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Focal nodular hyperplasia and hepatocellular adenoma: The value of shear wave elastography for differential diagnosis

Thomas Brunel[a,*], Aymeric Guibal[b], Camille Boularan[b], Christian Ducerf[c], Jean-Yves Mabrut[c], Brigitte Bancel[d], Loïc Boussel[a], Agnès Rode[a]

[a] Service de Radiologie, Hôpital de la Croix-Rousse, 103 Grande rue de la Croix-Rousse, 69004 Lyon, France
[b] Service d'imagerie abdominale, Hospices Civils de Lyon, Hôpital Edouard Herriot, 69437 Lyon cedex 03, France
[c] Service de Chirurgie Digestive, Hôpital de la Croix-Rousse, 103 Grande rue de la Croix-Rousse, 69004 Lyon, France
[d] Service d'Anatomie et de Cytologie Pathologiques, Hôpital de la Croix-Rousse, 103 Grande rue de la Croix-Rousse, 69004 Lyon, France

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ABSTRACT

Objective: This study assessed the clinical usefulness of shear wave elastography (SWE) during ultrasound for differentiating between focal nodular hyperplasias (FNHs) and hepatocellular adenomas (HAs).
Materials and methods: SWE was performed on 56 patients presenting with 76 liver lesions (57 FNHs and 19HAs) that were confirmed by MRI and contrast-enhanced ultrasound (CEUS) ($n = 55$) or by histology ($n = 21$). A mean elasticity value was obtained for each lesion. The ratios of the elasticity of the lesions to the elasticity of the surrounding liver were determined. The optimal elasticity cut-off value for distinguishing between the two lesion types was determined using ROC analysis. All lesions that were classified as "undetermined" after CEUS were reclassified using the elasticity values.
Results: The mean elasticity value was 46.99 ± 31.15 kPa for FNHs and 12.08 ± 10.68 kPa for HAs ($p < 0.0001$). The mean relative elasticity ratio values were 7.94 ± 6.43 and 1.91 ± 1.70, respectively ($p < 0.0001$). The ROC analysis showed a maximal accuracy of 95% for identification with a cut-off of 18.8 kPa for lesion elasticity (accuracy of 96% with a cut-off of 1.98 for the relative elasticity ratio). A total of 68CEUS were performed, and 17 lesions (25%) were classified as "undetermined" after CEUS. With these cut-off values 16 lesions (94.1%) were correctly reclassified as FNHs.
Conclusion: SWE is a useful adjunctive tool for differentiation between FNH and HA during ultrasound examination.

1. Introduction

The two main types of benign hepatocellular tumors are focal nodular hyperplasias (FNHs) and hepatocellular adenomas (HAs) [1]. Differentiating between these two lesions is essential because of differences in their management. Specifically, follow-up is not necessary for FNHs, while the majority of HAs should be resected because of the risk of hemorrhage and the possible development of hepatocellular carcinoma [2–5]. Several imaging methods can be used to make a non-invasive diagnosis: ultrasound imaging (US), contrast-enhanced ultrasound imaging (CEUS), and magnetic resonance imaging (MRI) [6–12]. These tumors develop mainly in asymptomatic young women, and avoiding invasive procedures is a priority.

Many studies have documented the different stages of hepatic fibrosis in chronic hepatopathy [13], and a few preliminary studies show that elastography methods can be used to visualize elements in focal liver lesions to make a differential diagnosis. These technologies, principally acoustic radiation force impulse elastography (ARFI) and shear wave elastography (SWE), are integrated into a conventional US system, providing both qualitative images and quantitative elasticity metrics. Both ARFI and SWE use acoustic radiation force to transiently deform soft tissues and then measure the dynamic displacement response of the tissues. In a previous study [14], we examined the quantitative spatial variations in the stiffness of varied focal benign and malignant liver lesions, and we noted a difference between FNHs and HAs. The aim of this study was to assess whether the elasticity characteristics of FNHs and HAs are

Abbreviations: ARFI, acoustic radiation force imaging; CEUS, contrast-enhanced ultrasound; FNH, focal nodular hyperplasia; HA, hepatocellular adenoma; SWE, shear wave elastography.

* Corresponding author.
E-mail addresses: thomasbrunel20@gmail.com (T. Brunel), aymeric.guibal@gmail.com (A. Guibal), camilboul@hotmail.fr (C. Boularan), christian.ducerf@chu-lyon.fr (C. Ducerf), jean-yves.mabrut@chu-lyon.fr (J.-Y. Mabrut), brigitte.bancel@chu-lyon.fr (B. Bancel), loic.boussel@chu-lyon.fr (L. Boussel), agnes.rode@chu-lyon.fr (A. Rode).

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Table 1
Characteristics of lesions and main elastography's results.

	FNH	HA
Number of lesions	57	19
Number of patients	50	10
Female	47	10
Male	3	0
Average age (years)	38.6	39.9
CEUS	55 (96.5%)	11 (57.9%)
MRI	50 (87.7%)	18 (94.7%)
Histologic prelevement	7 (12.3%)	19 (100%)
Average size (mm)	46.9	57.2
Patients with steatosis	5 (8.8%)	1 (5.3%)
Average elastography value in healthy liver (kPa)	6.7	6.7
Average elastography value in the lesions (kPa)	47	12.1
Minimal average value of elastography (kPa)	7.5	5.5
Maximal average value of elastography (kPa)	189.8	51.8
Relative elasticity ratio (RER) lesion / healthy liver	7.9	1.9
Minimal RER	1.4	0.9
Maximal RER	38	7.9
Average standard deviation	9.9	2.7

significantly different in order to help characterize these benign liver tumors and thereby avoid invasive diagnostic procedures in atypical cases.

2. Materials and methods

2.1. Patient selection

This prospective study was performed in two radiology departments, one at Hôpital de la Croix-Rousse and one at Hôpital Edouard Herriot, Lyon, France, between March 2010 and March 2014. The study was approved by the local ethics committee at our institutions. All participating patients provided oral informed consent.

The inclusion criteria were as follows: one or more benign hepatocellular tumors in otherwise normal livers (no notion of hepatopathy, no history of cancer, no dysmorphic liver in the different imaging examinations) and presentation at the radiology departments for tumor characterization. In most cases, patients were seeking a second opinion about diagnoses that were difficult for radiologists who lacked experience in hepatic imaging. Definite diagnosis was achieved using a combination of two imaging techniques (e.g., MRI and CEUS) according to previously defined imaging criteria [6–12]. All patients underwent CEUS and/or MRI plus elastography performed by two radiologists who specialized in liver disease (AR, with 20 years of experience and AG, with 10 years of experience). The exclusion criteria were no formal diagnosis by imaging or histology, cirrhosis or chronic hepatopathy, history of cancer or chronic disease, small lesions <1 cm, and failed SWE acquisition (inconsistent results because of tumor depth or location, because of heartbeat in the left lobe preventing precise measures). A total of 71 patients (67 women, 4 men; average age, 38 years) were considered for inclusion, with 94 undetermined benign hepatocellular lesions. Of these, 18 lesions in 16 patients were excluded before the analysis: 5 lesions did not have a certain final diagnosis, and 13 (13.8%) were elastography failures. The causes of the elastography failures included failed acquisition due to tumor depth or location or the tumors were too small ($n = 5$); heartbeat in the left lobe ($n = 3$); important steatosis that prevented accurate measures ($n = 2$); technical problems ($n = 2$); and proximity to the portal vessel ($n = 1$).

Thus, 76 lesions in 56 patients were included in the analysis, including 57 FNHs and 19HAs. (Table 1)

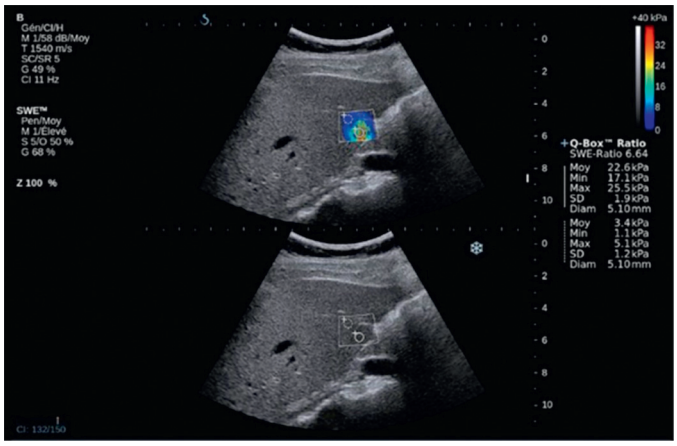

Fig. 1. Shear wave elastography (SWE) acquisition of a focal nodular hyperplasia in a 51-year-old woman.
Up: SWE mode with real-time evaluation of tissue elasticity. In this case, the analysis window shows two ROIs (one ROI in the lesion and the other in the normal liver).
Bottom: B-mode ultrasound helped locate the lesion.

2.2. Imaging protocols

2.2.1. SWE elastography

Elastography values were collected using an Aixplorer ultrasound system (SuperSonic Imaging) with a curved array transducer. In most cases, the radiologist knew the MRI results and the suspected diagnosis. B-mode US was performed before SWE to locate the lesions. The size of the SWE Window was adapted to the size of the tumor in cases of small lesions, otherwise it was a standard SWE color box of approximately 2 × 3 cm. The measurements were performed in a 1 cm diameter region of interest (ROI) into the SWE color box. SWE acquisitions with breath holding were performed for each lesion, with central placement of the ROI to target the stiffest part of the lesion (Fig. 1). Three acquisitions per lesion were performed. For each acquisition we obtained a quantitative evaluation of the lesion elasticity in kilopascals (kPa). A single value (the average of three acquisitions) was obtained for the elasticity of each lesion. Two additional acquisitions were performed in a healthy part of the liver near the lesion, and we calculated the ratio of the elasticity of the lesion to that of the surrounding liver.

2.2.2. MRI

MRI was performed with a protocol specific for liver exploration. The protocol consisted of transverse T1-weighted chemical shift sequences in-phase and out-phase, a transverse respiratory-triggered T2-weighted fast spin-echo sequence with spectral fat saturation, and a dynamic contrast-enhanced 3D gradient-echo volumetric interpolated breath-hold examination before and after administration of gadolinium-BOPTA (Multihance®, Bracco, Italy) at a dose of 0.1 mmol/kg of body weight (2 mL/s). These sequences were performed with an arterial, portal, and late phase (3 min) after injection using a bolus tracking technique.

2.2.3. CEUS technique

US was performed using an Aixplorer ultrasound system (SuperSonic Imagine) or a Logic 9 system (General Electric) with a curved array transducer. CEUS was performed after injection of a bolus of 2.4 mL of the contrast agent SonoVue® (Bracco, Milan) followed by 10 mL of saline; subsequently, we activated the chronometer and analysis archiving software. The exploration focused on the lesion. Arterial enhancement was analyzed in real-time, and the portal and late phases were analyzed with a scan at least 5 min after injection.