II Brazilian consensus statement on endoscopic ultrasonography

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ABSTRACT

Background and Objectives: At the time of its introduction in the early 80s, endoscopic ultrasonography (EUS) was indicated for diagnostic purposes. Recently, EUS has been employed to assist or to be the main platform of complex therapeutic interventions. Methods: From a series of relevant new topics in the literature and based on the need to complement the I Brazilian consensus on EUS, twenty experienced endosonographers identified and reviewed the pertinent literature in databases. The quality of evidence, strength of recommendations, and level of consensus were graded and voted on. Results: Consensus was reached for eight relevant topics: treatment of gastric varices, staging of nonsmall cell lung cancer, biliary drainage, tissue sampling of subepithelial lesions (SELS), treatment of pancreatic fluid collections, tissue sampling of pancreatic solid lesions, celiac neurolysis, and evaluation of the incidental pancreatic cysts. Conclusions: There is a high level of evidence for staging of nonsmall cell lung cancer; biopsy of SELs as the safest method; unilateral and bilateral injection techniques are equivalent for EUS-guided celiac neurolysis, and in patients with visible ganglia, celiac ganglia neurolysis appears to lead to better results. There is a moderate level of evidence for: yield of tissue sampling of pancreatic solid lesions is not influenced by the needle shape, gauge, or employed aspiration technique; EUS-guided and percutaneous biliary drainage present similar clinical success and adverse event rates; plastic and metallic stents are equivalent in the EUS-guided treatment of pancreatic pseudocyst. There is a low level of evidence in the routine use of EUS-guided treatment of gastric varices.

Key words: Consensus, endoscopic ultrasonography, endosonography, evidence-based medicine

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INTRODUCTION

At the time of its introduction in the early 80s, endoscopic ultrasonography (EUS) was indicated for diagnostic purposes. Classical indications included oncological staging and evaluation of subepithelial and pancreatic lesions. Histological sampling of peridigestive structures and intramural lesions of the gastrointestinal (GI) tract wall became possible in the 90s with the advent of EUS-guided fine-needle aspiration (EUS-FNA). More recently, EUS has been employed to assist or to be the main platform for complex therapeutic interventions, such as bile duct drainage, treatment of peripancreatic fluid collections (PFCs), celiac neurolysis, and embolization of gastroesophageal varices.

In 2009, a consensus group identified the best evidence supporting the use of EUS and compiled those evidences in the 1st Brazilian consensus on EUS. Based on that report, the consensus panel concluded that EUS provided useful information for the staging of esophageal cancer, differential diagnosis of subepithelial lesions (SELs), thickened gastric folds, assessment of peritoneal involvement in gastric cancer, evaluation of mucosa-associated lymphoid tissue lymphoma, diagnosis of common bile duct/gallbladder stones, diagnosis of chronic pancreatitis, differential diagnosis of a solid tumors in patients with chronic pancreatitis, differential diagnosis of pancreatic cysts, rectal cancer staging, and diagnosis and staging of nonsmall cell lung cancer. At that time, the consensus panel felt that several EUS indications would continue to emerge and require additional validation.

Seven years after publication of the first consensus, the Brazilian Society for Gastrointestinal Endoscopy encouraged the organization of a 2nd consensus meeting to reevaluate some of the conclusions of the 1st edition and to debate the evolving indications of therapeutic EUS.

METHOD

From a series of relevant new topics in the literature and based on the need to complement the I Brazilian consensus on EUS, twenty nationally renowned echoendoscopists were gathered to debate these topics.

Eight relevant topics were identified: EUS in the treatment of gastric varices, EUS in the staging of nonsmall cell lung cancer, EUS-guided biliary drainage, EUS tissue sampling of SELs of the GI tract wall, EUS-guided treatment of pancreatic fluid collections, EUS-FNA of pancreatic solid lesions, EUS-guided celiac neurolysis, and EUS for the evaluation of the incidental pancreatic cysts. The topics were transformed into questions which were presented to the experts 6 months before the definitive consensus meeting. The experts debated the questions, suggestions were raised, and the 19 resulting questions were distributed among the participants. Members of the consensus panel were asked to answer the questions based on the best available evidence and to rate the evidence degree found in the literature by adopting the Oxford System [Table 1]. Six months later, the 19 questions were discussed by the group during a consensus meeting, resulting in 43 recommendations. The recommendations were voted individually. When at least 70% of the participants were in agreement with the voted recommendation, consensus was considered to have been reached.

Three of the organizers (JFO, EQM, and FMF) wrote this report and sent it electronically to all the participants of the meeting who approved it for publication. None of them has any conflict of interest related to the consensus issues.

RESULTS

Comparison of endoscopic treatment versus endoscopic ultrasonography-guided treatment for obliteration of gastric varices

Gastric varices obliteration by cyanoacrylate endoscopic injection is effective.[4-7]

Recommendation: B – 100% vote; evidence level 2a.

EUS may be useful for evaluation of gastric variceal eradication in case of doubt.[4,5]

Recommendation: B – 100% vote; evidence level 2a.

EUS-guided treatment of varices type 1 isolated gastric varices (IGV1) and gastroesophageal varices 2 through the combination of cyanoacrylate injection and coil may be an option in the failure of conventional endoscopic treatment.[6,7]

Recommendation: C – 100% vote; evidence level 3a.

The EUS-guided treatment of gastric fundal varices presents similar efficacy to conventional endoscopic treatment, with a lower complication rate, especially pulmonary embolism, even asymptomatic.[8]
Discussion

The use of endoscopic injection of cyanoacrylate for the treatment of fundal gastric varices is supported by the high level of evidence.\[8\] Recently, EUS-guided embolization of gastric varices with coil and/or cyanoacrylate has been reported in some case series.\[4,6,7\]

A small retrospective comparative study suggests that EUS-guided coil embolization requires fewer sessions for gastric varices obliteration with fewer adverse events.\[6\]

The consensus panel discussed that EUS-guided coil embolization has important availability and cost issues compared with endoscopic injection of cyanoacrylate. On the other hand, the coil technique seems to reduce embolism events albeit it is recognized that most embolism events are asymptomatic. Those facts argue in favor of the use of EUS-guided coil embolization in patients at risk of embolism, such as the pediatric population (e.g., congenital cardiac conditions) or spontaneous portosystemic shunts (e.g., IGV1 large gastric varices).

**Endoscopic ultrasonography in the staging of nonsmall cell lung cancer**

It is recommended to perform EUS-guided puncture (EUS-FNA and/or endobronchial ultrasound [EBUS]-FNA) in patients with positron emission tomography-computed tomography (PET-CT) or CT demonstrating mediastinal lymph node enlargement.\[9-11\]

Table 1. Level of scientific evidence according to the type of study

| Level of recommendation | Level of evidence | Therapy/prevention - etiology | Diagnosis |
|-------------------------|-------------------|------------------------------|-----------|
| A                       | 1a                | SR (with homogeneity) of RCTs | SR (with homogeneity) of level 1 diagnostic studies; CDR with 1b studies from different clinical centers |
|                         | 1b                | Individual RCT (with narrow CI) | CDR with good reference standards or CDR tested within one clinical center |
|                         | 1c                | All or none                  | Absolute SpPins and SnNouts |
| B                       | 2a                | SR (with homogeneity) of cohort studies | SR (with homogeneity) of level >2 diagnostic studies |
|                         | 2b                | Individual cohort study (including low-quality RCT; for example, <80% follow-up) | Exploratory cohort study with good reference standards; CDR after derivation, or validated only on split-sample or databases |
|                         | 2c                | “Outcomes” research; ecological studies | |
|                         | 3a                | SR (with homogeneity) of case-control studies | SR (with homogeneity) of 3b and better studies |
|                         | 3b                | Individual case-control study | Nonconsecutive study; or without consistently applied reference standards |
| C                       | 4                 | Case-series (and poor quality cohort and case-control studies) | Case-control study, poor, or non-independent reference standard |
| D                       | 5                 | Expert opinion without explicit critical appraisal, or based on physiology, bench research or “first principles” | |

RCT: Randomized control trial, CDR: Clinical Dementia Rating, CI: Confidence interval, SR: Systematic review

Recommendation: C – 100% vote; evidence level 4.

EUS-FNA and/or EBUS-FNA are recommended in patients with PET-CT or CT with no evidence of mediastinal lymphadenopathy but presenting:

• Primary tumor of central location,
• Primary tumor with low uptake by PET-CT, or
• Presence of ipsilateral hilar lymph node enlargement (N1).\[9-11\]

Recommendation: C and D – 100% vote; evidence level 4 and 5.

Complementation with surgical staging (mediastinoscopy or other methods) is recommended in the case of nondiagnostic puncture by echoendoscopy.\[9-11\]

Recommendation: B – 100% vote; evidence level 2a.

Combined performance of EUS-FNA and EBUS-FNA is preferred to the execution of each method alone.

Recommendation: C – 100% vote; evidence level 4.

In patients with suspected left adrenal metastasis, it is suggested to perform EUS-FNA for diagnostic elucidation.\[9-11\]

Recommendation: C – 100% vote; evidence level 4.
Note: EBUS is not widely available in our country.

Discussion
It is recognized that EUS alone, EBUS alone, and combined EUS + EBUS have good sensitivity (83%–94%) for mediastinal staging of lung cancer. Therefore, in case of enlarged mediastinal lymph nodes on CT or PET-CT, EUS/EBUS with FNA is the first choice for tissue diagnosis. However, if lymph nodes are not present, the lesion is smaller than 3 cm and located in the outer third of the lung, surgery can be performed directly.[9]

The adrenal gland is the primary metastatic site of the lung cancer, this way, it should always be evaluated during EUS. In the suspicion of metastatic lesion, tissue diagnosis is mandatory.[10]

Endoscopic ultrasonography-guided biliary drainage

Comparison of endoscopic ultrasonography-guided biliary drainage versus transparietohepatic (percutaneous biliary drainage) in endoscopic retrograde cholangiopancreatography failure
The technical and clinical successes of the EUS-guided and percutaneous access to endoscopic retrograde cholangiopancreatography (ERCP) failure for drainage of the extrahepatic biliary tract are similar. The adverse events of these accesses are different but with similar rate. Local expertise and availability should be taken into account when choosing the approach. Whenever possible, the choice of the access should be the result of a multidisciplinary approach.[3,12-14]

Recommendation: B – 85% vote; evidence level: 2b.

Extra- or intra-hepatic access?
For EUS-guided biliary drainage, either by the rendezvous (RV) or transluminal (TL) technique, intra- or extra-hepatic accesses may be used. There are few prospective studies comparing both techniques. Current evidence suggests similar results but with lower rates of complications with the extrahepatic access. There is a lack of better quality studies comparing EUS-guided biliary drainage with intra- and extra-hepatic accesses.[15-17]

Recommendation: B – 95% vote; evidence level: 2b.

Biliary drainage by rendezvous versus transluminal
When for the option of EUS-guided biliary drainage due to ERCP failure, two drainage techniques are available: RV and TL. There are few studies comparing these techniques, and they suggest similar results and safety. Unfortunately, there is a lack of better quality studies comparing EUS-guided biliary drainage by RV and TL techniques.[18]

Recommendation: B – 95% vote; evidence level: 2b.

Hepaticogastrostomy versus choledochoduodenostomy
For the EUS-guided biliary drainage by the TL technique, the techniques of hepaticogastrostomy and choledochoduodenostomy can be used. There are few prospective studies comparing these techniques. Current evidence suggests similar efficacies but with lower rates of complications in favor of choledochoduodenostomy. More studies of better quality comparing the TL EUS-guided biliary drainage by hepaticogastrostomy technique and choledochoduodenostomy are warranted.[19]

Recommendation: B – 100% vote; evidence level: 2b.

Endoscopic ultrasonography-guided biliary drainage: Plastic versus metal stents
We found only one study comparing metal and plastic stents for EUS-guided biliary drainage. The study suggests that the technical and clinical successes are similar although the rate of biliary fistula is higher with plastic stents. The consensus group recommends the use of partially or fully covered metal stents in the biliary drainage whenever possible. There is a need for better quality comparative studies.[16]

Recommendation: C – 100% vote; evidence level: 4.

Discussion
In the case of unsuccessful transpapillary drainage of the biliary tree, the available alternatives are surgery, EUS-guided biliary drainage, and percutaneous biliary drainage. The last two options present similar success and complication rates although the EUS access seems to be less invasive.[8,12-14]

There are major differences between RV versus TL and extra- versus intra-hepatic approaches. However, choledochoduodenostomy (extrahepatic) complication rate seems to be lower when compared with hepaticogastrostomy.[15-18]
In summary, indications and methods for EUS-guided biliary drainage are still being standardized, and therefore, the approach should be individualized for each patient based on the local expertise and patient’s conditions.

**Endoscopic ultrasonography for subepithelial lesions**

When is endoscopic ultrasonography-fine-needle aspiration is indicated for subepithelial lesions?

It is suggested to perform EUS-FNA of asymptomatic SELs of the muscularis propria of the stomach, duodenum, and rectum, larger than 10 mm. It is recognized that diagnostic yield is higher for lesions larger than 20 mm. Irregular borders, cystic areas, body/antrum location as well as age >60 years strengthen the indication. Unsampled lesions should undergo endoscopic and/or EUS reevaluation although there is no consensus of the interval and duration of the follow-up.

Recommendation: C – 95% vote; evidence level: 4.

The use of elastography and contrasts is an additional option for the selection of lesions to be sampled.[19,20]

Recommendation: C – 100% vote; evidence level: 4.

Half of the asymptomatic patients do not accept to remain in follow-up, and two-thirds of those in prolonged follow-up refuse resection in the case of enlargement of their lesions. Such facts could strengthen the need to obtain tissue diagnosis.[21]

Recommendation: C – 95% vote; evidence level: 4.

Asymptomatic SELs of the esophageal muscularis propria layer >3 cm should be biopsied to differentiate leiomyomas from other potentially malignant lesions.

No agreement – 40% vote; evidence level: 4.

In the suspicion of the following lesions, regardless of the lesion size, tissue confirmation is necessary:

- GI stromal tumor with indication of neoadjuvant therapy
- Intramural metastases
- Lymphoma
- Neuroendocrine tumors
- Extrinsic neoplasia.

Recommendation: D – 100% vote; evidence level: 5.

**Tissue diagnosis of subepithelial lesions of the digestive tract: Endoscopic ultrasonography-fine-needle aspiration X alternative methods**

EUS-guided puncture is the safest method for histopathological diagnosis of SEL of the digestive tract.[22]

Recommendation: A – 100% vote; evidence level: 1b.

The type of needle (aspiration/trucut/pro-core) or caliber does not alter the diagnostic accuracy of the EUS-guided puncture for the diagnosis of SEL. The choice of needle depends on the location of the lesion and the preference of the endoscopist.[22]

Recommendation: B – 100% vote; evidence level: 2b.

Alternative methods for histopathological diagnosis of SEL of the digestive tract (such as mucosectomy, unroofing) are better than EUS-FNA for lesions <20 mm. They are an option when EUS-FNA is not available but with significant rates of bleeding and perforation.[22-25]

Recommendation: C – 95% vote; evidence level: 4.

For SEL located above the muscularis propria, <2 cm, where the EUS-FNA results are usually less satisfactory, biopsy-on-biopsy, unroofing, or endoscopic resection, either by ligature, mucosectomy, or submucosal dissection is valid options.[23,24]

Recommendation: C – 100% vote; evidence level: 4.

Endoscopic resection of the SEL of the muscularis propria, whether by submucosal dissection/tunneling or transmural resection, are techniques under evaluation and should be performed in referral centers with expertise.[26]

Recommendation: D – 95% vote; evidence level: 5.

**Discussion**

Tissue sampling of a SEL of the GI tract should be indicated whenever a premalignant or malignant lesion cannot be ruled out by EUS imaging alone. In practical terms, hypoechoic lesions located in the muscularis propria measuring between 10 and 30 mm are the best candidates for tissue sampling. The consensus panel is
in agreement that gastric, duodenal, and rectal lesions have a higher malignant potential when compared with esophageal lesions.\textsuperscript{[22-25]}

The available literature does support the superiority neither of a specific technique nor a needle caliber or model for increasing the diagnostic yield of EUS-guided tissue sampling for SEL. The diagnostic yield of EUS-guided tissue sampling is around 65\%–70\%.\textsuperscript{[23]}

High-quality studies comparing EUS-FNA with alternative methods for histopathological diagnosis of SEL such as unroofing, mucosectomy, and submucosal dissection are lacking. Nevertheless, the use of these techniques is supported specially for lesions <20 mm of from the submucosal and inner muscular propria layers where the EUS-FNA accuracy is usually nonsatisfactory.\textsuperscript{[24]}

**Endoscopic ultrasonography for peripancreatic fluid collections**

**Endoscopic ultrasonography in the characterization of peripancreatic fluid collections**

Before endoscopic or EUS-guided drainage of PFCs, in addition to CT-scan/magnetic resonance imaging (MRI), EUS may be used for the differential diagnosis of pancreatic cystic neoplasia and detection of necrosis.\textsuperscript{[27]}

Recommendation: D – 100\% vote; evidence level: 5.

**Endoscopic ultrasonography-guided pancreatic pseudocyst drainage: Plastic versus metal stents**

Success rates in resolution of pancreatic pseudocyst, frequency of adverse events, and recurrence with plastic or metal stents are similar 85\%, 20\%, and 10\%, respectively.\textsuperscript{[28]}

Recommendation: B – 100\% vote; evidence level: 3a.

**Endoscopic ultrasonography-guided drainage of walled-off necrosis: Plastic versus metal stents**

Success rates in the resolution of pancreatic walled-off necrosis (WON), frequency of adverse events, and recurrence of the collection with plastic or metallic stents are similar 70\%–75\%, 20\%, and 10\%, respectively.\textsuperscript{[28]}

Recommendation: B – 100\% vote; evidence level: 3a.

**Endoscopic ultrasonography-guided drainage of peripancreatic fluid collection with luminal-apposing metallic stents**

The results of EUS-guided drainage of PFC with luminal-apposing metallic stents (LAMSS) are promising and can improve the results obtained so far.

Recommendation: D – 100\% vote; evidence level: 5.

**Discussion**

The majority of acute PFCs will resolve spontaneously and do not require intervention. The indications for drainage of a PFC are the presence of symptoms, infection, and resolution of infected or enlarging cysts. A study of 242 patients found that mortality was reduced as the time from hospital admission to intervention of the PFC was increased (0–14 days: 56\%; 14–29 days: 26\%; and >29 days: 15\%; \(P < 0.001\)). Approximately 60\% of patients with necrotizing pancreatitis can be managed without an intervention and with low mortality.\textsuperscript{[29]}

Endoscopic treatments usually result in shorter hospital stays, better patient physical and mental health, and lower treatment costs compared with surgery. Although endoscopic and EUS-guided transmural pseudocyst drainage have shown similar clinical efficacy, EUS-guided drainage is preferred even when there is a visible luminal bulging, in a patient with normal hemostasis and no portal hypertension with collaterals.\textsuperscript{[30-32]}

There was no difference in adverse event rates between metal and plastic stents for endoscopic drainage of pseudocyst, and in spite of the rational that the thick viscosity of necrotic fluid and solid debris present within WON might not be adequately drained using plastic stents, no difference in treatment success rates is shown in the literature. The use of the recently introduced LAMSS is promising, but high-quality comparative studies with plastic and conventional metallic stents are still lacking.\textsuperscript{[27]}

**Endoscopic ultrasonography-fine-needle aspiration of pancreatic solid lesions**

When to indicate endoscopic ultrasonography-fine-needle aspiration of pancreatic solid lesion? For surgically resectable lesions: consider EUS-FNA in suspected metastasis, lymphoma, neuroendocrine tumor, or autoimmune pancreatitis.\textsuperscript{[33-36]}

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For surgically unresectable lesions: EUS-FNA is indicated for oncologic treatment planning.\textsuperscript{33-36}

When surgical tumor resectability is doubtful: complete staging and if unresectable, EUS-FNA is indicated.\textsuperscript{33-36}

If EUS-FNA result is negative for neoplasia, but suspicion is still high, repeat EUS-FNA.\textsuperscript{33-36}

EUS-FNA is indicated in patients referred to neoadjuvant treatment for locally advanced, marginally resectable pancreatic adenocarcinoma.\textsuperscript{36}

Recommendation: B – 100% vote; evidence level: 2a.

Elastography and contrast-enhanced EUS are methods that intend to improve the negative predictive value of EUS-FNA, so they are useful as complementary tests, helping to differentiate between solid pancreatic neoplasms and other lesions, as well as guiding the choice of puncture site. However, it should be emphasized that its use does not replace the need of tissue sampling.\textsuperscript{36-38}

Recommendation: B – 100% vote; evidence level: 2b.

Endoscopic ultrasonography-fine-needle aspiration techniques for pancreatic solid lesions

There are conflicting data in the literature comparing the efficacy of 19-, 22-, and 25-gauge needles, with no superiority of one over the other.\textsuperscript{36,39-44}

Recommendation: B – 100% vote; evidence level: 2b.

The 25-gauge needle appears to have a diagnostic advantage in transduodenal punctures.\textsuperscript{36,39-44}

Recommendation: B – 100% vote; evidence level: 2b.

Transduodenal puncture should not be performed with a nonflexible 19-gauge needle due to technical difficulties.\textsuperscript{36,39-44}

Recommendation: B – 100% vote; evidence level: 2b.

There is no evidence in the literature demonstrating superiority of the techniques of aspiration suction, use or not of the stylet, or “slow pull.”\textsuperscript{36,39-44}

Recommendation: B – 100% vote; evidence level: 2b.

The “fanning” technique seems to reduce the number of punctures needed for the definitive diagnosis.\textsuperscript{36,39-44}

Recommendation: B – 100% vote; evidence level: 2b.

Discussion

EUS is a very important method for the diagnosis of solid pancreatic lesions, especially the adenocarcinoma. Besides its good accuracy for the diagnosis of pancreatic adenocarcinoma (higher than 85%),\textsuperscript{45-47} it is also very useful for tissue sampling of other conditions. It is well accepted that EUS-FNA does not impact survival or alters the results of patients with resected pancreatic cancer.\textsuperscript{28,33}

The use of new technologies, such as elastography and contrast-enhanced EUS, are complementary to the EUS imaging alone and can be useful to guide the puncture site, but available literature does not show relevant improvement in EUS-FNA diagnostic yield.\textsuperscript{36,37,48}

When analyzing different aspects of the techniques for puncture of pancreatic solid lesions, such as the needle caliber or type, as well as the type of aspiration, there is no evidence in the literature that favors anyone in particular. The most important endpoint is the satisfactory tissue acquisition and a good pathology analysis to achieve the expected diagnostic yield.\textsuperscript{36,39-44}

Endoscopic ultrasonography-guided celiac plexus neurolysis

Celiac plexus neurolysis: Unilateral versus bilateral injection

The technique of injection (unilateral or bilateral) does not influence the efficacy of the celiac plexus EUS-guided neurolysis.\textsuperscript{49,51}

Recommendation: B – 100% vote; evidence level: 1b.

Celiac plexus neurolysis versus celiac ganglia neurolysis

In patients with visible ganglia, celiac ganglia neurolysis (CGN) appears to lead to a better pain relief and is preferable compared to celiac plexus neurolysis (CPN).\textsuperscript{49,52-54}

Recommendation: B – 100% vote; evidence level: 1b.

Discussion

EUS-guided CPN (EUS-CPN) for pain relief is safe and effective, especially for patients with pancreatic...
cancer, while the results are modest for chronic pancreatitis.\textsuperscript{49} EUS-CPN complication rate is around 40%, and a self-limited hypotension is the most common one (20%).\textsuperscript{46}

It was suggested that bilateral injection would enhance the efficacy of celiac plexus EUS-guided neurolysis, but the studies available did not confirmed this suspicion.\textsuperscript{49-51} The view of the celiac ganglia is a predictor of good response to neurolysis, and this structure can be identified by EUS in 63%–88% of patients. In these cases, the injection should be performed directly in the ganglia as the results show better pain relief.\textsuperscript{16,52-54}

**Endoscopic ultrasonography for the evaluation of the incidental pancreatic cyst**

**When is endoscopic ultrasonography indicated for incidental pancreatic cyst?**

EUS is indicated for the evaluation of the incidental pancreatic cysts identified and characterized preferably by MRI, with a protocol dedicated to the study of the gland, whose result is a pancreatic cyst of indeterminate morphology.\textsuperscript{47,55,56}

Recommendation: C – 100% vote; evidence level: 4.

**When is endoscopic ultrasonography-fine-needle aspiration indicated for incidental pancreatic cyst?**

EUS-FNA is indicated in the incidental pancreatic cyst of indeterminate morphology when:

- Larger than 15 mm
- There is a suspicion of nodule or vegetation
- There are irregular or thickened internal walls
- There is an abrupt change of the caliber of the main pancreatic duct next to the cyst
- The main pancreatic duct measures between 5 and 9 mm.\textsuperscript{47,55,56}

Recommendation: C – 100% vote; evidence level: 4.

Notes:

- EUS-FNA is not indicated when cyst morphology on EUS is characteristic of a serous cystadenoma, regardless of its size
- The risk and benefit of EUS-FNA should be weighted against the presence of intervening vessels, main pancreatic duct, or more than 10 mm of normal parenchyma between the needle and lesion
- Antibiotic prophylaxis is indicated
- The aspirated material should be sent for dosage of carcinoembryonic antigen (CEA), amylase, glucose, and cytopathology, giving preference to CEA
- In the future, the molecular evaluation of the aspirated material will be available and will probably be useful for risk stratification of malignancy.

**Discussion**

Despite the relatively high incidence of pancreatic cysts in the population (3%–15%), the risk of malignancy is very low (<1%). Thus, the indication of any surgical procedure, which carries a morbidity of 20%–40%, should be balanced.\textsuperscript{56} EUS is important in the characterization of incidental pancreatic cysts in asymptomatic patients. The consensus panel found prudent to follow most of the recommendations of the International Association of Pancreatologists concerning the indication of EUS-FNA of incidental pancreatic cysts. However, the consensus panel reduced the threshold for EUS-FNA in lesions measuring at least 15 mm. This is due to the recent studies on molecular analysis of the fluid of incidental pancreatic cysts showing mutations associated with high-grade dysplasia and even cancer in small branch-duct intraductal papillary mucinous neoplasms.\textsuperscript{57,59}

**CONCLUSIONS**

There is a low level of evidence to support the routine use of EUS-guided treatment of gastric varices. There is a high level of evidence to support the use of EUS for staging of nonsmall cell lung cancer. There is a high level of evidence to support EUS-guided biopsy of SELs as the safest method to sample SELs of the GI tract wall. There is a moderate level of evidence to support that the yield of EUS-guided tissue sampling of pancreatic solid lesions is not influenced by the needle shape, gauge, or employed aspiration technique. There is a moderate level of evidence to support that EUS-guided biliary drainage and percutaneous drainage present similar clinical success and adverse event rates. There is a moderate level of evidence to support that plastic and metallic stents are equivalent in the EUS-guided treatment of pancreatic pseudocyst. There is a high level of evidence to support that unilateral and bilateral injection techniques are equivalent for EUS-guided celiac neurolysis, and in patients with visible ganglia, CGN appears to lead to better results.
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Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Tio TL, Tytgat GN. Endoscopic ultrasonography of an arteriovenous malformation in a gastric polyp. Endoscopy 1986;18:156-8.
2. Vilman P, Jacobsen GK, Henriksen FW, et al. Endoscopic ultrasonography with guided fine needle aspiration biopsy in pancreatic disease. Gastrointest Endosc 1992;38:172-3.
3. Maluf-Filho F, Dotti CM, Halwan B, et al. An evidence-based consensus statement on the role and application of endosonography in clinical practice. Endoscopy 2009;41:979-87.
4. Lee YK, Han FK, Ng EK, et al. EUS-guided injection of cyanoacrylate for bleeding gastric varices. Gastrointest Endosc 2000;52:168-74.
5. Fabbri C, Luigiano C, Lissoti A, et al. Endoscopic ultrasound-guided treatments: Are we getting evidence based – A systematic review. World J Gastroenterol 2014;20:424-48.
6. Romero-Castro R, Elfrichmann M, Ortiz-Moyano C, et al. EUS-guided coil versus cyanoacrylate for the treatment of gastric varices: A multicenter study (with videos). Gastrointest Endosc 2013;78:71-21.
7. BinmoellerKF, Weiert F, Shah JN, et al. EUS-guided transesophageal treatment of gastric fundal varices with combined coiling and cyanoacrylate glue injection (with videos). Gastrointest Endosc 2011;74:1019-25.
8. de Franchis R, Baveno VI Faculty. Expanding consensus in portal hypertension: Report of the Baveno VI Consensus Workshop: Stratifying risk and individualizing care for portal hypertension. J Hepatol 2015;63:743-52.
9. De Leyn P, Doms C, Kuzdzel J, et al. Revised ESTS guidelines for preoperative mediastinal lymph node staging for non-small-cell lung cancer. Eur J Cardiothorac Surg 2014;45:789-98.
10. Vilman P, Clements PF, Colella S, et al. Combined endobronchial and esophageal endosonography for the diagnosis and staging of lung cancer. European Society of Gastrointestinal Endoscopy (ESGE) Guideline, in cooperation with the European Respiratory Society (ERS) and the European Society of Thoracic Surgeons (ESTS). Endoscopy 2015;47:545-59.
11. ASGE Standards of Practice Committee, Jae TL, Sharaf RN, et al. Role of EUS for the evaluation of mediastinal adenopathy. Gastrointest Endosc 2011;74:239-45.
12. Artifon EL, Aparicio D, Paione JB, et al. Biliary drainage in patients with unresectable, malignant obstruction where ERCP fails: Endoscopic ultrasound-guided choledochoduodenostomy versus percutaneous drainage. J Clin Gastroenterol 2012;46:768-74.
13. Khashab MA, Valeshabad AK, Afghani E, et al. A comparative evaluation of EUS-guided biliary drainage and percutaneous drainage in patients with distal malignant biliary obstruction and failed ERCP. Dig Dis Sci 2015;60:557-65.
14. Gornals JB, Moreno R, Castellote J, et al. Single-session endosonography and endoscopic retrograde cholangiopancreatography for bilioduodenal disease is feasible, effective and cost beneficial. Dig Liver Dis 2013;45:578-83.
15. Khan MA, Akbar A, Baron TH, et al. Endoscopic ultrasound-guided biliary drainage: A systematic review and meta-analysis. Dig Dis Sci 2016;61:684-703.
16. Khashab MA, Levy MJ, Itoi T, et al. EUS-guided biliary drainage. Gastrointest Endosc 2015;82:900-1001.
17. Dhir V, Bhandari S, Bapat M, et al. Comparison of transhepatic and extraneoplastic routes for EUS-guided rendezvous procedure for distal CBD obstruction. United European Gastroenterol J 2013;1:103-8.
18. Khashab MA, Valeshabad AK, Modayil R, et al. EUS-guided biliary drainage by using a standardized approach for malignant biliary obstruction: Rendezvous versus direct transmural techniques (with videos). Gastrointest Endosc 2013;78:734-41.
19. Tsuji Y, Kusano C, Gotoda T, et al. Diagnostic potential of endoscopic ultrasonography-elastography for gastric submucosal tumors: A pilot study. Dig Endosc 2016;28:173-8.
20. Sakamoto H, Kitano M, Matsu S, et al. Estimation of malignant potential of GI stromal tumors by contrast-enhanced harmonic EUS (with videos). Gastrointest Endosc 2011;73:227-37.
21. Kushnir VM, Keswani RN, Hollander TG, et al. Compliance with surveillance recommendations for foregut subepithelial tumors is poor: Results of a prospective multicenter study. Gastrointest Endosc 2015;81:1378-84.
22. Zhang XC, Li QL, Yu YF, et al. Diagnostic efficacy of endoscopic ultrasound-guided needle sampling for upper gastrointestinal subepithelial lesions: A meta-analysis. Surg Endosc 2016;30:2431-41.
23. Mekky MA, Yamao K, Sawaki A, et al. Diagnostic utility of EUS-guided FNA in patients with gastric submucosal tumors. Gastrointest Endosc 2010;71:913-9.
24. Watson RR, BinmoellerKF, Hameski CM, et al. Yield and performance characteristics of endoscopic ultrasound-guided fine needle aspiration for diagnosing upper GI tract stromal tumors. Dig Dis Sci 2011;56:1757-62.
25. Hamada T, Yamasuga H, Nakai Y, et al. Rarity of severe bleeding and perforation in endoscopic ultrasound-guided fine needle aspiration for submucosal tumors. Dig Dis Sci 2013;58:2634-8.
26. Eckardt AJ, Jessen C. Current endoscopic ultrasound-guided approach to incidental subepithelial lesions: Optimal or optional? Ann Gastroenterol 2015;28:160-72.
27. ASGE Standards of Practice Committee, Muthusamy VR, Chandrasekhara V, et al. The role of endoscopy in the diagnosis and treatment of inflammatory pancreatic fluid collections. Gastrointest Endosc 2016;83:481-8.
28. Bang JY, Haves R, Bartolucci A, et al. Efficacy of metal and plastic stents for transmural drainage of pancreatic fluid collections: A systematic review. Dig Endosc 2015;27:486-98.
29. van Santvoort HC, Bakker OJ, Bollen TL, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. Gastrointestology 2011;141:1254-63.
30. Park DH, Lee SS, Moon SH, et al. Endoscopic ultrasound-guided versus conventional transmural drainage for pancreatic pseudocysts: A prospective randomized trial. Endoscopy 2009;41:842-8.
31. Kahahe M, Shami VM, Conaway MR, et al. Endoscopic ultrasound drainage of gastric pseudocysts: A prospective comparison with conventional endoscopic drainage. Endoscopy 2006;38:355-9.
32. Varadarajulu S, Christen JD, Tamhane A, et al. Prospective randomized trial comparing EUS and EGD for transmural drainage of pancreatic pseudocysts (with videos). Gastrointest Endosc 2008;68:1102-11.
33. ASGE Standards of Practice Committee, Eloubeidi MA, Ducker GA, et al. The role of endoscopy in the evaluation and management of patients with solid pancreatic neoplasia. Gastrointest Endosc 2016;83:17-28.
34. Beane JD, House MG, Coté GA, et al. Outcomes after preoperative endoscopic ultrasonography and biopsy in patients undergoing distal pancreatectomy. Surgery 2011;150:844-53.
35. Ngarumwengphong S, Swanson KM, Shah ND, et al. Preoperative endoscopic ultrasound-guided fine needle aspiration does not impair survival of patients with resected pancreatic cancer. Gut 2015;64:1105-10.
36. Dumonceau JM, Polkowski M, Larghi A, et al. Indications, results, and clinical impact of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Clinical Guideline. Endoscopy 2011;43:987-912.
37. Kitano M, Kamata K, Imai H, et al. Contrast-enhanced harmonic endoscopic ultrasonography for pancreaticobiliary diseases. Dig Endosc 2015;27 Suppl 1:560-7.
38. Karstensen J, Cartana T, Pia K, et al. Endoscopic ultrasound-guided needle confocal laser endomicroscopy in pancreatic masses. Endosc Ultrasound 2014;3 Suppl 1:52-3.
39. Wallace MB, Kennedy T, Durkalski V, et al. Randomized controlled trial
of EUS-guided fine needle aspiration techniques for the detection of malignant lymphadenopathy. *Gastrointest Endosc* 2001;54:441-7.

40. Puri R, Vilmann P, Saftoiu A, et al. Randomized controlled trial of endoscopic ultrasound-guided fine-needle sampling with or without suction for better cytological diagnosis. *Scand J Gastroenterol* 2009;44:499-504.

41. Erickson RA, Sayage-Rabie I, Beissner RS. Factors predicting the number of EUS-guided fine-needle passes for diagnosis of pancreatic malignancies. *Gastrointest Endosc* 2000;51:184-90.

42. LeBlanc JK, Ciaccia D, Al-Assi MT, et al. Optimal number of EUS-guided fine needle passes needed to obtain a correct diagnosis. *Gastrointest Endosc* 2004;59:475-81.

43. Turner BG, Cizginer S, Agarwal D, et al. Diagnosis of pancreatic neoplasia with EUS and FNA: A report of accuracy. *Gastrointest Endosc* 2010;71:91-8.

44. Jani BS, Rzouq F, Saligram S, et al. Endoscopic ultrasound-guided fine-needle aspiration of pancreatic lesions: A systematic review of technical and procedural variables. *N Am J Med Sci* 2016;8:1-11.

45. Gress F, Schmitt C, Sherman S, et al. Endoscopic ultrasound-guided celiac plexus block for managing abdominal pain associated with chronic pancreatitis: A prospective single center experience. *Am J Gastroenterol* 2001;96:409-16.

46. Wiersma MJ, Wiersema LM. Endosonography-guided celiac plexus neurolysis. *Gastrointest Endosc* 1996;44:656-62.

47. Tanaka M, Fernández-del Castillo C, Adsay V, et al. International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. *Panreatology* 2012;12:183-97.

48. Mei M, Ni J, Liu D, et al. EUS elastography for diagnosis of solid pancreatic masses: A meta-analysis. *Gastrointest Endosc* 2013;77:578-89.

49. Fusaroli P, Jenssen C, Hocke M, et al. EFSUMB guidelines on interventional ultrasound (INVUS), part V. *Ultraschall Med* 2016;37:77-99.

50. LeBlanc JK, Al-Haddad M, McHenry L, et al. A prospective, randomized study of EUS-guided celiac plexus neurolysis for pancreatic cancer: One injection or two? *Gastrointest Endosc* 2011;74:1300-7.

51. Tellez-Avila Fl, Romano-Munive AF, Herrera-Esquibel Jde J, et al. Central is as effective as bilateral endoscopic ultrasound-guided celiac plexus neurolysis in patients with unresectable pancreatic cancer. *Endosc Ultrasound* 2013;2:153-6.

52. Levy MJ, Topazian MD, Wiersema MJ, et al. Initial evaluation of the efficacy and safety of endoscopic ultrasound-guided direct ganglia neurolysis and block. *Am J Gastroenterol* 2008;103:98-103.

53. Doi S, Yasuda I, Kavakami H, et al. Endoscopic ultrasound-guided celiac ganglia neurolysis vs. celiac plexus neurolysis: A randomized multicenter trial. *Endoscopy* 2013;45:362-9.

54. Ascunce G, Ribeiro A, Reis I, et al. EUS visualization and direct celiac ganglia neurolysis predicts better pain relief in patients with pancreatic malignancy (with video). *Gastrointest Endosc* 2011;73:267-74.

55. Del Chiaro M, Verbeke C, Salvia R, et al. European experts consensus statement on cystic tumours of the pancreas. *Dig Liver Dis* 2013;45:703-11.

56. Scheiman JM, Hwang JH, Moayyedi P. American gastroenterological association technical review on the diagnosis and management of asymptomatic neoplastic pancreatic cysts. *Gastroenterology* 2015;148:824-48.e22.

57. Springer S, Wang Y, Dal Molin M, et al. A combination of molecular markers and clinical features improve the classification of pancreatic cysts. *Gastroenterology* 2015;149:1501-10.

58. Singh AD, Zeh HJ, Brand RE, et al. American Gastroenterological Association guidelines are inaccurate in detecting pancreatic cysts with advanced neoplasia: A clinicopathologic study of 225 patients with supporting molecular data. *Gastrointest Endosc* 2016;83:1107-17.e2.