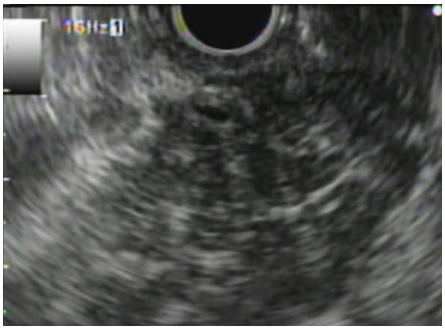
Mistakes in endoscopic ultrasonography and how to avoid them

Andrada Seicean and Rodica Gincul

Examination of the pancreas and biliary and digestive structures by endoscopic ultrasonography (EUS) can be tricky and using it to make a diagnosis can be challenging. Understanding anatomical variations and postoperative modifications is vital when undertaking EUS, as is choosing the correct linear echoendoscope for the structures being examined (e.g. the hilum of the liver versus the tail of the pancreas). There can also be difficulties with tissue acquisition related to tumour location and internal structures, and there are situations when sampling is contraindicated. Consideration also needs to be given to the use of contrast with special settings and difficulties in differential diagnosis (pancreatic solid lesions, indeterminate biliary strictures, gastric neuroendocrine tumours). The role of EUS assessment after neoadjuvant therapy should also be considered. Here we discuss the most frequent mistakes that are made in pancreatobiliary and digestive EUS imaging.



Mistake 1 Failing to understand the anatomical structure of the pancreatobiliary region

Pancreatic echogenicity on ultrasound is normally equal to or slightly greater than that of the liver.[1] However, sometimes the lobular architecture of the pancreas is so pronounced it is suspicious for chronic pancreatitis (figure 1). Increased echogenicity in the pancreatic parenchyma is not uncommon and can be mistaken for chronic pancreatitis during EUS examination. Hyperechoic pancreatic changes are frequently encountered in elderly and obese patients,[2,3] and understanding the possible variations in pancreatic echostructure and echogenicity is fundamental for accurate EUS diagnosis. The lack of pancreatic parenchyma calcifications and especially the presence of a normal pancreatic duct can help exclude chronic pancreatitis.[4]

On EUS, the ventral anlage of the uncinate process is often hypoechoic in appearance and may be suggestive of a hypoechoic focal lesion (figure 2a).[5] However, the absence of clear margins and a nondilated common bile duct (CBD) and pancreatic duct may help differentiate the ventral anlage from a pancreatic tumour. In case of diagnostic doubt, contrast-enhanced harmonic EUS imaging (CH-EUS)—a new sonographic technique that depicts intratumoural vessels in real time—can be helpful. CH-EUS improves the characterization of pancreatic lesions and discriminates between malignant and benign ones. In several studies, the hyposignal (hypoenhancement compared with the surrounding parenchyma) was a highly accurate sign of malignancy.[6] In the absence of a focal lesion, the entire parenchyma is enhanced homogeneously (figure 2b).

EUS is the most sensitive imaging procedure for the detection and characterization of pancreatic tumors;[7] however, the diagnostic performance for detection of pancreatic malignancy can be altered when associated with the following factors: chronic pancreatitis, a diffusely infiltrating carcinoma, a prominent ventral/dorsal split and a recent (<4 weeks) episode of acute pancreatitis.[8,9] CH-EUS may be useful for diagnosing pancreatic carcinoma in these situations, because its high negative predictive value (NPV) is greater than that of EUS-FNA (fine needle aspiration).[10] If there a high clinical suspicion of pancreatic cancer and EUS examination is negative, a repeat EUS after 2–3 months may be necessary to detect the missed neoplasm.[8]

EUS is of great value for the diagnosis of bile duct lithiasis, but it can be challenging in the presence of a periampullary diverticulum, particularly if it is large and obstructed with debris. Intradiverticular papilla can also confuse matters because of air artifacts that can produce a false stone-like image leading to unnecessary endoscopic retrograde cholangiopancreatography (ERCP). Filling the duodenum with water so that the papilla is submerged and free of air bubbles can avoid this issue.

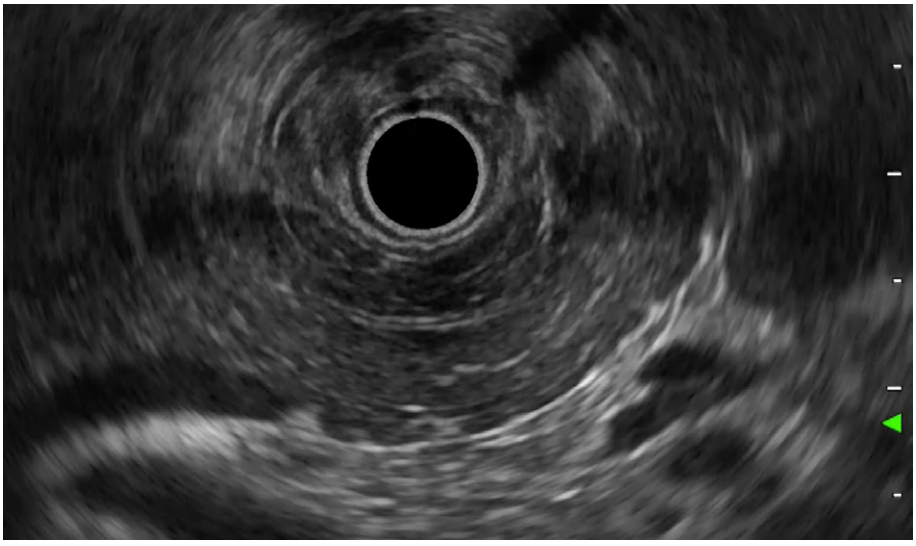


Figure 1 | Pronounced lobular architecture of the pancreas may seem suspicious for chronic pancreatitis with a normal main pancreatic duct.

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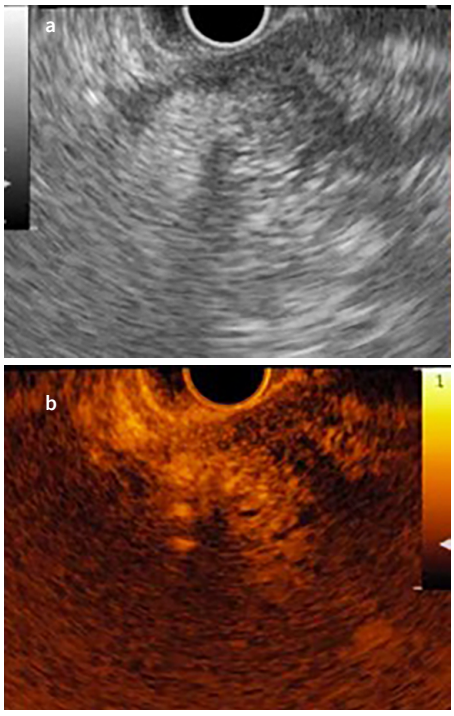

Figure 2 | False-positive diagnosis of pancreatic tumour. **a** | Hypoechoic appearance of the ventral anlage of the pancreatic uncinate process suggesting a focal lesion with a nondilated upstream pancreatic duct. **b** | The parenchyma is enhanced homogeneously, excluding the focal lesion.

Mistake 2 Choosing the incorrect echoendoscope

Examination of the hepatic hilum, which contains the portal triad (formed by the main portal vein, proper hepatic artery and common hepatic duct), is mandatory for exploration of hilar strictures. Most hilar strictures are a concern for underlying malignancy, such as hilar cholangiocarcinoma, gallbladder carcinoma, portal hepatic lymph nodes, and less frequently benign conditions, such as primary sclerosing cholangitis or postsurgical complications.[11]

EUS has been used for imaging hilar cholangiocarcinoma;[12–14] however, although imaging of the CBD can be done by both radial and linear techniques, depending on the operator's expertise, imaging of the hepatic hilum is difficult, and sometimes even impossible with a radial scope. The imaging capability of the curved linear array is superior to radial scanning for interrogating the area between the hepatic portal region and the superior bile duct.[15] EUS exploration of the hepatic hilum with a linear scope is possible and this should be the choice when investigating cases of hilar obstruction (figure 3).[16]

Pancreatic tail lesions are traditionally accessed through the gastric fundus by following the aorta until the coeliac take-off is seen, at which point it bifurcates into the hepatic and splenic artery. Once the splenic artery is detected, it can be followed with a slightly clockwise rotation and pulling out of the scope movement. This movement allows complete examination of the pancreatic body and tail up to the splenic hilum. However, in some cases (about 20%), the pancreatic tail is distant from the gastric wall and cannot be fully explored, especially with a radial scope. Several studies show that the lowest sensitivity of EUS for detecting pancreatic lesions is in the tail (37–40%) compared with the body (79%) and the head (83–92%).[17–19] Thus, in some clinical situations (unexplained acute pancreatitis, intraductal papillary mucinous neoplasm [IPMN] follow-up, secretory syndrome with normal conventional imaging or screening for a genetic predisposition for pancreatic neoplasia syndrome), a linear scope should be chosen for pancreatic body–tail exploration (figure 4).

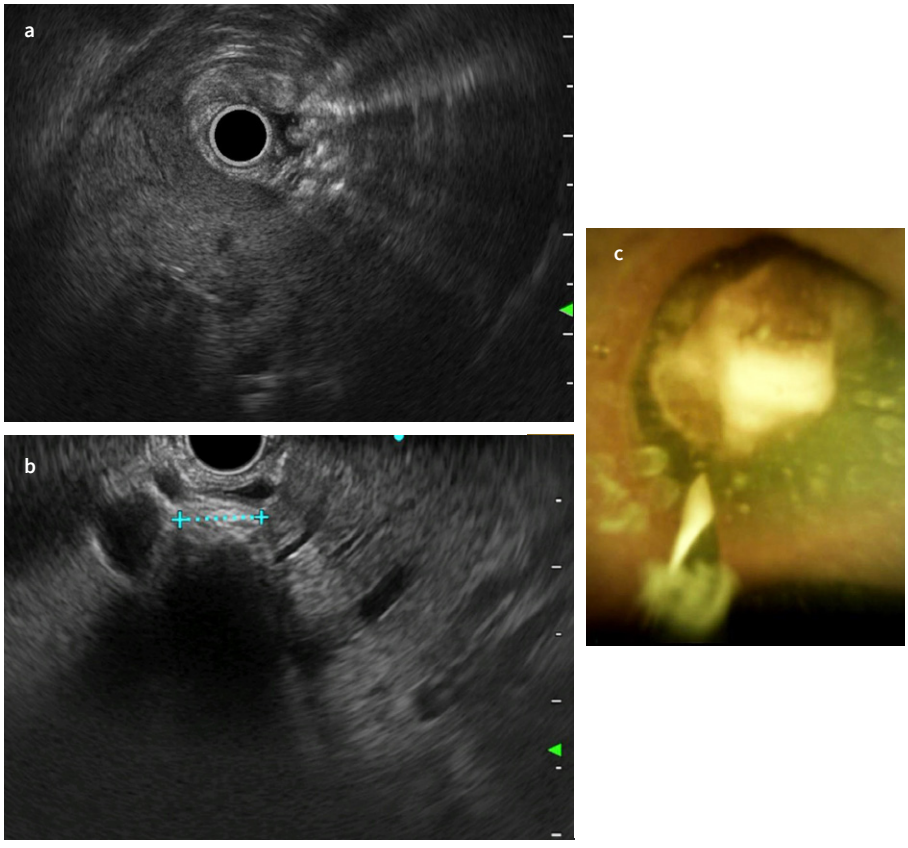

Figure 3 | Cholangitis with dilated left hepatic duct and no evident cause of biliary obstruction at imaging. **a** | An impacted bile stone in left hepatic duct invisible with EUS radial scope. **b** | The stone is diagnosed with a linear scope. **c** | Fragmentation of the impacted stone by Spyglass-guided electrohydraulic lithotripsy.

Mistake 3 Having the incorrect position to reach the target lesion during EUS-guided tissue acquisition

When performing EUS-FNA or FNB (fine needle biopsy) the EUS transducer should be placed as close as possible to the target lesion. The uncinate process is difficult to reach when excessive torqueing of the echoendoscope in the second part of the duodenum is necessary. Another difficult location to reach is near the fornix and greater curvature from the stomach, in which case the long position of the echoendoscope in the stomach can be helpful—the needle can push the stomach wall and a rapid and strong push of the needle is needed to pass the gastric wall. Diverticula or interposing vessels should be avoided by slight modification of the transducer position to puncture the gastrointestinal wall outside the vessels, followed by changing the needle direction towards the direction of the target lesion. In such awkward duodenal positions, the use of thinner FNA needles represents a technical advantage.

Previous surgery, especially gastrectomy or pancreatectomy, can make the detection of pancreatic lesions difficult. The surgical procedure and type of gastrointestinal anastomosis should be well documented before starting the EUS procedure. Scanning of the pancreas should be as extensive as possible, following the splenic vein and the pancreatic duct. For body/tail pancreatic lesions, the puncture is done easily from the remnant stomach or from the level of esophagojejunal anastomosis without passing the anastomosis. Lesions situated in the head of the pancreas are more challenging in case of previous surgery. In patients with a Billroth type I gastroduodenal anastomosis, they can be targeted from the duodenum after passing the anastomosis. In patients who have undergone

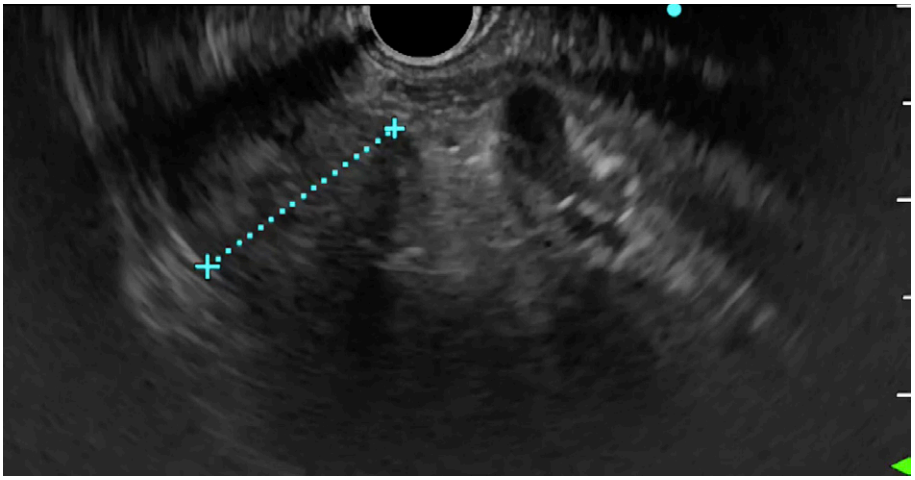

Figure 4 | A patient with a past history of renal cancer. A pancreatic tail lesion missed by a radial scope and detected with linear one.

gastrojejunal anastomosis with Billroth II and Roux-en-Y reconstructions, EUS-FNA/FNB is performed via the jejunal limbs using a linear echoendoscope by gradual insertions followed by scanning under fluoroscopy. In case of total gastrectomy with Roux-en-Y reconstruction and jejunal interposition it is more difficult to reach the lesions in the head of the pancreas.[20,21] The risk of perforation is 1–6% and placing a guidewire or a catheter using a balloon-assisted enteroscope may increase safety.[20] The use of a forward-viewing echoendoscope is effective for evaluating the periampullary area in 75% of patients with an existing Billroth II reconstruction, but not in those with a Roux-en-Y anastomosis.[22]

Passing the echoendoscope through a malignant oesophageal stenosis (15–42% of cases) may be difficult and increase the risk of perforation.[23] Regardless of the use of EUS-FNA/FNB in patient management, a fully expanded covered stent allows guidewire-assisted passage of the echoendoscope (to avoid accidentally impinging of the stent) under fluoroscopic control. A duodenal stenosis caused by an ulcer, scarring or by external compression related to a pancreatic head tumour impedes the passage of the echoendoscope at the closest point to access the tumour by EUS-FNA/FNB.[24] Using the long position of the echoendoscope in the duodenal bulb or sampling from the stomach should be performed, but placing too much pressure on the duodenal wall must be avoided because of the risk of mechanical injury and perforation.

Mistake 4 Not tailoring the approach of EUS tissue acquisition within the target lesion

A negative result after sampling a solid lesion that's surrounded by parenchyma with features of chronic pancreatitis should be treated with caution. These features might obscure the presence of pancreatic tumour and diminish the accuracy of pancreatic sampling (54% and 74% versus 89% and 91% in the presence versus the absence of chronic pancreatitis, respectively),[25,26] even in the case of small pancreatic lesions <1 cm in diameter (80% versus 98%).[27] These lesions are difficult to see especially when lobularity is present without honey-combing.[27]

Contrast highlights an adenocarcinoma as a hypoenhanced lesion caused by important fibrosis and the upward dilated ducts are more clearly visualised.[28] CH-EUS can guide EUS sampling within a lesion by avoiding the necrotic areas, although for adenocarcinoma in a normal pancreas it did not increase the accuracy of sampling.[29] Performing tissue acquisition, preferably with FNB needles for procuring core biopsy samples, eventually under CH-EUS guidance and even repeating the procedure, establishes the correct diagnosis.

The presence of a metallic biliary stent placed for biliary obstruction may affect the EUS result due to acoustic shadowing. This impedes correct visualization of the tumour behind the stent and the diagnostic yield is lower (Table 1).[30–35] Torqueing or changing to the long position of the echoendoscope provides a better window for passing the needle; some authors even recommend stent removal before tissue acquisition. When a plastic stent is placed, the orientation of the needle inside the lesion should avoid the stent to stay away from further dysfunctionalities, but the accuracy of tissue sampling is not influenced.[30]

The orientation of the needle inside the lesion should be established using the fanning technique. However, the presence of necrosis inside a mass impedes diagnosis and the needle should avoid this part of the lesion.[36] In such

Author, year and reference number	Number of patients with stents	EUS needle	ROSE (%)	Diagnostic accuracy rate of TA (%)		Influence of stents on TA diagnostic rate
				Stent	No stent	
Bekkali (2019)[31]	141 SEMS 149 PS 341 no stent	FNB	16	81 PS 79 SEMS	84	Yes Odds ratio = 1.96 for SEMS
Antonini (2017)[30]	56 PS 74 no stent	FNB	23	89	86	No
Kim (2015)[32]	65 PS 11 SEMS 105 no stent	FNA or FNB	45	77	89	Yes No difference PS-SEMS
Siddiqui (2012)[33]	577 PS 100 SEMS	FNA	100	100 vs 99	–	No
Ranney (2012)[34]	105 PS 45 SEMS 64 no stent	FNA	100	64	89	No
Fisher (2011)[35]	98 PS 72 no stent	FNA	90	88	92	–

Table 1 | Influence of biliary stents on EUS-guided tissue acquisition yield. FNA, fine-needle aspiration; FNB, fine-needle biopsy; PS, Plastic stent; SEMS, self-expandable metal stent; TA, Tissue acquisition.

inhomogeneous lesions, contrast enhancement shows the necrosis as an unenhanced area and hyperenhances the vessels to facilitate their avoidance.

The isoechoic appearance of some lesions, such as schwannomas in the gastrointestinal wall or neuroendocrine tumours (NETs) within the pancreas, can be better seen when contrast enhancement is used, making their sampling easier.[37] For hard lesions, a 25G needle is preferred because a 19G needle or a 22G needle cannot penetrate inside the lesion and may even move the entire lesion during the fanning technique.

Mistake 5 Performing unnecessary EUS-guided tissue acquisition

EUS-guided tissue acquisition is generally a safe procedure with few complications, and serious complications are rare. The incidence of adverse events may be reduced by performing a careful review of the indication for EUS-guided tissue acquisition and having knowledge of any coagulation disorders.

Pain, bleeding, pancreatitis and infection are the most frequently reported complications. In a meta-analysis and systematic review of more than 50 studies, the overall complication rate was 0.98% and the mortality rate was 0.02%, related to cholangitis and pancreatitis.[38] Pancreatitis and bleeding are usually seen in patients after EUS-FNA of pancreatic cysts.[39] Some studies have shown as high a frequency of intracystic bleeding as 6% after EUS-FNA of pancreatic cystic lesions, whereas a recent meta-analysis reported a pooled bleeding rate of only 0.69%.[40–42] However, EUS-guided sampling in patients who continue to take antithrombotic agents may result in severe bleeding.

Prospective and controlled trials are lacking concerning the risk of bleeding following EUS-FNA in patients on uninterrupted antithrombotic agents. One prospective clinical study demonstrated a 2.4% bleeding risk in patients in whom anticoagulant therapy was not stopped prior to EUS-FNA for fear of thromboembolic events.[43] The risk of both thromboembolic events and bleeding complications should be evaluated before performing EUS-guided tissue acquisition on patients being treated with antithrombotic agents.

Aspirin treatment may be continued in patients undergoing EUS sampling of solid lesions, but should be stopped for sampling of pancreatic cystic lesions.[44] However, EUS-guided sampling should be avoided in those treated with oral anticoagulants or thienopyridines.[44]

Infection or bacteraemia is rare in patients undergoing EUS-guided tissue acquisition of solid lesions, and, therefore, antibiotic prophylaxis is not recommended. By contrast, EUS-FNA of pancreatic cystic lesions is considered to be associated with an increased risk of infection rate, and the European Society of Gastrointestinal Endoscopy (ESGE) guidelines recommend prophylactic administration of antibiotics while sampling pancreatic cystic lesions.[45]

It is also important to remember that because of the high risk of infection, EUS-FNA of mediastinal cysts and vestigial retrorectal cystic tumours is usually not recommended and should be avoided. Several cases of mediastinitis caused by EUS-FNA of bronchogenic cysts have been reported.[46–48] Recognition of these usually asymptomatic lesions is, therefore, essential—on EUS they appear as paraoesophageal or intramural lesions (mostly originating from the muscularis propria) that are well-delineated, hypo- or anechoic, and compressible by a transducer.[48] EUS findings of vestigial retrorectal cystic tumors are hypo- or anechoic, uni- or multilocular.[49]

If mediastinal and retrorectal cystic lesions have an elevated protein content they can appear as a heterogeneous EUS-echostructure mimicking a solid mass. MRI and contrast-enhanced EUS (CE-EUS) may be helpful for differential diagnosis because these lesions have a typically high intensity signal in T2-weighted images on MRI and nonenhancement on CH-EUS.

Mistake 6 Failing to optimise contrast enhancement

Ultrasound contrast agent (UCA) is highly echogenic and produces intense scattering. The adequate mode of administration of UCA is an intravenous (IV) bolus (rapid rhythm of injection) via the cubital vein, to attain the proper concentration of the contrast substance in the blood, followed by 10 ml saline flushing. SonoVue®, the only available UCA in Europe, should be avoided in cases of severe cardiopulmonary events, but it is allowed in cases of renal insufficiency.[50]

The EUS settings should use a low mechanical index (0.14–0.4), and lower ultrasound frequencies are preferred to avoid rapid bubbles destruction in case of lesions situated far from the transducer. The gain of the harmonic image should be decreased because the aim of using contrast is to evaluate the vascularity and the tissue signals are subtracted. The dynamic range should be set at a medium level to avoid generating too many tones of grey. The focus should be positioned below the lesion of interest. If possible, including an arterial vessel in the scanned area can allow a better comparison with the contrast aspect within the vessel. The presence of calcifications produces posterior shadowing and their interposition between the transducer and the lesion should be avoided.

The counter should be started as soon as the contrast is injected and before the saline flushing, because the arterial phase is considered to be the first 25–30 seconds after the injection. The hypoenhancement, isoenhancement or hyperenhancement of the lesion is compared with that of the surrounding parenchyma and the homogenous or inhomogenous aspect of enhancement should be noticed. The venous phase should be followed on the contrast image until 45 seconds. The aspect during the late venous phase characterizes the slow or fast washout and it is important for diagnosing malignancy.

There are classic indications for the assessment of solid and cystic pancreatic lesions. The current application is for differentiation of solid pancreatic masses where a hypoenhanced aspect is suggestive of adenocarcinoma and has a high diagnostic yield even for small pancreatic tumours.[6,28] Hyperenhanced pancreatic lesions can be NETs, inflammatory masses related to chronic pancreatitis, accessory spleen, pseudosolid serous cystadenomas, a solid pseudopapillary tumour or metastasis.[6,10,51,52] Another use of CH-EUS is to highlight the vascularity of mural nodules or a solid mass in case of cystic pancreatic lesions, raising the suspicion of malignancy and this helps to differentiate the nodules from mucus. In case of IPMN, an enhanced nodule >5 mm represents a criterion for resection and a nodule <5 mm represents a relative indication for surgery.[53]

A special indication for CH-EUS might be following up patients with resected IPMN,[54] because the carcinoma incidence rates increase from 3.3% at 5 years to 15% at 15 years, and almost half of them are concomitant pancreatic adenocarcinoma.[55]

Contrast assessment can be used for differentiating malignant GISTs from benign subepithelial lesions, but it cannot replace EUS-FNB.[56] A metastatic lymph node from a solid tumour is inhomogenously hypoenhanced during CE-EUS, but a hyperenhanced homogenous lymph node can be seen in lymphoma or in benign and inflammatory lymph nodes, so their differentiation, based exclusively on qualitative assessment of contrast images, might be difficult.[57,58]

Mistake 7 Overdiagnosing solid pancreatic lesions as cancer

Inflammatory lesions represent 15–25% of all focal pancreatic solid masses.[10,28,51,52,59] On the other hand, 6–10% of surgical specimens from Whipple's procedure performed for suspected cancer are benign lesions, 25% of them being autoimmune pancreatitis (AIP).[60] Two distinct subtypes of AIP have been established based on the clinicohistopathological profile—type 1 and type 2.[61] Current international consensus diagnostic criteria for the diagnosis of AIP include five categories: characteristic imaging findings of the pancreatic parenchyma and duct,

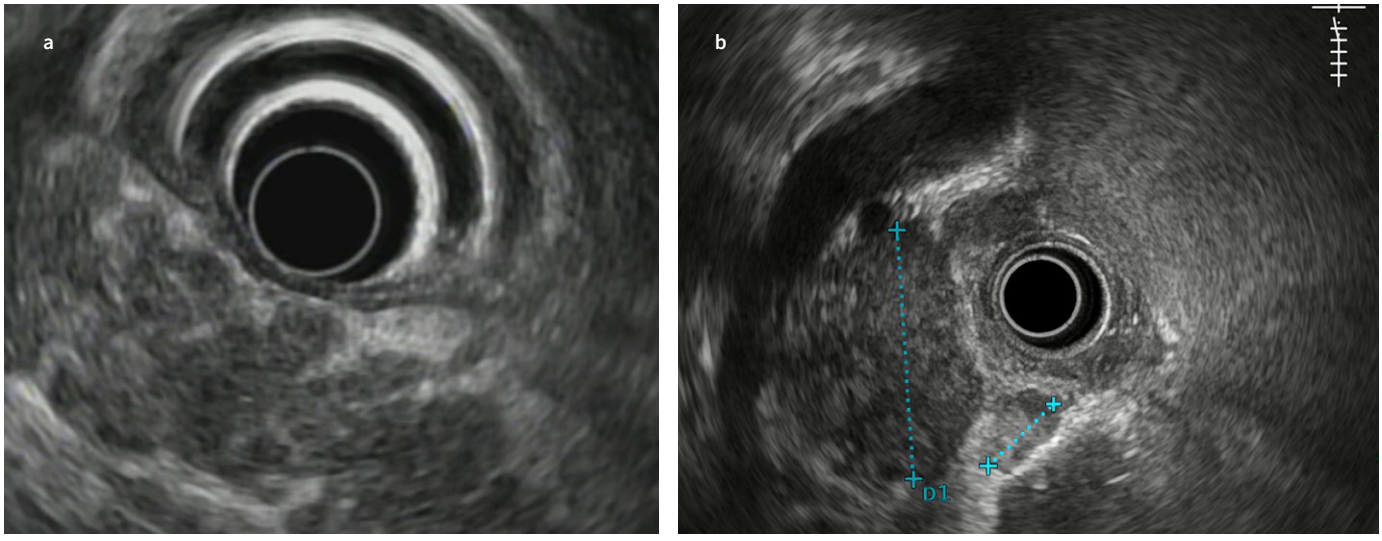

Figure 5 | Autoimmune pancreatitis. **a** | A diffuse pancreatic enlargement with hypoechoic, patchy and heterogeneous parenchyma. **b** | A focal hypoechoic mass, located in the pancreatic head-neck inducing 'mass-effect' on splenoportal confluence and lymphadenopathy.

serology, other organ involvement, pancreatic histopathology, and response to steroid treatment.[62] Type 1 AIP (referred to as a lymphoplasmacytic sclerosing pancreatitis) is the pancreatic manifestation of a systemic disease (so-called IgG4 disease) and is frequently associated with other organ involvement.[63] Type 2 AIP is also known as idiopathic duct-centric pancreatitis. Despite consensus diagnostic criteria, the diagnosis of AIP often remains challenging.[64,65] The IgG4 serum level is helpful to establish the diagnosis of type 1 AIP, but lacks sensitivity and specificity, and only 22–23% of patients fulfil the criteria to diagnose an IgG4-related disease.[63,66]

Patients with AIP present with typical acute pancreatitis or abdominal pain, but also with jaundice and/or a pancreatic mass that often mimics pancreatic carcinoma. The classic EUS findings for AIP include diffuse pancreatic enlargement with hypoechoic, patchy and heterogeneous parenchyma (figure 5a).[67–69] EUS may also demonstrate a focal hypoechoic mass, most frequently located in the pancreatic head, induce main pancreatic duct (MPD) narrowing with duct-wall thickening and usually without upstream dilation. Sometimes, the mass may appear to involve peripancreatic vessels (figure 5b), induce upstream MPD dilation, associated with enlarged peripancreatic lymph nodes, mimicking pancreatic cancer.[67,68] The presence of diffuse pancreatic enlargement, a hypoechoic thickened MPD and/or bile-duct wall, hypoechoic peripancreatic halo has been seen more frequently in patients with a confirmed AIP diagnosis than pancreatic cancer.

A key feature and clue to the presence of AIP is the finding of IgG4-associated cholangitis with markedly thickened bile ducts and in some cases gallbladder wall.[70,71] In contrast with pancreatobiliary malignancies, in which the biliary involvement is more irregular, the bile duct thickening in AIP IgG4-cholangitis is regular, homogeneous, with smooth inner and outer margins. The thickening may be extended to the cystic duct and gallbladder (figure 6).

Given the lack of pathognomonic EUS features for the differential diagnosis of a pancreatic solid mass, several imaging-enhancing techniques have been developed. CH-EUS allows the assessment of pancreatic tumour enhancement using ultrasound contrast

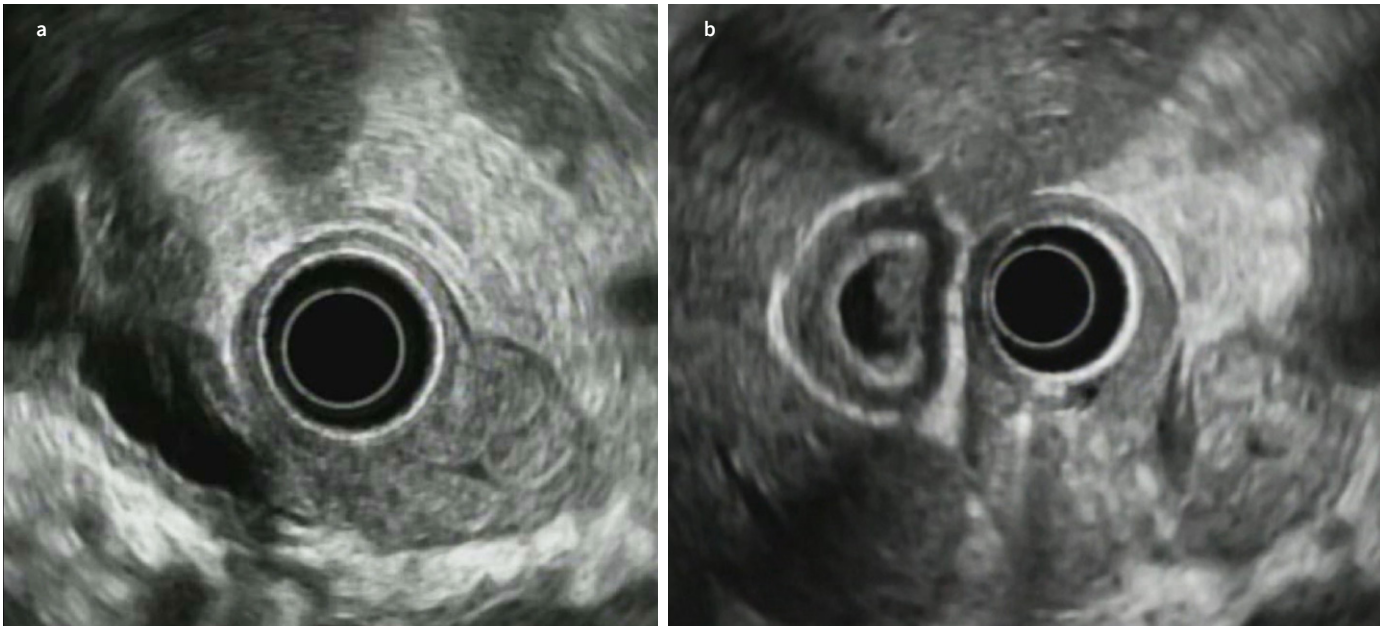

Figure 6 | EUS images of patients with IgG4-disease-related cholangitis. **a** | Regular bile-duct thickening extended to the cystic duct. **b** | gallbladder.

agents in real time with imaging-specific methods and appear to improve their characterization.[6,10,51,52,72] AIP-related focal pancreatic masses and also bile-duct thickening shows hyper- or isoenhancement at CH-EUS (figure 7), while a hypoenhanced lesion is strongly suggestive of adenocarcinoma.[6,10,51,52,73]

Ultrasound elastography (US-EG) is a diagnostic method based on tissue elasticity characterization. Qualitative EUS-elastography, based on a tissue's stiffness by measuring tissue strain, is useful for the characterization of pancreatic lesions and lymph nodes, but has low reliability and reproducibility.[74,75] Shear wave elastography (SWE) is a quantitative elastography based on measurements of shear wave propagation,[75] recently implemented into EUS systems, demonstrated to be useful to detect pancreatic fibrosis, chronic pancreatitis and recently, the correlation between disease activity and pancreatic elasticity in AIP.[75,76]

EUS-guided tissue acquisition is useful for obtaining adequate tissue sampling for the histological diagnosis of AIP, which is particularly important for the diagnosis of type 2 AIP, "seronegative" AIP, (normal or <2 ULN IgG4 serum level), but predominantly to exclude pancreatic cancer, especially in case of a focal mass. AIP is a particularly 'tricky' entity from a cytological point of view. The samples obtained by 22G/25G FNA needles are usually small and lack tissue architecture, hence they produce false-positive results for atypical cells that may mimic malignancy.[77,78] To overcome this limitation, larger calibre or cutting biopsy needles have been used for the diagnosis of AIP.[79]

Newly developed EUS-FNB needles have emerged, including ProCore® (Cook Ireland, Limerick, Ireland), SharkCore™ (Covidien/Medtronic, Boston, Massachusetts) and Acquire™ (Boston Scientific, Marlborough, Massachusetts), and have demonstrated, with a low complication rate, the ability to obtain core biopsy specimens and a high diagnostic yield in AIP, with the superiority of 22G Franseen-tip needle compared with a 20G forward-bevel needle for the diagnosis of type 1 AIP in one study.[80–83] The specific EUS findings and EUS-guided core biopsy have greatly improved the differential diagnosis between AIP and pancreatic cancer, avoiding unnecessary surgery.

Mistakes 8 Forgetting EUS in the assessment of indeterminate extrahepatic biliary strictures

The differentiation of benign from malignant biliary strictures is very challenging. Biliary strictures can be related to extraluminal compression from hepatic nodules or gallbladder cancer or lymph nodes. Intraluminal strictures are related to cholangiocarcinoma, benign cholangitis (primary sclerosing, IgG4-related, eosinophilic), biliary papillomatosis, response to infection, trauma (e.g. cholecystectomy) or ischaemia (e.g. liver transplantation). Some malignancies, such as bile-duct lymphoma or IPMN, can mimic cholangiocarcinoma.

Indeterminate strictures are those for which transpapillary sampling and imaging studies are not diagnostic. In such situations, EUS tissue sampling can increase the diagnostic yield. However, biliary stricture assessment cannot be done with a stent in place and stents should be removed before EUS. In patients who have an uncertain diagnosis for malignancy at the time of biliary drainage, a retrievable stent is, therefore, preferred.

EUS can assess the entire bile duct, and the involvement of the portal vein and/or hepatic artery. The location of the stricture, the layers affected and the multifocal stenosis are all important. A visible mass >5 mm or thick wall >3 mm are suitable for tissue acquisition, but it is more demanding in proximal strictures where there is the interposition of vascular structures.[84] A meta-analysis has recommended the ERCP approach for proximal strictures and the EUS approach for sampling the distal or external compressions.[85] Same session EUS-FNA and ERCP sampling is better than EUS-FNA alone.[86] The accuracy is 75%, which is better than brush cytology during ERCP, but a negative result does not rule out malignancy.[87] For strictures situated 2 cm below the hilum in a jaundiced patient, the first choice is EUS with or without FNA, followed by ERCP with or without cholangioscopy with biopsy samples. In case of proximal obstruction EUS-guided sampling is recommend, except if the patient is a candidate for transplantation, because there is a risk of peritoneal carcinomatosis.[88]

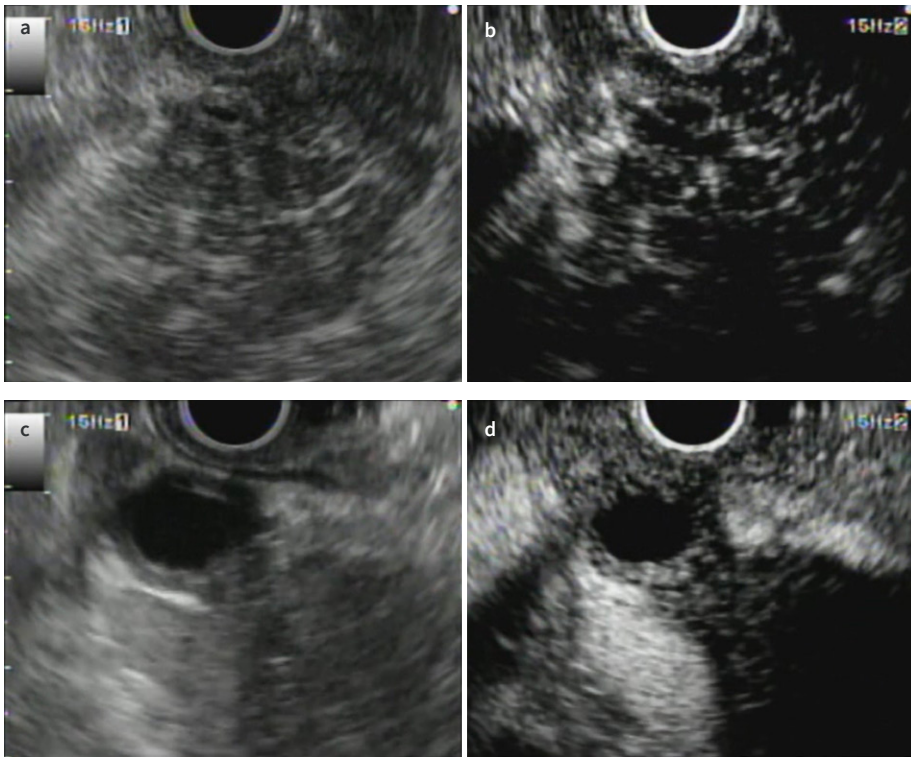

Figure 7 | IgG4-disease. **a** and **b** | Hyperenhancement of an AIP-related focal pancreatic mass after an intravenous bolus of SonoVue®. **c** and **d** | Hyperenhancement of bile-duct thickening.

Mistake 9 EUS misdiagnosing of gastric submucosal tumours involving the second or third layer

It is very difficult to establish by EUS the specific type of subepithelial lesion, although the layer of origin is well established. The EUS appearance of NETs is hypo- or isoechoic, homogenous, with smooth margins, originating from the second or third layer (more often third layer involvement is seen) (figure 8) and they are hypervascular on CH-EUS. Differential diagnosis is sometimes difficult with a leiomyoma or GISTs of muscularis mucosae. They are hypoechoic, but CH-EUS is helpful showing small vessels coming from the hilum of the lesion in case of leiomyoma or heterogenous vascularity in case of GISTs. A granular tumour is also hypoechoic, but with higher echogenicity compared to the muscle layer, heterogenous and arises from the same layers. An ectopic pancreatic tissue is hypoechoic or has mixed heterogenicity due to the presence of cysts or ductules, sometimes with a central depression. An inflammatory fibroid polyp is a sessile polyp, situated in the antrum, is hypo- or hyperechoic.[89]

The features of malignancy (i.e. irregular border or ulcerated lesion) or high-risk features of

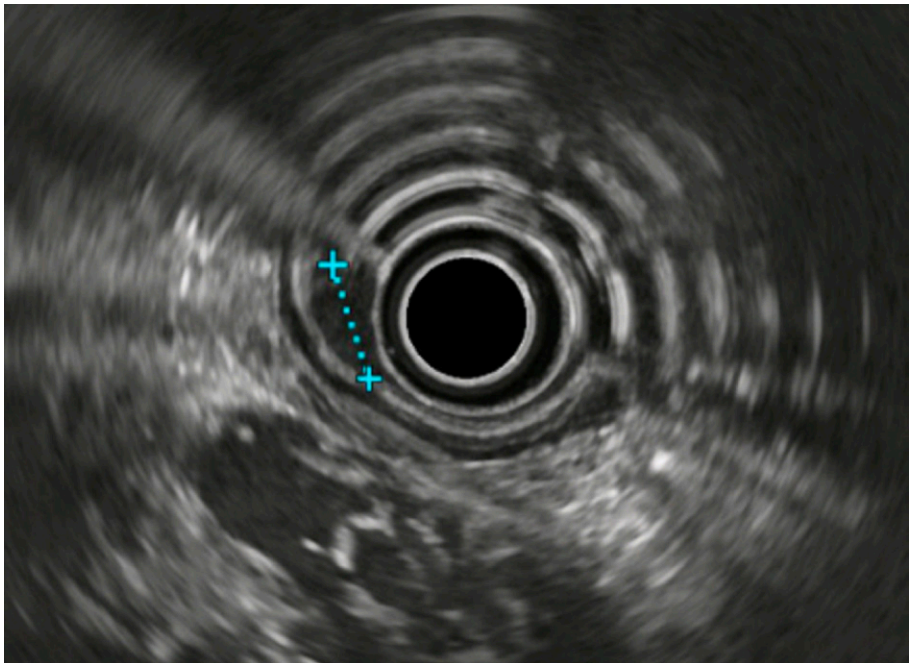

Figure 8 | A neuroendocrine gastric tumour. The gastric NET is visualised as a small, hypoechoic lesion in the second and third layer of the gastric wall.

malignancy (e.g. anechoic area, echogenic foci, or regional lymph node) are rarely seen for NETs associated with atrophic gastritis, but they can be found in type II or III NETs.

Tissue acquisition is necessary and easy in lesions situated in the second or third layer, the first step is to take a bite-on-bite biopsy sample, followed by ESD/EMR.[86,90] EUS-FNB or surgery are reserved for large lesions originating from the fourth layer with features of malignancy or high-risk features of malignancy.

Mistake 10 Relying on EUS morphology alone to assess residual cancer after neoadjuvant therapy

The optimal diagnostic strategy for the detection of the residual disease after the radiochemotherapy of oesophageal cancer involves positron emission tomography combined with computed tomography (PET-CT) and local assessment by oesophago-gastroduodenoscopy and forceps biopsy samples taken, combined with EUS and/or FNA of lymph nodes.[91] Chemoradiotherapy induces changes to the tumour size, but doesn't restore the normal mucosa layers. As a result, the accuracy of EUS assessment for the T stage is <30% for T1 and T2, 80% for T3 and <50% for T4. Mostly, EUS overstages the residual lesion. This is related to inflammatory and fibrous changes that cannot be distinguished from residual tumour and are more important in patients who have a good local response.[92–95] The size, shape, echogenicity and demarcated border of the lymph nodes in the coeliac trunk, lesser curvature, paraoesophageal, subcarinal, aortopulmonary window and mediastinal/paratracheal stations should be assessed in every case. The classic EUS criteria for suspicious lymph nodes (round shape, hypoechoic aspect and >5 mm in diameter) only identify 50% of malignant lymph nodes 10–12 weeks after radiochemotherapy.[96] To minimize missing residual disease from them, EUS-FNA should be performed even in cases with a low EUS suspicion.[97]

In case of gastric cancer, assessment of the clinical response after chemotherapy by EUS or CT is unable to predict the pathologic response.[98] The accuracy of EUS staging of rectal cancer after radiochemotherapy was 48–75% for the T stage and EUS is considered as unreliable for restaging.[37,99] Furthermore, EUS morphology alone is unreliable to identify the response to neoadjuvant chemotherapy in pancreatic cancer. The ambiguous periarterial soft tissue cuffing the major vascular structures (mesenteric vessels, coeliac trunk, hepatic artery) should be assessed by EUS-guided tissue acquisition before considering the patients as surgical candidates.[100]

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Your EUS briefing

UEG Week

- "Improving quality in EUS" session at UEG Week Virtual 2020 [https://ueg.eu/library/session/improving-quality-in-eus/161/2755].
- "Complications related to ERCP and EUS" presentation at UEG Week Virtual 2020 [https://ueg.eu/library/complications-related-to-ercp-and-eus/235086].
- "EUS-guided therapy" session at UEG Week Virtual 2020 [https://ueg.eu/library/session/eus-guided-therapy/161/2664].
- "EUS" presentation in the "Endoscopy: What's new in 2019?" session at UEG Week 2019 [https://ueg.eu/library/eus/212829].
- "Quality in ERCP and EUS: Who should stop and who can continue?" session at UEG Week 2019 [https://ueg.eu/library/session/quality-in-ercp-and-eus-who-should-stop-and-who-can-continue/156/2231].
- "Therapy update: Advanced endoscopic bilio-pancreatic interventions" session at UEG Week 2019 [https://ueg.eu/library/session/therapy-update-advanced-endoscopic-bilio-pancreatic-interventions/156/2172].
- "EUS: What's new in 2018?" session at UEG Week 2018 [https://ueg.eu/library/session/eus-whats-new-in-2018/153/2074].

Standards and Guidelines

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