



ARFI elastography in patients with chronic autoimmune liver diseases: A preliminary study

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KEYWORDS

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cholangitis.

Abstract *Objective:* Acoustic radiation force impulse (ARFI) is a new software-based technique that evaluates liver stiffness during B-mode ultrasonography. The purpose of this study was to evaluate the accuracy of ARFI in distinguishing patients with chronic autoimmune liver disease from healthy subjects.

Material and methods: We enrolled 9 adult patients (8 women, 1 man; age 48.1 ± 12.8 years) with chronic autoimmune disease (primary biliary cirrhosis (PBC, $n = 3$), autoimmune hepatitis (AIH, $n = 2$), primary sclerosing cholangitis (PSC, $n = 1$) and overlap syndromes, ($n = 3$) who underwent a liver biopsy and 11 healthy volunteers (age 34.7 ± 10.4 years; 7 women, 4 men). Liver stiffness was evaluated and expressed as the shear wave velocity (SWV) in m/sec. We used a US scanner Siemens-Acuson S2000, evaluating the right liver lobe and the left liver lobe. *Results:* The SWV was significantly higher in cases (right lobe: 1.51 ± 0.44 ; left lobe: 1.57 ± 0.40) than in controls (right lobe: 1.08 ± 0.10 ; left lobe: 1.12 ± 0.13) (right lobe: $P = 0.002$; left lobe: $P = 0.013$). We found no significant correlation between right and left lobe SWVs in cases ($P = 0.779$) or controls ($P = 0.385$). The SWV cut-off that best distinguished cases from controls was 1.25 m/sec (accuracy: AUC = 0.885; sensitivity: 70.6%; specificity: 95.5%).

Conclusions: ARFI elastography is a noninvasive ultrasonographic technique that can differentiate healthy subjects from patients with fibrotic stages of chronic liver disease.

Sommario *Introduzione:* L'elastografia ARFI è una tecnologia integrata all'ultrasonografia convenzionale B-mode in grado di determinare la rigidità tissutale. L'obiettivo di questo studio è stato valutare se l'elastografia ARFI sia in grado di differenziare pazienti affetti da patologie epatiche croniche autoimmuni e soggetti normali.

Materiali e metodi: Sono stati arruolati 9 pazienti affetti da epatopatia cronica autoimmune sottoposti a biopsia epatica (età 48.1 ± 12.8 anni; femmine/maschi: 8/1; 3 PBC, 2 AIH, 1 PSC e 3 overlap) e 11 volontari sani (età 34.7 ± 10.4 anni; F/M: 7/4). La rigidità epatica è stata valutata mediante l'elastografia ARFI ed espressa come "shear wave velocity" (SWV) in m/sec. È stato utilizzato un ecografo Siemens-Acuson S2000 valutando entrambi i lobi epatici. Le

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misurazioni sono state eseguite a respiro bloccato, ad una profondità compresa tra 2 e 5 cm. **Risultati:** La SWV è risultata significativamente più elevata nei casi (Dx: 1.51 ± 0.44 ; Sn: 1.57 ± 0.40) rispetto ai controlli (Dx: 1.08 ± 0.10 ; Sn: 1.12 ± 0.13) (Dx: $P = 0.002$; Sn: $P = 0.013$). Sia nei pazienti con epatopatia cronica ($P = 0.779$) che nei controlli ($P = 0.385$) non è stata rilevata una differenza statisticamente significativa della SWV fra i due lobi. Il valore ottimale di SWV per discriminare i casi dai controlli è risultato 1.25 m/sec (accuratezza: AUC = 0.885; sensibilità: 70.6%; specificità: 95.5%).

Conclusioni: L'elastografia ARFI è una metodica ultrasonografica utile nel differenziare soggetti sani da pazienti affetti da epatopatia cronica in evoluzione fibrotica.

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Introduction

The prognosis and management of chronic liver diseases depends largely on the extent and progression of hepatic fibrosis, which involves replacement of the hepatic parenchyma by extracellular matrix [1]. Liver biopsy is considered the gold standard method for assessing hepatic fibrosis because it is a direct method [2]. The main limitation of this procedure is its invasiveness, which in rare cases can lead to both minor and major complications [2–4]. Abdominal pain is associated with the procedure in roughly 25% of all cases, and procedure-related complications that require hospitalization are reported in 1–3% [5–7].

Other limitations include the risk of sampling errors [8–11] and operator-dependent variability in interpreting the results [12], which can result in under – as well as overestimation of the degree of liver fibrosis. In addition, the procedure is expensive, and it cannot be repeated frequently to monitor the evolution of the disease. There are also situations in which liver biopsy are contraindicated, including patients with coagulation disorders, those who uncooperative, and those who refuse to undergo biopsy.

Because of the limitations of liver biopsy and the dynamic nature and prognostic/therapeutic relevance of hepatic fibrogenesis in patients with chronic liver disease, several simple noninvasive methods have been proposed over the last decade to obtain simple, low-cost estimates of the extent of this process, which are also accurate, repeatable, and reproducible. These methods have been widely evaluated in patients with viral liver disease caused by hepatitis virus B or C and in those with nonalcoholic fatty liver disease (NAFLD), but there is much less information on their use in rarer forms of chronic autoimmune liver disease, such as primary biliary cirrhosis (PBC), autoimmune hepatitis (AIH), primary sclerosing cholangitis (PSC), and the AIH-PBC overlap syndrome.

The new methods used to evaluate liver fibrosis include biologic tools based on the use of direct and indirect biochemical markers and instrumental methods. Among biologic tools, those that have been most widely tested are the Fibrotest and the APRI score (AST to platelet ratio index). Instrumental approaches include impulse-based elastography (FibroScan) and ultrasound-based elastography (acoustic radiation force impulse elastography – ARFI – and real-time elastography).

The FibroScan has been proposed for assessment of liver stiffness as an indirect index of hepatic fibrosis. It is based

on the use of mechanical waves generated by vibrations. The diagnostic performance of this method in patients with HCV-related liver disease has been evaluated in three important multicenter studies [13–15], and it has also been tested in patients with NAFLD [16]. Data on its use in patients with autoimmune liver disease are not as clear or concordant [17,18].

A more recently developed approach, ultrasound-based elastography, is a technique used with conventional B-mode sonography to evaluate the elastic properties of tissues. It has been employed mainly for the differentiation of malignant and benign thyroid, breast, and prostate lesions and for characterization of atherosclerotic plaques [19–23].

Recent studies have evaluated its use in the study of hepatic fibrosis in patients with chronic liver disease (viral in most cases), and the results have shown good concordance with histological data [24,25]. Takahashi et al., for example, found that liver stiffness measured with ARFI correlates with Metavir scores of liver fibrosis. Again, however, there are fewer data on the less common autoimmune liver diseases.

The main objective of this study was to determine patients with chronic autoimmune liver disease can be distinguished from normal subjects with comparative analysis of ARFI elastographic findings in the right and left lobes of the liver.

Materials and methods

The study population included male and female patients with chronic autoimmune liver disease who underwent liver biopsy in the Dept. of Digestive Tract Diseases and Internal Medicine of Saint Orsola-Malpighi Policlinic in Bologna, Italy. The criteria for enrollment were: a) age ≥ 18 years; b) diagnosis of one of the following diseases: PBC, AIH, PSC, or an overlap syndrome; c) indications for liver biopsy; d) patient consent to participation in the study. The diagnosis of PBC was based on the criteria of Lindor et al. [26]. AIH was diagnosed on the basis of the simplified criteria described by the International AIH Group [27]. The diagnosis of PSC was based on the criteria of Lindor et al. [28], and the criteria of Boberg et al. were used to diagnose overlap syndromes [29]. Exclusion criteria were: a) multifactorial liver disease (other than an overlap syndrome); b) ascitic decompensation; c) previous liver transplantation (OLT); d) pregnancy; e) liver tumors; f) alcohol abuse

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