Editorial

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A brief report on EFSUMB Guidelines and Recommendations for elastography and contrast-enhanced ultrasound in non-hepatic applications

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The importance of ultrasound is well recognized all around the world, and for the past two decades, innovative technologies found their way in this field. Among the most important, ultrasound elastography and contrast enhanced ultrasound (CEUS) are undoubtedly a major breakthrough in the evolution of ultrasonography.

Basic principles of elastography have not been changed since the first time they were described. Moreover, since 2003 when transient elastography (TE) was proposed as a tool in assessing liver fibrosis, other approaches for evaluating the stiffness of the liver have been tried in predicting the evolution of chronic liver disease [1]. Given the growing general interest indicated by the scientific evidence in this field and the novel proposed technical approaches, it is important to have a comprehensive understanding of the various techniques of elastography, a guidance for clinical applications that can promote consistency among clinicians and high-quality education. Regarding CEUS, the interest in this technique has grown for the past 20 years and it has reshaped the role of ultrasound in clinical practice. This concept dates back in the late 1960s [2] and it regained the specialists' attention 20 years later [3], numerous papers published in the last 30 years have been confirming its value and potential for more extended future applications.

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For the first time, in 2013, a group of experts from the European Federation of Societies of Ultrasound in Medicine and Biology (EFSUMB) published the elastography guidelines. These were updated for the liver in 2017 and will be updated for non-hepatic applications in 2019. The first guidelines for CEUS were published by EFSUMB in 2004, followed by updates in 2008 and 2012. In 2013, the World Federation for Ultrasound in Medicine and Biology (WFUMB) and EFSUMB released the worldwide "CEUS in the liver" guidelines and updated them in 2017 for non-hepatic applications, as well as for use in pediatric applications. These guidelines provide a comprehensive understanding of the current clinical status of each commercially available technology for elastography and CEUS applications. Also, the guidelines offer educational support on the basic physical principles and technology, practical advantages and disadvantages for each technique, guidance for the scanning technique, image interpretation and specific artefacts [4-6].

Many papers on ultrasound elastography and CEUS focused mainly on liver applications showing great advances in the field of hepatology. This approach made it possible for the clinicians to take fast decision for their patients, in terms of management and disease progression, and more importantly to decrease the number of liver biopsies. But these ultrasound technologies hold a great potential for non-hepatic application as well, for the characterization and the detection of focal lesions in organs like pancreas, spleen, kidney, thyroid, breast and other systems.

Three approaches can be used to assess the elastographic properties of the pancreas: transabdominal, endoscopic and intraoperative, all of them with their own advantages and disadvantages. In acute pancreatitis, the pancreatic parenchyma becomes stiffer, although the use of this technique is questionable in some studies. Elastog-

raphy cannot distinguish chronic pancreatitis from malignant tumors, although it can be used as an additional imaging tool for diagnosis and grading. In characterizing solid pancreatic lesions, transabdominal ultrasound is not indicated, but endoscopic ultrasound elastography can be used as a complementary imaging tool. For non-hepatic applications, the pancreas is another organ of interest for CEUS, providing a clear distinction between solid and cystic lesions and a differentiation between cystic neoplasms and pseudocysts. Solid pancreatic lesions detected on conventional ultrasound can be characterized as ductal adenocarcinoma by CEUS, evaluating the lesion as typically hypo-enhancing in all phases, compared to neuroendocrine tumors that are hyper-enhancing lesions in the arterial phase. CEUS can be used to assess the lesion size, the margins of a pancreatic lesion and the relation to the peripancreatic vessels, as well as to differentiate vascular from avascular components of a pancreatic lesions [5,6].

Bowel wall lesions can be investigated using strain elastography (SE) and shear wave elastography (SWE), but most of the studies are based on SE, with main focus on the distinction between fibrous and inflammation strictures in Chron's disease (CD) and also in distinguishing rectal adenoma from adenocarcinoma. EFSUMB recommends SE for the characterization of the bowel wall lesions in CD, with ultrasound elastography as an add-on to endoscopic rectal ultrasound, and magnetic resonance imaging for improving rectal cancer staging. CEUS of the gastrointestinal tract can provide important vascular information, evaluating the vascularity of the gastrointestinal wall or tumor. In inflammatory bowel disease, CEUS can estimate more adequate than Power Doppler between disease activity stages, discern between fibrous and inflammatory stricture in CD, as well as monitoring the effect of treatment. Moreover, in CD it can be used to detect abscesses and to confirm and track the route of fistulae [5,6].

Spleen stiffness assessed by elastography correlates well with hepatic vein portal gradient, recommended as an additional non-invasive method to evaluate portal hypertension. Conventional US has a low accuracy in the diagnosis of splenic solid lesions, whilst CEUS improves the detection of focal abnormalities, as well as the identification of benign lesions with a persistent enhancement pattern in the late phase. Like other parenchymal organs, CEUS can also be used for diagnosing splenic infarction [5,6].

Renal elastography has limited applications, SE being used only for superficial kidneys, a situation encountered in renal transplantation. It would be of a great help as a non-invasive test, in order to avoid repeated biopsies for assessing histological lesions. Current recommendation is to be used as an additional tool in the diagnosis of chronic allograft nephropathy. On the other hand, CEUS can characterize focal renal lesions and it has similar detection rates of renal ischemia as CT imaging. EFSUMB recommends the use of CEUS to differentiate between renal tumors and "pseudotumors" whenever conventional US is equivocal, to characterize complex cysts, indeterminate renal lesions and renal abscesses in complicated acute pyelonephrytis. Also, CEUS can offer informations in non-surgical renal lesions follow-up [5,6].

The use of CEUS and elastography for focal lesions has decreased the drastic approach in testicular pathology. CEUS represents a solution to differentiate between hypovascular and avascular lesions, providing a practical solution in segmental testicular infarction and in discriminating non-viable regions in testicular trauma. CEUS may be a convenient method to exclude prostate malignancy by distinguishing vascular from non-vascular lesions. It brings no additional information in pathologies such as spermatic cord torsion and it has a limited use in extratesticular intrascrotal focal lesions. Testicular elastography is recommended to be adjunctive to other ultrasound techniques, as there is an overlap in findings between benign and malignant neoplasms [5,6].

Regarding the prostate, some studies reported improvement in biopsy guidance when using SE, but it was invalidated by others. The recommendation is for using transrectal ultrasound elastography to identify the suspicious target region for biopsy, increasing the rate of positive biopsy cores. CEUS cannot be recommended for clinical use in the detection and diagnosis of prostate cancer [5,6].

SE and SWE are used as add-ons to conventional B-mode examination in characterizing breast lesions, and thus increasing diagnosis confidence. In addition, BI-RADS 3 lesions should be considered for biopsy if they appear stiffer on breast ultrasound elastography. Numerous studies investigated CEUS in differentiating breast masses, but no specific pattern could indicate malignancy and at this moment it cannot be recommended for clinical use. For assessing the status of axillary lymph nodes, CEUS was used by injecting the ultrasound contrast agent intradermally, but it is still being studied and it is not recommended for clinical use [5,6].

Elastography, particularly the semi-quantitative methods, used for assessing thyroid abnormalities, should be used as a complementary tool to B-mode US. The assessment could provide additional information of thyroid nodule characteristics and thus supports the clinical decision of fine-needle aspiration biopsy. The use of CEUS in the diagnosis of thyroid malignancy is still an

active research as there are several limitations in the interpretation of tumor microvascularity, due to the overlapping data between quantitative and qualitative evaluation. Therefore, it cannot be recommended for clinical use [5,6].

Currently, CEUS is not recommended to assess lymph nodes in clinical practice but elastography can be used as an additional tool to differentiate between benign and malignant lymph nodes, in both superficial and mediastinal lymph nodes. Another recommendation is to use ultrasound elastography to help clinicians make decisions on targeted fine-needle aspiration biopsy of the most suspicious lymph nodes and/or suspicious areas within the lymph nodes [5,6].

Current advances in ultrasound technology have dramatically changed the management in various areas, especially by reducing the number of biopsies, whilst newer technologies emerge with a range of applications that are currently being investigated. This high pace might seem inciting but at times it can be overwhelming for the clinician and thus, the need of guidelines is essential. This strategy could increase the quality of care by reducing the costs of a final diagnosis and by answering rapidly and accurately to a clinical question.

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