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Original Article

Quantitative assessment of liver fibrosis in chronic viral hepatitis C patients using shear wave elastography with elastography point quantification feature

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ABSTRACT

Introduction: Hepatic fibrosis is the underlying pathological condition in chronic hepatitis C virus (HCV) infection. Shear wave elastography (SWE) with elastography point quantification (ElastPQ) feature is a recently developed method for measuring tissue elasticity.
Aim of this study: To evaluate the diagnostic value of SWE with ElastPQ feature for the quantitative assessment of liver fibrosis in patients with chronic HCV infection.
Patients and methods: This prospective study included 60 patients with chronic HCV infection and 50 healthy controls. All participants underwent imaging with ElastPQ technique for evaluation of the liver stiffness (LS). All patients underwent ultrasound guided liver biopsy. The METAVIR scores of fibrosis were illustrated.
Results: The study participants included 50 controls (mean LS 3.12 ± 0.40 kPa), 5 patients with F0 score (mean LS 3.77 ± 1.44 kPa); 10 patients with F1 score (mean LS 7.50 ± 0.68 kPa), 23 patients with F2 score (mean LS 8.45 ± 0.62 kPa), 17 patients with F3 score (mean LS 9.64 ± 1.20 kPa) and 5 patients with F4 score (mean LS 12.61 ± 1.41 kPa). There was a highly significant correlation between the METAVIR scores of liver fibrosis and LS measurements assessed by ElastPQ SWE ($p > 0.0001$).
Conclusion: The ElastPQ SWE technique appears as a reliable non-invasive tool that can provide an optimal way to monitor liver tissue stiffness in patients with chronic HCV infection with high accuracy (97.6%) in recognition of the earlier fibrosis stage (F2).

1. Introduction

Chronic viral hepatitis infections are the most important public health problems leading to a significant rate of morbidity and mortality. Hepatitis C virus (HCV) infection in Egypt carries the highest prevalence worldwide [1], which is estimated to be 14.7% in the 15–59 years age group, reflecting a national level epidemic [2]. A wide variety of liver diseases usually ends in hepatic fibrosis which is responsible for most of the clinical complications in patients with chronic HCV infection. Fibrosis is a dynamic pathological scarring condition in which chronic inflammation leads to the production and accumulation of collagen and extracellular matrix proteins with potential progression to cirrhosis [3]. Furthermore, the clinical management and prognosis in patients with chronic liver disease depend largely on the degree of fibrosis [4].

Liver biopsy (LB) is still considered as the standard reference for the evaluation of liver fibrosis and degree of histo-pathological damage in patients with chronic liver disease [3]. However, this method is not suitable for frequent monitoring due to its invasive nature which may be associated with some complications, in addition to technical limitations derived from small sampling or intra-observers and inter-observer variability in staging of fibrosis. All these limitations have motivated the efforts to search for new

Abbreviations: SWE, shear wave elastography; ElastPQ, elastography point quantification; LB, liver biopsy; LS, liver stiffness.

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non-invasive approaches [5,6]. In the last decade, ultrasound-based techniques have become commercially available to quantify the degree of liver fibrosis [3].

Shear wave ultrasonographic elastography (SWE) with elastography point quantification (ElastPQ) feature is a recently developed, non-invasive method for measuring tissue elasticity, which gives a local assessment and measurement of the shear wave propagation speed at each point of interest of an organ in kilopascals (kPa). This imaging method is operator-independent, reproducible, and quantitative [7–9]. It works by generating electronic voltage pulses, which are transmitted to the transducer. In the transducer, a piezo electric array converts the electronic pulse into an ultrasonic pressure wave [10,11]. The maximum penetration depth of ElastPQ is 8 cm. Therefore, it may offer an ideal way to monitor liver tissue stiffness [10].

The aim of this study is to prospectively evaluate the diagnostic value of SWE with ElastPQ feature as a non-invasive method for the in vivo quantitative assessment of liver fibrosis in patients with chronic hepatitis C virus and compare the results with fibrosis stage assessed by the histological METAVIR scoring system and biopsy samples as the reference methods.

2. Materials and methods

2.1. Study participants and study design

The current study is a prospective study, carried out in the period between March 2015 and May 2016. Study participants, recruited from the Hepatology outpatient clinic in our institutions, included sixty consecutive patients with chronic HCV infection, in addition to fifty consecutive healthy volunteers served as a control group. The patients were 38 males and 22 females; their ages ranged between 25 and 69 years, while controls were 32 males and 18 females; their ages ranged between 18 and 65 years. Patients were recognized on the basis of clinical data, and laboratory findings including the liver function tests, and polymerase chain reaction (PCR) for HCV. Serum aspartate transaminase (AST) and serum alanine transaminase (ALT) levels were estimated in all subjects. Serum levels of AST and ALT above 37 unit/liter and 40 unit/liter, respectively, were considered abnormal. However, so as to avoid inclusion of transient episodes of acute hepatitis, only patients with stable AST and ALT within the last 6 months and thereafter were included in this study. The patients' characteristics, epidemiological data and biochemical test results were recorded. Assessment of liver fibrosis with the liver stiffness (LS) measurements was prospectively estimated in all subjects by using ElastPQ SWE.

The study criteria excluded patients with history of decompensated liver diseases or co-infection with chronic hepatitis B virus or other liver disease that may have influenced the hepatic parenchyma and the extent of liver stiffness such as; congestive heart disease, liver failure, chronic renal disease, hemchromatosis, hepatolenticular degeneration, biliary obstructive disease and fatty liver. Patients with liver tumor or gross ascites, and patients who received antiviral and/or interferon therapy during the study period were also excluded.

The control group consisted of healthy volunteers, who visited the Hepatology outpatient clinic of our institution for medical checkup. They did not receive any medications and did not show history of chronic liver disease. They all had normal B-mode ultrasonographic examination, normal liver function tests, and negative PCR.

An official permission to perform this work was achieved from the local medical research ethical committee. A written informed consent was also obtained from all study participants.

2.2. Ultrasound and ElastPQ shear wave elastography technique

Initially, all study participants underwent B-mode liver ultrasound scanning with iU22 ultrasound system (iU22, Philips Medical Systems, Bothell, WA, USA), which was adapted to generate shear waves via its ElastPQ feature (Fig. 1A). During ultrasound examination, quantitative evaluation of the LS was performed by ElastPQ using a convex transducer C5-1 (1–5 MHz; C5-1, Philips Healthcare). Sub-costal and intercostals scans were used to reach and visualize the 8 liver segments (I–VIII).

The maximum penetration depth of ElastPQ is 8 cm. [10]. Each region of interest (ROI) was simulated by a fixed sample box with predefined size of 15×5 mm, which was placed by moving a trackball, in a hepatic parenchymal area that did not include large vasculature, biliary structures and away from the heart, diaphragm, liver/kidney interface, or liver capsule (at least 1.5–3 cm below the Glisson's capsule). The study participants were all instructed to suspend their breath during the actual scanning with breathing rehearsals were allowed while measurements were obtained. Furthermore, for all study participants; three 10-measurement elastographic cine clips were obtained at each of the following locations in the liver: (a) left lobe, (b) upper right lobe, and (c) lower right lobe. So, to provide a more comprehensive evaluation, total of thirty measurements were obtained across the liver for off line analysis. We considered the median values of LS measurements, which were automatically calculated, were reliable if 10 valid successful measurements (out of the 30 measurements) of both hepatic lobes in each study participant were obtained. These measurements were expressed either in meters/seconds (m/s) or kilopascals (kpa). However, if we could not obtain 10 valid measurements after 20–25 attempts, we considered these cases as invalid failed measurements and they were excluded from the study [3,11]. The means of the median values were then statistically calculated in the group of patients and compared with those of the control group.

The median values of LS measurements card (which is displayed to the left of the image; as shown in Fig. 1B) and the bias reference table were automatically calculated and displayed on the screen over a B-mode ultrasound image. The bias reference table is a reference table which describes the potential variation that obtained at different sample depths in m/s and does not vary by patient (Fig. 1C). Finally a sample report was generated at the end of examination (Fig. 1D).

The average of these measurements was then used to estimate the degree of liver stiffness, which was correlated with a predicted biopsy METAVIR score. The mean values of each fibrosis stage were statistically calculated and then they were compared with each other.

2.3. Liver biopsy and histopathological evaluation

All patients underwent ultrasound guided liver biopsy, which was performed in the same day, immediately after ElastPQSWE. The liver biopsy was carried out through a semi-automatic 18G needle by experienced interventional radiologist. All the biopsy specimens were analyzed by a qualified pathologist using the METAVIR scoring system [12], which evaluates both necro-inflammatory changes as well as degree of fibrosis. The fibrosis score was assessed on a five-point scale (F0 = no fibrosis, F1 = portal fibrosis without septa, F2 = few septa, F3 = numerous septa without cirrhosis, F4 = cirrhosis).

2.3.1. Statistical analysis

The SPSS for Windows version 18.0 software package (SPSS Inc, Chicago, IL) was used for statistical data analysis. Data of continuous variables were reported as mean ± standard deviation (SD),

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