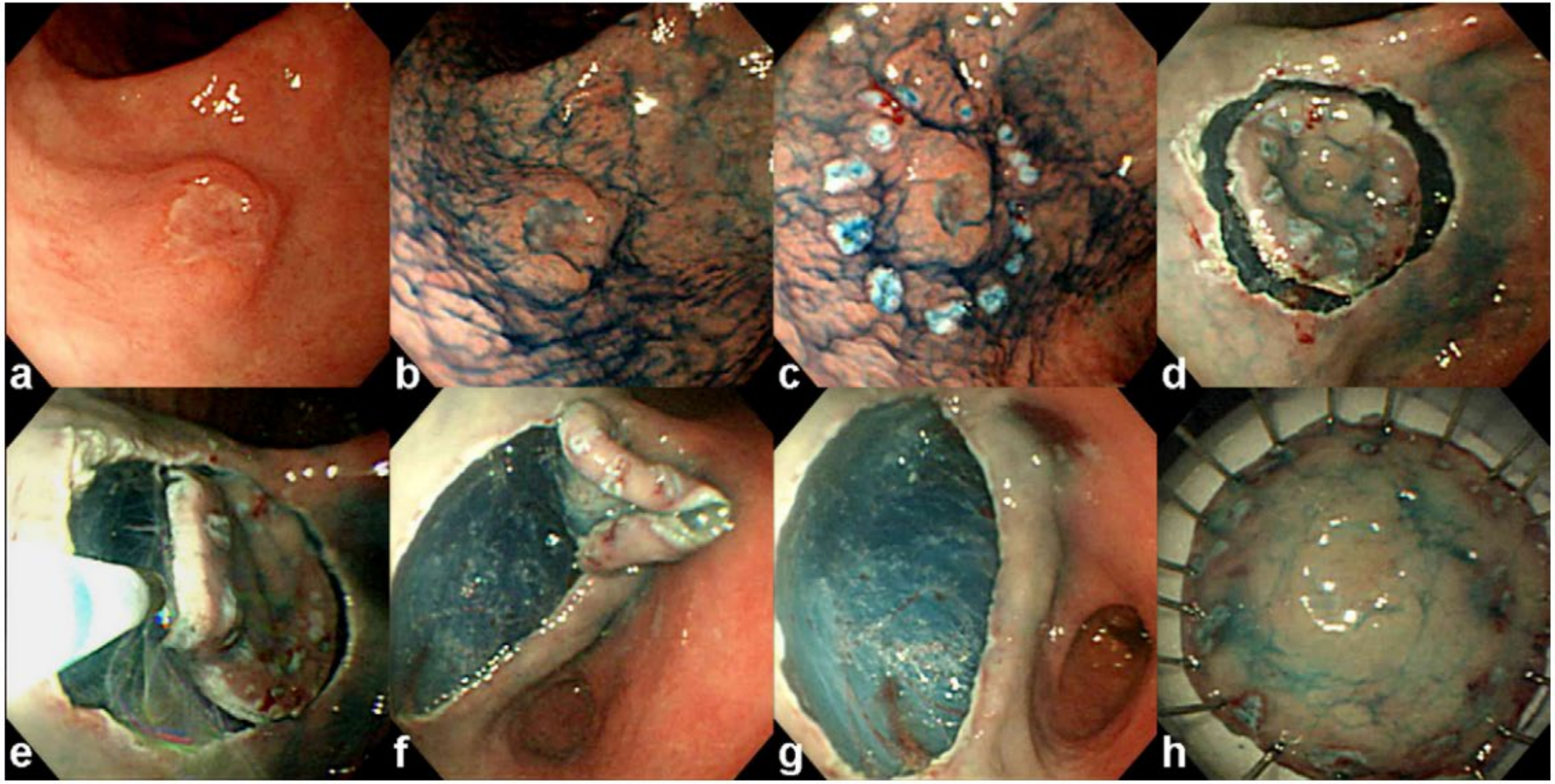
# ESD Negatives

- More Time consuming
- Higher risk of perforation (few caveats)
- Higher skill and fewer practioners
- More costly
- Potentially can be hard to retrieve specimen en-bloc (I.e. very large lesions)

# ESD Key Steps



# Conventional ESD

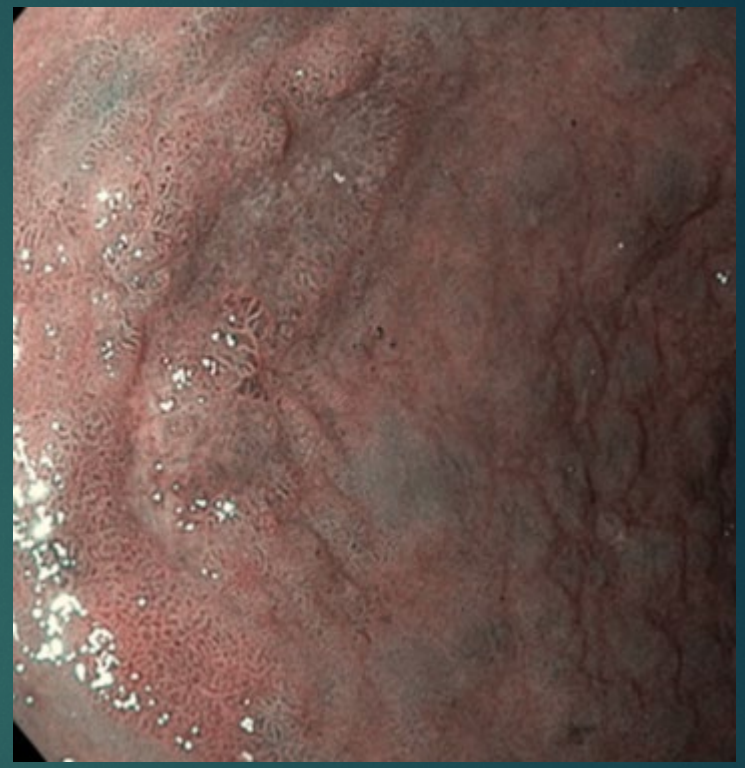




- Min, B. H., Lee, J. H., Kim, J. J., Shim, S. G., Chang, D. K., Kim, Y. H., ... & Rhee, J. C. (2009). Clinical outcomes of endoscopic submucosal dissection (ESD) for treating early gastric cancer: comparison with endoscopic mucosal resection after circumferential precutting (EMR-P). *Digestive and Liver Disease*, *41*(3), 201-209.

# Marking

- Mark around 2mm outside of specimen
- Can either cut through markings or cut just outside of marking
- Soft coagulation setting with a knife



# Marking

- Mark around 2mm outside of specimen
- Can either cut through markings or cut just outside of marking
- Soft coagulation setting with a knife
- I usually mark distal first, then proximal, then the lateral sides (4 marks)
- I then connect the four marks
- Markins is the MOST important step

# Injection

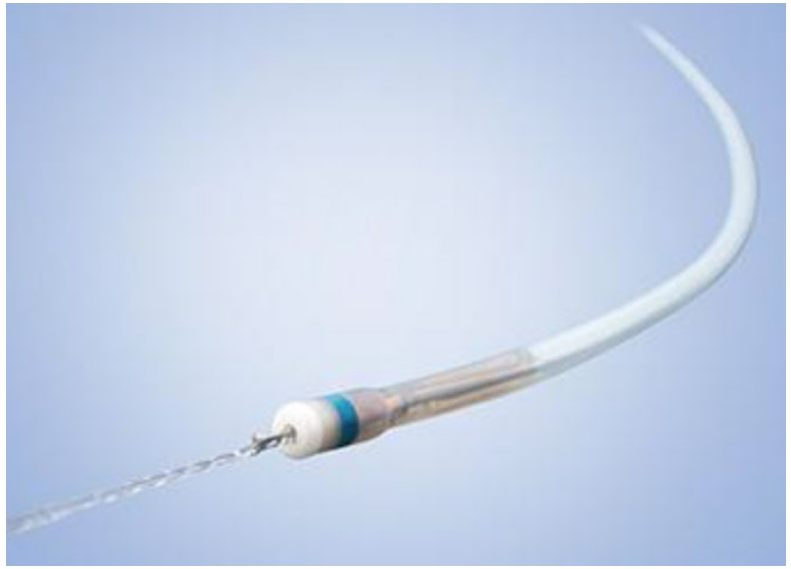
- Normal Saline IV bag + Epinephrine + Methylene Blue
- Other solutions
  - 6% Hetastarch
  - Commercial Lifting Agents
- Methods of lifting
  - Needle
  - Knife Itself
  - Use of a Pressure Jet

# The Submucosal Plane

- Target: between lesion and muscularis propria
- White fibers = safe dissection zone
- Blue-stained cushion improves orientation
- Loss of plane increases perforation risk

# Dissection

- Straight Knives
- Insulated Tip Knives
- Hook Knives
- Injection knives
- Scissors
- Snare (hybrid ESD)
- Traction
- Coagulation Graspers



# Dissection

- Straight Knives
- Insulated Tip Knives
- Hook Knives
- Injection knives
- Scissors
- Snare (hybrid ESD)
- Coagulation Graspers
- Traction

# ESD Specimen

- Allows for pathology to review intact architecture
- Orientation of margins
- Depth assessment
- Allows for assessment of invasion or more importantly confidently exclude it

# Safety and efficacy of endoscopic submucosal dissection vs endoscopic mucosal resection in managing gastrointestinal tract tumors: a systematic review and meta-analysis

Adnan Bhat [1], Ajay Kumar [2], Humza Saeed [3], Zahra Ali [4], Anchit Chauhan [5], Muhammad Hamza [6], Unaiza Iftikhar [7], Adil Ahmed [8], Peter Draganov [9]

Affiliations + expand

PMID: 41487547 PMCID: PMC12758251 DOI: 10.1080/08998280.2025.2583724

- 25 studies with 5283 Patients
- ESD results in higher En-bloc Rates
- Higher Procedural Risks (Delayed bleeding and perforation risk higher)

# EMR vs ESD

=

# EMR vs ESD

- The true question is not EMR vs ESD. It is do we need piecemeal or do we have to have this lesion En-bloc?

***DIAGNOSIS:***

**A. Small bowel, duodenal carcinoid D margins, biopsy:**
**- Well-differentiated neuroendocrine tumor, 0.4 cm, grade 1**
**- Deep and peripheral margins (including part B) are negative for tumor**
**- Pathologic stage pT1: Tumor invades the mucosa or submucosa only, and is less than or equal to 1 cm in greatest**

**B. Small bowel duodenal EMR side margins, biopsy:**
**- Duodenum mucosa with no significant histopathologic changes**
**- Side margins are negative for neuroendocrine tumor**

# Diagnostic Uncertainty

- When EMR performed and it is not en-bloc there can be pathologic uncertainty in staging. This can lead to unnecessary surgeries like esophagectomy (high morbidity)
- If piecemeal EMR is performed and showed adencaricnoma will not be able to exclude deeper invasion or complete resection
  - Referral to surgery (may or may not be necessary)
- ESD En-bloc resection of same lesion with negative deep and lateral margins helps you risk stratify risk of invasion and whether surveillance is reasonable.
- How can we identify when there is a concern for malignancy? So that the correct endoscopic modality can be performed.

| | EMR | ESD |
|---|---|---|
| En bloc resection | 47% | 92% |
| Curative resection | 42% | 82% |
| Local recurrence | 12% | 1% |
| Perforation | 1.4% | 5.7% |

Fujiya et al. Gastrointest Endosc. 2015

- Clinical Outcomes

Table 2
Clinical outcomes of EMR-P and ESD for all study subjects

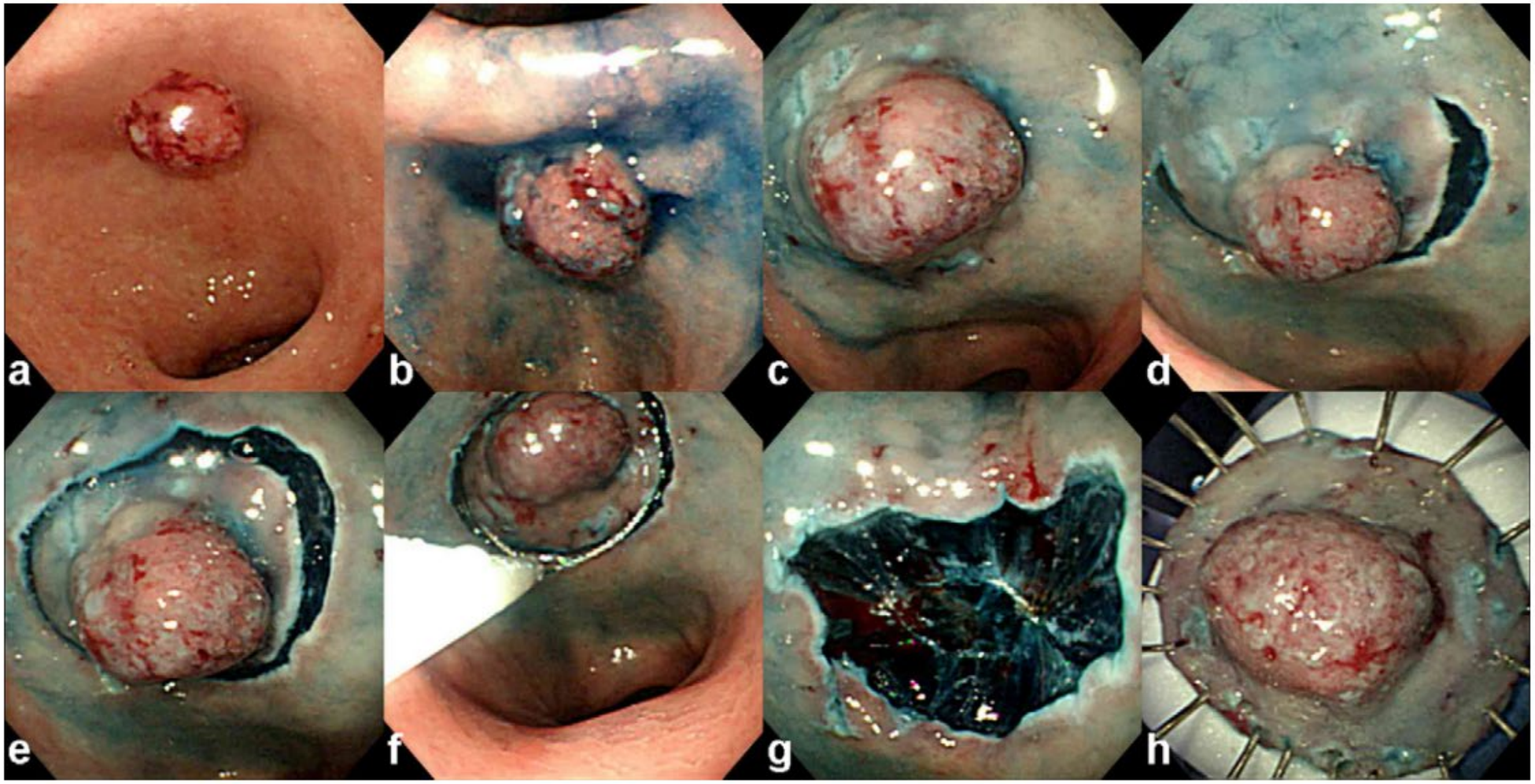
| Characteristics | EMR-P ($n = 103$) | ESD ($n = 243$) | *P*-value |
|---|---|---|---|
| En bloc resection (%) | 80 (77.7) | 233 (95.9) | <0.001 |
| R0 resection (%) | 92 (89.3) | 226 (93.0) | 0.251 |
| En bloc plus R0 resection (%) | 78 (75.7) | 216 (88.9) | 0.002 |
| Procedure time (min)[a] | 24.3 ± 16.2 | 33.4 ± 16.6 | <0.001 |
| Bleeding (%) | 4 (3.9) | 13 (5.3) | 0.564 |
| Perforation (%) | 2 (1.9) | 11 (4.5) | 0.359 |

EMR-P, endoscopic mucosal resection after circumferential precutting; ESD, endoscopic submucosal dissection.

[a] The value was expressed as mean ± standard deviation.

Min, B. H., Lee, J. H., Kim, J. J., Shim, S. G., Chang, D. K., Kim, Y. H., ... & Rhee, J. C. (2009). Clinical outcomes of endoscopic submucosal dissection (ESD) for treating early gastric cancer: comparison with endoscopic mucosal resection after circumferential precutting (EMR-P). *Digestive and Liver Disease*, *41*(3), 201-209.

# Hybrid ESD

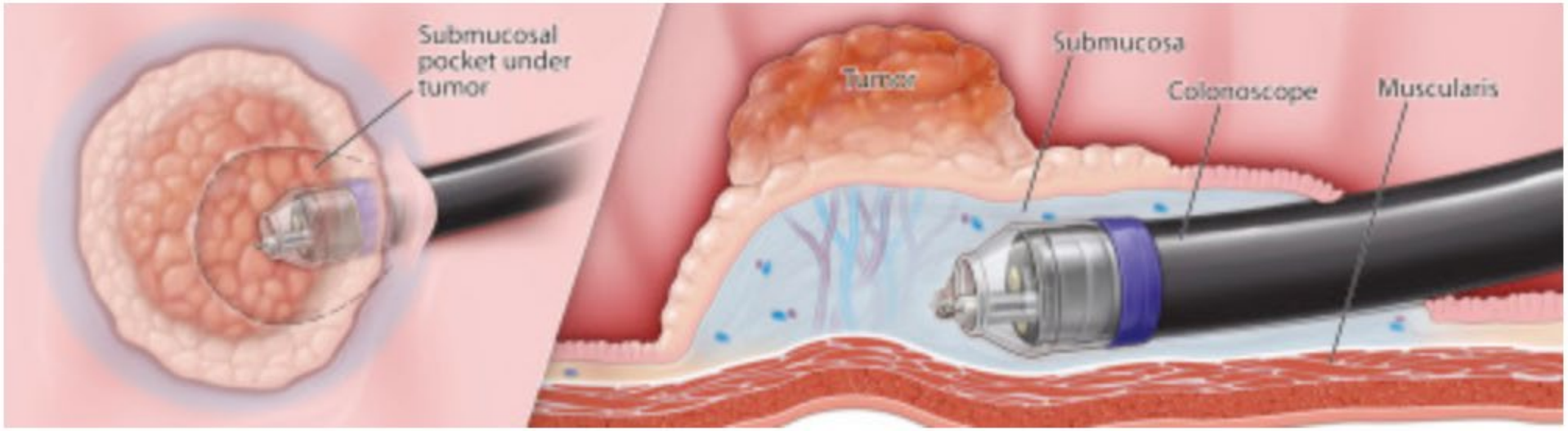




- Min, B. H., Lee, J. H., Kim, J. J., Shim, S. G., Chang, D. K., Kim, Y. H., ... & Rhee, J. C. (2009). Clinical outcomes of endoscopic submucosal dissection (ESD) for treating early gastric cancer: comparison with endoscopic mucosal resection after circumferential precutting (EMR-P). *Digestive and Liver Disease*, *41*(3), 201-209.

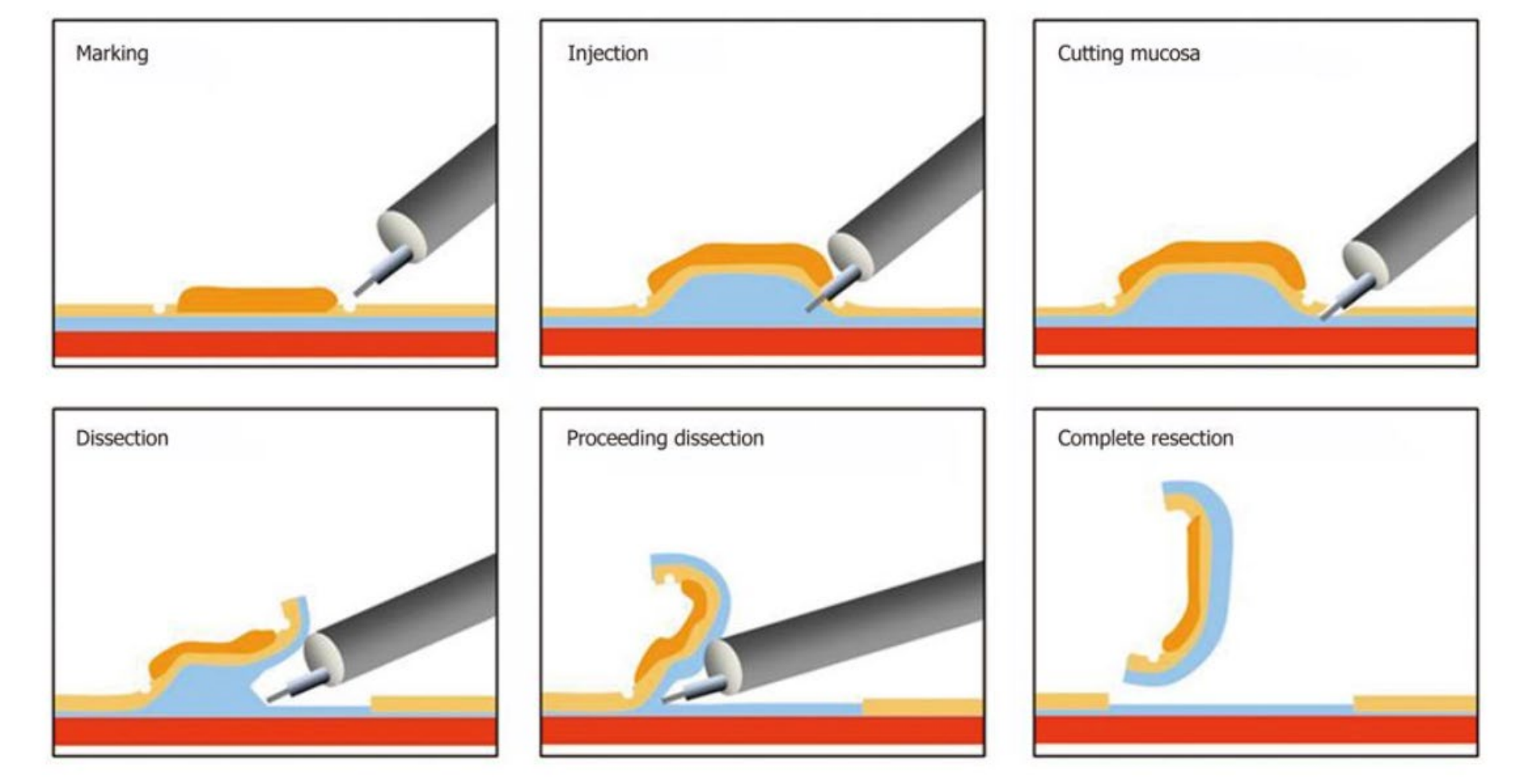
# ESD

## Graphical abstract



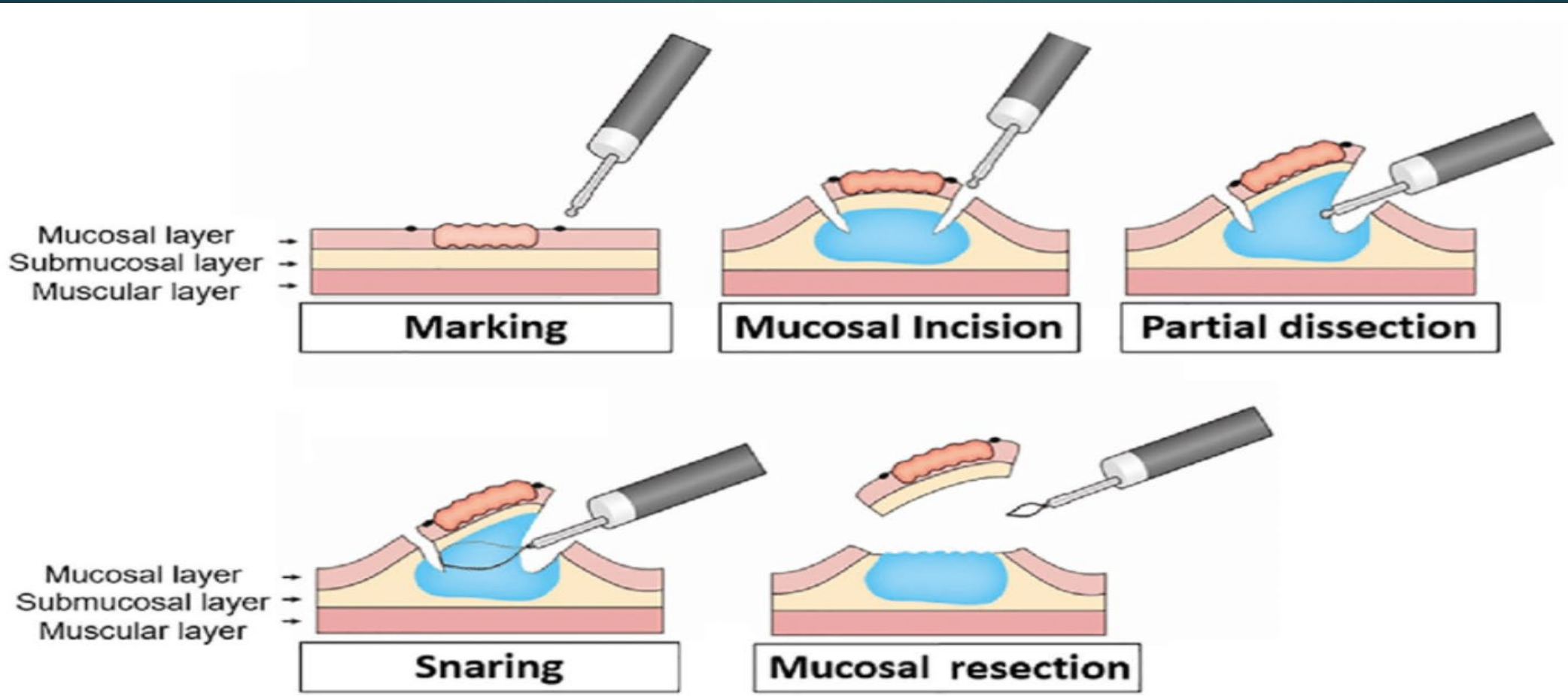

Takezawa, T., Hayashi, Y., Shinozaki, S., Sagara, Y., Okada, M., Kobayashi, Y., ... & Yamamoto, H. (2019). The pocket-creation method facilitates colonic endoscopic submucosal dissection (with video). *Gastrointestinal endoscopy*, *89*(5), 1045-1053.

# Conventional ESD




Asano, M. (2012). Endoscopic submucosal dissection and surgical treatment for gastrointestinal cancer. *World journal of gastrointestinal endoscopy*, *4*(10), 438.

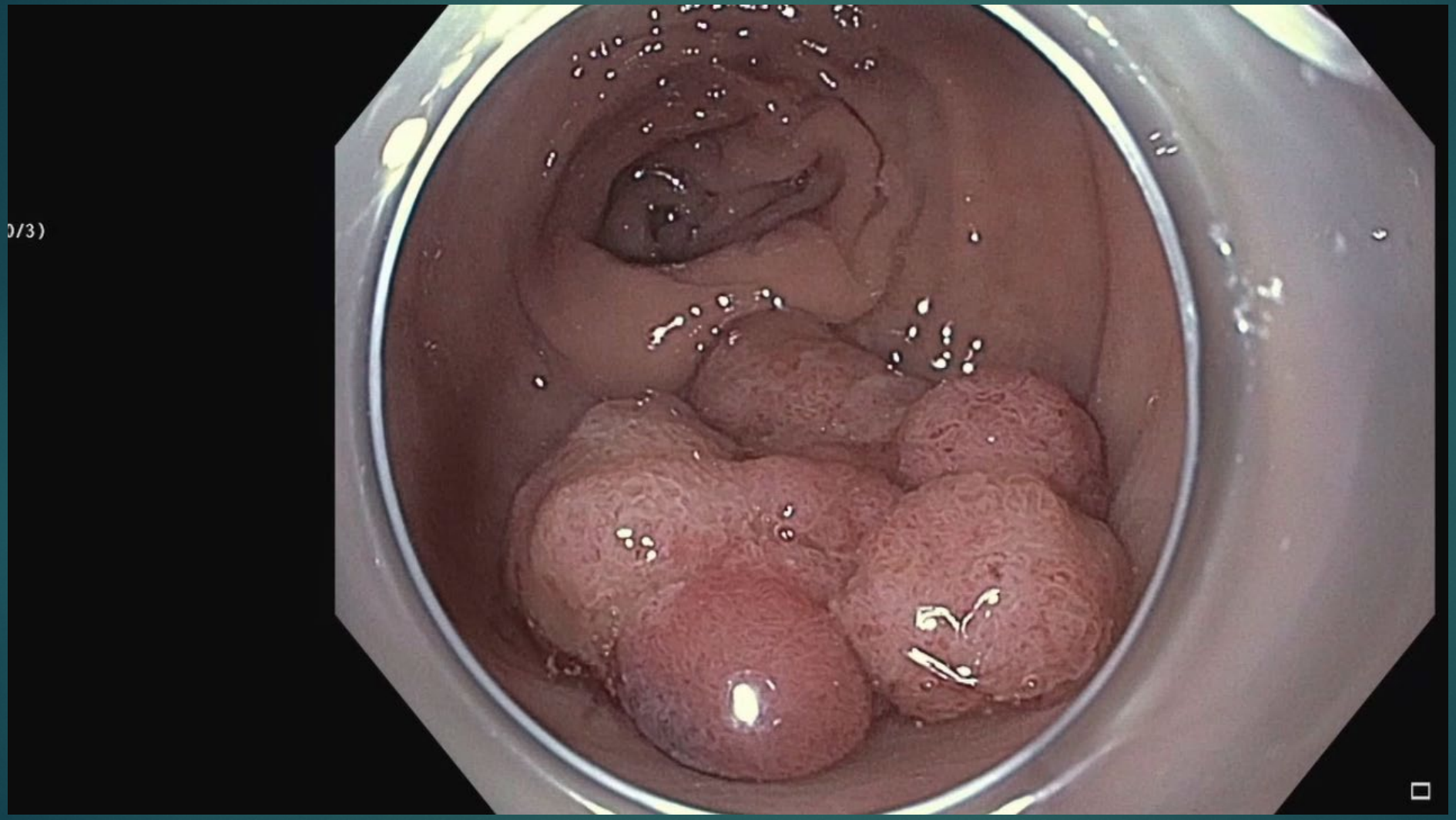
# Hybrid ESD



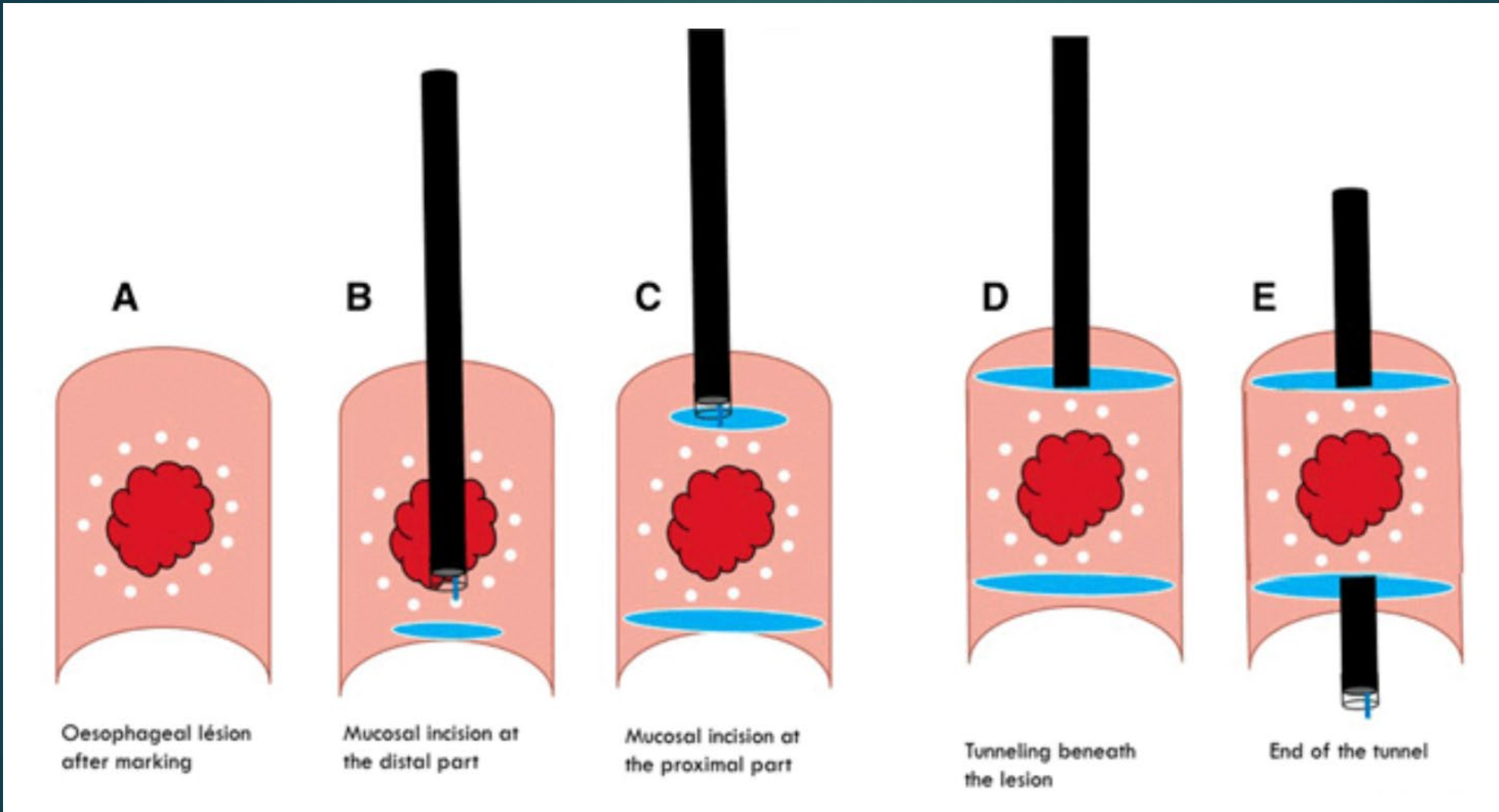

The procedures of H-ESD. (A-E) The schemas show each step of the H-ESD procedure: marking (A), mucosal incision (B), partial dissection (C), snaring (D), and mucosal resection (E). H-ESD, hybrid endoscopic submucosal dissection.

Esaki, M., Suzuki, S., Horii, T., Ichijima, R., Yamakawa, S., Shibuya, H., ... & Gotoda, T. (2020). Reduction in the procedure time of hybrid endoscopic submucosal dissection for early gastric neoplasms: a multi-center retrospective propensity score-matched analysis. *Therapeutic advances in gastroenterology*, *13*, 1756284820939420.

# Rectal ESD Hybrid

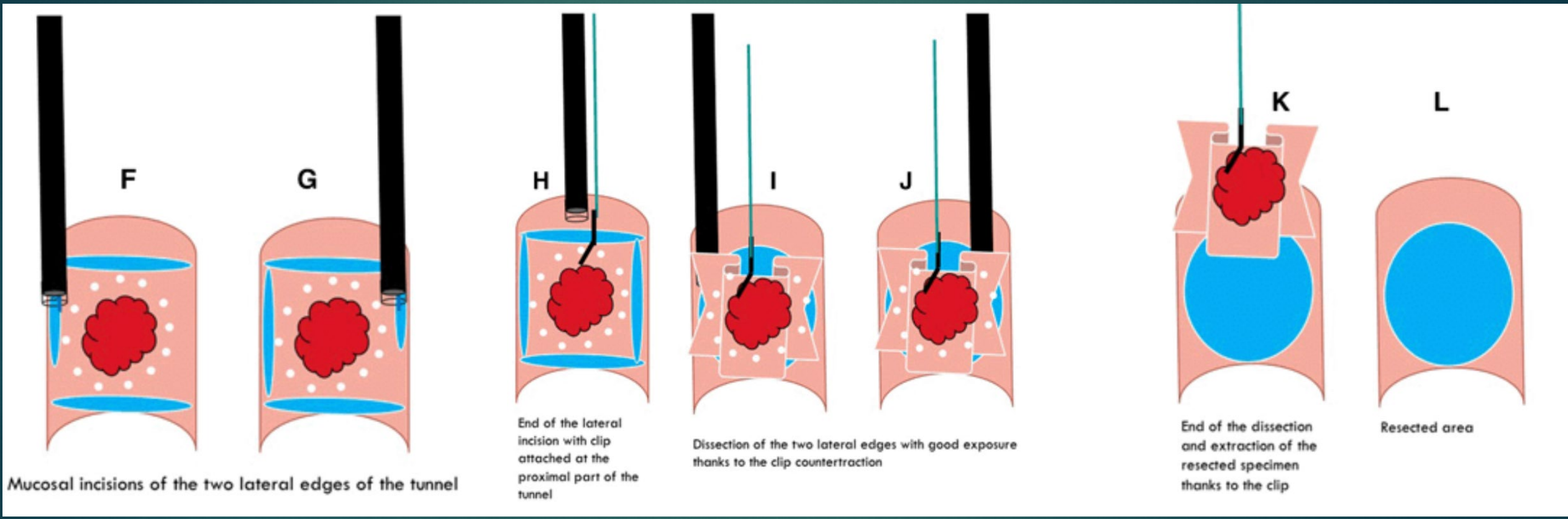


# Tunnel ESD



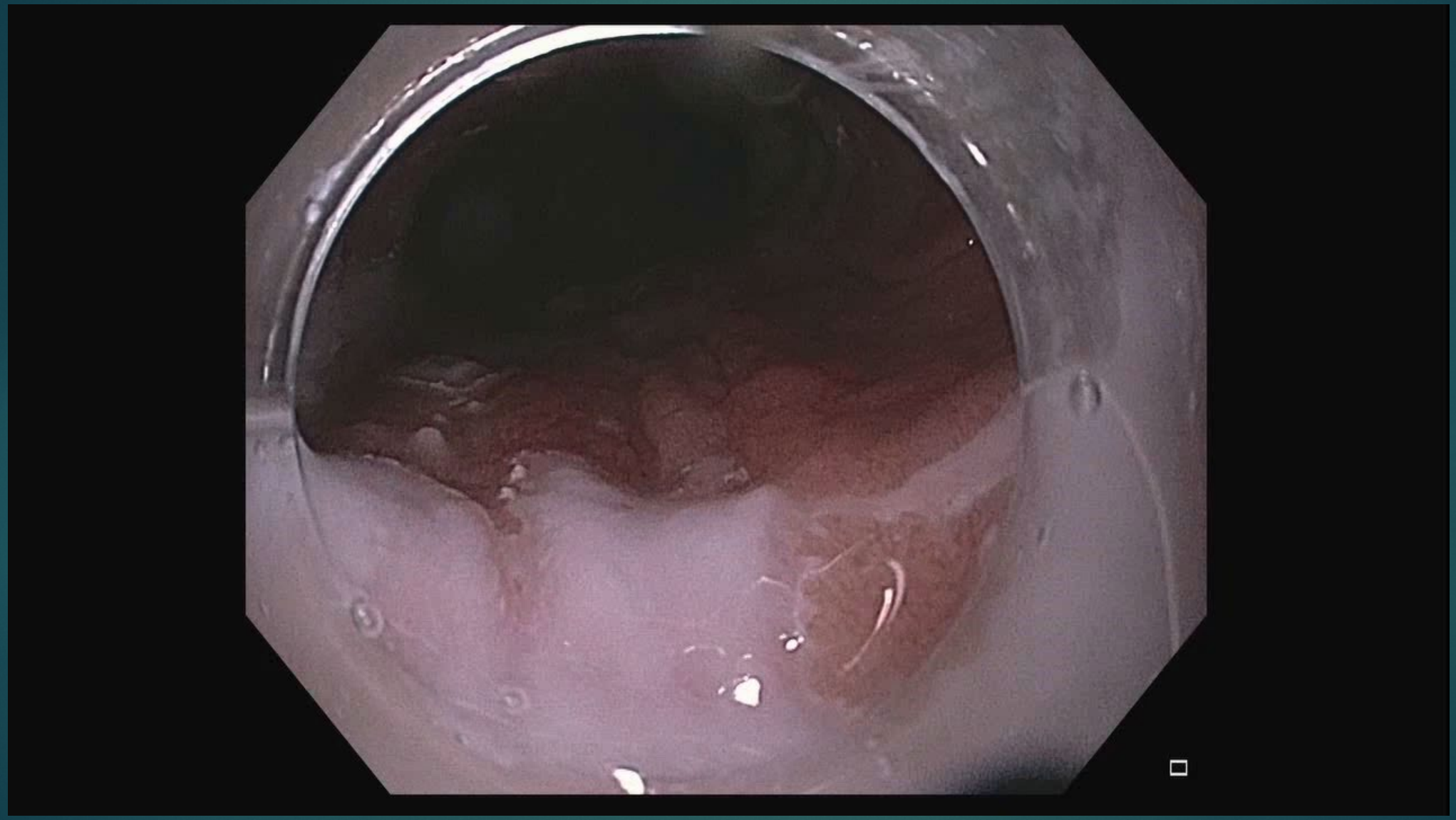

Jacques, J., Legros, R., Rivory, J., Charissoux, A., Sautereau, D., Ponchon, T., & Pioche, M. (2017). The “tunnel+ clip” strategy standardised and facilitates oesophageal ESD procedures: a prospective, consecutive bi-centric study. *Surgical endoscopy*, *31*(11), 4838-4847.

# Tunnel ESD

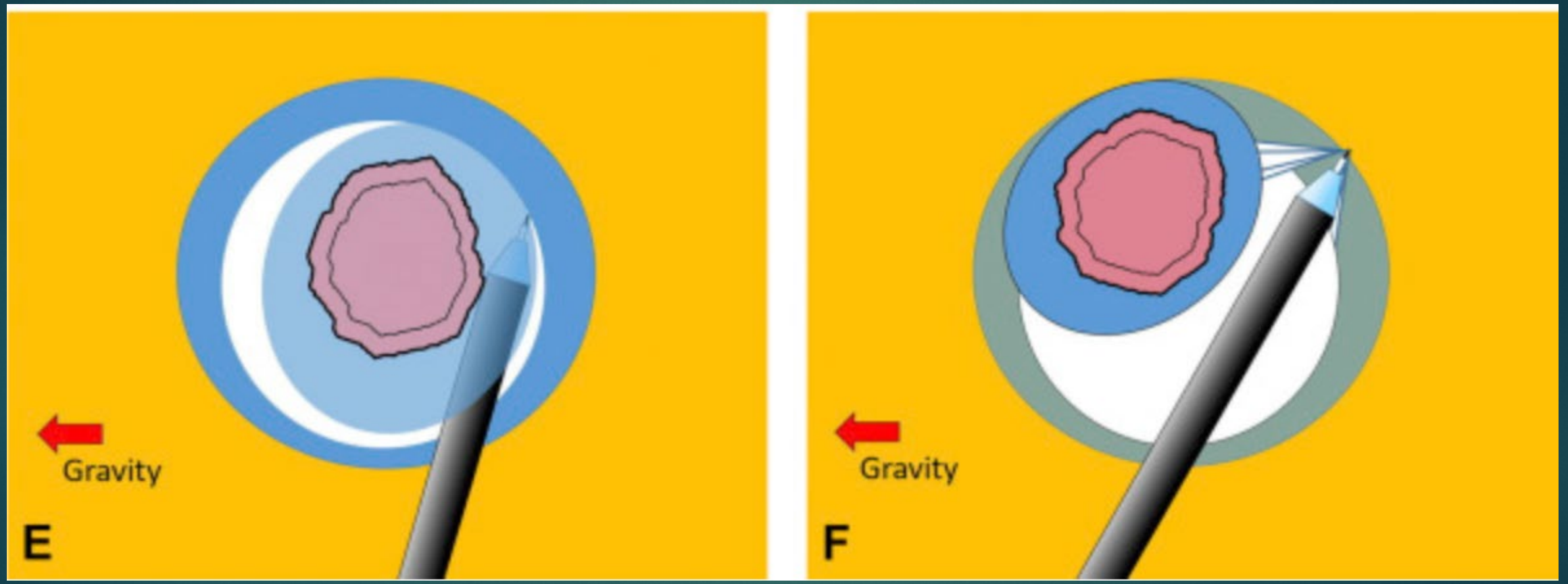



Jacques, J., Legros, R., Rivory, J., Charissoux, A., Sautereau, D., Ponchon, T., & Pioche, M. (2017). The “tunnel+ clip” strategy standardised and facilitates oesophageal ESD procedures: a prospective, consecutive bi-centric study. *Surgical endoscopy*, *31*(11), 4838-4847.

# BE Intramucosal Adenocarcinoma Tunnel



# Pocket Creation Method

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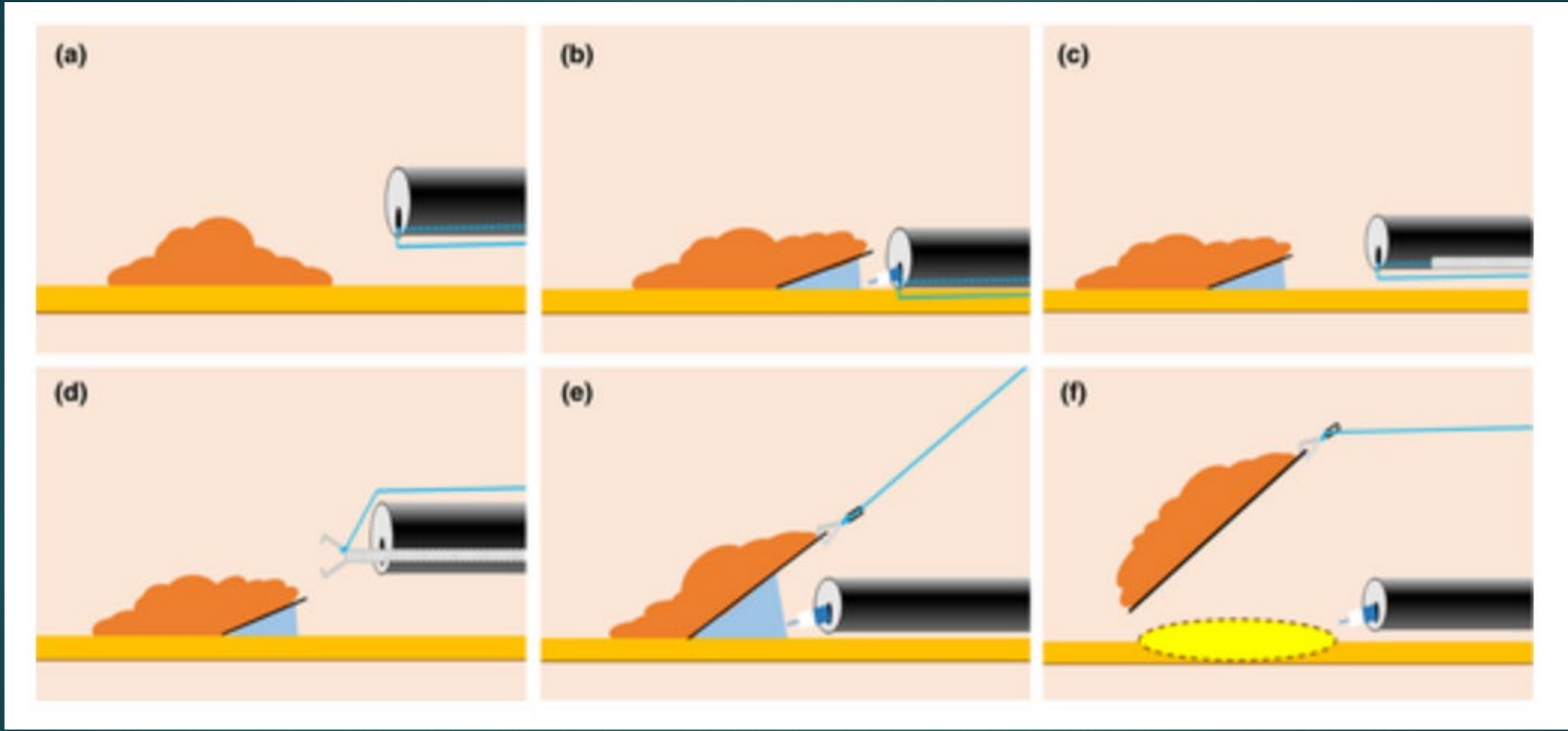
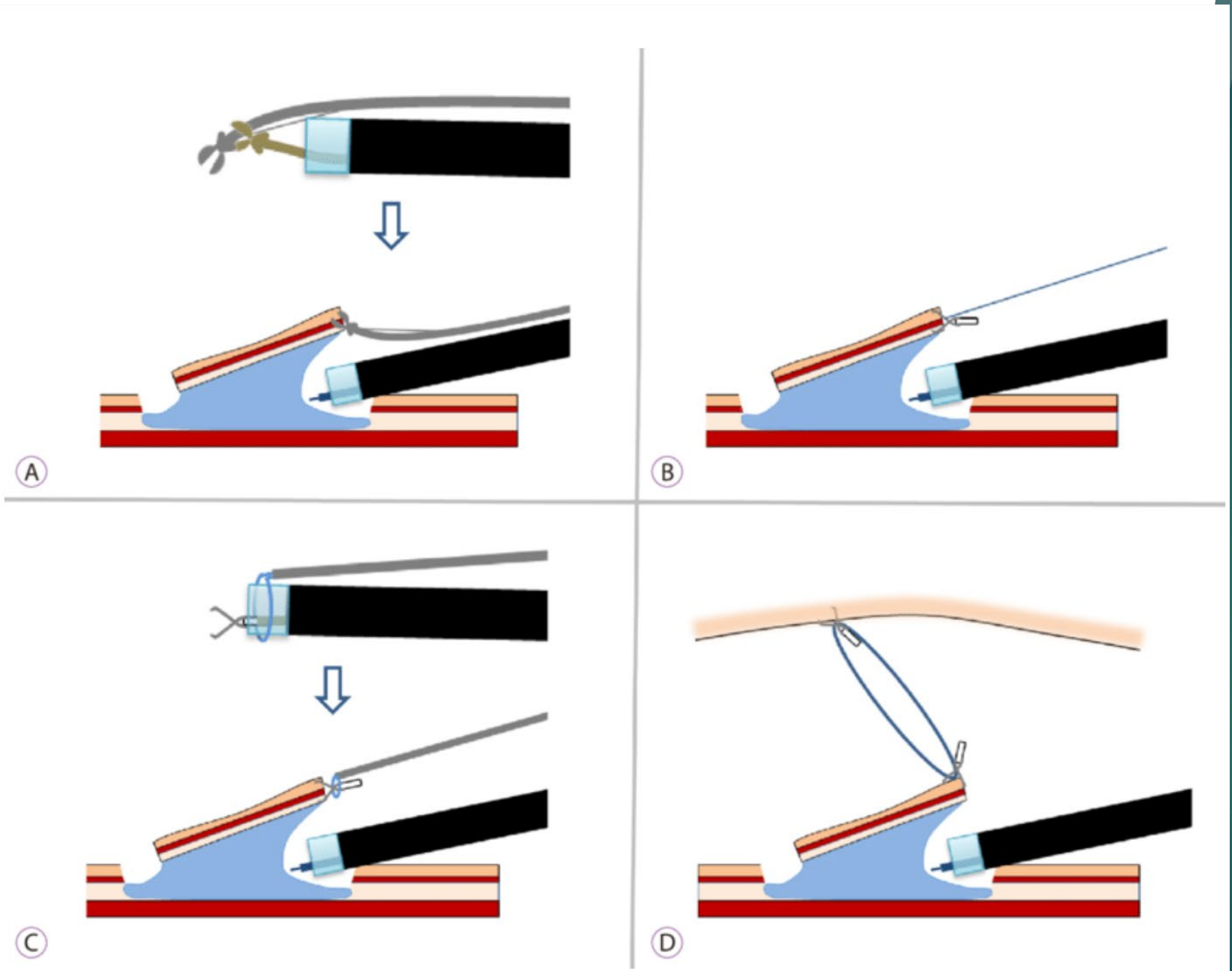
# Traction for Assistance



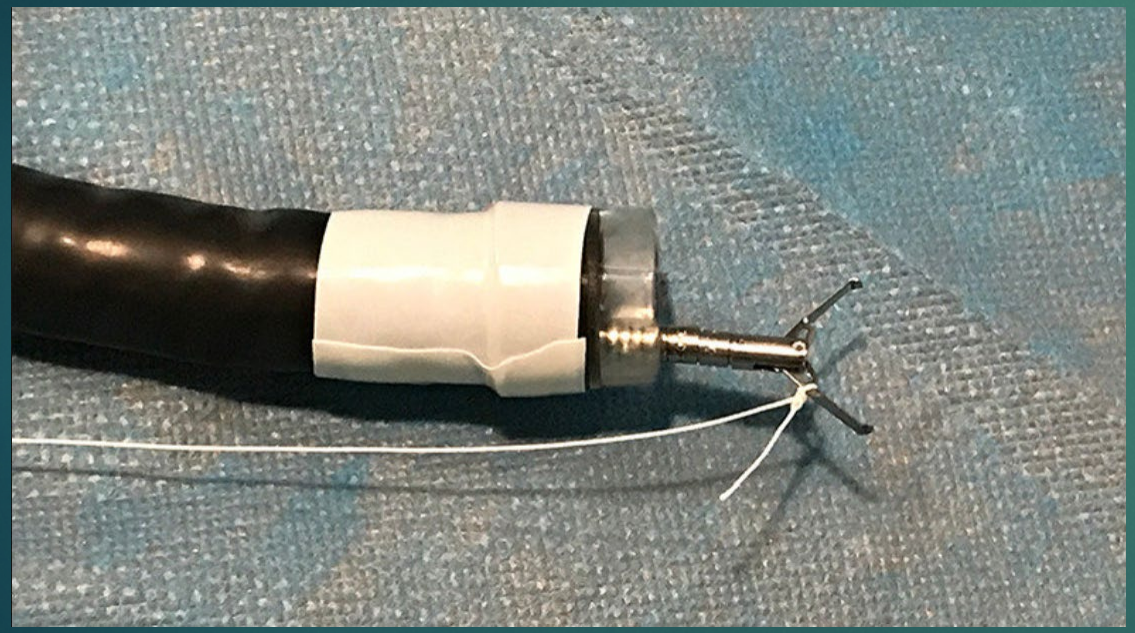

Yamasaki, Y., Takeuchi, Y., Uedo, N., Kanesaka, T., Kato, M., Hamada, K., ... & Iishi, H. (2018). Efficacy of traction-assisted colorectal endoscopic submucosal dissection using a clip-and-thread technique: A prospective randomized study. *Digestive Endoscopy*, *30*(4), 467-476.

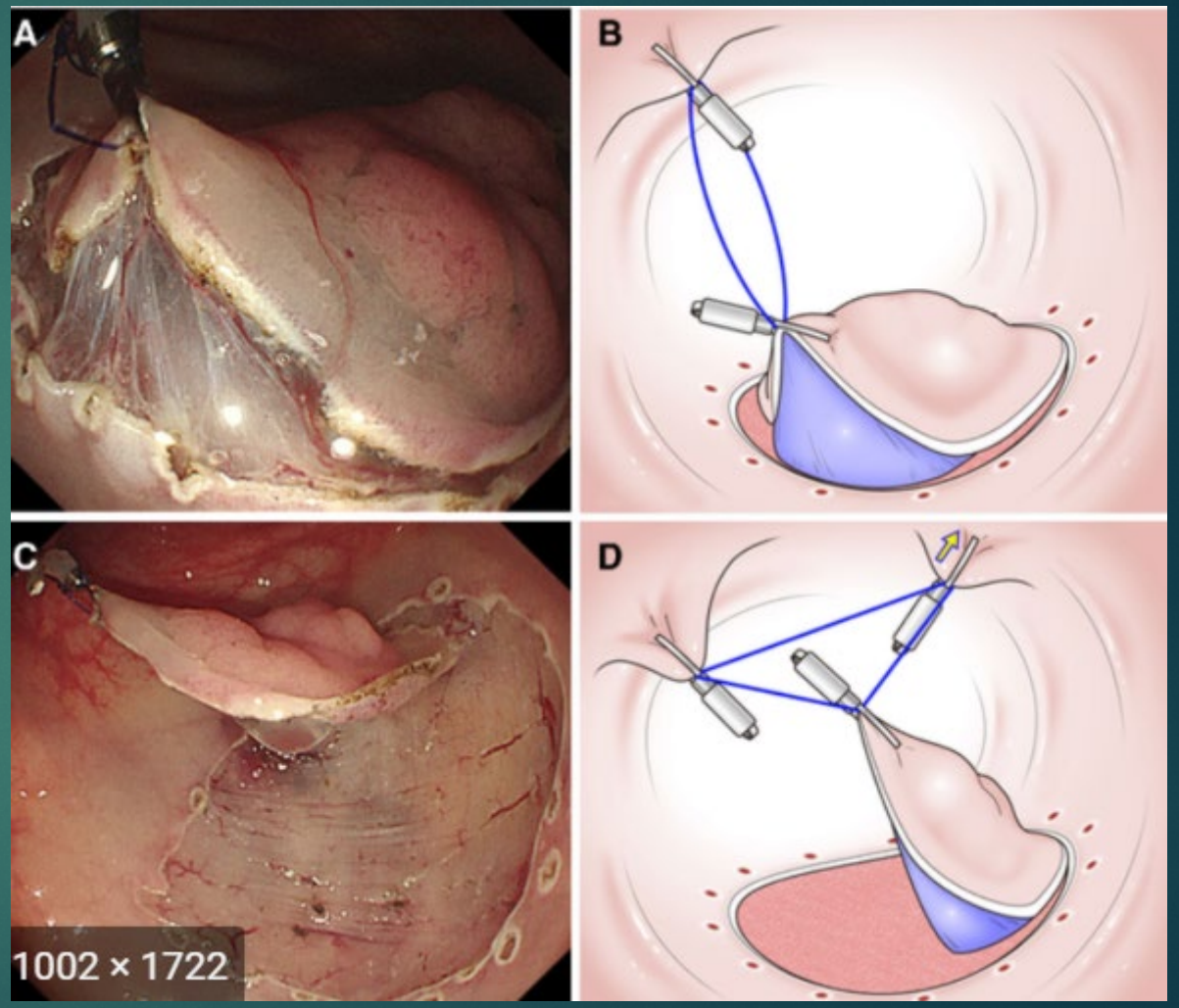
# Various Traction Methods

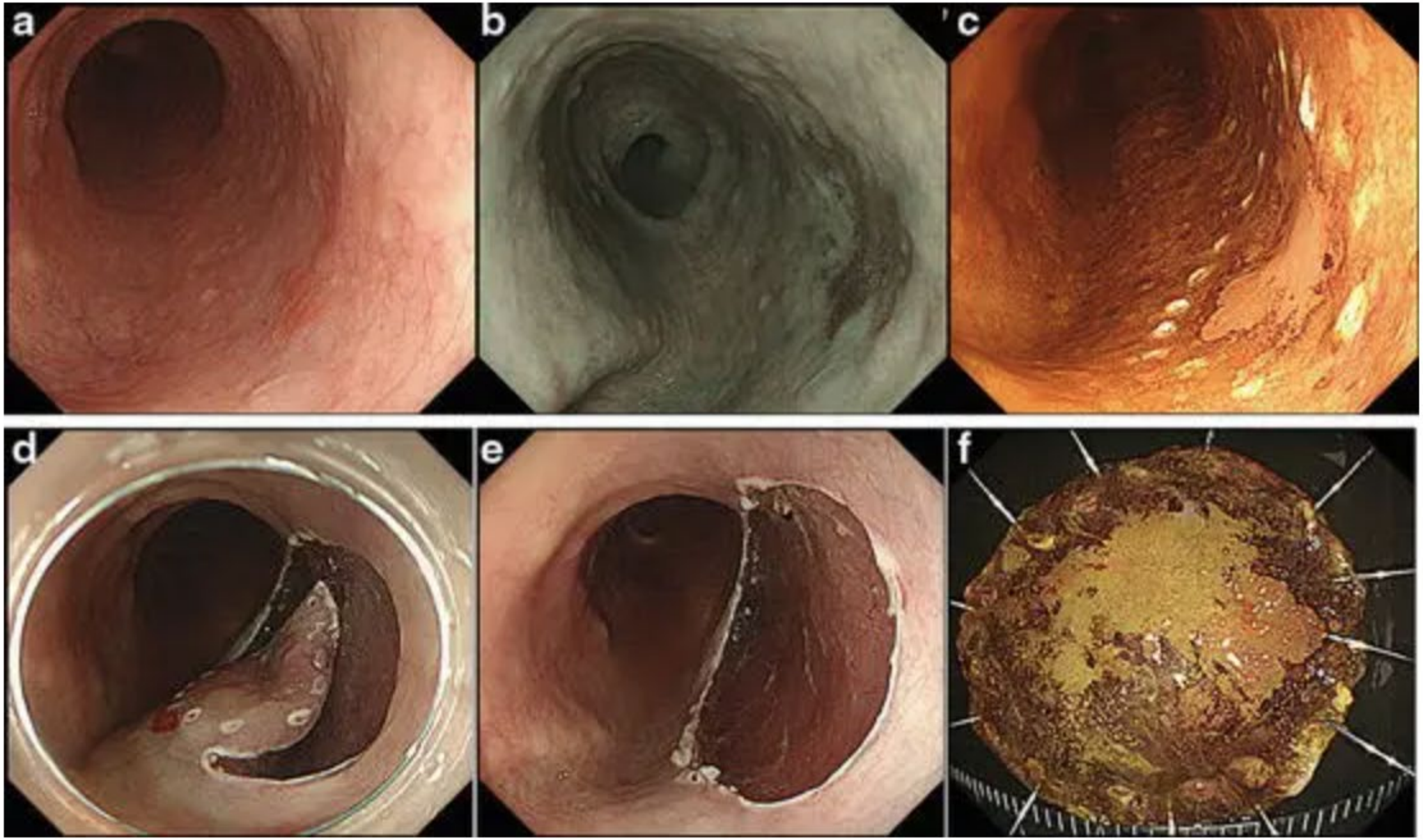



Traction methods. (A) External forceps method. (B) Clip-with-line method. (C) Clip-and-snare method with a pre-looping technique. (D) Clip-with-loops method.

# Hemoclip Traction Device

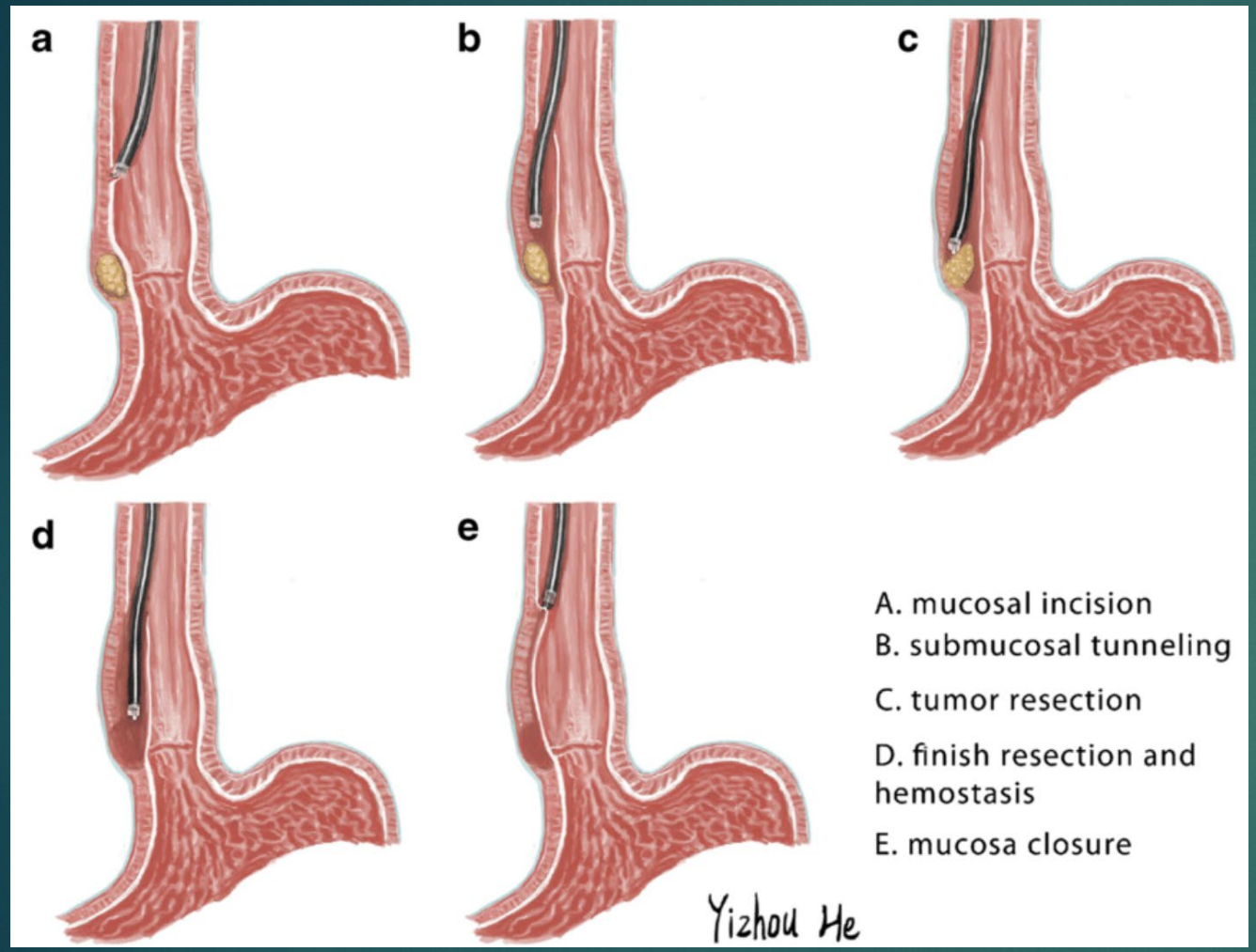





a
b
c
d
e
f

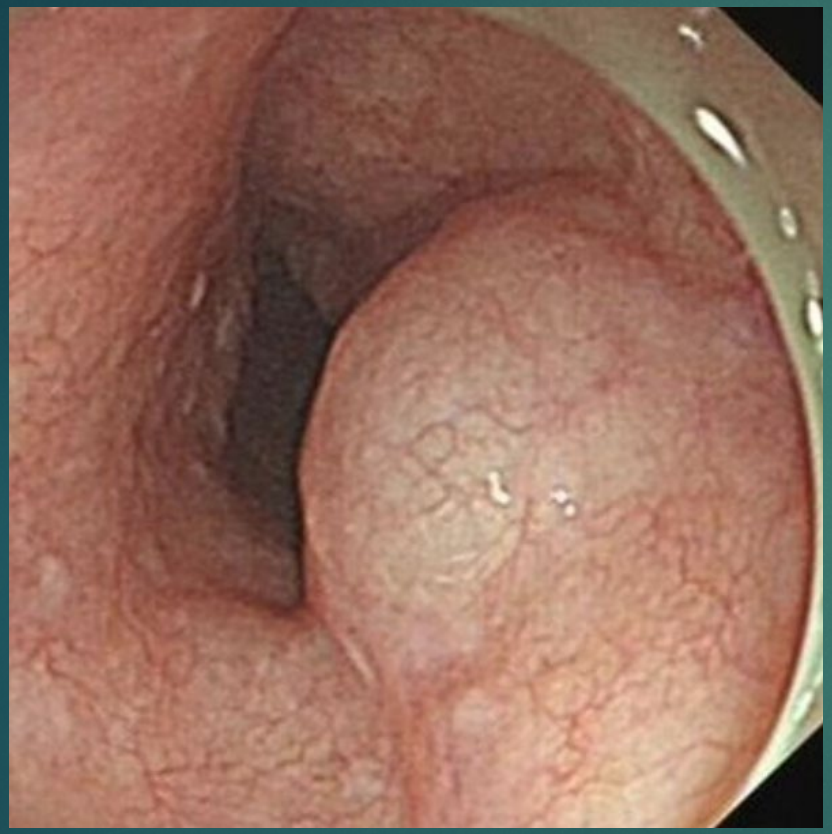
# STER: Submucosal Tunneling w/ Endoscopic Resection

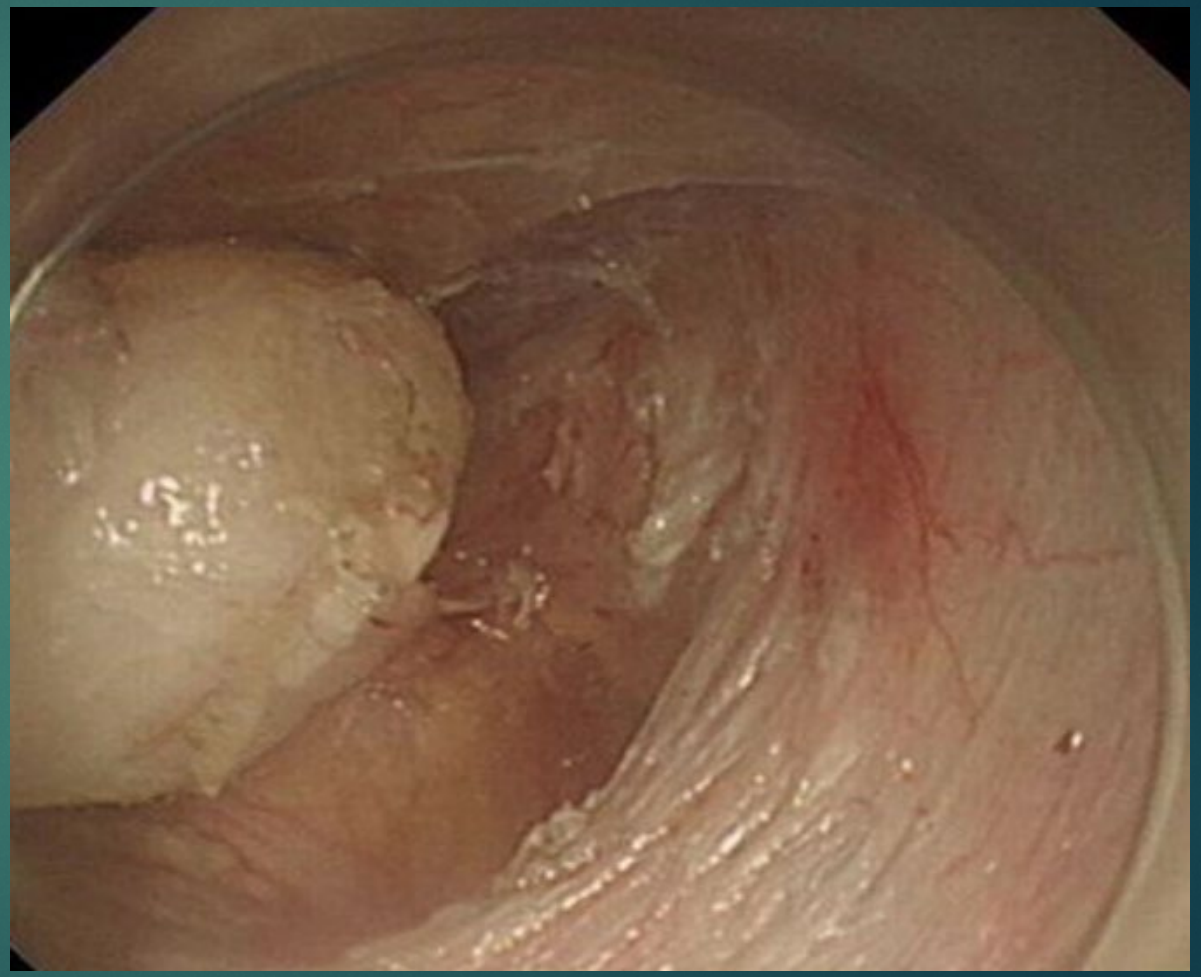
- Combination of POEM + ESD
- Create an entry and tunnel distal past the lesion
- Dissect around the lesion/mass and expose the adventitia/serosa
- Use of a roth net or snare to atraumatically remove through the tunnel
- Close the entry with clips/suture



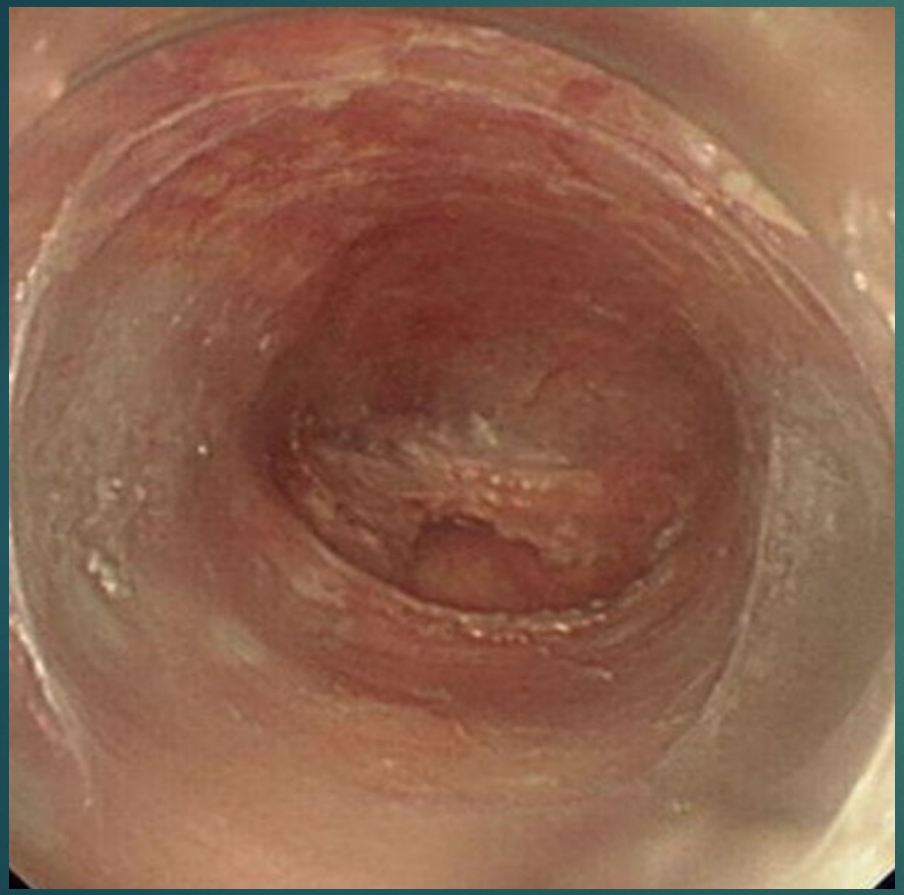

# STER: Submucosal Tunneling w/ Endoscopic Resection

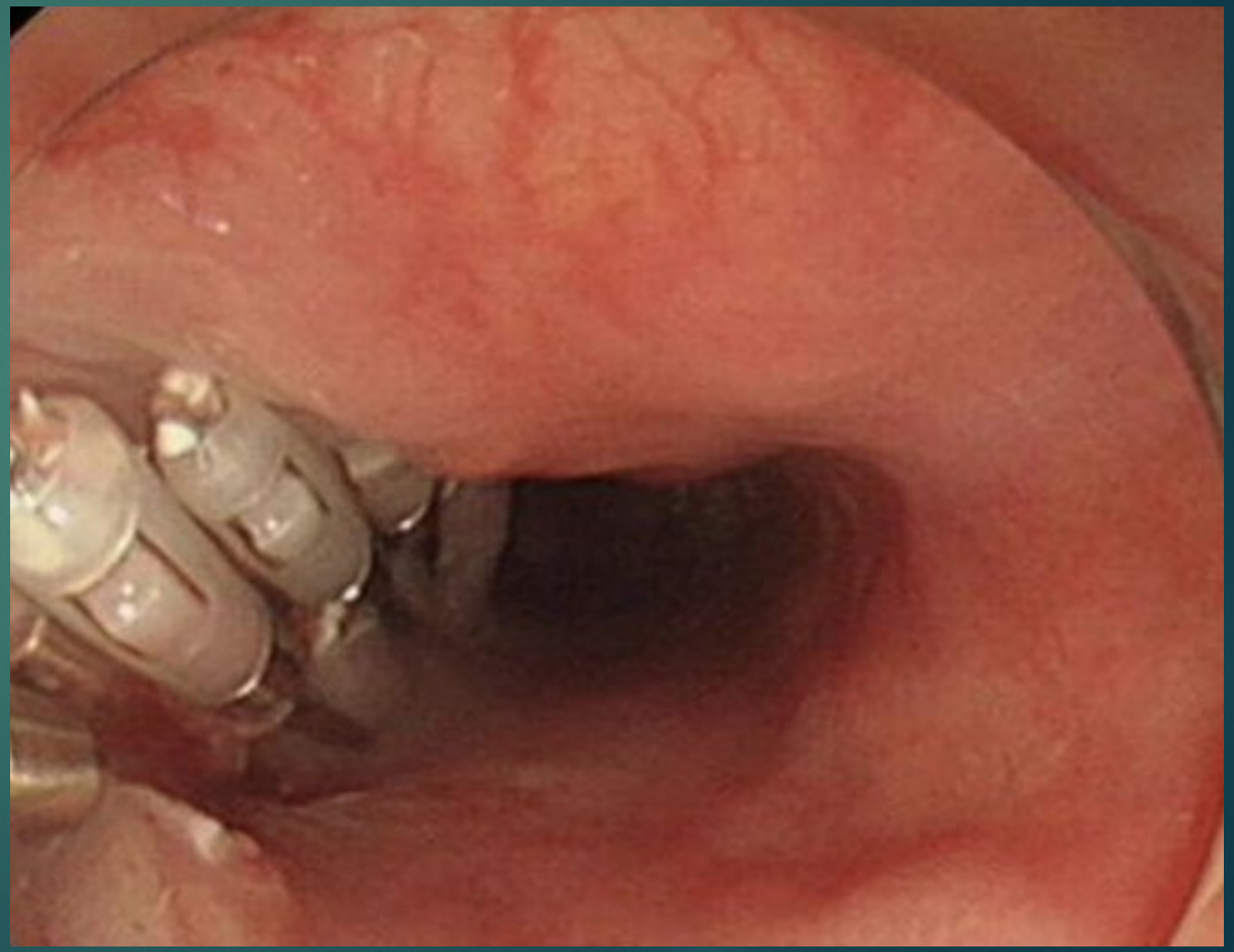
# STER Esophageal Leiomyoma





# STER Esophageal Leiomyoma





# STER Esophageal Leiomyoma

# Indications for STER

- Esophagus
  - Leiomyoma (dysphagia)
  - Rarely GIST
- Stomach
  - GIST Typically 2-3cm in size

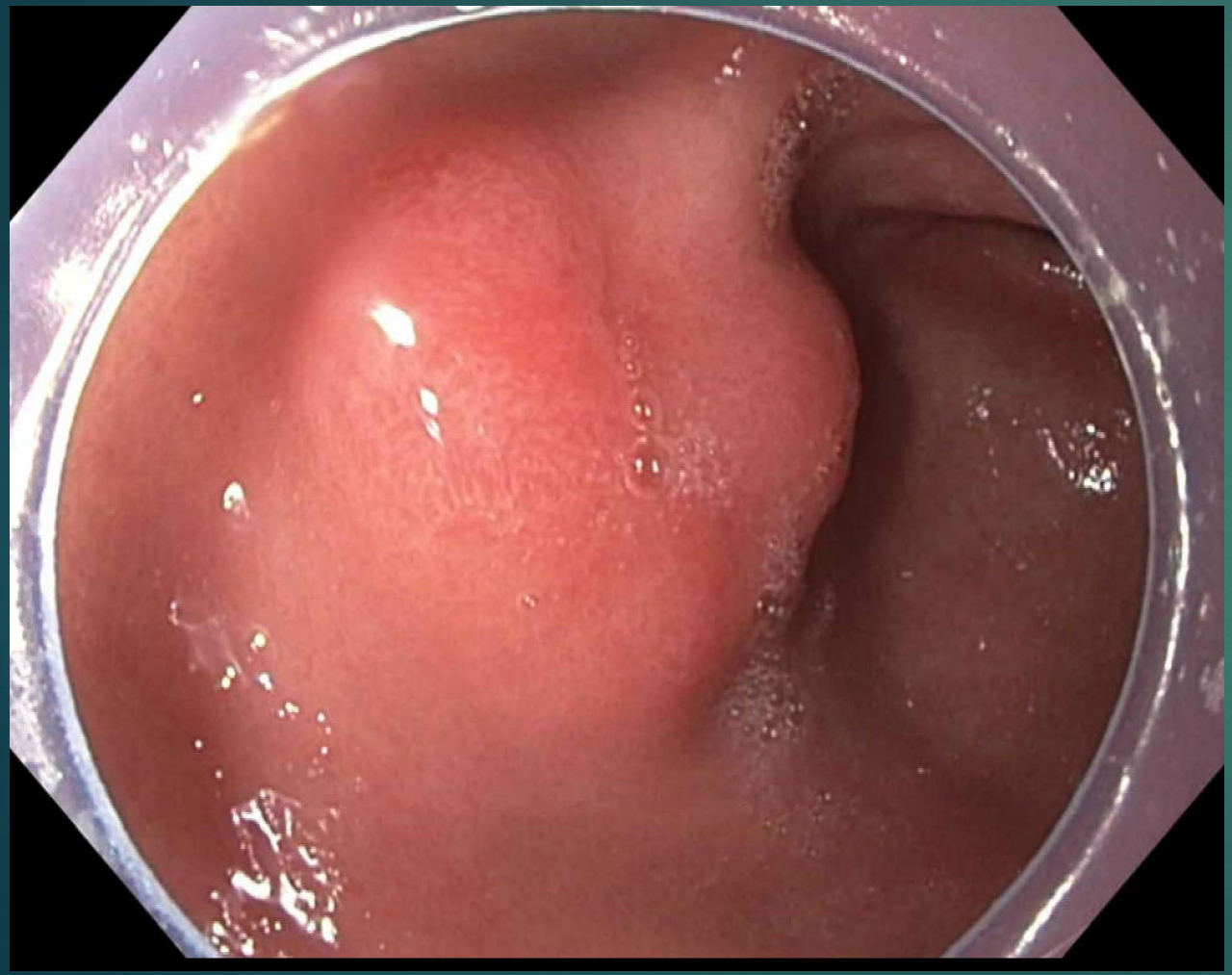
# ESD Limitations

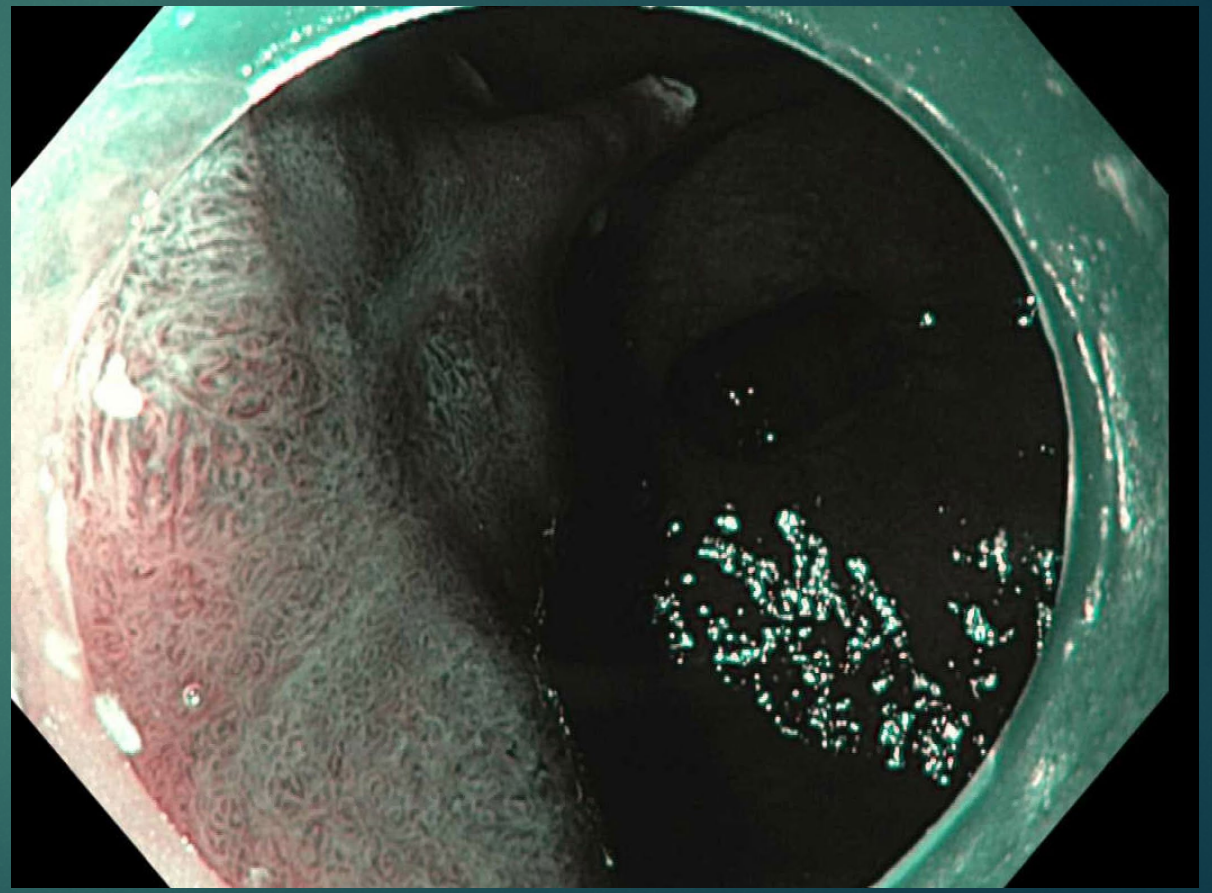
- General Anesthesia and Paralysis
- Ability to physically remove the specimen in a single piece after dissection
- Scar tissue (planes between muscle/tattoo/fibrosis can be an issue)
- Device Cost
- Time and Re-imbursement
- Higher risk of perforation

# Gastric Case Report

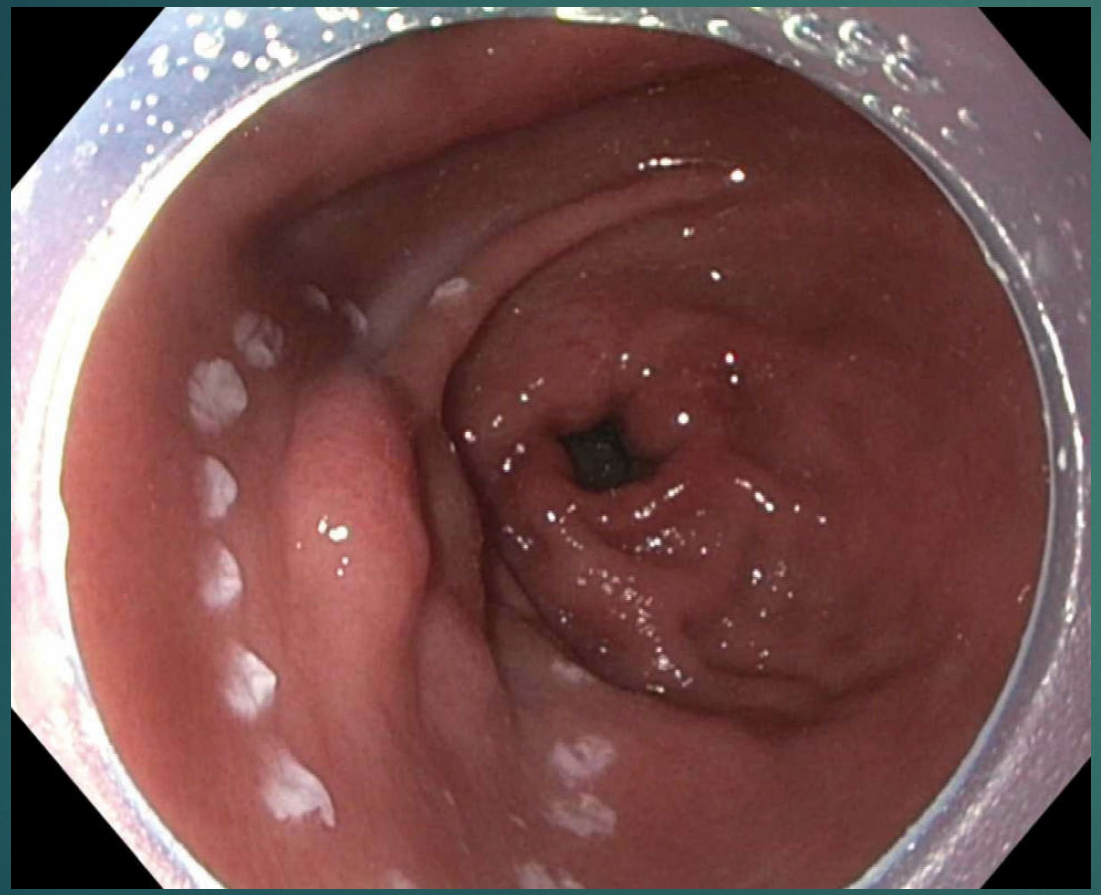
- 44y/o F hx of MASH Cirrhosis with portal HTN on imaging
- Outside biopsy with concern for adenocarcinoma, antral nodule, no ulceration
- Referral to surgical oncology
- Given Severe portal HTN on imaging referral for ESD was made

# Antral Gastric Adenicarcinoma

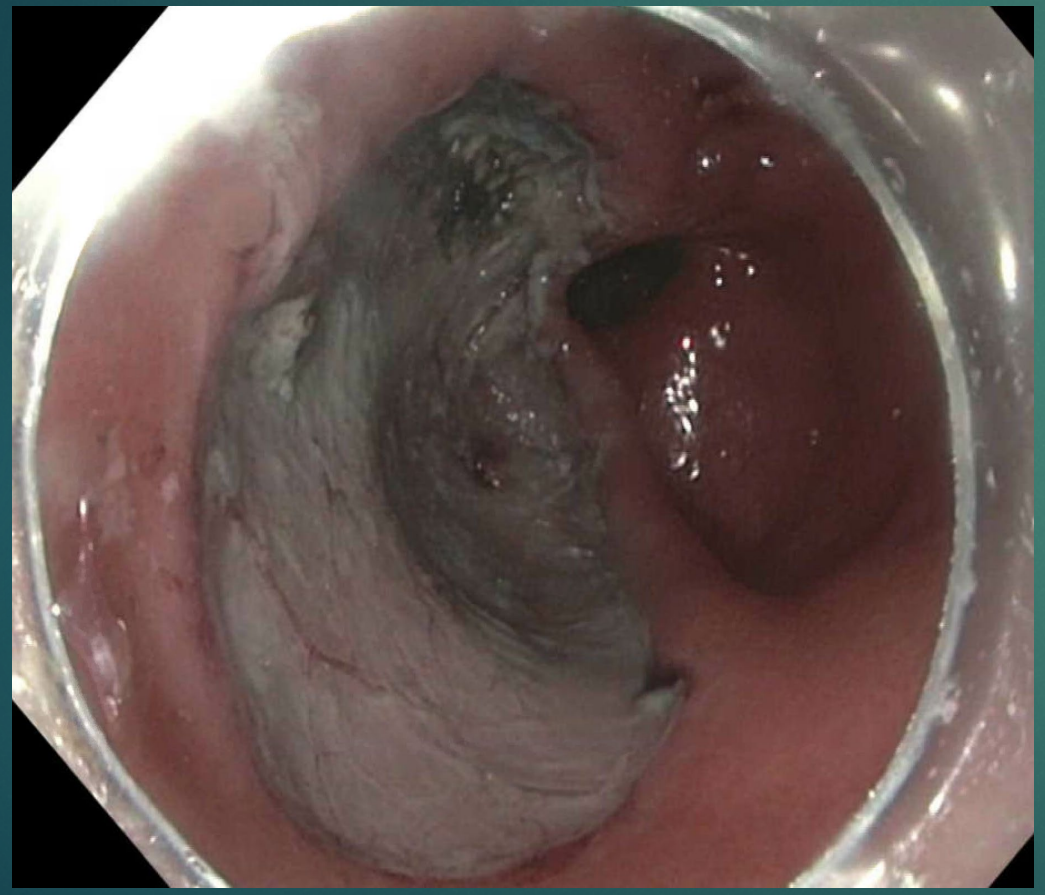


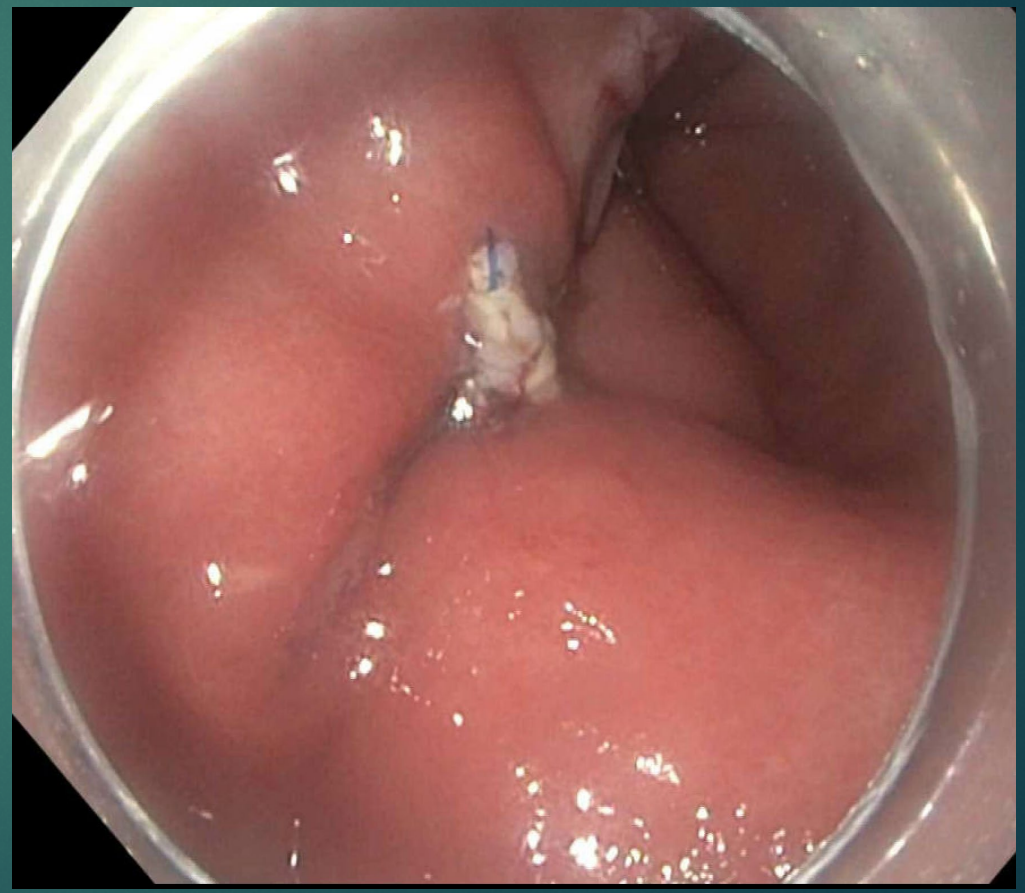


# Antral Gastric Adenocarcinoma



# Post ESD and Closure





# Pathology Review

***DIAGNOSIS:***
**Gastric mass, endoscopic mucosal resection:**
**- Adenocarcinoma.**

**Synopsis:**
**- Procedure: Endoscopic resection**
**- Tumor Site: Antrum**
**- Tumor Size: 15 mm**
**- Histologic Type: Adenocarcinoma, diffuse (signet-ring) type**
**- Histologic Grade: G3, poorly differentiated**
**- Tumor Extension: Tumor invades submucosa**
**- Margins: All margins are free of tumor**
**- Treatment Effect: No known presurgical therapy**
**- Lymphovascular Invasion: Not identified**
**- Perineural Invasion: Not identified**
**- Regional Lymph Nodes: No lymph nodes submitted**
**- Pathologic Stage: pT1**

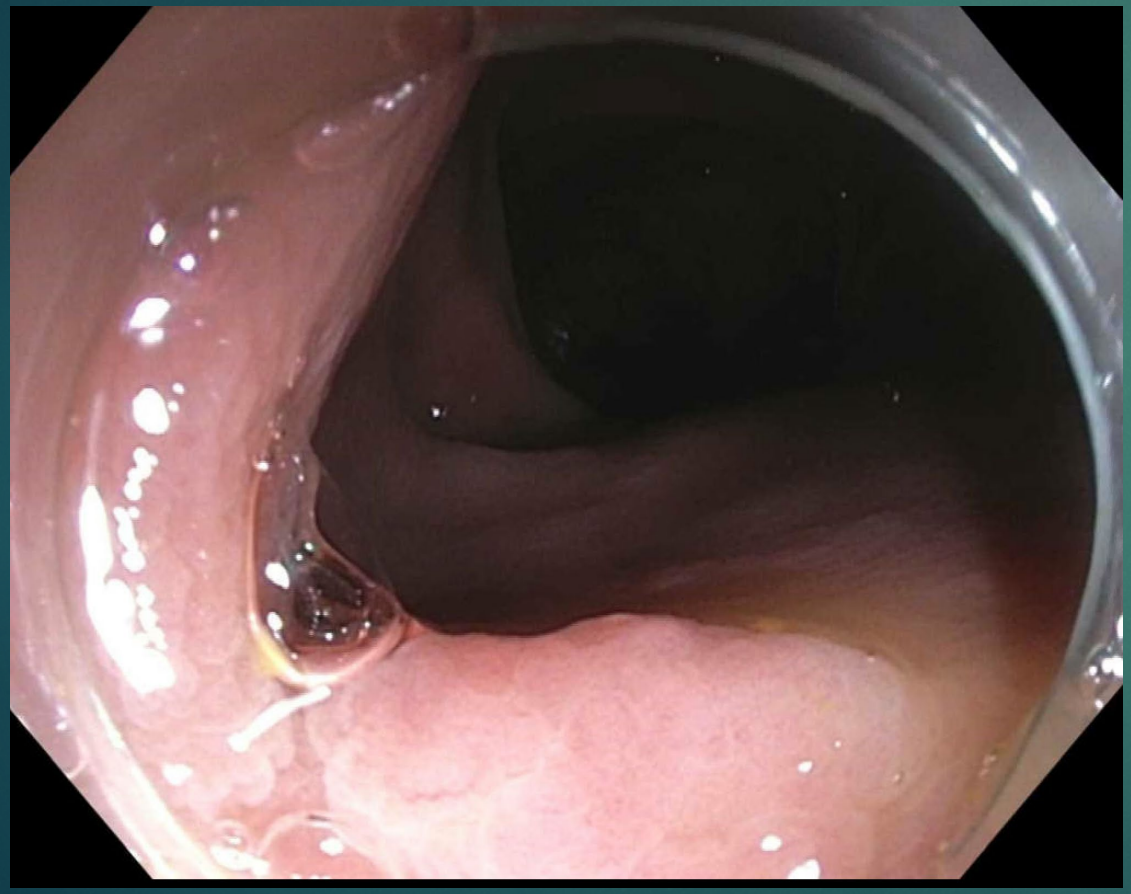
**Note:**
**- Immunohistochemistry for CKAE1/3 and CK20 is positive, and GATA-3, CDX2, and ER are negative.**

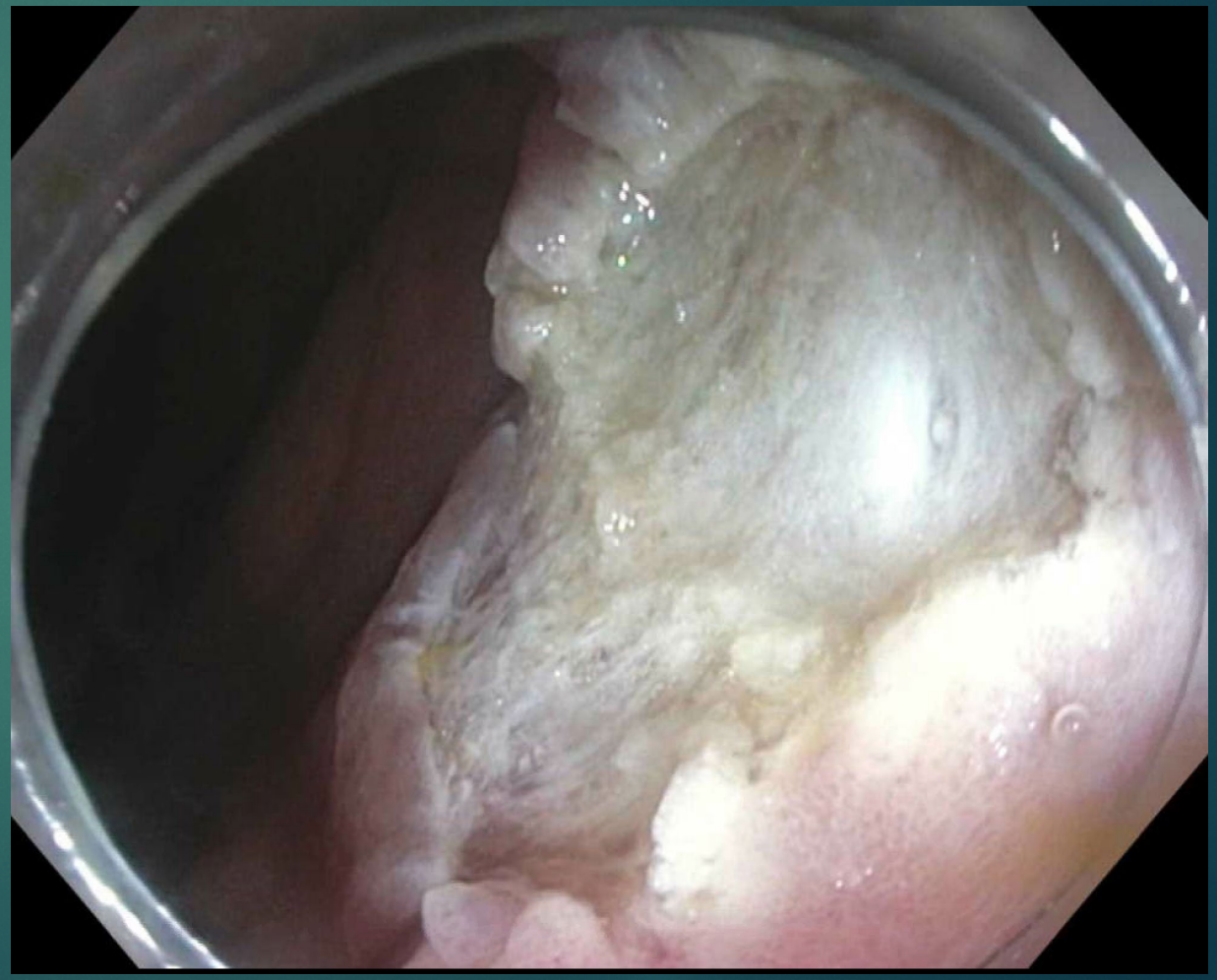
***ADDENDUM:***
The tumor invades submucosa to a depth of 4 mm.

# Post Op

- Tumor boards with Surgical Oncology/Medical Oncology
- Endoscopic surveillance only
- EGD at 6 months with gastric mapping and re-biopsy of the site
- PET/CT scan negative 2 years out

# Ascending Colon ESD





# T1 Invasive CRC Adenocarcinoma

**DIAGNOSIS: (Verified)**
**A. Colon, ascending polyp, biopsy:**
**- Sessile serrated adenoma (WHO 2019: sessile serrated lesion)**

**B. Colon, ascending polyp, biopsy:**
**- Invasive adenocarcinoma, moderately differentiated, arising from tubulovillous adenoma**
**- No lymphovascular invasion**
**- Tumor budding: low**
**- Carcinoma invades into the submucosa (pT1)**
**- Carcinoma is 0.8 millimeter from the deep cauterized margin**
**- Margins are negative for dysplasia or carcinoma**
**- Microsatellite stable (MSS) phenotype by immunohistochemistry**

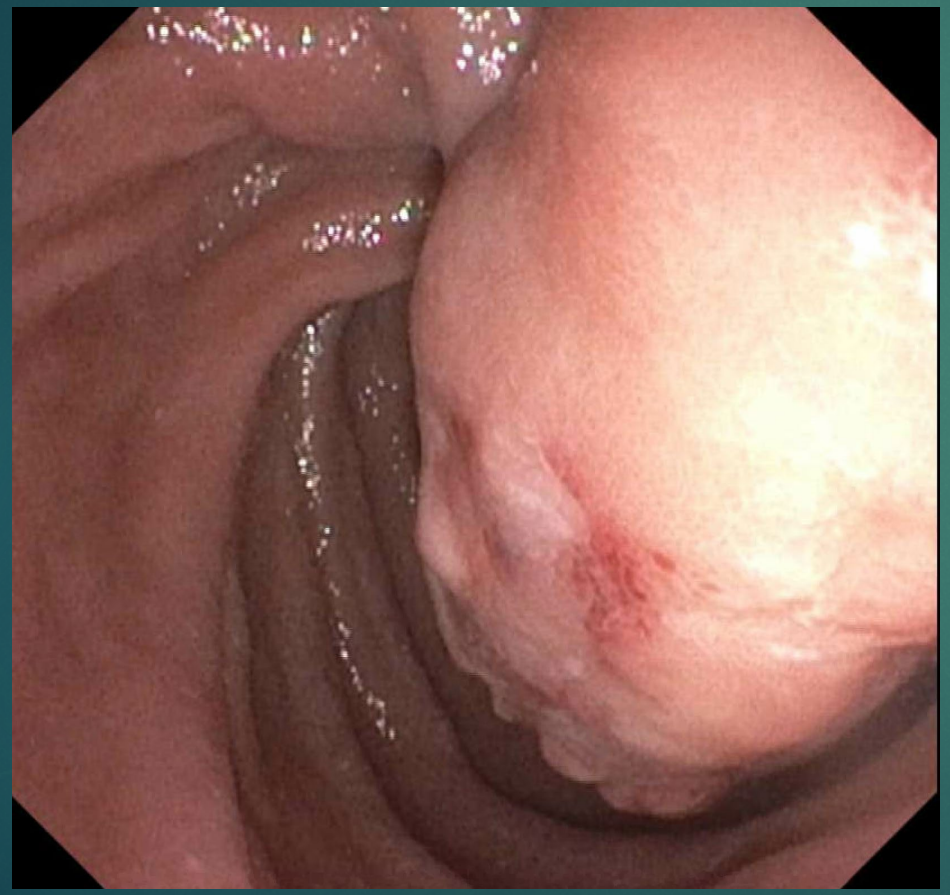
**C. Colon, side margins, biopsy:**
**- Negative for dysplasia or carcinoma**

- Referral to sugery, right hemi-colectomy performed, single lymph node positive. Chemo/radiation post op
- PET/CEA negative 2 years out

# Ampullary NET S/P ERCP w/ Ampullectomy Underwater EMR En-Bloc

- 75y/o F, hx of HTN, DM
- Known carcinoid found incidentally on EGD
- EUS with outside provider with biopsy proven carcinoid
- Followed for 3 years, with 10mm growth Ki-67 4%, moderately differentiated
- PET Dotate scan with focal uptake at the ampulla
- No biliary dilation on MRCP, no previous pancreatitis
- Referral to Surgical oncology for Whipple
- Declined Whipple sent to GI for second opinion

# Ampullary NET  S/P ERCP w/ Ampullectomy Underwater EMR En-Bloc



# Post Resection

# Ampullary NET S/P ERCP w/ Ampullectomy Underwater EMR En-Bloc

***SYNOPTIC REPORT:***

**CASE SUMMARY: (DUODENUM AND AMPULLA NEUROENDOCRINE TUMOR)**
**Standard(s): AJCC-UICC 9**
**Procedure: Ampullectomy**
**Tumor Site: Duodenum, second portion, see Comment**
**Histologic Type and Grade: G2, well-differentiated neuroendocrine tumor**
**Histologic Grade Determination:**
**Mitotic Rate: 3 mitoses per 2 mm2**
**Ki-67 Labeling Index: 5%**
**Tumor Size: 1.8 cm**
**Tumor Focality: Unifocal**
**Tumor Extent: Duodenal Tumor, Invades muscularis propria**
**Lymphatic and / or Vascular Invasion: Not identified**
**Margin Status: All margins negative for tumor**
**Closest Margin(s) to Tumor: Deep**
**Distance from Tumor to Closest Margin: 0.12 cm**
**Regional Lymph Node Status: Not applicable (no regional lymph nodes submitted or found)**
**Distant Site(s) Involved, if applicable: Not applicable**
**pTNM CLASSIFICATION (AJCC Version 9): pT2**
**Additional Findings: Mucosal erosions and granulation tissue.**

***GROSS DESCRIPTION:***

A. Received in formalin labeled with the patient name, MRN, and "ampullectomy specimen". The specimen consists of a 3.0 x 2.4 x 1.5 cm fragment of pink-tan polypoid tissue. The specimen is inked, sectioned and entirely submitted in blocks A1-A7.

# Post-Op

- ERCP 1 month later for stent removal
- PET-Dotate scan 3 months later negative with oncology
- ERCP/EUS Surveillance negative q 6 months, 2 years out now

# My Personal Practice EMR vs ESD

- Review of the patients age and comorbidities
- Variance dependent on Location and Tumor Size and pathology
- Careful lesion assessment, for TA lesions that are low risk I typically EMR for time, and safety reasons (pathology does not usually do synoptic reports for TA lesions)
- Scope position and Access is very important
- ESD I book 2 hours of block time and may increase if the lesion is reviewed prior
- May perform EUS to allow review of the lesion and then subsequent scheduling of ESD
- Review of previous op reports, if previous lifted and partially resected and non malignant appearing ESD carries higher risks

# Take Home Message

- Many different approaches to resection
- Multiple factors involved
- Endoscopy should be considered first line unless deeply invasive
- Within EMR and ESD there are many different ways of performing these procedures
- STER can aide us in resection of small lesions with the MP/advential plane
- Third Space Endoscopy has opened

# Things to do with Barrett Esophagus

- Accurately describe the position of the lesion
- Describe if flat vs nodularity
- Intramucosal/invasive adenocarcinoma  with a well defined lesion consider EMR/ESD
- Synopitc report with staging

# Things Not to do with colon large polyps

- If you cannot make a 100% effort to remove completely…DON'T
- If you don't feel confident in removal of the polyp..DONT
- Do not biopsy aggressively if anticipate resection
- Place tattoo well away from the polyp >3 cm. Just distal
- Tattoo technique
  - -Inject 1-2cc of saline first, after submucosal pillow then place 2cc of spot and conclude

# Words of Wisdom

- “A superior pilot uses their superior judgement to avoid situations which require the use of their superior skill”
  - Frank Borman, Apollo 8

- The Patients who benefit the most from endoscopy are the worst surgical candidates
  - -Unknown