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Elastography of the Pancreas, Current View

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Ultrasound elastography (USE) of the pancreas allows pancreatic tissue stiffness assessment by virtual palpation. Two main types of USE are used. For the pancreas strain elastography applying by endoscopic ultrasound has been established for the characterisation of small solid pancreatic lesions (SPL). In larger SPL >30 mm the results are less convincing mainly due to the heterogenicity of the lesions but also by concomitant changes of the surrounding pancreatic parenchyma. The current role of shear wave elastography has to be determined. This article reviews the current use of elastography of the pancreas. **Clin Endosc 2019;52:533-540**

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INTRODUCTION

Ultrasound elastography (USE) of the pancreas allows pancreatic tissue stiffness assessment by palpation. Prerequisite of all kinds of elastography is the entire visualization of the gland.[1-3] Two main types of USE are used: Ultrasound strain elastography (SE) using the endoscopic and transcutaneous route and ultrasound shear wave elastography (SWE) only using the transcutaneous route.[4-6] The types of USE vary on how the stress is applied and tissue displacement (strain) is measured. SE can be performed with qualitative and semi-quantitative information and SWE with qualitative and quantitative data. The description of the basic principles and the terminology has been generally accepted.[4,5] SE allows the semi-quantitative evaluation of the strain-ratio (SR) between two regions of interest and the strain-histograms (SH) of a

certain pancreatic region of interest.[7-10] Computer-aided diagnostic techniques using artificial neural networks might additionally improve the accuracy for the differential diagnosis of focal pancreatic masses.[8,11] The advantages of SWE are used for assessment of liver fibrosis,[4,5,12-17] but only few studies used this technique for the pancreas.

Recommendations have been published for the endoscopic and the transcutaneous approach of strain imaging on how to improve performance.[18,19] SE applied by endoscopic ultrasound (EUS) has been established for the characterisation of small solid pancreatic lesions (SPL). In larger SPL >30 mm, the results are less convincing mainly due to desmoplastic reaction and the heterogenicity of larger lesions with regressive changes but also by concomitant changes of the surrounding pancreatic parenchyma. The current role of the transcutaneously applied SWE is less clear today compared to endoscopically applied strain imaging and has to be determined. This article reviews the current use of elastography of the pancreas.

HOW TO USE STRAIN IMAGING OF THE PANCREAS?

Ultrasound SE is a qualitative technique where a comparison is performed and relative stiffness differences of the pancreatic tissue are displayed by colours.[8,9,12,18-23] The trans-

cutaneous examination technique has been described for the examination of lymph nodes[24-29] with similiar elastographic features compared to the endoscopic USE approach to examine peripancreatic and other lymphadenopathy.[25,30-33]

We prefer to denote blue as stiffer and red as softer but there are no convincing reasons for this except the historical use. The technical principles of real-time tissue elastography have been recently described in detail by the European Federation of Societies for Ultrasound in Medicine and Biology and the World Federation for Ultrasound in Medicine and Biology.[4,5,12,13,16,17,34-36]

Important parameters of SE to take into consideration are listed in the following check list.

- appropriate transducer
- frequency selection
- frame rate
- line density
- palpation speed and amplitude
- noise filters
- persistence
- dynamic range of elasticity
- other qaulity parameters (e.g., strain graph display)

Since strain imaging displays the relative stiffness of tissue, the relation to enough sufficient normal or reference tissue surrounding the lesion is of major interest. The best image quality can be achieved when the lesion of interest covers up to 50% of the region of interest.[18,19,37] Too strong pre-compression should be avoided to achieve consistent, reproducible elastograms. The contact of the endoscopic transducer should be strictly applied to the center of the lesion to avoid falsely too stiff estimation. Care should be taken to avoid assessment of tissue adjacent to stiff areas, as soft tissue will strain more when it is above hard tissue.[19]

EUS strain imaging allows the imaging of elasticity properties of SPL but is not suitable for examining larger pure cystic lesions. The blue/green/red sign is a useful artefact to determine the cystic nature of small pancreatic cystic lesion.[38]

NORMAL STIFFNESS OF THE PANCREAS

The entire pancreas has an intermediate stiffness and the shear wave speed is about 1.4 m/sec.[39] Pancreatic stiffness increases during aging which is true for SE[40,41] and SWE.[42-44] Size, body weight, body mass index and gender do not significantly influence pancreatic stiffness[42-46] but published data are sparse.

ACUTE AND CHRONIC PANCREATITIS, AUTOIMMUNE PANCREATITIS

Necroses in acute pancreatitis are softer as compared to the healthy pancreatic parenchyma. Acute pancreatitis induces complex changes of the pancreas with no clear cut stiffness values.[46-49] The value of elastography for the diagnosis of chronic pancreatitis is controversially discussed[40,44,46,48,50-68] with stiffer parenchyma during the course of the disease both using SE (SR and SH)[40,69] and SWE.[44,46,56,57,70] Typically a heterogeneous (honeycombed) stiffness pattern can be displayed with predominantly stiff strands and calcifications. EUS elastography is especially helpful in identifying patients with autoimmune pancreatitis since the entire organ shows stiffer tissue (and hypervascularity) before B-mode changes are visible (Fig. 1).[20,71-74]

Tuberculosis is also stiffer.[75,76] Elastogaphic methods have also been used to estimate the risk of fistula formation after pancreatic surgery. Interestingly, the softer values are risk factors analysed by SWE[50,51,67,77] and SE.[54,59,68]

STRAIN IMAGING

Recently a study was performed with 218 patients with SPL ≤15 mm and a definite diagnosis.[23] It could be shown that in patients with small pancreatic lesions, EUS elastography can rule out malignancy with a high level of certainty if the lesion is displayed as soft (Fig. 2).

A stiff lesion can be either benign or malignant.[78] The most important differential diagnosis of pancreatic ductal adenocarcinoma (PDAC) (Fig. 3) are pancreatic neuroendocrine tumors (Fig. 2).

Other SPL include metastases (e.g., renal cell, lung and colorectal carcinoma) (Fig. 4), lymphoma, serous microcystic neoplasia with only microscopically detectable cysts mimicking a solid lesion, mesenchymal pancreatic tumors and and intrapancreatic accessory spleens. These may present as stiffer or softer lesions compared to the surrounding pancreatic parenchyma.[38-42]

In patients with SPL lesions <15 mm, it is more likely to diagnose lesions other than ductal adenocarcinoma compared to larger SPL. In multivariate analysis a lesion size of ≥15 mm was associated with PDAC with an Odds ratio of 20.2.[79] In small pancreatic tumors (≤25 mm), the risk of ductal adenocarcinoma was correlated to increasing size with a risk of ductal adenocarcinoma of 4.3% in lesions ≤15 mm, of 22.8% of lesions measuring 16–20 mm, and of 42.1% of leasions measuring 21–25 mm.[80] In a large cohort of solid pancreatic tumors (3.4–130 mm; median 32 mm) diagnosed using
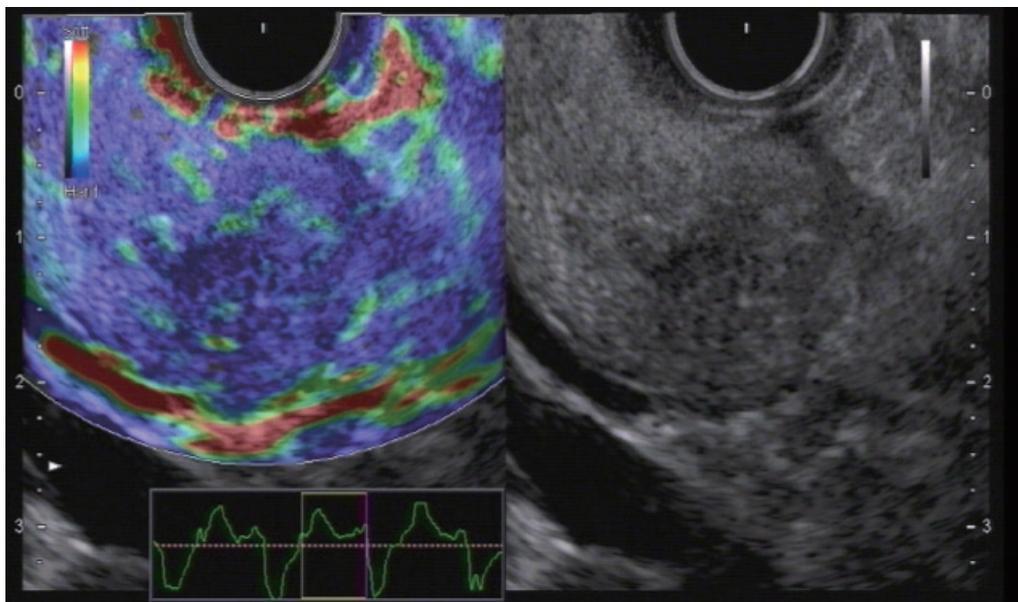
Fig. 1. Autoimmune pancreatitis. The entire organ shows diffuse stiffness. In comparision, pancreatic cancer shows circumscriptive stiffness only.
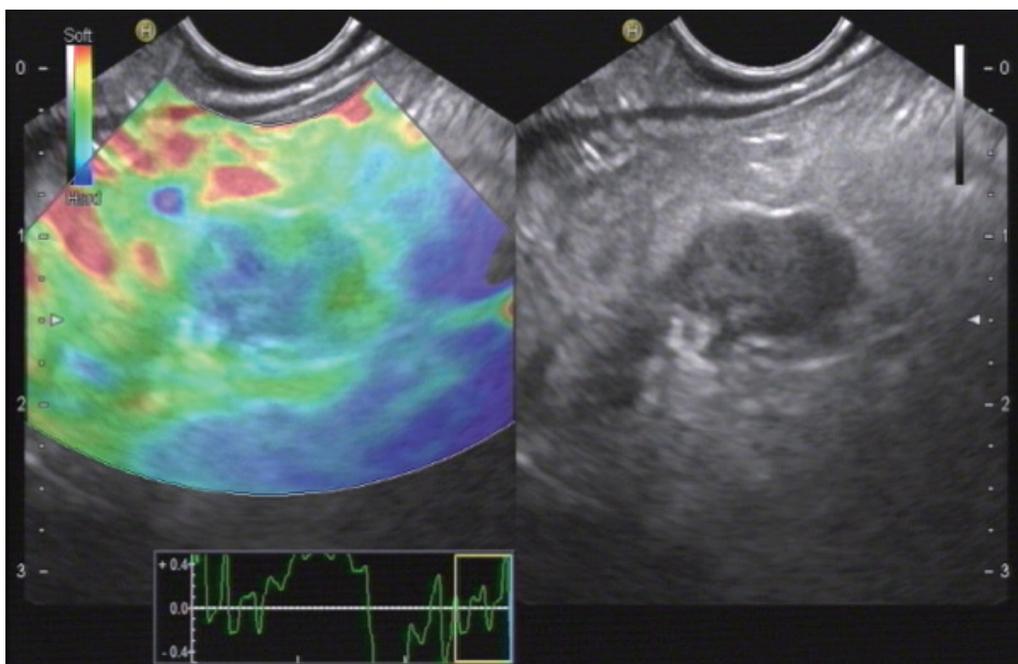

Fig. 2. Neuroendocrine tumour, benign. Endoscopic ultrasound elastography can rule out malignancy with a high level of certainty if the lesion is displayed as soft.

EUS-guided fine needle aspiration (EUS-FNA), 40 lesions were ≤10 mm in diameter, 121 had a diameter of 10–20 mm, and 835 >20 mm. In the group of lesions ≤10 mm, only 22.5% were diagnosed to be PDAC, but 40% proved to be pancreatic neuroendocrine tumours (P-NET). In the group with lesions of intermediate size (10–20 mm) 58.7% were ductal adenocarcinoma and 14% were NET. In lesions larger than 20 mm PDAC was by far the most common diagnosis (81.8%), and

only 2.8% of lesions were P-NET.[81] Dawwas et al. reported modest accuracy for differentiating malignant lesions.[82] They studied 104 patients with evidence of a solid pancreatic mass on cross-sectional imaging and/or endosonography, with 111 quantitative EUS elastography procedures. Multiple elastographic measurements of the mass lesion and soft-tissue reference areas were undertaken, and the corresponding SRs calculated. Malignant masses had a higher SR (p=0.01) and
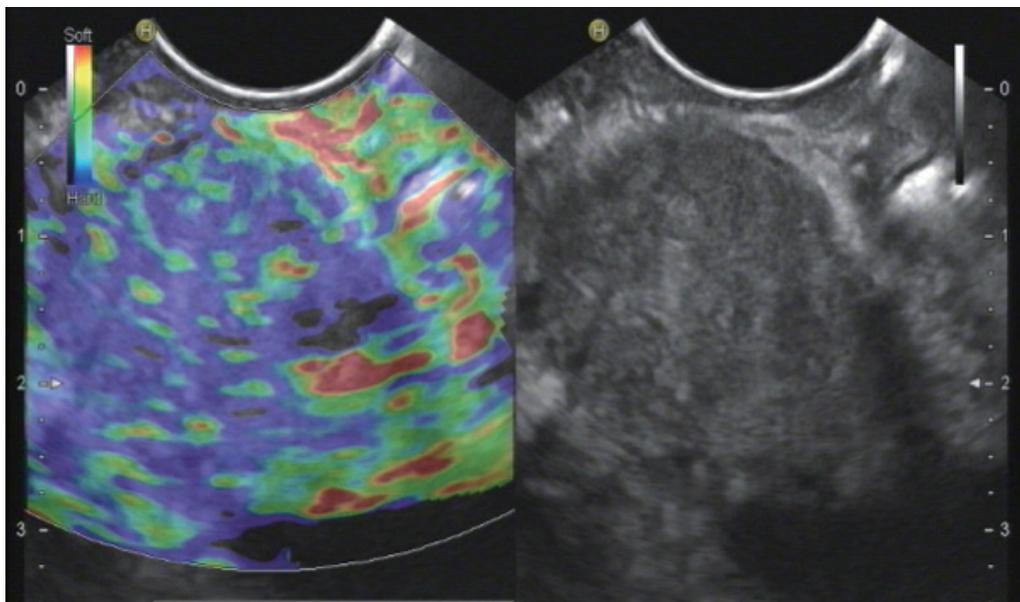
Fig. 3. Pancreatic ductal adenocarcinoma. Elastography show a typical heterogenous stiff pattern.
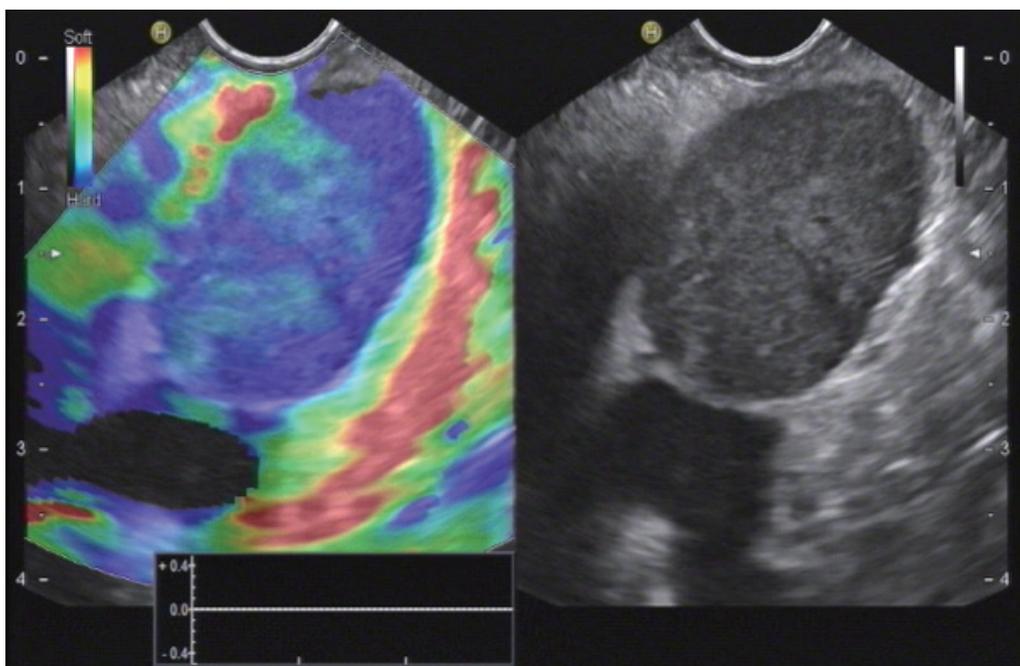

Fig. 4. Pancreatic metastasis of colorectal carcinoma. Elastography show a typical homogenous stiff pattern.

lower mass elasticity (p=0.003) than inflammatory lesions. The areas under the receiver-operating characteristic curve for the detection of pancreatic malignancy of both SR and mass elasticity were 0.69 and 0.72, respectively. At the cut-off points providing the highest accuracy in this cohort (4.65% for SR and 0.27% for mass elasticity), quantitative EUS elastography had a sensitivity of 100.0% and 95.7%, specificity of 16.7% and 22.2%, positive predictive value of 86.1% and 86.4%, negative predictive value of 100.0% and 50.0%, and overall accuracy of 86.5% and 83.8%, respectively.[82] The authors suggested that EUS-SE may only supplement rather than supplant the role of pancreatic tissue sampling in the future.

EUS elastography was reported to be useful for the differentiation of focal pancreatic masses, particularly between pseudotumoral chronic pancreatitis and pancreatic cancer, and in the presence of a strong suspicion of pancreatic cancer

and false-negative EUS-FNA results.[83] In a retrospective study design, 109 patients with SPL were assessed by EUS elastography. Tissue elasticity distribution and elasticity semiquantification, using the SR of tissue elasticity, were used. Elastography for all PDAC patients showed intense blue coloration, indicating hard tissue. In contrast, mass-forming pancreatitis presented with a mixed coloration pattern of green, yellow, and low-intensity blue. Normal controls showed an even distribution of green to red. The mean SR was 23.66±12.65 for mass-forming pancreatitis and 39.08±20.54 for PDAC. Semiquantitative analysis of elasticity using the SR may allow the differentiation of mass-forming pancreatitis from PDAC.[84] Mass forming pancreatitis seems to be a computed tomography phenomenon since it relies mainly on swelling whereas EUS shows most often focal lesions.

One prospective study from 2008, of 70 patients with undifferentiated pancreatic masses, reported a much lower overall sensitivity of elastography for malignancy of 41%, specificity of 53%, and accuracy of only 45% in larger lesions. The subanalysis revealed much better results for smaller lesions.[21]

Recent efforts to improve the reproducibility, accuracy, and clinical utility of elastography in pancreatic imaging have moved toward developing quantitative scoring systems for elastography to better delineate the relative differences in the elasticity of solid pancreatic masses.[9] SR is a tool used for quantifying relative tissue stiffness, normally used to measure the stiffness of a discrete mass lesion.[18] Histogram analysis has been applied in diffuse chronic pancreatic diseases, where the colour pattern displayed in the elastogram is related to the fibrous structure caused by the chronic inflammatory disease.[18] Both topics have been extensivle discussed elsewhere.[18,19,23,85]

SHEAR WAVE ELASTOGAPHY

Shear wave velocities are significantly higher in PDAC compared to the surrounding pancreatic parenchyma[46,86,87] with shear wave velocities >3 m/s.[46,86-88]

CONCLUSIONS

Ultrasound based SE allows improved visualisation and relative quantification of pancreatic tissue stiffness, an area not accessible to direct palpation. SE[5,8-11,19-21,31,32,40,41,44,52-54,57-63,69,78,84,89-112] and SWE[5,39,42-47,50,51,53,55-57,86-90,113-115] have been widely used to examine the pancreatic parenchyma and to differentiate SPL. The EUS approach has been established for the differential diagnosis of small SPL. A hypoechoic SPL <30 mm on B-mode with low strain signal (hard) in otherwise healthy pancreatic parenchyma can be malignant or benign whereas a soft SPL is almost always benign. The transcutaneous and intraoperative approaches are promising as well but data are less extensive and less convincing. Elastographic methods are not able to decisively differentiate focal pancreatitis from PDAC. Transabdominal and endoscopic USE may be also helpful tools for diagnosing and staging of chronic pancreatitis. Strain imaging is also of use in diagnosing autoimmune pancreatitis. Finally, the combination of imaging methods should be used.

Conflicts of Interest

The authors have no financial conflicts of interest.

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