Spleen assessment by Acoustic Radiation Force Impulse Elastography (ARFI) for prediction of liver cirrhosis and portal hypertension

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Abstract

Aim: To establish the values of spleen stiffness (SS) assessed by Acoustic Radiation Force Impulse (ARFI) in healthy subjects and in cirrhotic patients, and to evaluate its predictive value for the presence of cirrhosis and for the presence and severity of esophageal varices (EV).

Patients and methods: Our study included 82 subjects (15 healthy volunteers, 57 cirrhotic patients, 10 with various grade of liver fibrosis), 38 women and 44 men. Of these, 42 cirrhotic patients had varices, 30 had significant EV and 11 had a history of variceal bleeding. We performed 10 measurements in each patient expressed in meters/second (m/s) and a median value was obtained.

Results: The mean SS values (m/s) were: 2.04±0.28 in healthy subjects and 3.10±0.55 in cirrhotic patients (p<0.001). For a cut-off value of >2.51 m/s of SS, ARFI had 85.2% Se, 91.7% Sp, 95.8% PPV, 73.3% NPV, 87.1% accuracy (AUROC=0.91) for predicting liver cirrhosis. No significant differences regarding SS were observed between patients with and without EV, also between those with and without a history of variceal bleeding.

Conclusion: SS evaluated by means of ARFI had a very good predictive value for the presence of cirrhosis (AUROC=0.91, accuracy=87.1%), but could not predict the presence or severity of EV, also the risk of variceal bleeding.

Keywords: spleen stiffness, liver stiffness, liver cirrhosis, esophageal varices, ARFI (Acoustic Radiation Force Impulse)

Introduction

In chronic hepatopathies, the evaluation of liver fibrosis is essential. Until some years ago, the evaluation of fibrosis was made only by liver biopsy (LB), considered to be the “gold standard” for hepato pathological evaluation [1], but in the latter years non-invasive methods (recently developed) are beginning to replace this invasive procedure. The non-invasive methods for the evaluation of liver fi-
brosis using ultrasound waves are: transient elastography (TE) (FibroScan) [2,3,4]; SonoElastography (Real-Time Tissue Elastography) (RT-E) [5-9] and ARFI (Acoustic Radiation Force Impulse Elastography) [10-13].

ARFI imaging technology involves the mechanical excitation of tissue using short-duration acoustic pulses (push pulses) in a region of interest chosen by the examiner, producing shear waves that spread away from the region of interest, generating localized, micron-scale displacements in the tissue [14,15]. Simultaneously, detection waves of lower intensity than that of the push pulse are generated. The push pulse uses a few hundred cycles and different voltage compared to the short cycle B-mode pulse. The moment of interaction between the shear waves and detection waves marks the period of time elapsed between the generating of shear waves and their entire crossing of the region of interest. By recording the shear wave front at several locations and correlating these measurements with the elapsed time, the shear wave velocity (m/s) can be quantified; generally, the stiffer a region in the tissue, the greater the shear wave velocity as it travels through this region [13,16-18].

Aim:
The aim of this paper was to establish the values of spleen stiffness assessed by ARFI in healthy subjects, in patients with liver cirrhosis and to evaluate its predictive value for the presence of cirrhosis, the presence and severity of esophageal varices (EV) and the risk of bleeding due to ruptured varices.

Patients and methods:
We obtained written informed consent from all the subjects involved in the study and the approval of the University Ethics Committee.

We studied a number of 82 subjects, mean age 52.4±15 years, 38 women and 44 men. In each patient we measured liver stiffness (LS) by means of ARFI in the right liver lobe, 1cm below the liver capsule, by intercostal approach, with the patient lying in left lateral decubitus (fig 1); and spleen stiffness (SS) by means of ARFI, 1 cm under the spleen capsule, by intercostal approach, with the patient laying in right lateral decubitus (fig 2). ARFI measurements were performed with a Siemens Acuson S2000ultrasound system. In each patient 10 valid ARFI measurements were performed in the liver and in the spleen and the median values were calculated, the results being expressed in meters/second (m/s).

Our study included 15 healthy volunteers, without known liver pathology, 10 patients with various degrees of liver fibrosis (patients with liver biopsy) and 57 patients with liver cirrhosis. 52 had had recent gastroscopies (in the last 6 months). Of them, 42 (73.6%) had varices, 30 (52.6%) had significant EV (grade II or III) and 11 (19.2%) had a history of variceal bleeding.

The data we obtained from our patients were collected in a Microsoft Excel file, the statistical analysis being performed using the MedCalc program. ARFI measurements were numeric variables, so the mean and standard variation were calculated. The t test was used to compare the ARFI values.

The diagnostic performances of ARFI elastography were assessed by using receiver operating characteristics (ROC) curves that were built for the detection of cirrhosis. Optimal cut-off values were chosen to maximize the sum of Sensitivity (Se) and Specificity (Sp). Se, Sp positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated according to standard methods. Exact confidence intervals (CI) of 95% were calculated for each predictive test and used for comparing AUROC curves.
Results:

In 4 of the subjects we could not obtain valid measurements (4.8%), due to the poor cooperation of the patient and ultrasound window. Table I presents the means values of ARFI in the spleen (in those 78 patients with valid measurements) according to the liver pathology.

We observed a statistically significant difference between SS in subjects without hepatic pathology and those with liver cirrhosis (p<0.001), between healthy volunteers and the patients with chronic hepatopathies with various degrees of fibrosis (p=0.03) and between the cirrhotic patients and those with various degrees of fibrosis (p<0.001).

The best SS cut-off value for predicting cirrhosis was 2.51 m/s (AUROC 0.91, p<0.0001, with 85.2% Se, 91.7% Sp, 95.8% PPV, 73.3% NPV and 87.1% accuracy) (fig 3).

Regarding LS evaluated by means of ARFI, for a cut-off value of 1.8 m/s (values resulted from our previous studies) [19], LS had 96.4%Se, 92%Sp, 96.4%VPP, 92% VPN and 95% accuracy for predicting cirrhosis.

Using LS and SS combined values for predicting cirrhosis under cut-off values mentioned are obtained on these sensitivity and specificity: when one of the methods are positive-98.1%Se, 95.8%Sp, 98.1%VPP, 95.8%VPN and 95% accuracy and when the both methods are positive-94.7%Se, 96%Sp, 98.1%VPP, 88%NPV and 95% accuracy.

No significant differences were observed regarding the mean SS values in patients with and without EV (p=0.16), also between those with different degrees of EV (grad I vs. grad II-p=0.88, grad I vs. grad III-p=0.46 and grad II vs. grad III-p=0.37).

No significant differences were found between the mean SS values in cirrhotic patients with esophageal varices regarding the history of variceal bleeding (p=0.53) (Table III).

No significant differences were observed regarding the mean SS between patients with liver cirrhosis without varices or small varices (grad I) and those with large varices (grad II and III): 3.02±0.64 m/s vs. 3.21±0.50 m/s (p=0.23).

Discussions

In a meta-analysis performed by Friedrich-Rust [20] and co-workers on 50 studies, Transient Elastography (TE)-FibroScan had a very good predictive value for the diagnosis of liver cirrhosis (AUROC=0.94).

Stefanescu et al [21] used TE, to determine SS in cirrhotic patients and its use in predicting the presence of esophageal varices. The study included 135 cirrhotic patients and for a cut-off value> 52.5 kPa, SS predicted the presence of EV with 75.2% accuracy. For a LS value>
28 kPa the presence of EV was predicted with 72.2% accuracy. Using the LS and SS combined, with the cut-off values mentioned above, the presence of EV in cirrhotic patients was predicted with 89.6% accuracy.

Calvaruso et al [22] also published a study using FibroScan determination in spleen and liver for predicting cirrhosis and esophageal varices. For a cut-off value of 47 kPa, SS had 79% Se and 70% Sp for predicting cirrhosis. The AUROC curve of LS and SS for predicting the presence of EV had similar values (0.76 vs. 0.73), but LS had higher sensitivity than SS (0.84 vs. 0.72) for predicting the presence of large varices.

In our study, ARFI technique had a good predictive value for the diagnosis of cirrhosis, with 85.2% Se, 91.7% Sp and 87.1% accuracy (AUROC = 0.91). The accuracy increased when we combined SS with LS, but we could not predict the presence of EV or variceal bleeding occurrence.

Gallotti et al [23] performed the first ARFI measurements in the spleen and they have published the only existing article in the literature so far. SS as well as the stiffness of other abdominal organs (liver, spleen, kidney, and pancreas) were evaluated in 35 healthy volunteers, the mean values being 2.44 m/s which conferred to the spleen the status of the toughest abdominal organ. In our study we obtained slightly lower SS values in patients without liver pathology (2.04 ± 0.28 m/s).

**Conclusions**

SS assessment by means of ARFI can be performed in most of the patients (95.2%). In our study, for a cut-off value of 2.51 m/s, SS evaluated by means of ARFI had a very good predictive value for the presence of cirrhosis (AUROC = 0.91, accuracy = 87.1%). The accuracy for the diagnosis of liver cirrhosis increased in combination with LS. These data suggest that SS evaluated by means of ARFI can be used in patients with indeterminate ARFI or TE measurements in the liver. Also, in our study no significant differences were found between SS mean values in cirrhotic patients with and without esophageal varices, with or without a history of variceal bleeding. Further studies are needed to confirm these data.

**Conflict of interest:**

None

**References**


