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# Can Shear -Wave Elastography be used to detect liver decreased stiffness in liver due to hepatic steatosis?

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**Introduction:**

The most common liver disorder in developed countries is the Non-alcoholic fatty liver disease (NAFLD) [1,2]. Insulin resistance and the metabolic syndrome are both related to NAFLD [3]. The disease occurs up to 80% of obese people [4]. The most extreme form of NAFLD is Non-alcoholic steatohepatitis (NASH) which is the major cause of cirrhosis of the liver of unknown cause [5]. More commonly NAFLD is detected routine blood tests followed by diagnosed abnormal liver function tests. In the presence of insulin resistance and metabolic syndrome (obesity, combined hyperlipidemia, diabetes mellitus (type II), and high blood pressure ) NAFLD may seen often [3,5]. A spectrum of disease activity is being considered to cover in NAFLD. This spectrum begins as fatty accumulation in the liver (hepatic steatosis). A liver can remain fatty liver could work without any disturbing liver function, but by varying mechanisms and possible insults to the liver may also progress to become non-alcoholic steatohepatitis (NASH), a state in which steatosis is combined with inflammation and fibrosis (steatohepatitis). NASH is a progressive disease: over a 10-year period and also up to 20% of patients with NASH may develop cirrhosis of the liver, and 10% will suffer death related to liver disease [6].

**Materials and Methods:**

The study was approved by the Institutional Ethics Committee, and all volunteers provided with written informed consent. In this prospective study, 110 patients with NAFLD, followed by a general internal medicine outpatient clinic (57 male 53 female mean age 50,17) and a control group of 50 healthy adults (26 males 24 females mean age 48,26) without liver disease and sonographically grade 0 steatosis were admitted to the study. Anyone having any other liver diseases (HBV, HCV infection, chronic alcohol abuse, cholestatic chronic hepatitis, autoimmune chronic hepatitis, haemochromatosis, Wilson's disease) and using any medication were excluded from the accompanying study in patients groups. Volunteers selected were completely healthy. Radiological evaluation in the liver of the study and the control group was carried out between November 2015 and April 2016.

B Mode Ultrasound Grading of diffuse hepatic steatosis on ultrasound has been used to communicate to the clinician about the extent of fatty changes in the liver. Grade I; increased hepatic echogenicity with visible periportal and diaphragmatic echogenicity, grade II; increased hepatic echogenicity with imperceptible periportal echogenicity, without obscuration of diaphragm, grade III; increased hepatic echogenicity with


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imperceptible periportal echogenicity and obscuration of diaphragm. Craniocaudal lenght of the liver was measured midclavicular line averages 10-12,5 cm. Any liver that had a craniocaudal length longer than 15.5 cm in the midclavicular line was considered enlarged.

**ARFI measurement (Acoustic Radiation Force Impulse Imaging)**

The patients and control subjects underwent an ARFI examination using a commercial scanner (Siemens Acuson S3000™ 4 MHz (6C1) probe, Siemens Medical Solutions USA, Inc., Mountain View, CA, USA), which was performed by an US physician with three months of experience in ARFI elastography. The patients were examined in the left lateral decubitus position with the right arm elevated above the head. Scanning was performed with minimal scanning pressure applied by the operator; the patients were asked to stop breathing to minimize motion. The operator positioned the probe over the following region of interest: right lobe of the liver parenchyma, away from motioand vessels, including at least two times every segment at a depth between 3.0 and 4.0 cm. Ten SMV measurements were made for each person. A median value was calculated for every patient. SMV average values were obtained in all patients. Quantitative assessment of the tissue stiffness was made with VTQ. In VTQ, an acoustic push pulse and detection pulses were used to calculate SWV, which increases with increasing tissue stiffness. The presence of steatosis and ratings were determined by sonographic criteria.

**Laboratory tests:**

SMV values and laboratory values simultaneously received were compared. Routine liver function tests were performed immediately and patients with elavation of aminotransferases (ALT and AST) > 5 times the upper limit of normal were excluded from the further examination. Lipid profile were examined for triglycerides, very low density lipoprotein (VLDL ), low density lipoprotein (LDL), and total cholesterol. We calculated body mass index (BMI) of patients and control group.

**Statistical analysis**

Statistical analysis was performed using SPSS 14.0 software package (SPSS Inc, Chicago, IL, USA). Data were expressed as means ± standard deviation (SD) $p< 0.05$ was considered statistically significant. The normal distribution for each variable was examined via the Kolmogorov-Smirnov test.

Spearmann correlation was used. However, it was not used to compare the normal and pathology groups; instead it was used to reveal one to one interrelationships between SMW values and other variables. Student's t-test and analysis of variance (ANOVA) were used for continuous variables with normal distribution. Nonparametric tests (Mann–Whitney U test and Kruskal Wallis test) were used for variables that were not normally distributed in the studied population.

**Results:** SMV values average speed value is calculated to be 2,26 ± 0.57 m/s in patient group (Fig-1); 1.71 ± 0.34 m/s in the control group (Fig-2), (Table-I);

| | n | SMV Mean | SD |
|---|---|---|---|
| Patient | 110 | 2,260 | 0,565 |
| Control | 50 | 1,706 | 0,336 |

**Table I**: SMV values in patient and control groups.

**Figure 1:** Image of liver stiffness measurement by ARFI in patients with hepatic steatosis ( SMV: 2,50 m/sn).

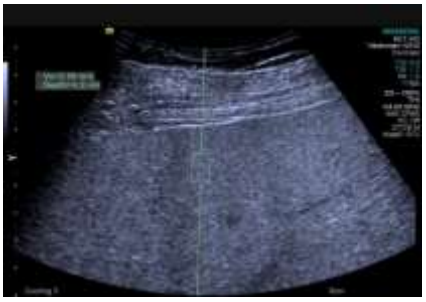


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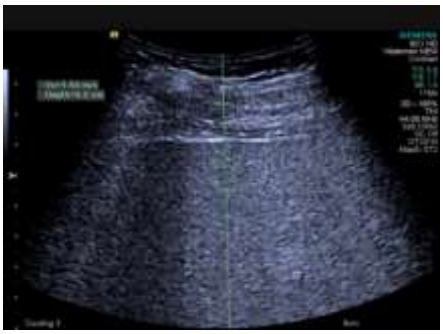
**Figure 2:** Image of liver stiffness measurement by ARFI in control group (SMV: 1,50 m/sn).



SMV values average speed value is calculated 2,15 ± 0.63 m/s in patients with grade I steatosis; 2.25 ± 0.42 m/s in patients with grade II steatosis, 2.72 ± 0.43 m/s in patients with grade III steatosis (Table-II).

| Liver Grade | N | SMV Mean | Std. Deviation | Std. Error |
|---|---|---|---|---|
| | | | | |
| 1,00 | 43 | 2,1513 | ,63535 | ,06501 |
| 2,00 | 54 | 2,2551 | ,42632 | ,08646 |
| 3,00 | 13 | 2,7285 | ,43556 | ,12080 |
| Total | 110 | 2,2601 | ,56501 | ,05387 |

**Table II:** SMV values in the degree grade of hepatic steatosis SMV values indicate a statistically significant difference in patient and control groups (p < 0,003) (Table-III).

**Table III:** SMV values indicate a statistically significant difference in patient and control groups (p < 0,003).

| SMV | Sum of Squares | df | Mean Square | F | Sig. |
|---|---|---|---|---|---|
| Between Groups | 3,492 | 2 | 1,746 | 5,968 | ,003 |
| Within Groups | 31,304 | 107 | ,293 | | |
| Total | 34,796 | 109 | | | |

SMV values with statistically insignificant differences were detected between the degrees of hepatic steatosis grade.

The triglicerid (p < 0,000), AST (p < 0,000), ALT (p < 0,001) show a significant difference between normal and pathological groups for SMV mean values. Liver craniocaudal length with increased triglycerides (p < 0,021), VLDL (p < 0,043), AST (p < 0,012) and ALT (p < 0,029) showed a statistically significant correlation with each increase in value.

The trigliserid, VLDL, AST, ALT show a significant difference between normal and pathological groups for hepatomegaly liver size mean values. Similarly, the grade increases with increasing degree of liver craniocaudal length and an increasing values of BMI, AST and ALT. Hence, an increase in the value of SMV indicated a statistically significant correlation. SMV values did not indicate any statistically significant difference between the groups with normal BMI and those with high BMI values. SMV values did not show any statistically significant difference between patients with hepatomegaly andthose having normal liver sizes.

**Discussion:**

Liver biopsy is not recommended in NAFLD patients because of conventional Bmode imaging can be inaccurate in NAFLD patients and due to its risk of complications. To measure liver stiffness which is a phenomenon which correlates well with liver fibrosis, astutely combined elastography and conventional B-mode ultrasonography which called ARFI elastography is a promising imaging technology, a phenomenon which correlates well with liver fibrosis [7,8,9]. In this systematic review and meta-analysis, we found that ARFI elastography was modestly accurate (i.e., summary sensitivity: 80.2%; summary specificity: 85.2%; diagnostic odds ratio: 30.13) in detecting significant fibrosis (defined as 4>F≥2) in NAFLD patients. The SWV increases with the degree of fibrosis observed by histopathology was shown in the vast majority of studies [10,11]. Thus, ARFI elastography provides both a qualitative measure of displacement as well as a quantitative measure of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SMV as opposed to conventional elastographic methods, which provides an advantage in assessing hepatic fibrosis [8,9]. In the presence of steatosis and hepatic inflammation in the NAFLD liver,SMV measurement by ARFI elastography may be complicated and it shown in the previous studies [7,10]. Although Palmeri et al. [11] found no relationship between SMV values and hepatocyte ballooning or inflammation another study reported significant SMV decreases in proportion to increasing steatosis severity [7,12]. Some of NAFLD patients with different hepatic inflammatory activity levels shows significantly varied SMV values [1,13]. Therefore, based on the foregoing evidence, steatosis appears to decrease SMV values, while hepatic inflammation and steatosis appears to increase SMV values in NAFLD patients undergoing ARFI elastography [7]. Our study demonstrates in NAFLD patients that ARFI elastography was modestly accurate in detecting significant fibrosis, this type of data is not typically reported in ARFI elastography studies thats why we could not specifically assess the effects of steatosis and hepatic inflammation upon ARFI elastography's accuracy. Therefore, future trials of ARFI elastography in NAFLD patients should histopathologically assess hepatic inflammation and steatosis in order to better determine their effects upon SMV values. There are several limitations to this study. First, this study has not been extensively investigated in NAFLD patients because ARFI elastography is a relatively new technology. Second, this study could not provide a head-to-head comparison of ARFI elastography versus transient elastography, RTE, MRE, or other more novel elastographic imaging technologies (e.g.. two-dimensional shear wave elastography, strain elastography) in NAFLD patients due to the paucity of these comparative trials [7,10]. Third, as the included studies failed to report on observed technical failures of ARFI elastography (if any), we are uncertain as to whether any technical failures did occur, and if so, what the nature of such technical failures were. Fourth, previous research has reported losses in diagnostic accuracy in obese patients [10,14,15]. Aim of this study was to assess the use of ARFI elastography in detecting decreased stiffness in liver on NAFLD patients. SMV values were compared to liver biopsy in previous studies in the evaluation of fatty liver fibrosis. Our case series is more than the other study which was planned as non-invasive. As conclusion, the presence and severity of hepatic steatosis measured shear wave velocity values by ARFI elastography. SMV values were increased with the degree of hepatic steatosis. ARFI imaging can be used as a preliminary assessment examination with laboratory tests and at least 10 measurements, using the average value so that it may be more accurate. To detect decreased stiffness in liver (on average 2 and over SMV values) with increased of triglycerides, AST and ALT in patients ARFI can be most usefull. This study shows that ARFI is a useful non-invasive tool for evaluation of decreased stiffness in liver on NAFLD.

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