



Factors associated with the impossibility to obtain reliable liver stiffness measurements by means of Acoustic Radiation Force Impulse (ARFI) elastography—Analysis of a cohort of 1031 subjects

Simona Bota*, Ioan Sporea¹, Roxana Sirli¹, Alina Popescu¹, Mirela Danila¹, Ana Jurchis¹, Oana Gradinaru-Tascau¹

Department of Gastroenterology and Hepatology, "Victor Babes" University of Medicine and Pharmacy Timisoara, Romania

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ABSTRACT

Introduction: Acoustic Radiation Force Impulse (ARFI) elastography is a non-invasive technique for liver fibrosis assessment.

Aim: To assess the feasibility of ARFI elastography in a large cohort of subjects and to identify factors associated with impossibility to obtain reliable liver stiffness (LS) measurements by means of this technique.

Methods: Our retrospective study included 1031 adult subjects with or without chronic liver disease. In each subject LS was assessed by means of ARFI elastography. Failure of ARFI measurements was defined if no valid measurement was obtained after at least 10 shots and unreliable in the following situations: fewer than 10 valid shots; or median value of 10 valid measurements with a success rate (SR) < 60% and/or an interquartile range interval (IQR) \geq 30%.

Results: Failure of LS measurements by means of ARFI was observed in 4 subjects (0.3%), unreliable measurements in 66 subjects (6.4%), so reliable measurements were obtained in 961 subjects (93.3%). In univariate analysis, the following risk factors were associated with failed and unreliable measurements: age over 58 years (OR = 0.49; 95% CI 0.30–0.80, $p = 0.005$), male gender (OR = 0.58; 95% CI 0.34–0.94, $p = 0.04$), BMI > 27.7 kg/m² (OR = 0.23, 95% CI 0.13–0.41, $p < 0.0001$). In multivariate analysis all the factors mentioned above were independently associated with the risk of failed and unreliable measurements.

Conclusions: Reliable LS measurements by means of ARFI elastography were obtained in 93.3% of cases. Older age, higher BMI and male gender were associated with the risk of failed and unreliable measurements, but their influence is limited as compared with Transient Elastography.

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1. Introduction

Acoustic Radiation Force Impulse (ARFI) elastography is a non-invasive method for liver fibrosis assessment, valuable for predicting significant and severe fibrosis and with excellent results for predicting liver cirrhosis [1–3]. This elastographic technique has

applications also in other organs, such as spleen [4,5], thyroid [6,7], breast [8], kidney [9] or prostate [10].

The principle of ARFI elastography is based on the compression of the examined tissue that induces a smaller strain in hard tissues than in soft ones. The ultrasound probe automatically produces an acoustic “push” pulse that generates shear-waves which propagate into the tissue. Their speed, measured in meters/second (m/s), is displayed on the screen. Also, shear wave speed may be quantified, in a precise anatomical region, focused on a region of interest, with a predefined size (10 mm in length and 5 mm in width), provided by the system [11,12].

Published studies showed high percentages of patients in whom liver stiffness (LS) could be evaluated by means of ARFI elastography [13–16], but no data are available regarding the factors associated with the impossibility to obtain reliable LS measurements by means of this elastographic technique.

The aim of this study was to assess the feasibility of ARFI elastography in a large cohort of subjects and to identify factors associated

* Corresponding author at: Department of Gastroenterology, University of Medicine and Pharmacy, 2, Intrarea Martir Angela Sava str., 300742 Timisoara, Romania. Tel.: +40 721 656147; fax: +40 256 488003.

E-mail addresses: bota.simona1982@yahoo.com, simona.doctor@yahoo.com (S. Bota), isporea@umft.ro (I. Sporea), roxanasirli@gmail.com (R. Sirli), alinamircea.popescu@gmail.com (A. Popescu), mireladanila@gmail.com (M. Danila), ana.jurchis@yahoo.com (A. Jurchis), bluonmyown@yahoo.com (O. Gradinaru-Tascau).

¹ Address: 10, Bd. Iosif Bulbuca, 300736 Timisoara, Romania. Tel.: +40 256488003; fax: +40 256488003.

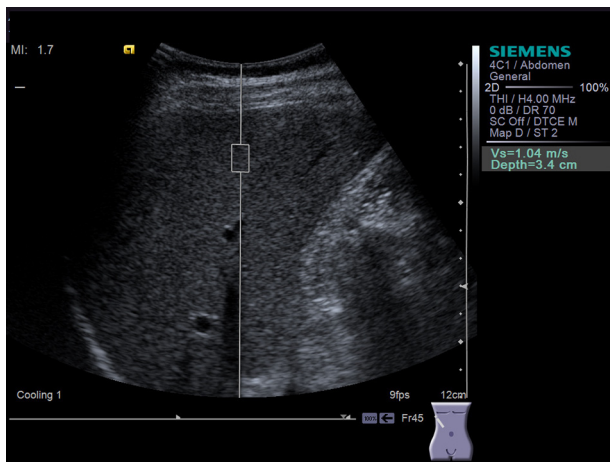


Fig. 1. Liver stiffness measurement by means of ARFI elastography (valid measurement).

with impossibility to obtain reliable LS measurements by means of this technique.

2. Subjects and methods

2.1. Subjects

Our retrospective study included 1031 adult subjects with or without chronic liver disease evaluated in our department between October 2009 and December 2012. We included in our study: healthy volunteers – defined as subjects without a history of hepatopathies, with a normal abdominal ultrasound, but additional tests as aminotransferases or viral markers were not performed; patients with chronic hepatitis B and C evaluated by means of ARFI elastography and liver biopsy (LB); patients diagnosed with liver cirrhosis by means of clinical, biological, ultrasound, endoscopic and/or laparoscopic criteria; patients with non-cirrhotic ascites – including patients with demonstrated peritoneal carcinomatosis with histological proof, acute pancreatitis with ascites, which was later resolved, or lymphatic ascites; and patients with focal liver lesions in the absence chronic liver disease.

At the time of ARFI measurements, besides the epidemiological and demographic data, the following serum biological parameters were determined in all subjects included in our study, with the exception of healthy volunteers: aminotransferases, alkaline phosphatase, gamma-glutamyl transpeptidase, total bilirubin, albumin, cholinesterase, prothrombin time.

All subjects signed an informed consent; the study was approved by the local Ethics Committee and was in accordance with the Helsinki Declaration of 1975.

2.2. ARFI elastography

ARFI was performed in all patients, in fasting condition, with a Siemens Acuson S2000™ ultrasound system (Siemens AG, Erlangen, Germany), software version 2.0, with a 4C1 ultrasound probe. Scanning was performed between the ribs with the patient in supine position, in the Vth or VIIIth segment of the right liver lobe, 1–2 cm under the capsule, with minimal scanning pressure applied by the operator, while the patients were asked to stop breathing for a moment, in order to minimize breathing motion. In every patient, we aimed for 10 valid acquisitions in the same place of the right liver lobe, and a median value was calculated, the result being measured in m/s (Fig. 1). If the measurement was not valid, “X.XX” was displayed on the screen (Fig. 2).

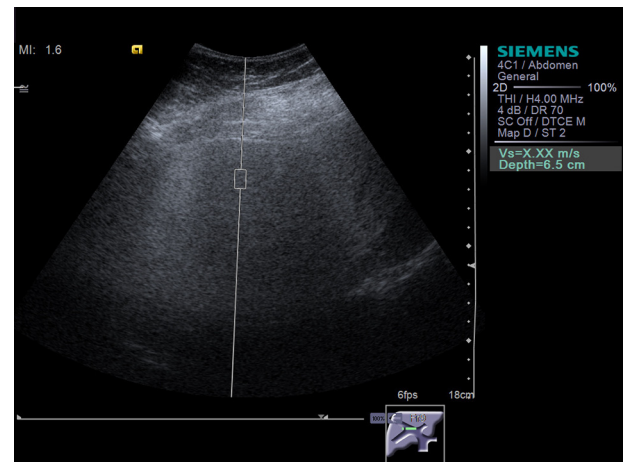


Fig. 2. Invalid liver stiffness measurement by means of ARFI elastography in an obese subject.

Even if the device's manufacturer did not make any indication regarding the quality of ARFI measurements, published studies [17,18] demonstrated that to have a better concordance of LS measurements by means of ARFI elastography with histological fibrosis, quality parameters should be used, similar with Transient Elastography (TE) measurements. The quality parameters that we used were: interquartile range interval (IQR = the difference between the 75th percentile and the 25th percentile, essentially the range of the middle 50% of the data) and success rate (SR = the ratio of valid shots to the total number of shots).

Reliable ARFI measurements were defined as: median value of 10 valid LS measurements with a SR \geq 60% and an IQR < 30%. Failure of ARFI measurements was defined as no valid measurement obtained after at least 10 shots, and a measurement was considered as unreliable in the following situations: fewer than 10 valid shots; or median of 10 valid measurements with SR < 60% and/or IQR \geq 30%.

The operators who performed ARFI measurements were blinded to all patients' clinical, serologic, and histological data.

2.3. Abdominal ultrasound

Abdominal ultrasound examination was performed in all subjects included in the study by using a Siemens Acuson S2000™ ultrasound system (Siemens AG, Erlangen, Germany) with a 4C1 ultrasound probe. We recorded in all cases the liver structure, the presence of focal liver lesions, the presence of ascites, and the antero-posterior diameter of the spleen.

2.4. Liver biopsy

Liver biopsy was performed echo-assisted in the same session with ARFI measurements in patients with chronic hepatitis B and C, using Menghini type modified needles, 1.4 and 1.6 mm in diameter.

The LBs were assessed according to the Metavir score, by a senior pathologist, blinded to the results of ARFI measurements and to all patients' clinical, serologic, and histological data. Fibrosis was staged on a 0–4 scale: F0 – no fibrosis; F1 – portal fibrosis without septa; F2 – portal fibrosis and few septa extending into lobules; F3 – numerous septa extending to adjacent portal tracts or terminal hepatic venules and F4 – cirrhosis..

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