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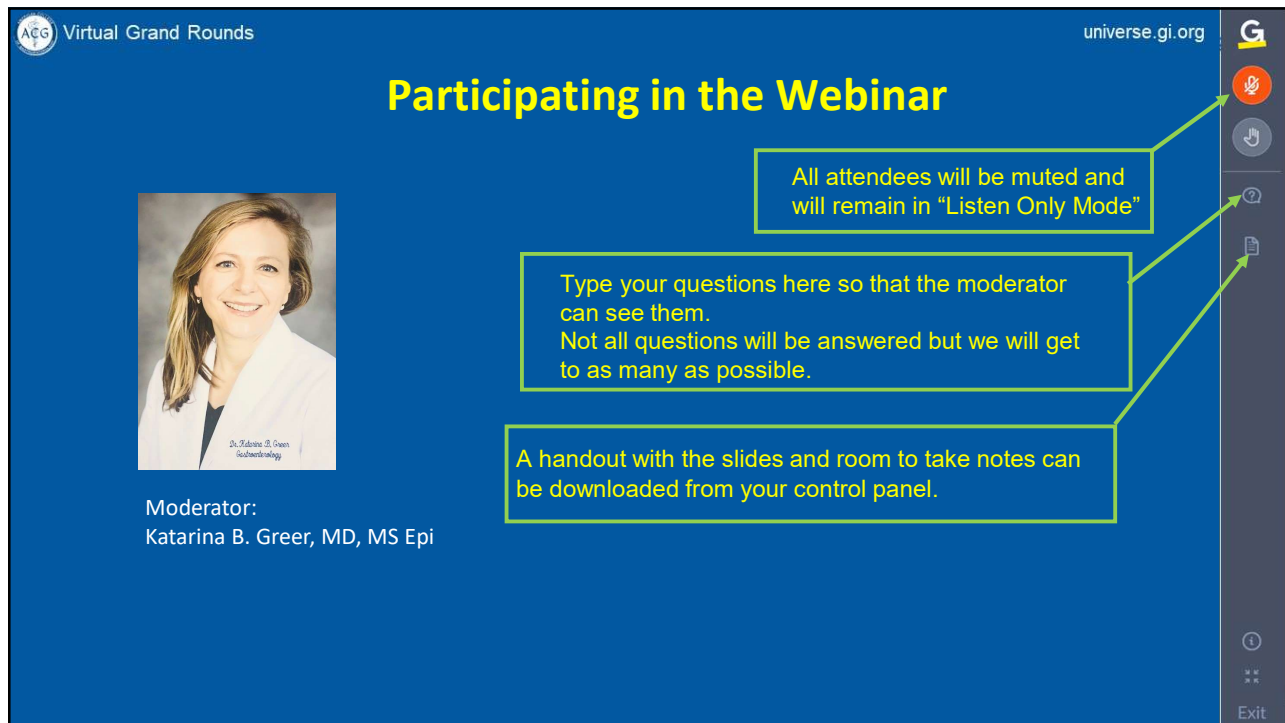
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**Moderator:**  
Katarina B. Greer, MD, MS Epi

All attendees will be muted and will remain in "Listen Only Mode"

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

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 Management of Patients With Acute Lower Gastrointestinal Bleeding: An Updated ACG Guideline  
 Faculty: Neil Sengupta, MD  
 Moderator: Lisa L. Strate, MD, MPH, FACC  
**At Noon and 8pm Eastern**




**Week 35 – Thursday, August 31, 2023**  
 ACG Clinical Guideline: Diagnosis and Management of Biliary Strictures  
 Faculty: Jennifer L. Maranki, MD, MSc  
 Moderator: Anna Tavakkoli, MD  
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**Brian C. Jacobson, MD, MPH, FACP**  
Dr. Jacobson has no relevant financial relationships with ineligible companies.



**Katarina B. Greer, MD, MS Epi**  
Department of Defense (Award W81XWH2110586). This grant supports study of diagnostic accuracy of Esocheck/Esoguard for esophageal cancer screening. I also serve as local site investigator for the CONFIRM study at the Cleveland VA Medical Center. I have no conflicts of interest to disclose.

*\*All of the relevant financial relationships listed for these individuals have been mitigated*

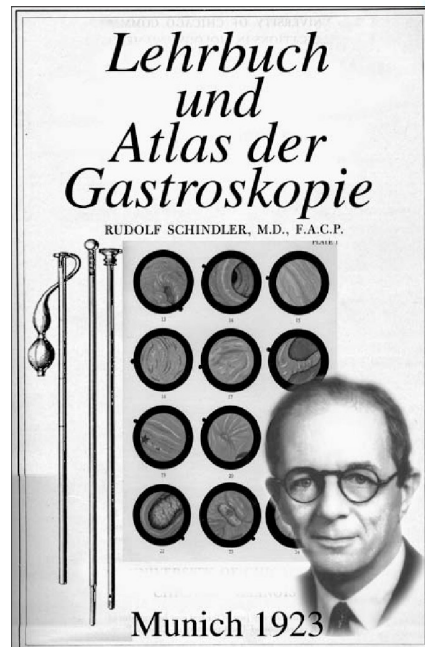
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# ACG Clinical Guideline: Diagnosis and Management of Gastrointestinal Subepithelial Lesions



Brian C. Jacobson, MD, MPH, FACG  
Associate Professor of Medicine, Harvard Medical School  
Director of Program Development for GI, Massachusetts General Hospital

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From "Gastroscopy: the endoscopic study of gastric pathology" by Rudolf Schindler, 1937

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## GI Stromal Tumor



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CME

## ACG Clinical Guideline: Diagnosis and Management of Gastrointestinal Subepithelial Lesions

Brian C. Jacobson, MD, MPH, FACP<sup>1</sup>, Amit Bhatt, MD<sup>2</sup>, Katarina B. Greer, MD, MS<sup>3</sup>, Linda S. Lee, MD<sup>4</sup>, Walter G. Park, MD, MS<sup>5</sup>, Bryan G. Sauer, MD, MSc, FACP<sup>6</sup> and Vanessa M. Shami, MD, FACP<sup>6</sup>

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### “Subepithelial” not (or maybe not) “submucosal”

- The term subepithelial lesion (SEL) describes a mass or mass-like structure that projects into the GI lumen
- Arises from a non-mucosal layer within the GI tract wall or outside the wall

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**Table 1. Subepithelial lesions and causes of extrinsic compression**

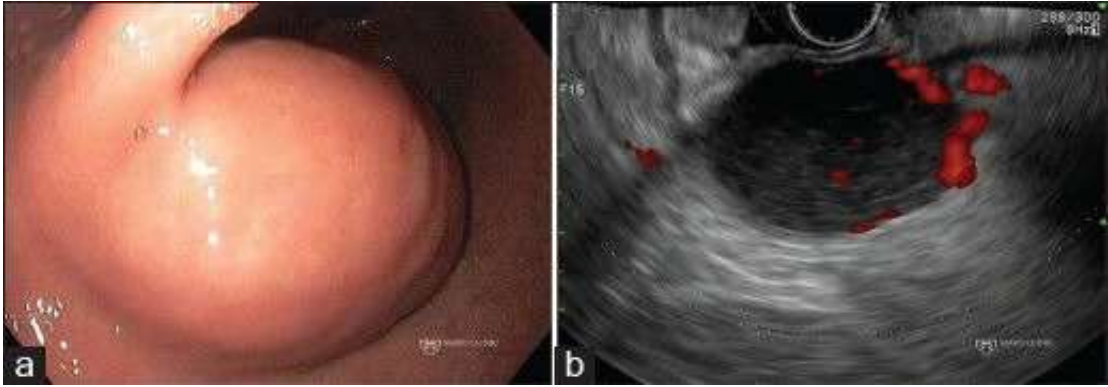
Subepithelial lesion or cause of extrinsic compression	Location in wall	Typical site(s) where found in GI tract <sup>a</sup>	Malignant potential	Tissue acquisition required for diagnosis
Spine	Extrinsic	Esophagus	No	No
Leiomyoma	MM, MP	Esophagus	No	Yes
Granular cell tumor	MM, SM	Esophagus	Yes (rare)	Yes
Duplication or bronchogenic cyst	Any including extrinsic	Esophagus/mediastinum	Yes (extremely rare)	No
Varices	SM	Esophagus	No	No
Xyphoid	Extrinsic	Fundus of stomach	No	No
Neuroendocrine tumor	SM, MP	Stomach, duodenum, rectum	Yes	Yes
GI stromal tumor	MM, MP	Stomach	Yes	Yes
Heterotopic pancreas	MM, SM, MP	Stomach (antrum)	Yes (extremely rare)	No
Schwannoma	SM, MP	Stomach	No	Yes
Gallbladder	Extrinsic	Antrum of stomach or Duodenal bulb	No	No
Lymphangioma	MP	Small intestine	No	Yes
Lipoma	SM	Colon	No	No
Metastasis	Any layer including extrinsic	Anywhere	Already malignant	Yes

GI, gastrointestinal; MM, muscularis mucosa; MP, muscularis propria; SM, submucosa.  
<sup>a</sup>While additional sites have been reported, this site(s) is the most common.

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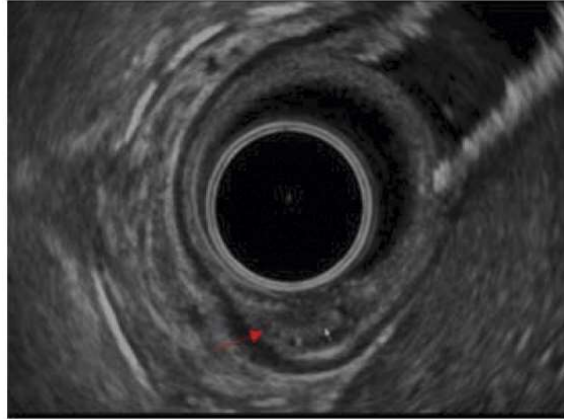
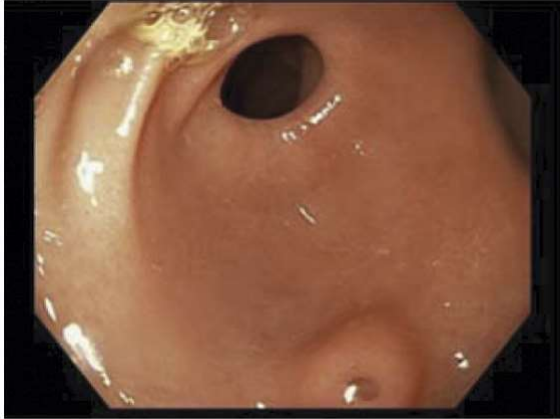
## GI Stromal Tumor



Source: Endoscopic ultrasound. 2014;3(1):35-45

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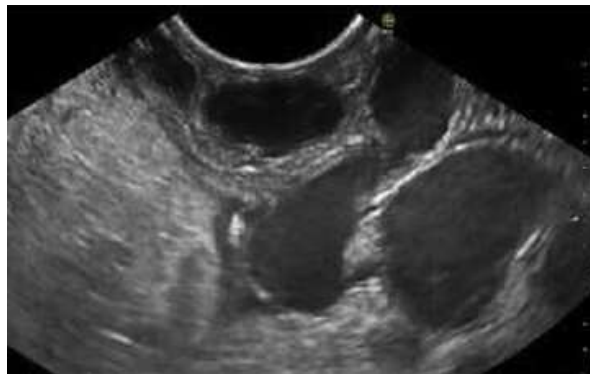
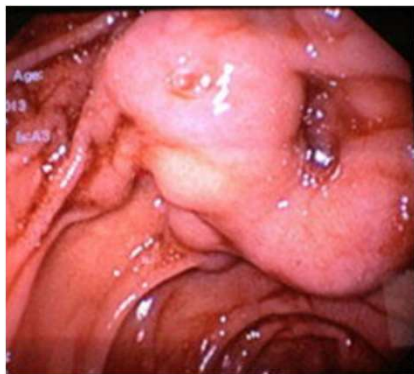
# Pancreatic Rest (Ectopic pancreas)



Source: Case reports in gastrointestinal medicine. Volume 2021; Article ID 8853120; <https://doi.org/10.1155/2021/8853120>

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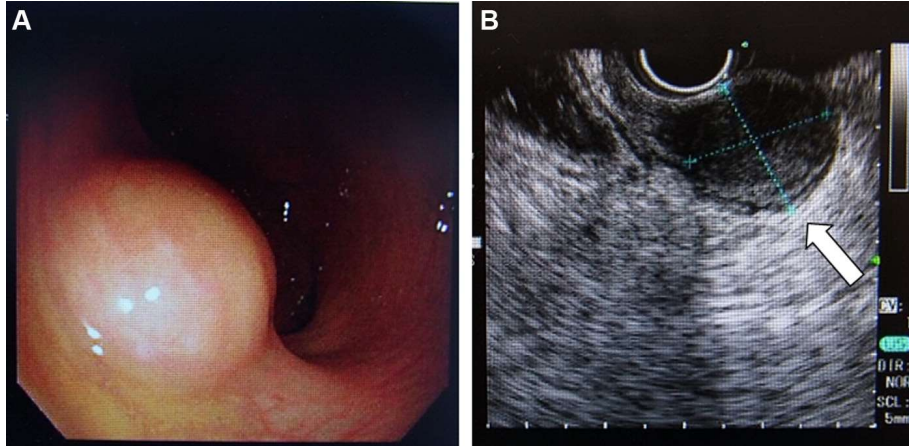
# Duodenal varix



Sources: VideoGIE 2020; DOI:10.1016/j.vgie.2020.09.007; GE Portuguese Journal of Gastroenterology 2015  
DOI: 10.1016/j.jpge.2015.03.008

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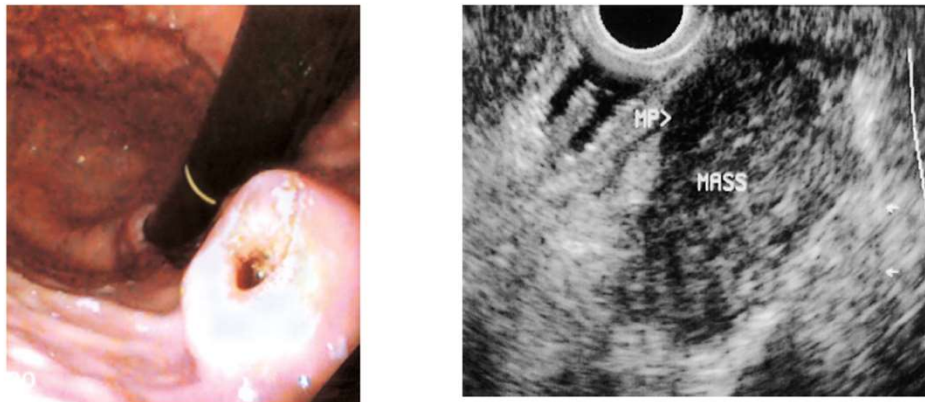
# Rectal Schwannoma



Source: Int J Surg Case Reports. Volume 5, Issue 12, 2014, Pages 1193-1196

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# Ovarian cancer metastasis in stomach



Source: Gastrointest Endosc. 2003;58:933-935

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## How was the guideline prepared?

- Research librarians aided the panel in formulating 15 questions deemed clinically important using the PICO format:
  - P = population in question
  - I = intervention
  - C = comparator
  - O = outcomes of interest
- Example: Among asymptomatic individuals with a SEL (P), is EUS-FNB (I) more accurate than EUS-FNA (C) for diagnosing subepithelial lesions (O)?

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## How was the guideline prepared?

- PICO questions were then investigated by comprehensive literature search (1/2000 – 12/31/2020): EMBASE, PubMed, Cochrane Reviews, and the Cochrane Central Register of Controlled Clinical Trials
- 444 citations for review
- PICO questions evolved into a final set of 11 recommendations

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## Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology:

### Quality of Evidence

“High” quality of evidence = Confident that true effect lies close to estimate of the effect

“Moderate” = True effect is likely to be close to the estimate of the effect

“Low” = True effect may be substantially different from the estimate of the effect

“Very low” = Very little confidence in the effect estimate

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## Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology:

### Strength of Recommendation

“Strong recommendation” = The desirable effects of the intervention clearly outweigh the undesirable effects

Most patients should be managed according to the recommendation

“Conditional recommendation” = offered when the tradeoffs are less certain.

Some, but not all, patients may derive benefit. In general, conditional recommendations require a thorough consideration of individual clinical situations

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## Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology:

### Strength of Recommendation

Strength of the recommendation derives from the quality of the evidence and an assessment of potential risks and benefits

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### “Key Concepts”

- Statements to which the GRADE process was not applied
- May also include definitions and epidemiological statements rather than diagnostic or management recommendations

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## Diagnostic and Management Algorithm

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Is an SEL found at endoscopy (or on imaging)  
causing symptoms or anemia?

- If yes, then it should be resected
- If no, then let's figure out what it is

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## Key Concept #1

- If an SEL is causing symptoms or GI bleeding, then resection may be justified regardless of the size of the lesion and without a pre-resection diagnosis
- The one exception is in the case of a large GIST, in which case tissue confirmation may be needed to permit the use of neoadjuvant imatinib to reduce tumor size

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“Ok, so we’re gonna try to diagnose this thing”

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## Recommendation #1

We suggest EUS be performed preferentially compared with endoscopy or contrast-enhanced cross-sectional imaging for the diagnosis of nonlipomatous SEL (conditional recommendation; very low quality of evidence)

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## Lipomas

- Lipomas can present anywhere within the GI tract, have a slightly yellow appearance and demonstrate a “pillow sign”
- In one small prospective study, endoscopy alone had a 99% specificity for the diagnosis of lipomas based on the presence or absence of a pillow sign (99%), although the sensitivity was low (40%)
- While granular cell tumors and small neuroendocrine tumors may also look yellow, they are typically firm and fail to demonstrate a pillow sign

Sources: Gastrointest Endosc Clin N Am 2012;22(2):187–205; Gastrointest Endosc 2005;62(2):202–8; Scand J Gastroenterol 2011;46(2):142–7.

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## Up to one-third of suspected SEL are extrinsic

- For the determination of the location (specific intramural layer vs extrinsic to the GI lumen) of a suspected SEL, EUS is superior to endoscopy
- In one multicenter study, the sensitivity and specificity of correctly differentiating an intramural from an extramural lesion with endoscopy alone was 87% and 29%, respectively
- EUS improved the sensitivity and specificity to 92% and 100%

Sources: Gastrointest Endosc 2005;62(2):202–8; Scand J Gastroenterol 2002;37(7):856–62; Endoscopy 1994;26(02):239–42.

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## What about cross-sectional imaging?

- Case series show EUS has greater accuracy than CT for pre-resection diagnosis of gastric SEL (64% vs 51%, respectively)
- CT has difficulty identifying small (e.g. <11mm) SELs
- The data suggest that while cross-sectional imaging may detect lesions identified incidentally during EGD, there is little diagnostic gain over EUS

Sources: Clin Endosc 2019;52(6):565–73; Abdom Imaging 2012;37(6):1074–8; Abdom Imaging 2012;37(4):519–30.

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## Key Concept #2

- When seeking a diagnosis, contrast-enhanced imaging may add clinically useful information, but this should be reserved for situations when EUS is unavailable
- In such instances, and depending on the differential diagnosis being considered, strong consideration should be given to referral to a center where EUS is available

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## Recommendation #2

We do not recommend one type of echoendoscope (forward viewing vs oblique viewing) when evaluating SEL (strong recommendation; low quality of evidence)

38

## Forward vs Oblique-Viewing Scopes

- Three randomized studies have compared forward-viewing echoendoscopes with standard oblique-viewing linear echoendoscopes with no significant differences in diagnostic yield for SEL (21–23)
- While there may be certain situations that favor a forward-viewing echoendoscope, there is no clear superiority of one type over the other
- The choice of echoendoscope for any particular case should be left to the discretion of the operator

Sources: Endoscopy 2019;51(5):444–51; Gut Liver 2015;9(5):679–84; Gastrointest Endosc 2015;82(2):287–95.

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## Recommendation #3

We do not suggest bite-on-bite biopsies in the evaluation of SEL before EUS (conditional recommendation; very low quality of evidence)

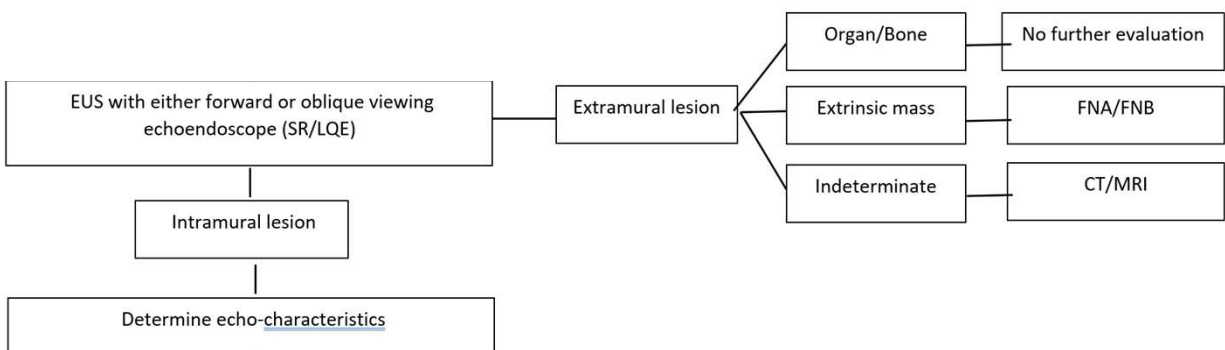
40

## Bite on Bite

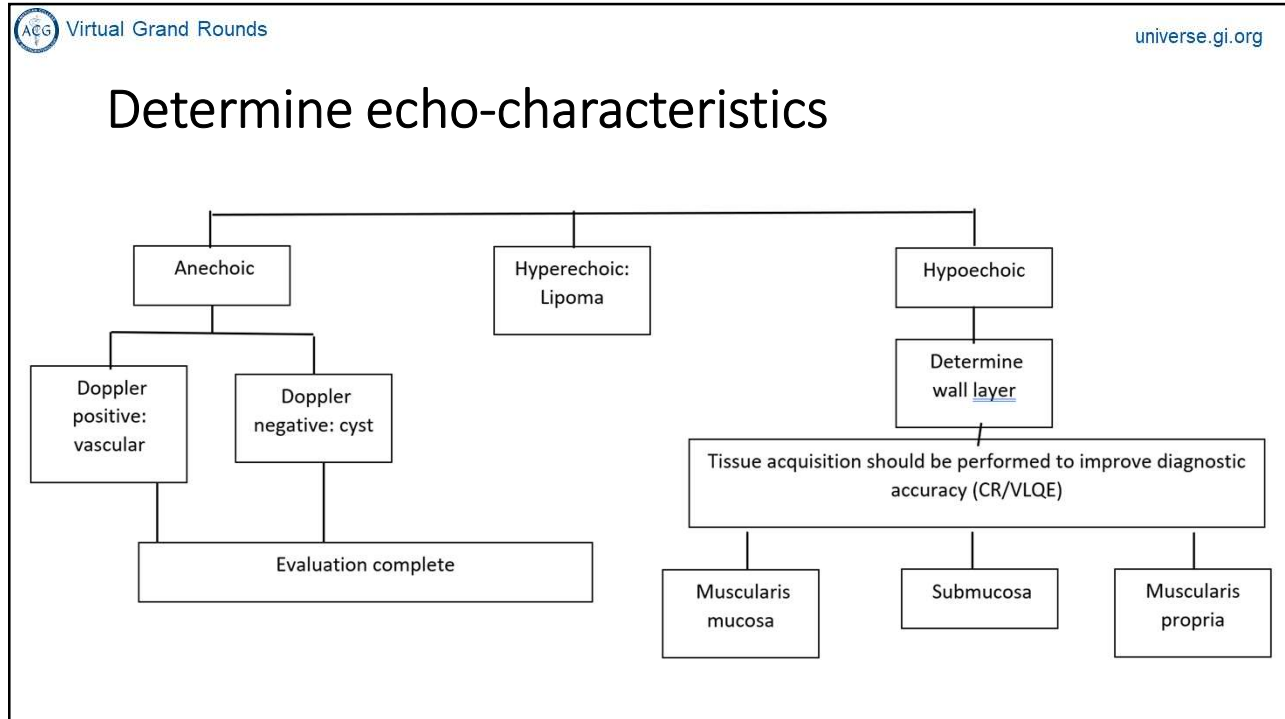
- Very limited data – EUS done ahead of time
- May help with tiny lesions if FNA/FNB won't be feasible
- **Must** be sure vascular lesions are excluded

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## So now you're doing your EUS



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## Recommendation #4

We suggest EUS with tissue acquisition to improve diagnostic accuracy in the identification of solid non-lipomatous SEL (conditional recommendation; very low quality of evidence)

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## “Tissue is the Issue”

- The addition of tissue acquisition increases the diagnostic accuracy from a range of 30%–50% to a range of 73%–84%
- Interobserver agreement was good to excellent for cysts and lipomas but only poor to fair for other SEL including leiomyomas and vascular lesions

Sources: Gastrointest Endosc 2001;53(1):71–6; Turk J Gastroenterol 2018;29(4):436–41; Gastrointest Endosc 2011;74(3):504–10; Medicine (Baltimore) 2016;95(44):e5246; Gastrointest Endosc 2009;69(7):1218–23.

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## Key Concept #3

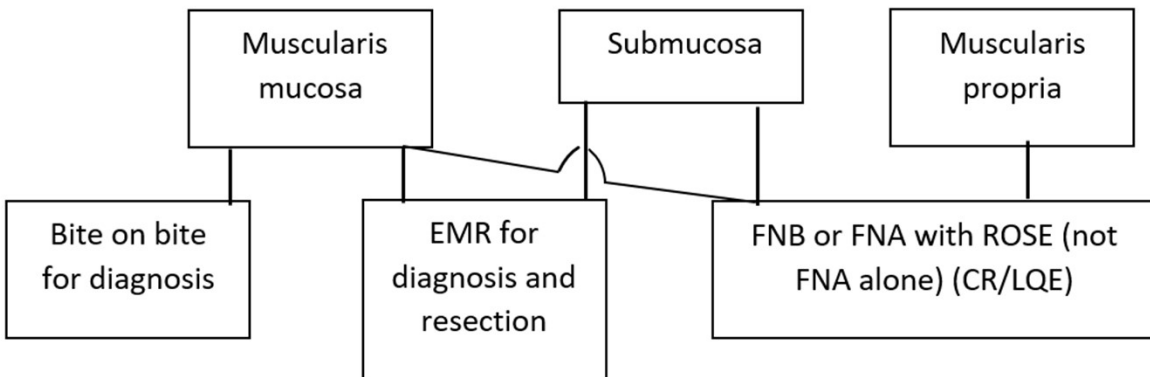
In the absence of a tissue diagnosis and/or resection of an SEL, the patient should be enrolled in some form of surveillance plan unless there is a high degree of confidence that the SEL has no malignant potential

46

“Ok, so how’re we gonna sample this thing?”

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### Employ location-based sampling



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## Recommendation #5

We suggest EUS-FNB alone or EUS-FNA with rapid on-site evaluation (ROSE) sampling of solid nonlipomatous SEL compared with EUS-FNA without ROSE (conditional recommendation; low quality of evidence)

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## FNB vs FNA with ROSE

- A meta-analysis of 10 studies (including 6 randomized trials) with a total of 669 patients compared EUS-FNA with FNB of SEL
- FNB yields higher rates of adequate samples and histologic cores, yields greater diagnostic accuracy, and requires fewer numbers of needle passes
- However, when ROSE was available in these studies, no significant differences between FNA and FNB were noted

Source: Gastrointest Endosc 2020;91(1):14–22 e2.

50

## Needle Size

- One retrospective study compared 19- and 22-gauge FNA needles for gastric SEL in the fourth layer of the wall and demonstrated significantly higher diagnostic yield with the 19-gauge FNA needle (92% vs 71%)
- Regarding FNB, there are insufficient data in the setting of SEL to know whether needle size correlates with diagnostic yield

Source: Arq Bras Cir Dig 2018;31(1):e1350.

51

## Key Concept #4

- There is no fixed cutoff in size below which FNA/FNB may not be attempted
- Small SEL should be managed on a case-by-case basis depending on the location, ease of sampling, clinical history, perceived risks and benefits of a surveillance approach, and potential for primary endoscopic resection

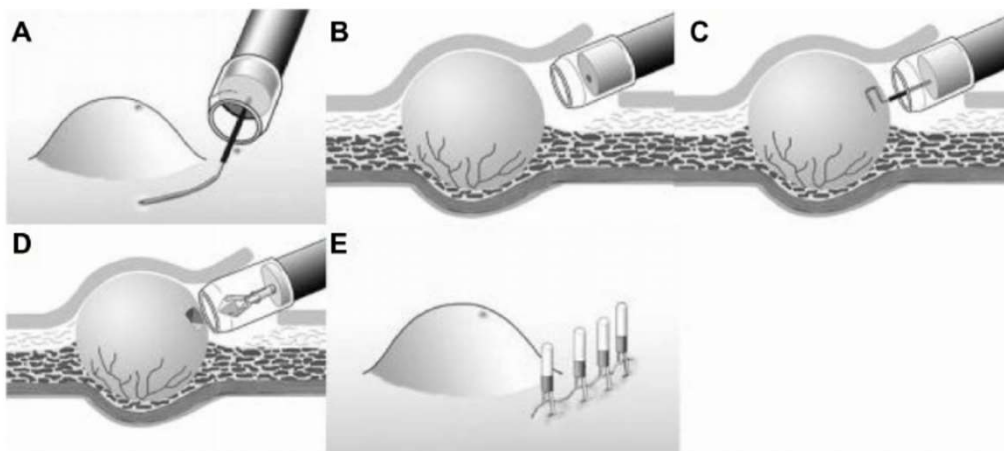
52

## Recommendation #6

We suggest using an unroofing technique when a pre-resection definitive diagnosis of an SEL is necessary and when EUS-FNA or FNB is nondiagnostic (conditional recommendation; low quality of evidence)

53

## Submucosal Tunnel Biopsy



Source: Kobara et al. Submucosal tunneling techniques: Current perspectives. *Clinical and Experimental Gastroenterology* 2014;7:67-74

54

## Submucosal Tunnel Biopsy

- One prospective study (n=68) compared STB with primary surgical resection
- STB in 40 pts achieved a diagnostic yield of 90% without complications and 13 pts avoided surgery
- Among the 28 pts who underwent primary surgical resection without a preop diagnosis, 12 (43%) were confirmed to have benign lesions
- Note, this may cause fibrosis, hampering future endoscopic resection

Source: Endoscopy 2014;46(10):845–50

55

## Mucosal incision–assisted biopsy (MIAB)

- Mucosa is cut in a freehand fashion using a needle knife to expose the SEL for direct biopsy
- A systematic review of MIAB that included 7 studies with a total of 159 patients reported a diagnostic yield of 89%
- Mean tumor size was 2.1 cm, and 95% were located in the stomach
- GI bleeding in 5%; close defect with clips

Source: Ann Gastroenterol 2020;33(2):155–61.

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## Diagnosis obtained... now what?

- Surveillance may be an option
- Resection method depends on the diagnosis, size, location and patient-specific factors

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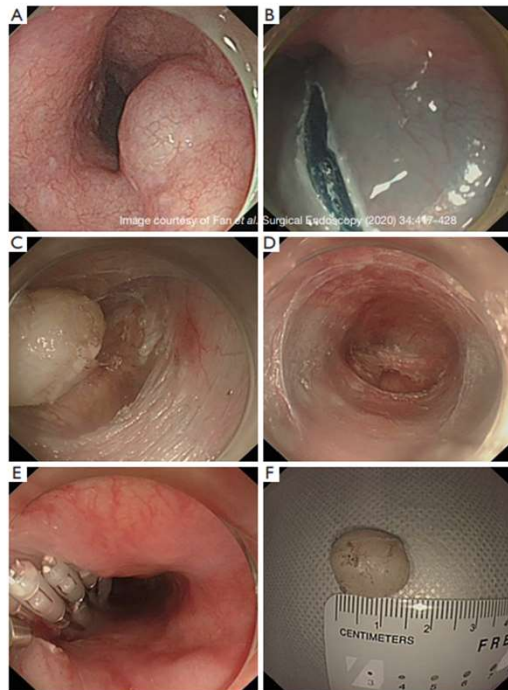
Suppose the SEL is in the muscularis propria in the esophagus or GE junction

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## Recommendation #7

We suggest either submucosal tunneling endoscopic resection (STER) or surgical resection for the management of SEL originating from the muscularis propria layer of the esophagus and gastroesophageal junction when resection is necessary (conditional recommendation; very low quality of evidence)

59



### Endoscopic resection techniques of benign esophageal tumors: literature review

Yahya Alwatari, Dawit Ayalew, Athanasios E. Sevdalis, Daniel Scheese, Vignesh Vudatha, Walker Julliard, Rachit D. Shah

Ann Esophagus 2023;6:17 | <https://dx.doi.org/10.21037/aoe-21-32>

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## SEL in the MP of the esophagus or GE junction

- Retrospective study compared outcomes of patients who underwent STER (n=91) or thoracoscopic enucleation (TE; n=75) for large (>5 cm) symptomatic SEL in the esophagus and esophagogastric junction.
- en bloc resection rates: STER = 85%, TE =87%; Shorter procedures and hospital LOS with STER; similar AE rate
- More technical difficulties, piecemeal resection, and adverse events with STER for tumors >3.5 cm and with irregular shapes

Source: J AmColl Surg 2017;225(6):806–16

61

Suppose the diagnosis is GI stromal tumor  
(GIST)

62

## Recommendation #8

- There is insufficient evidence to recommend surveillance vs resection of gastric GIST <2 cm in size
- Owing to their malignant potential, we suggest resection of gastric GIST >2 cm and all non-gastric GIST (conditional recommendation; very low quality of evidence)

63

## Management of GISTs <2 cm is controversial

- Metastatic rate approaches 0% regardless of the mitotic rate
- Per National Comprehensive Cancer Network guidelines, surveillance reasonable if no high-risk features
  - Irregular borders, cystic spaces, ulceration, echogenic foci, or heterogeneity
- However, resect in the presence of high-risk features

Gastrointest Endosc 1997;45(6):468–73; Semin Diagn Pathol 2006;23(2):70–83;  
NCCN ([https://www.nccn.org/login?ReturnURL=https://www.nccn.org/professionals/physician\\_gls/pdf/gist.pdf](https://www.nccn.org/login?ReturnURL=https://www.nccn.org/professionals/physician_gls/pdf/gist.pdf)). Accessed March 3, 2022..

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## Key Concept #5

- For GIST < 2 cm, if the clinical decision is to resect, endoscopic methods may be considered as acceptable alternative therapies compared with surgery
- There is insufficient data to suggest any one endoscopic method as superior

65

## Resect larger GISTs

- For GISTs > 2 cm, the rate of metastatic spread increases with the size of the lesion and may be as high as 86% for lesions greater than 10 cm with a high mitotic rate
- Several non-randomized studies comparing surgical and endoscopic resections, with good outcomes for both, however...
- Typically, the endoscopic methods are done in patients with smaller GISTs (typically around 2 cm)

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## Suppose the diagnosis is gastric neuroendocrine tumor (gNET)

67

## First a word about gNETs

- Three types based on behavior and clinical setting
- Types 1 and 2 gNETs are associated with chronic hypergastrinemia
- Excess gastrin due to atrophic gastritis in type 1 gNET and due to tumor-produced gastrin in type 2 gNET (e.g. MEN-1)
- Type 3 gNET are sporadic tumors that develop without hypergastrinemia and behave more aggressively than types 1 and 2

Source: Gastroenterology 1993;104(4):994–1006.

68

## Recommendation #9

We suggest EMR or ESD for the resection of type 1 gNETs (conditional recommendation; very low quality of evidence)

69

## Type 1 gNETs

- National Comprehensive Cancer Network recommends endoscopic resection of prominent tumors
- One retrospective study of type 1 gNET  $\leq 10$  mm resected by EMR (n=48) or ESD (n=39) showed negative margin resection rate (R0 resection) was higher with ESD (95%) than EMR (83%); P=0.17) with better deep margin control
- Given the indolent nature, unclear if superiority of ESD is clinically relevant

Sources: J Natl Compr Canc Netw 2018;16(6):693–702; Gastroenterol Res Pract 2014;2014:1–7.

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## Key Concept #6

- Endoscopic resection of prominent type 2 gNET can be undertaken if the goal is debulking or management of ongoing blood loss
- It is not clear whether ESD is superior to EMR in this setting, and choice of resection method may depend on local expertise

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## Recommendation #10

We suggest ESD over EMR for the resection of low-grade, small type 3 gNET without radiologic or EUS evidence of lymphadenopathy that do not undergo surgical resection (conditional recommendation; very low quality of evidence)

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## Type 3 gNETs

- One retrospective study compared outcomes among pts with type 3 gNETs who underwent EMR (n=41) or ESD (n=9)
- Positive margins were seen in 7/41 (15%) in the EMR group and in 1/9 (11%) in the ESD group (P=0.25)
- Considering the findings in type 1 gNETs, ESD may result in higher R0 resection rates than EMR
- Because a positive margin requires surgery, when expertise is available, ESD should be considered for small, low-grade type 3 gNETs

Source: World J Gastroenterol 2016;22(42):9400–10.

73

Suppose the diagnosis is rectal  
neuroendocrine tumor

74

## Recommendation #11

We do not suggest one type of endoscopic therapy (EMR vs ESD) for the resection of small (<1 cm), low-grade rectal NET (conditional recommendation; very low quality of evidence)

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## Rectal NETs

- Some retrospective studies have found higher R0 resection rates with ESD compared with EMR with submucosal injection and snare resection (90%–97% vs 71%–77%, respectively)
- However, 2 studies with a combined 159 patients compared band ligation EMR with ESD finding significantly higher R0 resection rates with band ligation EMR compared with ESD (EMR: 96%–100%; ESD 54%–75%)

Sources: Clin Res Hepatol Gastroenterol 2018;42(1):24–30; Gastrointest Endosc 2010;72(1):143–9; Gastroenterol Res Pract 2016;2016:1–6; Gastroenterol Res Pract 2019; 2019:1–10.

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## Rectal NETs

- A retrospective study compared underwater EMR with ESD for small rectal NETs, finding both achieved an R0 resection in 86% of cases
- Underwater EMR had significantly shorter procedure time than ESD (6 +/- 3 vs 27 +/- 13 minutes, P=0.001)

Source: Gastrointest Endosc 2020;91(5):1164–71.e2.

77

## A final word on rectal NETs

- While all rectal NETs should be removed, EUS to assess for adenopathy may not be necessary in small (< 10 mm), incidental rectal NETs
- Primary excision may be performed during the initial colonoscopy when they are first encountered
- Data suggest band or underwater EMR better than inject-and-lift/snare resection

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## Future Directions

- As our resection methods improve (e.g. FTRD, STER), we should clarify the role of primary resection vs pre-resection diagnosis
- Safe and efficient unroofing techniques may limit need for EUS
- Is there a diagnostic role for artificial intelligence?

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## Future Directions

- Head-to-head resection comparisons needed (including surgery)
- A standardized lexicon of terminology is needed for sampling and resection techniques

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## The reference for those interested

ACG Clinical Guideline: Diagnosis and Management of  
Gastrointestinal Subepithelial Lesions

*Am J Gastroenterol 2023;118:46–58*

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A promotional graphic for the ACG 2023 meeting in Vancouver, Canada. The background is an aerial view of the city and harbor. A large blue speech bubble with a white dotted pattern contains the text: "I'm going to ACG 2023 JOIN ME in Vancouver, Canada". In the bottom right corner, there is a logo for "ACG 2023" with the dates "OCTOBER 20-25, 2023" and "VANCOUVER, CANADA". Below the logo, it says "For more information, visit acgmeetings.gi.org".


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## Questions



Brian C. Jacobson, MD, MPH, FACP



Katarina B. Greer, MD, MS Epi

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# CONNECT AND COLLABORATE IN GI



ACG & CCF IBD Circle



ACG GI Circle

Connect and collaborate within GI



ACG Hepatology Circle



ACG Functional GI  
Health and Nutrition Circle



ACG Women in GI Circle

**ACG's Online Professional Networking Communities**

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