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Liver and spleen elastography using supersonic shear imaging for the non-invasive diagnosis of cirrhosis severity and oesophageal varices

Christophe Cassinotto[a,b,*], Anne Charrie[a], Amaury Mouries[a], Bruno Lapuyade[a], Jean-Baptiste Hiriart[c], Julien Vergniol[c], Delphine Gaye[a], Arnaud Hocquelet[a], Maude Charbonnier[c], Juliette Foucher[c], François Laurent[d], Faiza Chermak[c], Michel Montaudon[d], Victor de Ledinghen[b,c]

[a] Department of Diagnostic and Interventional Imaging, Hôpital Haut-Lévêque, Centre Hospitalier Universitaire de Bordeaux, Pessac, France
[b] INSERM U1053, Université Bordeaux, Bordeaux, France
[c] Centre d'investigation de la fibrose hépatique, Hôpital Haut-Lévêque, Centre Hospitalier Universitaire de Bordeaux, Pessac, France
[d] Department of Diagnostic and Interventional Imaging, Hôpital Haut-Lévêque, CHU and University of Bordeaux, Pessac, France

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ABSTRACT

Background: Elastography is a promising non-invasive approach for assessing liver fibrosis. We assessed diagnostic performances of liver and spleen stiffness using supersonic shear imaging for diagnosing cirrhosis severity and oesophageal varices.
Methods: 401 consecutive cirrhotic patients were prospectively enrolled from November 2012 to March 2014. All patients underwent liver and spleen stiffness measurement with supersonic shear imaging and Fibroscan.
Results: Failures of measurement were 6.2% and 29.2% for liver and spleen stiffness (supersonic shear imaging), and 18.4% for liver stiffness (Fibroscan). Liver and spleen stiffness were correlated with severity of cirrhosis, with values increasing according to Child–Pugh subclasses and presence of complications. With a negative predictive value ≥90%, liver stiffness cut-offs for high-risk oesophageal varices, history of ascites, Child–Pugh B/C, variceal bleeding and clinical decompensation were 12.8, 19, 21.4, 30.5, and 39.4 kPa, respectively. Areas under the curve of spleen and liver stiffness (supersonic shear imaging), and liver stiffness (Fibroscan) were 0.80, 0.77 and 0.73 respectively for detection of oesophageal varices.
Conclusion: Liver stiffness using supersonic shear imaging is a relevant diagnostic tool for assessing cirrhosis severity and its complications. Spleen stiffness shows promising results for the detection of oesophageal varices but is not yet sufficiently robust for clinical practice owing to high failure rates.

1. Introduction

Liver elastography is one of the most promising techniques to have emerged in the past years in the field of chronic liver diseases. Liver stiffness measurement (LSM) using transient elastography (FibroScan®) is a widely accepted method to predict the severity and prognosis of liver disease [1–3]. LSM is efficient for diagnosing cirrhosis and its severity, with values increasing according to the presence of clinical complications such as portal hypertension [4]. In cirrhotic patients, LSM can also be used to predict clinically significant portal hypertension (hepatic venous pressure gradient [HVPG] ≥10 mmHg) or severe portal hypertension (HVPG ≥12 mmHg) [5–7]. However, it is not considered sufficiently accurate for the prediction or the grading of oesophageal varices (EVs) in clinical practice [8].

The ability of a non-invasive approach to predict accurately the presence and size of EVs in cirrhotic patients is of great clinical interest, especially for selecting a target population that would benefit from endoscopic screening programmes and/or prophylactic therapy [8–10]. The assessment of portal pressure and varices in patients with liver cirrhosis using spleen stiffness measurement (SSM) has been proposed in recent studies [11–13]. The increase in spleen stiffness is likely due to spleen congestion that leads to increased organ stiffness. Thus, several authors have reported an excellent correlation of SSM with CSPH and EVs using either Fibroscan [11] or Acoustic Radiation Force Impulse (ARFI) [12,13],

* Corresponding author at: Department of Diagnostic and Interventional Imaging, Hôpital Haut-Lévêque, CHU and University of Bordeaux, 1, Avenue de Magellan, 33604 Pessac cedex, France. Tel.: +33 5 57 65 64 44; fax: +33 5 57 65 64 72.
E-mail address: christophe.cassinotto@chu-bordeaux.fr (C. Cassinotto).

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exploring the feasibility of using elastographic techniques as non-invasive diagnostic and prognostic tools in cirrhotic patients.

Recently, a new technology in the field of liver elastography was proposed. Supersonic shear imaging (SSI), also named Shear Wave™ elastography, is based on an ultrasound device (Aixplorer, Supersonic Imagine, Aix-en-Provence, France). Unlike the ARFI or Fibroscan methods in which a single shear wave is emitted temporarily at a single frequency for each measurement, the ultrasound transducer in SSI emits many pulse wave beams at increasing depths, allowing the synchronous evaluation of the velocity of several shear wave fronts over a wide frequency range [14,15]. By generating a real-time colour mapping of the elasticity encoded pixel by pixel in an image superimposed on the standard B-mode, SSI allows quantitative imaging of the tissue elasticity. Preliminary results on this novel method are promising, showing a higher diagnostic accuracy than Fibroscan or ARFI for the non-invasive assessment of liver fibrosis [16–18]. However, no study has ever evaluated the clinical impact of SSI among cirrhotic patients for the non-invasive diagnosis of cirrhosis severity and the detection of EVs.

In the present study, we aimed to assess the diagnostic performances of LSM and SSM using SSI for the non-invasive diagnosis of cirrhosis severity and the detection of EVs.

2. Materials and methods

2.1. Patients

Between November 2012 and March 2014, all consecutive patients with cirrhosis referred for liver ultrasound (US) examination at our radiology department were prospectively included. Inclusion criterion was cirrhosis either biopsy-proven or diagnosed on combined physical, biological, and radiological evidence. Exclusion criteria were as follows: idiopathic portal vein thrombosis, presence of trans-jugular intra-hepatic porto-caval shunt, cardiac congestive liver, regenerative nodular hyperplasia, hepatocellular carcinoma (HCC) graded as Barcelona Clinic Liver Cancer (BCLC) B or C.

For each patient, LSM and SSM were performed using SSI (LSM-SSI and SSM-SSI, respectively). LSM with Fibroscan (LSM-Fibroscan) was performed the same day as the SSI examination using the Fibroscan M probe (Echosens, Paris, France). All physicians who performed the LSM examinations were blinded to the results of other non-invasive tests. An ethics committee approved the study design and written informed consent was obtained for all patients.

2.2. SSI technique

SSI was integrated in a conventional ultrasound device (Aixplorer™, Supersonic Imagine, Aix-en-Provence, France). Elastography was performed with the convex probe routinely used for abdominal US examination. Details of the technique and the examination procedure have been described in previous reports [14–18].

2.3. US examination and stiffness measurements

After overnight fasting, patients underwent a complete upper abdomen US examination by one of four experienced abdominal imaging radiologists. The following criteria were recorded and analysed: left and right liver lobe diameter, large and small splenic axis and portal vein diameter in millimetres, portal vein velocity in cm/s, presence of steatosis (defined as an increased visual hepatic/renal echogenicity ratio), and ascites. Immediately after, LSM and SSM were performed with the same probe, the patient lying in dorsal decubitus with the arms in maximal abduction, on the right lobe of the liver for LSM and on the inferior pole of the spleen for SSM, through the intercostal spaces. The operator, who was assisted by a real-time B-mode ultrasound image, targeted in a patient with apnoea, a region with a good spatial resolution on B-mode US image. In both LSM-SSI and SSM-SSI, a colour mapping with complete and homogeneous fulfilling was obtained in this zone. Then, a region of interest of 15 mm of diameter was positioned in the centre of the colour mapping, in a zone free of large vascular structures and 15 mm below the capsule. The mean value of the 5 LSM-SSI and 5 SSM-SSI measurements (with their standard deviation) expressed in kiloPascals (kPa) was used as the representative measurement. Measurements were classified as failed when no or little signal was obtained in the SSI box for all acquisitions.

2.4. Fibroscan

LSM-Fibroscan was performed by two trained nurses with more than 5000 LSM experience who were blinded to clinical, biological and SSI results. The objective was to obtain a total of 10 valid measurements (defining a successful liver stiffness measurement examination), with the maximum number of attempts set at 20. LSM-Fibroscan was considered as unreliable when IQR/LSM was >0.30 in patients with LSM ≥7.1 kPa [19].

2.5. Morphological and biological parameters

The following parameters were determined for all patients at the time of US examination. Clinical parameters included age, gender, body mass index (BMI), history of diabetes and hypertension, past history of ascites or variceal bleeding, presence of ascites and hepatocellular carcinoma. These parameters were used to classify patients according to their clinical status: compensated cirrhosis, compensated cirrhosis with past history of decompensation, and decompensated cirrhosis. Decompensated cirrhosis was defined by the presence of clinically significant ascites, variceal bleeding, jaundice, or hepatic encephalopathy. Biological parameters included platelet count (Plt), prothrombin time (PT), total bilirubin levels, gamma-glutamyl transpeptidase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), albumin, hyaluronic acid levels, and renal function. These parameters were then used to calculate the FIB-4 score [20], the aspartate aminotransferase/alanine aminotransferase ratio index (AST/ALT) [21], the aspartate-to-platelet ratio index (APRI) [22], and the platelet count/spleen diameter ratio (PLT/Spleen diameter) [23]. The liver stiffness * spleen diameter/platelet count ratio score (LSPS) was calculated as previously described by Kim and colleagues as: LSM-Fibroscan X spleen diameter/platelet ratio (LSPS-Fibroscan) [24]. LSPS was also calculated according to the same formula but using LSM-SSI instead of LSM-Fibroscan (LSPS-SSI). Child–Pugh score and model for end-stage liver disease (MELD) score were calculated according to the published formulae [25,26].

2.6. Upper endoscopy

For statistical analysis, we included endoscopic examinations performed within 3 months of SSI examinations for patients with EVs and within 6 months for patients without EVs (n = 305 patients). Endoscopic examinations were performed by experienced operators in the endoscopy unit of our hospital, which performs more than 2000 upper endoscopies per year. Varices were graded as follows: grade 0, absence of EVs, grade I, varices were flattened by insufflation; grade II, non-confluent varices protruding in the lumen despite insufflation; grade III, confluent varices were not flattened by insufflation. According to the Baveno V criteria, EVs with high risk of rupture (high-risk EVs) were defined as (i) grade II or III EVs, or (ii) grade I EVs with red signs or Child–Pugh class C [27].