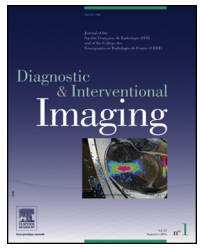
Diagnostic and Interventional Imaging (2016) **97**, 91—99



ORIGINAL ARTICLE /*Gastrointestinal imaging*

Shear wave elastography: An accurate technique to stage liver fibrosis in chronic liver diseases

A. Guibal [a,b,*], G. Renosi [a], A. Rode [c], J.Y. Scoazec [d], O. Guillaud [e], L. Chardon [f], M. Munteanu [g], J. Dumortier [e], F. Collin [b], T. Lefort [a]

[a] *Service de radiologie, hôpital Édouard-Herriot, hospices civils de Lyon, 69437 Lyon, France*
[b] *Service de radiologie, centre hospitalier de Perpignan, 20, avenue du Languedoc, 66046 Perpignan cedex 9, France*
[c] *Service de radiologie, hôpital de la Croix-Rousse, hospices civils de Lyon, 69317 Lyon, France*
[d] *Service d'anatomo-pathologie, hôpital Édouard-Herriot, hospices civils de Lyon, 69437 Lyon, France*
[e] *Fédération des spécialités digestives, hôpital Édouard-Herriot, hospices civils de Lyon, 69437 Lyon cedex 03, France*
[f] *Fédération de biochimie, hôpital Édouard-Herriot, hospices civils de Lyon, 69437 Lyon, France*
[g] *Hepatology research unit, biopredicitive, 75007 Paris, France*

KEYWORDS
Elastography;
Sonoelastography;
Cirrhosis;
Liver fibrosis;
Elasticity imaging techniques

Abstract
Objectives: The goals of this study were to assess the diagnostic accuracy of shear wave elastography (SWE) using the results of histopathological analysis as a standard of reference and compare the results of SWE and those of transient elastography (TE) to the degree of fibrosis as evaluated by histomorphometry.
Patients and methods: Adult patients who were scheduled to undergo liver biopsy were prospectively enrolled in the study. The diagnostic performances of SWE were assessed using AUROC curve analysis according to fibrosis thresholds defined by $\geq$F2 (significant fibrosis), $\geq$F3 (advanced fibrosis) and F4 (cirrhosis). Additional analyses using the Obuchowski measures for pairwise comparisons of fibrosis stages were performed. In a subgroup of 55 patients, the relationships between stiffness as measured using SWE and TE and the percentage of fibrosis were compared using Spearman's rank coefficient.

Abbreviations: SWE, shear wave elastography; TE, transient elastography; (w)AUROC, (weighted) area under the receiver operating characteristic; CI, confidence interval; ARFI, acoustic radiation force impulse; HBV, hepatitis B virus; HCV, hepatitis C virus; BMI, body mass index; ROI, region of interest; kPa, kilopascals; ICC, intra-class correlation coefficient; IQR, inter-quartile range; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, gamma glutamyltransferase.

* Corresponding author. Service de radiologie, centre hospitalier de Perpignan, 20, avenue du Languedoc, 66046 Perpignan cedex 9, France.
E-mail address: aymeric.guibal@gmail.com (A. Guibal).

http://dx.doi.org/10.1016/j.diii.2015.11.001

Results: Among the initially enrolled 170 patients, 148/170 (87%) had successful SWE acquisition and formed the study population. SWE sensitivity and specificity were respectively 85.1% and 82.7% (≥ F2), 88.9% and 90.3% (≥ F3), 93.3% and 98.3% (F4). The AUROC curves of SWE along with their 95% confidence intervals (CI) were respectively 0.904 (95%CI: 0.845—0.946) for fibrosis ≥ F2; 0.958 (95%CI: 0.912—0.984) for fibrosis ≥ F3 and 0.988 (95%CI: 0.955—0.999) for fibrosis = F4. The global Obuchowski measure was 0.953 ± 0.007. In the subgroup study, a significant correlation was found between the percentage of fibrosis and stiffness as assessed by SWE ($r = 0.77$; 95%CI: 0.63—0.86; $P < 0.0001$) and by TE ($r = 0.65$; 95%CI: 0.47—0.78; $P < 0.01$).
Conclusion: SWE is accurate to assess liver fibrosis in patients with chronic liver disease.

Chronic liver diseases are major public health concerns, with an estimated mortality of 1.5 million per year worldwide due to cirrhosis and its complications [1]. The assessment of liver fibrosis is a key element to determine prognosis, to manage treatment, to monitor disease progression and assess response to therapy in patients with chronic liver disease. Histopathological assessment using liver biopsy remains the standard of reference to evaluate liver fibrosis. However, this procedure is painful and may lead to hemorrhage (0.3%) or death (0.01%). In addition, the biopsy analysis depends on the experience of the pathologist, the size of the biopsy sample (usually about 1/50,000 of the total liver mass) and the site of sampling [2]. The heterogeneous distribution of liver fibrosis as well as intra- and inter-observer variability explain why the diagnosis of cirrhosis can be missed in up to 30% [3].

To address these limitations, non-invasive methods have been investigated for estimating liver fibrosis in patients with chronic liver diseases. Among the available non-invasive approaches shear wave-based techniques such as FibroScan®, also named transient elastography (TE), or acoustic radiation force impulse (ARFI) have been developed [4]. With TE, liver stiffness is assessed by estimating the speed of shear waves mechanically generated at the surface of the skin. Several studies have reported good performances of TE in patients with specific causes of liver fibrosis (hepatitis C virus [HCV] or hepatitis B virus [HBV] infections, alcoholic liver disease [5], non-alcoholic steatohepatitis, non-alcoholic fatty liver disease [6], primary biliary cirrhosis or primary sclerosing cholangitis) [7]. However, TE does not allow measuring stiffness in patients with ascites and fails in up to 20%, particularly when body mass index (BMI) is high [8]. ARFI has the advantage to provide a steerable point estimate of liver tissue stiffness, which can be guided by ultrasound. When compared to the results of histopathological analysis, both techniques have shown similar diagnostic performances [6,9,10].

Shear wave elastography (SWE), also named supersonic shear imaging or two-dimensional (2D) SWE, implemented on the Aixplorer® unit (SuperSonic Imagine, Aix-en-Provence, France) provides in real-time, a 2D quantitative map of tissue stiffness, that can be used in several organs [11,12]. This image enables adjustment of the region of interest (ROI) to assess a region of tissue (up to 4 cm long, 4 cm wide), to perform the measurements while assessing artifacts from tissue movement pulsation around larger vessels and reverberation under the liver capsule [13]. In HCV- and HBV-infected patients, SWE allows assessment of severe fibrosis and cirrhosis as accurately as TE does with better diagnostic performances in livers with significant fibrosis [14,15].

The main objective of this study was to evaluate the diagnostic accuracy of SWE compared to the results of liver biopsy. We also assessed the relationships between stiffness and METAVIR fibrosis scores, METAVIR activity and steatosis as well as the inter-observer reproducibility of SWE. In a subgroup of patients, we compared the diagnostic accuracy of SWE and TE according to fibrosis thresholds and assessed the relationships between stiffness measured by SWE or TE and the percentage of fibrosis, evaluated by histomorphometry.

Materials and methods

Study population

All consecutive patients were eligible if they were at least 18 year old, if they were scheduled to undergo liver biopsy whatever its indication in the Department of Radiology at Lyon Hospitals (France) from September 2010 to May 2012. Exclusion criteria were a liver transplantation for less than 6 months or contra-indications for liver biopsy (marked coagulation abnormalities, anticoagulant therapy, cardiac insufficiency, ascites, acute liver disease). This study protocol conformed to the ethical guidelines of the 1975 declaration of Helsinki. Informed written consent was obtained from each patient.

Study procedures

After a 6-hour fasting period, venous blood samples were collected to assess liver function. A standard Doppler ultrasound examination was then performed to identify the site of biopsy and to perform SWE. An ultrasound machine Aixplorer® (SuperSonic Imagine, Aix-en-Provence, France) with the low frequency convex probe (SC6-1) suitable for liver imaging was used.

SWE was first performed in the segment 5 of the liver. The right arm was placed in maximum abduction to enlarge the space between the ribs. During SWE acquisition, the patient was asked to stop breathing during 5 seconds. The elastographic acquisition was repeated 5 times for each