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Assessment of Liver Stiffness by Shear Wave Elastography in Healthy Liver in a Tertiary Center

Adhikari K, Devkota K, Koirala S

Department of Radiodiagnosis and Imaging, BPKIHS, Dharan

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ABSTRACT

Introduction:
The main aim of this study was to determine the mean value of liver stiffness in healthy adults using S-Shear wave elastography and compare liver stiffness with gender, age and BMI.

Methods:
A hospital-based cross-sectional study was carried out in the Department of Radiology, BPKIHS over 6 months after taking ethical approval from the institutional review committee. Ninety-six adults referred for ultrasonography of the abdomen for various indications were included in the study

Results:
Mean shear wave velocity of the healthy liver in the study subjects was 1.267±0.151m/s.The corresponding mean value of liver stiffness was 4.91±1.15 kPa. The mean liver stiffness was higher in males compared to females (5.283±1.08 kPa vs. 4.689±1.13 kPa) which were statistically significant (p=0.0013). Mean liver stiffness was highest in the age group of 70-79 years (6.7±0.80 kPa) compared to other age groups. There were significant differences between the mean liver stiffness values among different age groups (p=0.01). Patients in the obese class I category showed higher mean liver stiffness value (5.54±0.42 kPa) than other BMI categories. However, mean liver stiffness values showed no significant difference among different BMI groups (p=0.322).

Conclusions:
Liver stiffness values measured using S-Shear wave elastography in healthy adults ranged between 2.4 kPA to 7.4 kPa.There were significant differences in mean liver stiffness values between men and women and among different age groups. However, no significant difference was found among different BMI categories.

Keywords: *Elastography; Shear Wave; Liver Stiffness*

Correspondence to: Dr Kapil Adhikari
Department of Radiodiagnosis and Imaging
BPKIHS
Dharan-18, Nepal
Email: *adhkapil123@gmail.com*

INTRODUCTION

Chronic liver disease is a common occurrence in our part of the world. Liver fibrosis is the main pathology behind the chronic liver disease.[1] Therefore, it is important to determine the severity of liver fibrosis for staging chronic liver disease which will be helpful for the clinician in taking the therapeutic decision and for determining the prognosis of the patients. A liver biopsy is still considered the gold standard method for establishing the diagnosis of hepatic fibrosis, especially in patients with chronic liver disease. However, a liver biopsy is an invasive procedure which is associated with an increased risk of complications.[2]

Shear wave elastography (SWE) is a non-invasive alternative to liver biopsy for the evaluation of liver stiffness and hence determine liver fibrosis. SWE is a technology that detects the velocity of the shear wave propagated through a targeted area in tissue and the shear wave propagation speed is used to calculate the stiffness of the tissue.[3] SWE displays the numerical measurement of elasticity (stiffness) as either shear wave velocity (m/s) or as Young's Modulus in kPa.[4] S-shear wave elastography (S-SWE; Samsung Medison Co. Ltd., Seoul Korea) is a recently developed shear wave elastography method. It is based on the same technical principle as the other point shear-wave methodologies using acoustic radiation pulse impulse imaging techniques.[5] To differentiate a healthy liver from a fibrotic liver, it is necessary to determine the normal values of liver stiffness in healthy individuals.[6] This study will determine the mean value of liver stiffness in healthy adults by using S-SWE and compare liver stiffness with gender, age and BMI.

METHODS

Ninety-six adults referred for ultrasonography (USG) of the abdomen for various indications from the inpatient and outpatient departments were included in our study after the exclusion of the patient with a history of liver disease, altered liver function, fatty changes in the liver and splenomegaly. The study was carried out over 6 months after ethical approval from the institutional review committee (IRC). Elastography was performed using a convex probe (CA1-7A) in Samsung's RS80A with Prestige ultrasound system using S- Shearwave technology. Patients were positioned in the left lateral decubitus position and scanning was done by intercoastal approach. Patients were kept nil per orally (NPO) at least 4 hours before the scan. The region of interest (ROI) box was placed in the right lobe of the liver >2 cm below the liver capsule away from any vasculature. (Figure 1) Ten valid shear wave velocity (m/s) measurements were taken. The measurements were conducted while the patient suspended respiration. The velocity of the shear wave was used to calculate the stiffness (kPa) of the targeted area within the ROI. Only the measurements with IQR (interquartile range interval) ≤30% and Reliability Measurement Index (RMI) ≥0.4 were considered reliable. (Figure 2) Numerical Data was collected in a Microsoft Excel file and statistical analysis was performed using Statistical Program for the Social Sciences (SPSS). Mean and standard variations of liver stiffness (kPa) according to different age groups, BMI and gender were tabulated. Student t-test was used to compare the mean stiffness values(kPa) between males and females and one-way analysis of variance (ANOVA) was to compare mean stiffness values among different age groups and body mass index (BMI) categories. P value <0.05 was considered statistically significant.

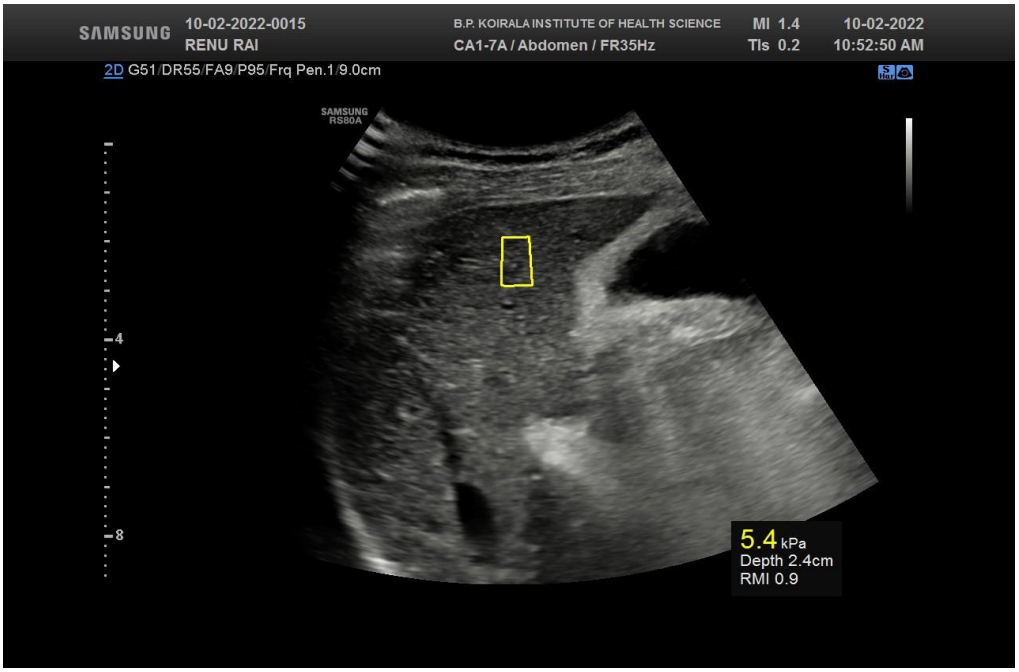

Figure 1: *Method of measuring S-SWE in the healthy liver where ROI box placed 2.4cm from the liver capsule and liver stiffness expressed in kPa with corresponding RMI of 0.9*

Figure 2: *Illustration of ten valid S-shear wave measurements with RMI >0.4 and IQR <30% taken at the depth of 2.3-2.5 cm from the liver capsule and median stiffness of liver expressed in kPa and m/s*

RESULTS

Out of 96 adult patients, there were 37(38.5%) male and 59(61.5%) female patients and their mean age was 43.41±15.05 years. Most patients (23 cases, 24%) were in the age group of 18-29 years. Likewise, 60 patients (62.5%) had normal BMI, 23 patients (24%) were overweight, 7 patients (7.3%) were class I obese and 6 patients (6.3%) were underweight. All 96 patients (100%) had valid liver stiffness measurements with an IQR <30% for kPa values with RMI ranging between 0.4 to 1. The mean depth of ROI from the liver capsule was 3.46±0.76 cm (depth ranging between 2.3 to 5.8 cm). The overall mean shearing wave velocity of the healthy liver in the study subjects was 1.267 ± 0.151m/s with values ranging between 0.89 to 1.57 m/s. The corresponding mean value of liver stiffness was 4.91±1.15 kPa with values ranging between

2.4 to 7.4 kPa. The mean liver stiffness value was higher in males compared to females (5.283 ±1.08 kPa; 1.316±0.14 m/s in males vs. 4.689±1.13 kPa; 1.236±0.15 m/s in females) which was statistically significant (p=0.0013 for kPa; p=0.001 for m/s). Mean liver stiffness was highest in the age group of 70-79 years (6.7 ± 0.80 kPa, 1.49± 0.92 m/s) compared to other age groups as shown in table 1. We found significant differences between the mean sliver stiffness values among different age groups (p=0.01 for kPa; p=0.002 for m/s). Patients in the obese class I category showed higher mean liver stiffness value (5.54±0.42 kPa, 1.35±0.04 m/s) compared to other BMI categories as shown in table 2. However, mean liver stiffness values showed no significant difference among different BMI groups (p=0.322 for kPa and p=0.312 for m/s).

Table 1. Liver stiffness values (kPa and m/s) of healthy adult livers by age group

Age group n=96	18-29 n=23	30-39 n=20	40-49 n=22	50-59 n=17	60-69 n=9	70-79 n=4	80-89 n=1	p-value
Mean ± SD (kPa)	4.37± 1.08	5.21±1.22	4.75±0.88	4.75±1.21	5.64±0.45	6.70±0.80	4.30	0.01
Mean ± SD (m/s)	1.19±0.15	1.30±0.16	1.24±0.12	1.24±0.15	1.37±0.05	1.49±0.09	1.20	0.002

Table 2. Liver stiffness values (kPa and m/s) of healthy adult livers by BMI category

BMI category	Normal (n=60)	Underweight (n=6)	Overweight (n=23)	Obese class 1 (n=7)	p-value
Mean ± SD (kPa)	4.94± 1.24	4.43±0.32	4.47±1.13	5.54±0.42	**0.32**
Mean ± SD (m/s)	1.27±0.16	1.21±0.04	1.24±0.14	1.35±0.04	**0.31**

DISCUSSION

Several studies have been done previously for the assessment of liver fibrosis using shear wave elastography in chronic liver diseases, however, there are only a few studies done for determining the normal range of liver stiffness in healthy subjects. Previous studies on mean liver stiffness in healthy normal livers using transient elastography (TE) showed values of normal liver ranged from 4.4 kPa to 5.6 kPa (Das et al., Colombo et al. & Kim et al.).[7,8,9] Using Acoustic Radiation Force Impulse (ARFI), the normal liver stiffness values ranged from 1.09 to 1.19 m/s (Madhok et al., Popescu et al., Goertz et al. & Horster et al. 2010).[6,10,11,12] and using shear wave elastography (SWE) the values ranged from 4.1 to 5.1 kPa (Mulabecirovic et al. 2018; Huang et al. 2014).[13,14] Our study revealed that the mean liver stiffness value of normal liver using S-Shear wave elastography (S-SWE) was 4.91±1.15 kPa which is within the range of measurements reported with TE and SWE in the above studies. However, the mean shear wave velocity of the liver in our study was slightly higher (1.267±0.151m/s) than the range of measurements previously reported with ARFI in the above studies.

Our study revealed that the mean liver stiffness was higher in men (5.28±1.08 kPa) than in women (4.68± 1.13 kPa) and the difference between the two groups was statistically significant (p=0.013). A similar finding was also noted in a study by Huang et al. and Colombo et al. where they reported that the median stiffness in men was significantly higher than in women.[8,14] Another study by Madhok et al. among 137 healthy subjects found no statistically significant difference in mean ARFI values between men and women.[6] Popescu et al. and Horster et al. in their studies also did not find gender as an influence of shear wave velocity in healthy subjects.[10,12] These variations in findings among different studies may be the result of different sample sizes, different ethnicities or different elastography techniques like SWE, TE and ARFI.

Multiple studies have been done previously to determine age as a variable factor for influencing liver stiffness in normal subjects. Popescu et al. and Horster et al. in their studies did not find age as an influence on shear wave velocity in healthy

subjects.[10,12] A study by Ling et al. also did not show the difference in liver stiffness values across age groups while a study by Colombo et al. 2011 found higher liver stiffness in the younger age group.[8,15] In our study, mean liver stiffness was highest in the older age group of 70-79 years (6.7±0.80 kPa, 1.49±0.92 m/s) compared to other age groups and the finding was statistically significant (p=0.01 for kPa; p=0.002 for m/s). Similar findings were noted in the study by Roulot et al. where they found higher liver stiffness in the older age group.[16] Bende et al. in their study also reported that age over 40 years was associated with higher liver stiffness.[17] Possibly the cause of higher liver stiffness in older age groups might be hepatic steatosis which is more prevalent in older populations.

In a study by Das et al., they found higher liver stiffness values in healthy subjects with underweight BMI as well as in obese subjects compared with normal-weight subjects.[7] Our study also demonstrated a higher liver stiffness in subjects with class I obesity (5.54±0.42 kPa, 1.35±0.04 m/s) compared to other BMI categories. However, the findings were not statistically significant (p=0.32 for kPa; p= 0.31 for m/s). Various other studies (Kim et al., Popescu et al. & Huang et al.) also found that liver stiffness was not significantly affected by BMI.[9,10,14]

There are a few limitations in our study. In our study, healthy subjects were considered on basis of normal liver function tests and the absence of fatty changes in the liver on ultrasound. A liver biopsy is an ideal choice for confirmation of healthy liver which is not practical in healthy subjects. Since our study was done in a small number of healthy subjects, further larger studies on healthy subjects are required to establish the normal liver stiffness measurement and use it as a reference to differentiate a healthy liver from a fibrotic liver.

CONCLUSION

In our study, the mean liver stiffness value obtained by S-SWE in healthy subjects was 4.91kPa (1.26 m/s) and we found significant differences in mean liver stiffness values between men and women and among different age groups. However, we did not find any significant difference in mean liver stiffness values among different BMI categories.

CONFLICT OF INTEREST

None

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None

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