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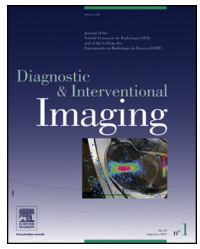

ORIGINAL ARTICLE /*Gastrointestinal imaging*

Ultrasonographic assessment of liver fibrosis with computer-assisted analysis of liver surface irregularities

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KEYWORDS
Ultrasound;
Liver fibrosis;
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Abstract
Purpose: The goal of this study was to evaluate the diagnostic accuracy of a software program that automatically analyzes the liver surface to diagnose significant fibrosis, by comparing it to the subjective analysis of a radiologist and to transient elastography (Fibroscan®).
Patients and methods: One hundred fourteen patients with chronic liver disease were included in the study. They underwent liver biopsy, FibroScan® and ultrasonographic examination of the liver surface. The liver surface was analyzed by a software program that gave a score of surface irregularities. This evaluation was compared to subjective analysis by a radiologist expert in liver imaging and by two general radiologists.
Results: Fifty percent of the patients had significant fibrosis according to the METAVIR score. The AUROC for the diagnosis of significant fibrosis by the software program was 0.80 (95%CI: 0.71—0.87), which was equivalent ($P = 0.86$) to that of FibroScan® (0.81; 95%CI: 0.71—0.89).

Abbreviations: AUROC, Area under the receiver operating characteristic (ROC) curve; NASH, Non alcoholic steatohepatitis; ROC, Receiver operating characteristic; HBV, Hepatitis B virus; HCV, Hepatitis C virus; HIV, Human immunodeficiency virus; NPV, Negative predictive value; PPV, Positive predictive value.

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Results of the subjective analysis by the expert radiologist were poorer than those of the software analysis ($P = 0.02$) (AUROC = 0.66; 95%CI: 0.56—0.75). Interobserver agreement among radiologists was poor ($0.25 < kappa < 0.37$).

Conclusion: Computer-assisted liver surface analysis was better than subjective analysis, and similar to that of the FibroScan®. This method could be useful for the diagnosis of significant fibrosis in patients with chronic hepatitis and complementary to the other non-invasive diagnostic tests.

Introduction

The development of fibrosis during follow-up of chronic liver disease, whatever the etiology, is a major prognostic factor. Precise analysis of the stage of fibrosis is essential to determine future management. Although liver biopsy is still considered to be the gold standard, it still has numerous limitations, in particular due to sampling errors. The rate of false negative findings for the diagnosis of cirrhosis can reach up to 20 to 30% [1,2]. Moreover, biopsy is invasive, expensive [3,4], and conveys a risk of severe complications (0.4%) and even death (0.03%) [5—7].

As a result, multiple non-invasive diagnostic tests have been developed to evaluate the liver as precisely as possible, to identify patients with significant lesions that could respond to treatment and to monitor disease progression. The most common complementary tools are blood tests, which consist of a combination of biological markers [8—11] and transient elastography (FibroScan®) to measure liver stiffness [12—18]. The morphological study of the liver by conventional ultrasonography (US) is also frequently used in daily clinical practice to confirm the diagnosis of cirrhosis [4,19,20]. Among the different criteria used, liver surface analysis using high resolution US helps diagnose liver fibrosis and differentiate between the early stages of fibrosis [21—23].

The goal of this study was to evaluate the diagnostic accuracy of a software program that automatically analyzes the liver surface to diagnose significant fibrosis, by comparing it to the subjective analysis of a radiologist and to transient elastography.

Materials and methods

Patients

One hundred fourteen patients (56 women, 58 men; mean age 51 ± 10.6 years old, range 18—82 years), presenting with unexplained persistent elevation of transaminases or chronic liver disease, were included in this prospective study. One hundred and five patients were hospitalized in the hepatogastroenterology unit of the Grenoble University Hospital to undergo liver biopsy and the remaining nine had clinically confirmed cirrhosis. US-guided percutaneous liver biopsy was performed by two hepatologists. Histological analysis of the liver biopsies was performed by an experienced pathologist. The degree of liver fibrosis was assessed using the 5 stages of the METAVIR scoring system, from F0 to F4 (absent, minimal, moderate, severe and confirmed cirrhosis). The study was consistent with the Declaration of Helsinki; data were collected as part of a biological collection authorized by the Institutional Review board and registered under the reference DC-2008-727.

Imaging protocol

One hundred four patients had liver stiffness measurement by two trained operators using the FibroScan® (Echosens, Paris, France) US analysis of the liver surface was performed by a radiologist using an Aplio® (Toshiba Medical Systems, Tokyo, Japan) US unit and a 7.2 MHz probe within between one and four hours after performing the liver biopsy or during a hospital stay in patients with cirrhosis. US cine loops were recorded for each patient using a right lateral intercostal approach. It should be noted that the choice was made to only analyze the right liver surface. Indeed, the correlation with the results of liver biopsy (also performed in the right liver) appeared more pertinent. Moreover, data from the expert radiologist, in addition to preliminary tests performed with the software, showed that the quality of the US recordings of the left liver surface were often insufficient for reliable analysis of regularity because of the deeper location and higher slant of the left liver capsule.

Image analysis

An extract of each video recording was selected by the operator by positioning a region of interest outside of areas of poor echogenicity, areas with artifacts due to shadowing posterior to the ribs or areas where the capsule did not appear perpendicular to the US beam. The video extracts were read by a radiologist expert specialized in liver imaging and two general radiologists. Interpretations were performed blinded to clinical data and histopathological results. A score of 0 to 4 was used: 0 for a smooth, thin and regular hyperechogenic surface, 1 for a nearly normal surface with some irregularities, 2 intermediate, 3 for an irregular spotty surface, and 4 for a totally irregular and deformed liver surface.

These video extracts were then analyzed using software developed at the Grenoble University Hospital allowing automated analysis of the contours of the liver surface by US. This software quantitatively evaluated the irregularity of the liver surface using a score between 0 and 100% (Fig. 1).

Statistical analysis

All data were recorded and analyzed using NCSS and MedCalc software. The reference test was the histopathological