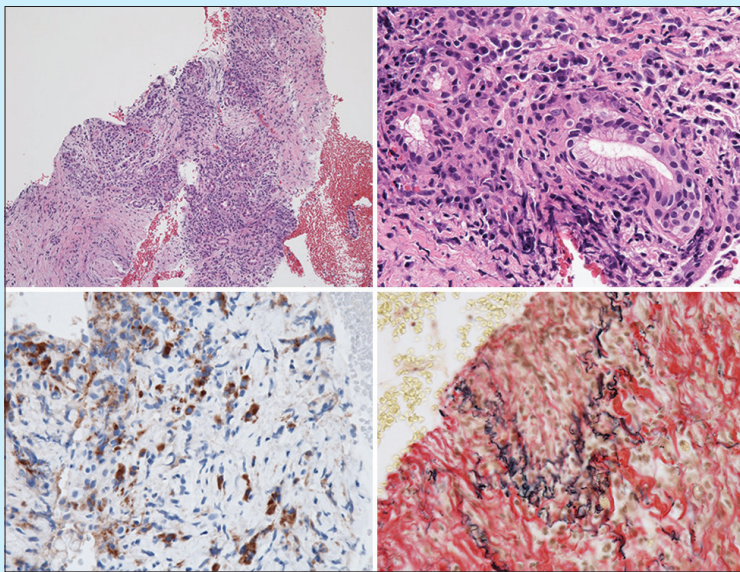




EUS

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HIGHLIGHT ARTICLES

- Robotic ultrasound and ultrasonic robot
- What should be known prior to performing EUS?
- Psychological impact of pancreatic cancer screening by EUS or magnetic resonance imaging in high-risk individuals: A systematic review
- Placement of lumen-apposing metal stents to drain pseudocysts and walled-off pancreatic necrosis can be safely performed on an outpatient basis: A multicenter study




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What should be known prior to performing EUS?

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Abstract

Direct referral of patients for EUS – instead of preprocedural consultation with the endosonographer – has become standard practice (like for other endoscopic procedures) as it is time- and cost-effective. To ensure appropriate indications and safe examinations, the endosonographer should carefully consider what information is needed before accepting the referral. This includes important clinical data regarding relevant comorbidities, the fitness of the patient to consent and undergo the procedure, and the anticoagulation status. In addition, relevant findings from other imaging methods to clarify the clinical question may be necessary. Appropriate knowledge and management of the patients' anticoagulation and antiplatelet therapy, antibiotic prophylaxis, and sedation issues can avoid unnecessary delays and unsafe procedures. Insisting on optimal preparation, appropriate indications, and clear clinical referral questions will increase the quality of the outcomes of EUS. In this paper, important practical issues regarding EUS preparations are raised and discussed from different points of view.

Key words: Coagulation tests, cost-effective, EUS, sedation

INTRODUCTION

Indications, clinical pathways, and techniques used for EUS may vary in different cultural contexts, countries, and EUS centers.^[1-9] Practicing EUS endoscopists from various regions across the world contributed to this review and discussed their standard practice with regard to currently available evidence and according to personal preference.

This study aims to discuss the pros and cons of several issues as follows:

- The “nihilistic” or “puristic” approach, “I need nothing prior to EUS” *versus* the clinical approach (“performing EUS as a clinician, I prefer to review as much clinical data as possible prior to EUS”)
- Knowledge of other imaging results before EUS
- Should transcutaneous ultrasound (TUS) and EUS be performed by the same operator?
- The use of esophagogastroduodenoscopy (EGD) prior to EUS
- Should consenting for EUS differ from consenting for EGD?
- Coagulation tests prior to EUS and interventions
- Other miscellaneous topics.

The authors declared that this study is not intended as a guideline, but rather an opportunity to document the current practice, allowing readers to evaluate their own pre-EUS procedures and to stimulate further discussion.

The nihilistic or puristic approach

“I need nothing prior to EUS” is the philosophy of some of the authors. For diagnostic EUS, they do

not need any test results. Ideally, EUS results should not be influenced by the pretest results. EUS is an endoscopic and imaging procedure and independently from previous findings should always be performed in a standardized manner.

In Great Britain, EUS is performed not only by gastroenterologists but also by radiologists. Therefore, endosonographers should be able to perform and interpret their examinations like a radiologist, with only basic clinical information and no prior imaging.

It is important that EUS is performed in an unbiased manner and that endosonographers develop the confidence to produce independent reports, especially if they disagree with the findings on other imaging procedures. It also forces the endosonographer to do a complete, systematic examination, instead of focusing only on previously described abnormalities. If there is discordance with other imaging modalities, it may be useful to compare EUS findings to previous imaging studies after the initial EUS assessment.^[10,11] The endosonographer may then decide whether it is worth prolonging the procedure to focus on a potential “missed-area” or to conclude the procedure. The protagonists of the nihilistic approach state that they never look at previous imaging studies prior to EUS. Despite this, the protagonists of the “puristic” approach claim that their results and outcomes are just as good as those in centers who do consult previous imaging procedure. In any case, there are no data proving that preprocedure consultation of computed tomography (CT) or ultrasound improves the yield of EUS.

The clinical approach

“I need to have clinical and image data available prior to EUS” is the paradigm of other authors. EUS should always be used and interpreted in a clinical context. In most countries, EUS is performed by gastroenterologists, surgeons, pneumologists, and other clinicians knowing the clinical history, laboratory findings, and previous imaging data of the patients. The protagonists believe that this is a great advantage compared with the puristic approach described above. The studies suggested that the results of EUS not blinded to patient’s history, clinical data, and previous imaging results are superior to the evaluation only of EUS video sequences.^[12,13]

Only by knowing the full clinical context of the EUS examination, the operator can interpret the findings correctly and decide properly on performing EUS-guided sampling and therapeutic procedures. Moreover, from a practical viewpoint, as EUS is minimally invasive, it is best for the patient to undergo a strategic diagnostic workflow, knowing the relevant clinical or image data at the time of the procedure. Knowledge of the results of previous examinations may help prevent adverse events, may inform the examiner on potentially useful auxiliary procedures such as contrast-enhancement or EUS-guided sampling, and can suggest the best choice of EUS scope. For instance, dilatation of the common bile duct without obvious cause of obstruction has a completely different meaning depending on whether the liver function tests are elevated or not and whether the patient has symptoms or not.^[14-17]

Possible underlying diseases should be known before examination.^[18-21] Missing relevant information preprocedure might result in the need to repeat the EUS procedure. Clinical and imaging information can guide a problem-orientated EUS approach that allocates the main procedure time to answering the clinically relevant question. One example is altered anatomy or pathology of the gastrointestinal (GI) tract (postsurgical, esophageal or duodenal diverticula, and stenosis), which may prompt the examiner to be especially careful to advance the scope; to use a small-diameter EUS scope (e.g., an endobronchial ultrasound [EBUS] scope for esophageal EUS), a US-miniprobe, or a forward-viewing scope; or to decide in favor of performing EGD prior to EUS. Another example is diagnosis of mediastinal lymphadenopathy, mediastinal tumors or mediastinal staging of lung cancer: the

choice of the scope (linear EUS scope *vs.* EBUS-scope) may depend on the location of the tumor or of the lymph nodes.^[22-24] In general, knowledge of radiological imaging is essential for planning of sampling strategies in oncological staging.^[25-27] In certain cases, knowledge of previous findings may help obviate invasive investigations with its attendant risks. In case of biochemical proof of insulinoma with EUS performed for localization, awareness of the biochemical test results means that EUS-guided sampling can be avoided.

DO WE NEED OTHER IMAGING MODALITIES BEFORE EUS?

Introduction

Combining TUS or other cross-sectional imaging with EUS may provide complementary information, for example, in oncological staging, but also in gastric, biliary and endocrine diseases, cystic and solid pancreatic lesions, or idiopathic acute and chronic pancreatitis.^[28-34] The topic was controversially discussed because the variety of authors represented different cultural behavior, institutional preference, and medical education ranging from gastroenterologists and surgeons to radiologists performing EUS. Some of the authors learned TUS as students and as mandatory part of the specializing curriculum whereas others never learned and used ultrasound and other radiological techniques. The use of US, CT, magnetic resonance imaging (MRI), and positron-emission tomography (PET) depends on the availability and legal and specific health-care rules and local habits. The topic of imaging in relation to EUS will be discussed in a planned separate paper. Initial demonstration of pathology by EUS may facilitate the finding of the same features using subsequent high-quality TUS equipment.

One recent study demonstrated that detection of pancreatic cysts by TUS was significantly improved with correlative images from CT, MRI, or EUS.^[35] In general, TUS is rarely used in oncological staging in Anglo-Saxon countries; however, investigating the reasons for this attitude is outside the purpose of this article and might be related to training policies in gastroenterology and availability of adequate equipment. On the other hand, cross-sectional imaging is routinely included in the staging protocols in these countries. Nowadays, new high-quality compact models of ultrasound processors that are compatible with EUS and EBUS scopes are emerging to meet the needs of physicians performing both

EUS^[3,8,9,25,26,36-40] and EBUS.^[41,42] Although these new processors are not compatible with the standard transabdominal probes, the basic principles of ultrasound and the normal anatomy should be well known by physicians who intend to performing EUS. No consensus could be reached between the authors regarding the specific roles of TUS, EUS, CT, and MRI in the four clinical scenarios noted below. This was particularly true with respect to the value of TUS.

Clear indications

A thorough clinical assessment is mandatory to establish the indications for EUS which is a minimally invasive method that carries a low, but not negligible risk. In addition, it may help minimize the EUS procedural risk by optimizing the coagulation status, creating awareness of altered anatomy, or comorbid conditions, allowing planning of invasive/interventional procedures, by intubation of unstable patients, or by examination after a prolonged fasting period in case of delayed gastric emptying. Less obvious is the definition of what should be mandatory clinical information prior to EUS. However, knowing the clinical symptoms, certain blood test results, particularly liver function tests, and previous findings of other investigations will support the quality and interpretation of the EUS results.^[43] However, this statement only reflects common clinical understanding/expert opinion, while hitherto only very few studies have been published.^[12] The need of TUS as prerequisite for EUS depends on its indication. MRI or CT is helpful to evaluate the whole extent of an inflammatory process such as necrotizing pancreatitis or tumor extent in oncological examinations. In patients with abdominal/retroperitoneal lymphadenopathy of unknown cause and in patients with (suspected) lung cancer, a thoracoabdominal (PET) CT is useful before EUS (\pm guided sampling) while Dotanoc/Dotatoc PET-CT is useful in neuroendocrine tumors. This helps in planning the most useful technique for tissue acquisition, a reasonable sequence for the diagnostic workup and the optimal site of biopsy. In cases with solid mediastinal mass lesions on CT, a mediastinal cyst has to be ruled out prior to EUS-guided sampling.

Oncologic indications

When EUS is indicated for locoregional staging of malignancy, TUS and/or other preliminary imaging methods such as MRI, CT, and PET might be appropriate to rule out metastatic disease, which

primarily determines the prognosis. CT is essential for staging of upper GI, pancreatobiliary, and thoracic malignancies and may guide the view of the endoscopist. If, for example, hepatic, lung, or skeletal metastases are detected, locoregional staging by EUS may become unnecessary. In fact, histological confirmation of metastases would determine the further therapy of the patients, while EUS would have no additional impact. In conclusion, if distant metastatic disease is found with cross-sectional imaging, in most cases, additional staging by EUS is not necessary.

The three imaging modalities (TUS, CT, and MRI) are sometimes complementary. EUS-guided sampling would be indicated if metastases are not detectable or reachable by percutaneous techniques.^[23,25-27,44,45] In patients with rectal cancer, CT is performed to exclude distant metastases, followed when negative by MRI to rule out or to confirm infiltration of the mesorectal fascia. In patients with distant metastases and locally advanced rectal cancer, EUS is not indicated.

For detecting metastases to the adrenals, the combined use of TUS and EUS is relevant as the right adrenal gland is better visualized with TUS and contrast-enhanced US (CEUS), whereas the left adrenal gland is more easily depicted with EUS.^[46-49]

The assessment of resectability of ductal pancreatic adenocarcinoma is difficult and is improved by complementary use of different imaging tools (CT, TUS, and EUS).^[50-52] The vascular involvement by pancreatic cancer is often more accurately assessed by CT or MRI than by EUS. If the information is available for the endoscopist, the correct diagnosis and staging can be achieved more easily.

Suspected choledocholithiasis

TUS should be performed first line in patients with suspected choledocholithiasis, since the direct confirmation of common bile duct stones or proof of dilated bile ducts in patients with elevated liver enzymes would result in direct referral to ERCP with endoscopic sphincterotomy and stone extraction. However, EUS or MRI cholangiography (MRCP) is still required prior to ERCP in cases with intermediate probability (10%–50%) of bile duct stones and no direct proof of common bile duct stones with TUS.^[53-56] An alternative approach in the intermediate probability setting would be early cholecystectomy with on-table cholangiography followed

by laparoscopic extraction or on-table ERCP in the case of positive findings. Recent meta-analysis show superiority of EUS over MRCP for the diagnosis of common bile duct stones, in particular in the case of small stones and microlithiasis.^[33,57] Miniprobe-EUS has shown promising results, but is rarely available.^[56]

Chronic pancreatitis

Advanced chronic pancreatitis can be diagnosed by TUS,^[58,59] while EUS due to its high spatial resolution may be more helpful to diagnose finer details in earlier stages or to exclude chronic pancreatitis. Therefore, together with secretin-enhanced MRCP, EUS may be considered the current “golden standard” for the diagnosis of chronic pancreatitis.^[13,34,60-64] TUS is appropriate before considering EUS to diagnose chronic pancreatitis. If the pancreas is well visualized (which is the case in the majority of patients),^[65,66] then EUS for the diagnosis of chronic pancreatitis may be avoided.^[58,59] On the other hand, EUS provides valuable additional information, e.g., on ductal anatomy (pancreas divisum)^[67,68] and on complications (splenic vein thrombosis and small visceral pseudoaneurysm) and therefore may help plan therapeutic procedures.^[63] If inflammatory masses need to be distinguished from neoplastic lesions, it also offers the option for EUS-guided sampling which may be less risky than percutaneous biopsy by TUS.

Pancreatic focal lesions

According to the current meta-analysis, all modern imaging tools have comparably high sensitivity for the diagnosis of pancreatic cancer.^[69] However, for the detection of small pancreatic lesions, TUS and CT are definitely inferior to MRI and EUS.^[10,52,70] In high-risk persons for pancreatic cancer, screening algorithms utilize a combination of MRI and EUS. Currently, EUS (in particular longitudinal) is the most sensitive technique to detect small solid and cystic pancreatic lesions. Nevertheless, it should be kept in mind that even a negative pancreatic EUS examination is not capable to completely exclude the presence of pancreatic cancer in patients with a high clinical suspicion.^[71-73] The number of incidentally detected small pancreatic lesions is increasing.^[10,11,74] To avoid unnecessary major surgery and to allocate these lesions correctly to treatment or surveillance, accurate classification into malignant, premalignant, and benign lesions is essential. However, accuracy of all modern imaging modalities to classify focal pancreatic lesions is limited.^[75] Therefore, often, the combination of various imaging techniques and

tissue diagnosis is necessary. CEUS has an approximately 90% of accuracy to differentiate pancreatic ductal adenocarcinoma from other solid pancreatic lesions and to differentiate between neoplastic and nonneoplastic pancreatic cysts.^[11,76,77] EUS elastography can rule out malignancy with a high level of certainty if the lesion appears soft. A stiff lesion can be either benign or malignant.^[78] From a technical standpoint with specific reference to optimal frequencies, the current CEUS techniques are considered more suitable for transabdominal use as opposed to EUS with Sonovue®.^[36-38,79-82] Therefore, TUS with CEUS should be performed in patients with suspected cystic and solid pancreatic lesions as an initial imaging tool.^[11,18-20,36,76,77,80]

TUS AND EUS: SHOULD THE EXAMINER BE THE SAME?

TUS should be performed by the same examiner as EUS

It is helpful and convenient if TUS and EUS are performed by the same person as the individual anatomy is then already familiar during the EUS examinations and pathologies detected by TUS can further be investigated and characterized by EUS. For logistic reasons, this will not always be possible.

TUS could be performed by any other examiner

In principle, a high-quality TUS report should precisely describe any pathological findings with respect to size, location, echogenicity, shape, delineation, as well as contrast- or elastography characteristics. It has to be taken into account that standardized reporting is mandatory for each imaging modality. Therefore, TUS could be performed by any experienced sonographer. However, good-quality images or better video sequences from the TUS examination should be available for the EUS examiner.

Points in favor of TUS and cross-sectional imaging before EUS

A high-quality TUS and/or radiological cross-sectional imaging should be performed prior to EUS in the following situations:

- To rule out distant metastases in oncological patients (comment: the use of PET in oncological patients varies widely in European countries)
- In patients with abdominal pain
- In patients with larger abdominal lesions
- In patients with suspected choledocholithiasis
- In patients with suspected cystic and solid pancreatic lesions

- In patients with ductal adenocarcinoma of the pancreas to evaluate resectability
- To guide the choice of echoendoscope (radial *versus* longitudinal, diameter).

In some cases, unambiguous results of TUS or cross-sectional imaging techniques may render additional EUS unnecessary, whereas ambiguous results may be clarified using EUS. Another advantage of performing TUS prior to EUS may be that after detailed EUS imaging, some lesions may be followed up by TUS. This may be the case, for example, in cystic pancreatic lesions^[35] and subepithelial GI tumors in certain locations.^[28] A TUS examination may be recommended and should be performed if the area of interest is the upper esophagus including for Zenker's diverticulum (since the upper 5 cm of the esophagus can be evaluated using US),^[83] lower esophagus (since the cardia and the surrounding tissue can be evaluated), stomach, perianal region,^[84-92] and pancreas.^[77,93-96] The use of mediastinal ultrasound is not well known in the community, but the supra- and prevascular as well as the paratracheal regions and the aortopulmonary window can be evaluated in almost all patients. We refer to two recently published reviews on the topic.^[22,23]

Points against TUS and cross-sectional imaging before EUS

A small number of indications for EUS are not associated with a potential benefit of a preliminary TUS or another cross-sectional imaging method. This includes the evaluation of subepithelial lesions in the GI tract where EUS offers the highest resolution at the point of interest compared to other techniques.^[13,97-100] TUS is not helpful in the evaluation of subepithelial lesions in the mid esophagus. Performing high-quality TUS of the entire abdomen before performing focused EUS examination is time-consuming.

Conclusion

In general, to know more is better than to know less. In the mirror of the clinical context, TUS and cross-sectional imaging techniques will often define whether EUS is really indicated. The strengths of EUS are the confirmation or exclusion of lesions suggested by the clinical picture or other imaging modalities, tissue confirmation, and staging of GI malignancies. Furthermore, the exact role of TUS prior to EUS is controversial, and it differs from country to country, depending on national and local traditions and available imaging technology. However, the EUS endoscopist should keep an open mind during

the examination and should not always totally rely on previous imaging findings.

DO WE NEED EGD PRIOR TO EUS?

Introduction

Little is known about the reasons to perform EGD prior to EUS. All recommendations in EUS textbooks originate from the personal opinions of the investigators. It seems logical to assume that a prior EGD could diminish the complication rate of EUS. The pros and cons of preliminary EGD are discussed in detail in the following paragraphs.

It is mandatory for the physician approaching EUS to know the echoendoscope very well. In particular, the length of the nonflexible tip (where the transducer is located) and the oblique viewing of echoendoscopes are the most peculiar features. This is true for the linear echoendoscopes and radial technology from Olympus, whereas the radial technology from Pentax and Fujinon uses the frontal view. Due to these features, some maneuvers may be more difficult or risky than with the standard endoscope, for example, the insertion in the upper esophagus and the advancement in the descending duodenum from the bulb.^[101] EUS plays an important role in preoperative staging for esophageal cancer. However, when the echoendoscope cannot be passed through a stenotic tumor, the role of predilatation is controversial due to the risk of perforation, and the probability that these patients have locally advanced disease is very high. In a recent study on 100 patients with malignant esophageal strictures, the gastroscope could not be advanced through the stricture in 46 patients. At staging with EUS, all these patients had locally advanced disease (T3 or T4 and N0/N+).^[102] Therefore, the current guidelines do not recommend dilatation and EUS staging of stenosing esophageal cancers.^[27,103,104]

Points in favor of EGD before EUS

Knowledge of the anatomy of the upper GI tract of a particular patient might lower the complication rate of EUS. However, up to now, this was not proven in studies. The perforation rates of EUS have been reported as being between 0.034% and 0.22%^[101] mainly in the esophagus and the duodenal bulb, respectively.^[101] In the study of Das *et al.*, 44% of the esophageal perforations occurred in patients who were difficult to investigate during EGD.^[105] Moreover, there is a significant risk to miss clinically meaningful luminal lesions when EUS is performed without prior EGD. This is related to

the fact that echoendoscopes are not as flexible as a standard gastroscope; for example, retroflexion in the fundus is much less efficient (or even not possible) using echoendoscopes. In addition, some types of echoendoscopes are not equipped with a high-definition endoscopic view while side-viewing endoscopes do not adequately visualize the esophagus. Therefore, in particular, side-viewing echoendoscopes may miss important mucosal findings within the upper GI tract. In patients undergoing EUS for pancreaticobiliary or mediastinal indications, three studies found clinically relevant luminal lesions of the upper GI tract in 20.5%–29.7% of cases.^[106-108] A multicentric prospective study reported that EGD performed prior to EUS found luminal lesions impacting the subsequent endosonography in 9.8% of cases.^[107] Therefore, routine performance of EGD before longitudinal EUS may be worthwhile. In addition, the endoscopic appearance of the lesion, especially mucosal or submucosal lesions, can influence the performance and the result of EUS. In case of lesions of the papilla Vateri, a good endoscopic view of the lesion is mandatory, because EUS alone cannot discriminate between adenomyomatosis, adenoma, and carcinomatous lesions.

The arguments in favor of EGD are described as follows:

1. A relevant proportion of indications for EUS are indications for EGD as well. Explanation: Detection of gastric or duodenal lesions may aid in exclusion of pancreaticobiliary pathology as the cause of the patient's clinical picture
2. EUS using side-viewing echoendoscopes may miss a number of clinically relevant luminal findings in the upper GI tract
3. The interpretation of endoscopic pictures after EUS where EGD is performed after and not before EUS is hampered by mucosal artifacts induced by EUS
4. The knowledge of anatomic difficulties such as a Zenker's or duodenal diverticulum may minimize the risk of perforation
5. A prior endoscopic inspection of a tumor or a subepithelial lesion is complementary to observation by EUS.

Points against EGD before EUS

Some radial echoendoscopes from manufacturers are equipped with forward viewing optics; thus, an extra previous EGD may not be necessary. In patients with upper GI symptoms, a single EUS examination using a radial EUS scope has a similar or even higher diagnostic yield compared with combination of TUS

and upper GI endoscopy, and therefore may be used as a first-line examination in these patients.^[109,110] The miss rate of clinically relevant lesions using a longitudinal echoendoscope to evaluate the luminal surface of the upper GI tract in one prospective multicenter study was not inferior to EGD.^[108] EGD always requires air insufflation. The removal of insufflated air for EUS may be time-consuming and incomplete. In the view of the authors, this does not pose a real problem. Performing an EGD before any EUS examination is time-consuming, and the added diagnostic information is assumed to be low in daily practice. Some of the authors believe that the endoscopic view of the echoendoscope still allows good general orientation. This statement does not reflect that most patients with an indication for EUS have an indication for a coincident EGD or had a prior EGD before. A complication rate of 0.034% for EUS and EUS-fine-needle aspiration (EUS-FNA) was reported according to a German survey.^[111] Furthermore, it was felt that this survey probably underestimated the risk of EUS. This low rate of complications following EUS suggests that systematic adoption of EGD prior to EUS would be unlikely to statistically increase the safety of the procedure. Finally, if the results of a recent EGD are known, an additional separate endoscopy may be skipped.

Conclusion

We suggest that EGD be performed prior to EUS in the following indications and circumstances:

1. In patients with upper esophageal pathology such as swallowing disorders, dysphagia, benign strictures, or a known Zenker's diverticulum and in patients with a history of difficult upper endoscopy, to reduce the risk of perforation
2. In patients with impaired gastric emptying to exclude gastric outlet obstruction
3. In patients with suspected or confirmed esophageal or gastric cancer to exclude stenosing lesions and to decide about the type of echoendoscope to use (*e.g.*, the EBUS scope could be used for stenosing esophageal cancer)
4. In patients with surgically altered anatomy
5. In patients where the endoscopic findings are subtle and difficult to identify (*e.g.*, small subepithelial tumors).

SHOULD CONSENTING FOR EUS DIFFER FROM EGD CONSENTING?

Diagnostic and therapeutic EUS will be discussed differently as the risk for each is notably different.

Introduction

Similar to other endoscopic procedures, adverse events could occur during or after EUS which may relate to the diagnostic or therapeutic intervention itself or to the applied sedation. In expert hands, EUS-related complications are generally rare, mainly bleeding and perforation and depend on the type of diagnostic or therapeutic intervention. As EUS-guided drainage procedures in biliary and pancreatic disease and other EUS-guided therapeutic applications evolve, the safety profile of interventional EUS is changing. Apart from the type of procedure, the incidence of complications is associated with the experience of the endoscopist, the nature of the disease, the general health condition of the patient, and the type of echoendoscope used.^[3,25-27,39,40,101,112-114] It is of importance that the endosonographer knows the potential risks involved for any endoscopic procedure he/she suggests for the patient and can explain the technique, intended benefit, and possible risks in simple terms.

Points in favor of the proposal that consent for EUS differs from EGD

Diagnostic EUS without EUS-guided sampling

Due to the transducer being located at the tip, radial as well as linear echoendoscopes have a nonflexible end of 4–5 cm, which makes them more rigid. The reported perforation rates of diagnostic EUS ranges between 0.03% and 0.09%, which is higher than for standard endoscopy of the upper GI tract.^[101] EUS-guided sampling may be indicated due to findings at EUS examination in a significant proportion of cases, in particular in patients with malignant disease.^[44] Therefore, for all patients receiving diagnostic EUS using a longitudinal echoendoscope, informed consent for EUS-guided sampling is advisable.

EUS-guided sampling

EUS-guided sampling is a procedure with an entirely different spectrum of adverse events compared to EGD. Patients who undergo EUS-guided sampling are approximately ten times more likely to suffer complications compared to patients undergoing diagnostic noninterventional EUS.^[111] In a systematic review, the overall rate of adverse events in EUS-guided sampling was estimated at 0.98%. However, the pooled complication rate of prospective studies was as high as 1.72%. The most common complications are postprocedural pain (34%), acute pancreatitis (34%), fever and infectious complications (16%), and bleeding (13%). Perforations, pneumothorax,

pneumoperitoneum, and bile leaks are very uncommon risks of EUS-guided sampling.^[115] Complication rate and spectrum of EUS-guided sampling are related to several factors including operator experience and needle target.^[101] In particular, it has been reported to be considerably higher in pancreatic lesions (1.03%; only prospective studies: 2.64%) than in mediastinal lesions (0.38%). Considering only pancreatic targets, the risk was higher for cystic lesions (2.75%; prospective studies: 5.07%) than for solid lesions (0.82%; prospective studies: 2.44%).^[115] In particular, there is a considerable risk of hemorrhage, pancreatitis, and infection after EUS-guided sampling of cystic pancreatic lesions.^[116] Although prospective studies are lacking, guidelines recommend antibiotic prophylaxis for EUS-guided sampling of cystic pancreatic lesions.^[25,26,104,114,117] There is, however, also a small risk of adverse events associated with periprocedural and antibiotics (0.28%).^[116]

Overall mortality rate after EUS-guided sampling is very low (0.02% in a systematic review).^[115] Mortality rate of EUS-FNA of pancreatic cystic lesions, however, was reported to be 0.19%.^[116] An extremely rare, but potentially catastrophic complication of EUS-guided sampling of potentially resectable tumors is tumor cell seeding.^[118-125] Therefore, the information given to the patient should specifically address the planned EUS-guided sampling procedure.

EUS-guided therapeutic interventions

EUS-guided therapeutic interventions are completely different from diagnostic procedures, with the degree of difference being dependent on what procedures are performed. EUS-guided treatment procedures carry a highly variable risk, determined by the particular type of intervention, specific patient-related factors, and the experience of the operator and the interventional team. For example, EUS-guided celiac plexus neurolysis carries a risk of major adverse events of only 0.2%, which is much lower than that of EUS-guided drainage of walled-off pancreatic necrosis or obstructed bile or pancreatic ducts, which may be as high as 10%–20%.^[39,40,112,113]

Points against the proposal that consent for EUS differs from EGD

Diagnostic EUS and EUS-guided sampling are safe procedures. The procedural experience and sensations in experts for the patients are similar to a standard endoscopy. The consent form could be the same for EGD and diagnostic EUS since the procedural risk for both is very low. In the commonly used consent

forms in Germany, the risk of perforation is mentioned but not as a higher risk than EGD. This obviously changes fundamentally if a therapeutic procedure is performed. EUS-FNA may be considered controversially discussed for small and resectable ductal adenocarcinoma, which can be directly referred to surgery. EUS-FNA is contraindicated in hilar cholangiocarcinoma in patients considered for liver transplantation, as a transperitoneal biopsy may preclude the liver transplantation procedure. EUS-FNA is controversial in GI stromal tumor (GIST) tumors due to its low sensitivity and accuracy, while most of the patients will need surgery anyway. This should be carefully considered during the informed consent process.

Conclusion

The consent process should enable the patient to make an informed decision balancing the individual risks of the procedure with its potential diagnostic benefit. Therefore, we need to explain the goals and techniques of diagnostic and therapeutic EUS which fundamentally differ from EGD and other diagnostic and therapeutic endoscopic techniques. The information provided to the patient before EUS-guided interventions should relate as specifically as possible to the intervention and should be based on a thorough consideration of risk factors and alternative procedures. All EUS performing units should have specific patient information leaflets and consent forms for EUS procedures available. Auditing and reviewing adverse events should be part of continuous quality improvement activities and might help reduce the occurrence of such complications in future.^[25,26,40,126,127]

In summary, a careful review of the indication for EUS procedures, optimal preparation, and knowledge of anatomical particularities which might increase the perforation risk, is mandatory to reduce the incidence of adverse events. The knowledge of the clinical background and any previous imaging, such as TUS, CT, and MR, are complementary in paving the way to achieve the best possible EUS outcome.

DO WE NEED COAGULATION TESTS PRIOR TO EUS-GUIDED SAMPLING? SHOULD ANTIPLATELET AND ANTICOAGULANT TREATMENT BE STOPPED BEFORE EUS-FNA?

Introduction and review of the literature

Bleeding associated with EUS-guided sampling is an infrequent event (0%–1.4% in large

prospective series),^[101] and clinically significant bleeding is a very rare complication (0.23% in a Japanese national registry).^[128] However, some guidelines list EUS-FNA as a high-risk procedure for bleeding.^[25-27,39,40,104,114,129-131] A previous meta-analysis showed that the rate of bleeding complications after EUS-FNA was 0.13%.^[115] Assessments of the Japanese national database reported that the rates of severe bleeding after EUS-FNA in patients with GI submucosal and pancreatic tumors were as low as 0.44% and 0.23%, respectively.^[128,132] However, EUS-guided sampling in patients with continuation of antithrombotic agents may result in severe bleeding. Unfortunately, there is a paucity of prospective and controlled trials investigating the “real-life” risk of bleeding following EUS-FNA in patients in whom anticoagulants cannot be withdrawn. One recent prospective clinical study assessed the bleeding risk in 2629 consecutive patients undergoing EUS-FNA for various indications, particularly solid tumors.^[133] In 85 of 2629 patients, anticoagulants could not be withdrawn prior to EUS-FNA for fear of thromboembolic events during withdrawal. Of this small group, 2 (2.4%) patients developed severe bleeding including hemothorax and melena, requiring blood transfusions and surgical therapy in one patient. However, no thromboembolic events were observed in the remainder. Given this risk, the performance of coagulation tests prior to EUS-guided sampling may help identify patients with coagulation disorders who are at greater risk of complications. When bleeding occurs, it is most often self-limiting with no clinical consequences. Three types of bleeding are described: extraluminal bleeding, described as an echopoor leakage adjacent to the sampled mass; intracystic bleeding in case of biopsy of cystic lesions, defined as a hyperechoic area within the cyst; and intraluminal bleeding in the GI tract at the site of the needle puncture that is visible and treatable endoscopically. The incidence of the first type is reported as between 1.3% and 2.6% of procedures.^[134,135] The frequency of intracystic bleeding in some studies was as high as 6%,^[136,137] whereas a recent meta-analysis reported a pooled bleeding rate after EUS-FNA of pancreatic cystic lesions of only 0.69%.^[116] Conservative management is recommended in cases of extraluminal bleeding.^[134,136] Additional endoscopic therapy has been described in rare cases of intraprocedural luminal bleeding,^[135] but the effectiveness of these measures is uncertain. After bleeding related to EUS-guided sampling, close postprocedural clinical observation should be instituted and a low threshold for CT angiography maintained.

Points in favor of routine pre-EUS coagulation testing

Although not evidence based, in some centers, coagulation tests are routinely requested prior to EUS-guided sampling. According to the guidelines, EUS-guided interventions should not be performed with a platelet count $<50000/\text{mm}^3$ and a prothrombin time (PT)–international normalized ratio (INR) >1.5 .^[25,26,104,114,138,139]

Routine coagulation tests are not expensive with the results available from all laboratories within a few hours. They may identify patients with undiagnosed coagulation disorders such as hemophilia or von Willebrand disease.^[140] Preprocedural coagulation testing may, therefore, identify patients in whom EUS-guided sampling should be avoided.

Points against of routine pre-EUS coagulation testing

In some studies, bleeding did not occur following EUS-guided sampling of solid organs.^[141,142] The main disadvantage of routine coagulation testing relates to its poor sensitivity and specificity in predicting postoperative bleeding.^[121,122,143] The PT, INR, and partial thromboplastin time (PTT) neither predict nor correlate with intraoperative or postoperative hemorrhage in the absence of clinical suspicion of a bleeding disorder or coagulopathy.^[144-147] An abnormal value of one of the above-mentioned tests cannot predict bleeding occurrence and a normal value does not ensure hemostasis.^[143,147-150] Furthermore, a platelet count is not routinely recommended without clinical suspicion of thrombocytopenia. A history of excessive bleeding, myeloproliferative disorder, use of medications that decrease the platelet count, or other risk factors elicited from the history and physical examination should be investigated with a platelet count.^[149,151,152] The ASGE states that, in the absence of clinical suspicion, abnormalities of hemostasis are uncommon and routine preoperative screening for coagulopathy with PT, INR, PTT, platelet count, or bleeding time, either alone or in combination, is not recommended.^[153] Given this evidence and recommendation, the routine performance of coagulation tests before EUS and EUS-guided sampling may be unnecessary.

Points in favor of stopping antiplatelet and anticoagulation medication

The risk of bleeding is moderately elevated in patients receiving nonaspirin antiplatelet^[133] or anticoagulant treatment,^[135,154] but not in patients receiving aspirin

monotherapy.^[133,135] The guidelines advise stopping anticoagulants, clopidogrel, and other thienopyridines before performing EUS-guided sampling and therapeutic interventions. Aspirin should be stopped only before EUS-guided sampling of cystic pancreatic lesions.^[25,26,104,138]

Con: Points against stopping antiplatelet and anticoagulation medication

Bleeding events after EUS-guided sampling are rare, despite the periprocedural continuation of antithrombotic agents (e.g., aspirin or cilostazol).^[25,39,40,135,155] A few case “series” show that EUS-guided sampling and EBUS-TBNA of mediastinal lymph nodes are not associated with a significantly increased risk of procedure-related bleeding in patients who continue thienopyridine treatment.^[156,157]

Conclusion

There is a paucity of strong evidence supporting the routine assessment of coagulation function prior to performance of EUS-guided sampling. However, guidelines do support the performance of these tests in patients at greater risk of a coagulation disorder, such as those individuals with a personal or family history suggestive of a coagulation defect or with another clear clinical indication such as cholestatic jaundice. Endoscopists should evaluate the risks of both thromboembolic events and bleeding complications before performing EUS-FNA on patients being treated with antithrombotic agents. Aspirin treatment may be continued in patients undergoing EUS sampling of solid lesions. However, EUS-guided sampling should be avoided in patients treated with oral anticoagulants or thienopyridines, regardless of the results of the coagulation tests.

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