

DIAGNOSTIC VALUE OF POINT SHEAR WAVE
ELASTOGRAPHY (pSWE) OF THE SPLEEN FOR
ASSESSMENT OF LIVER FIBROSIS IN PATIENTS
WITH CHRONIC VIRAL HEPATITIS

Katia Doykova¹, Daniel Doykov², Silvia Tsvetkova¹,
Vladimir Andonov²✉

Received on May 11, 2021

Presented by D. Damianov, Member of BAS, on July 30, 2021

Abstract

In recent years spleen stiffness (SS), assessed by point shear wave elastography (pSWE) has been a topic of interest as a more accurate indicator for the diagnosis of liver fibrosis in chronic viral hepatitis. For the first time in Bulgaria, a comprehensive research on the stiffness of the liver and spleen has been performed by pSWE in patients with chronic viral hepatitis, as well as evaluation of their correlation with the histological assessment of liver fibrosis. The aim of the research is to establish spleen and liver stiffness in patients with chronic viral hepatitis and their correlation with intermediate stages of liver fibrosis diagnosed histologically after biopsy. For the period 2018–2020, ninety patients with chronic viral hepatitis B and C (mean age 46.20 ± 14.55) from the department of Gastroenterology, University hospital Kaspela, Plovdiv, Bulgaria, have been examined, by abdominal ultrasound, pSWE of the liver and spleen, histological evaluation of liver fibrosis, data study on the presence of esophageal varices and ascites. The liver stiffness (LS) value distinguishing between F1 and F2 was 1.86 m/s ($rs = 0.769$, 95% CI: 0.652–0.850, $p < 0.001$). The spleen stiffness (SS) value distinguishing between F1 and F2 was 2.95 m/s ($rs = 0.838$, 95% CI: 0.749–0.898, $p < 0.001$). Liver stiffness is significantly affected by BMI, which reduces its diagnostic potential in obese patients. Spleen stiffness measured by pSWE can be used in the diagnosis of intermediate stages of liver fibrosis in patients with chronic hepatitis B and C.

Key words: chronic viral hepatitis, elastography, spleen stiffness, liver stiffness

<https://doi.org/10.7546/CRABS.2024.06.12>

Introduction. Chronic viral hepatitis B and C are the most common chronic liver diseases leading to cirrhosis and development of hepatocellular carcinoma. These infections are one of the leading causes of death.

The liver and spleen are connected to each other through the portal circulation. Liver fibrosis, which occurs in the liver parenchyma as a result of chronic damage, leads to portal hypertension. It is logical to assume that there is a correlation between the stiffness of the liver and that of the spleen.

Liver biopsy has been the ‘gold standard’ for the diagnosis of liver fibrosis for decades, although it is associated with a risk of serious complications [1], including a 0.01–1% risk of death [2, 3]. In 2017, the European Federation of Ultrasound Societies in Medicine and Biology approved ultrasound elastography of the liver as an alternative method of liver biopsy for the diagnosis of liver fibrosis. In 2017, EFSUMB established ultrasound elastography as an alternative method for diagnosing and monitoring patients with liver fibrosis [4].

Patients and methods. The study includes 90 patients with chronic viral hepatitis, of which 30 HBV, 30 with HCV and 30 with cirrhosis of viral etiology, with positive serological markers for the presence of chronic viral infection: HbsAg or anti-HCV for at least six months. All patients signed an informed consent to perform a biopsy to determine the stage of liver fibrosis and the activity of inflammation according to the METAVIR classification. Biopsy is not performed on patients with cirrhosis, which corresponds to stage F4 – the diagnosis is made by a specialist gastroenterologist based on anamnestic data, ultrasound signs, biochemical parameters – thrombocytopenia, hyperbilirubinemia, ascites. The control group consisted of 35 healthy adult volunteers with normal liver enzyme levels, negative viral markers, no history of heart, lung, and neoplastic disease, and no alcohol abuse. All patients are over 18 years of age.

Abdominal ultrasound was performed to each participant to assess the size, shape and US structure of the liver and spleen. Detection of structural pathology in the liver or spleen in the course of ultrasound examination is an exclusion criterion from participation. The ventro-dorsal size along the right medioclavicular line for the liver (mm), the longitudinal size of the spleen (mm), the size of the portal vein and the splenic vein (mm), the portal and lienal blood flow velocity (m/s) have been measured.

The study population was stratified according to BMI, following the limit values set by the World Health Organization: under 18.5 (underweight), 18.5–24.9 (normal weight), 25–29.9 (overweight), 30–34.9 (obesity 1), 35–39.9 (obesity 2) and with a body mass index over 40 (obesity 3).

Point shear wave elastography. Liver and spleen stiffness were assessed sequentially by point shear wave elastography (pSWE), which was activated by QElaXto[®] software to an Esaote MyLab[™] 9 eXP ultrasound machine. The same C1-8IQ appleprobe convex transducer was used. Ten elastographic measurements of both organs were performed with a mean interquartile range (IQR/M) validation criterion < 30.



Fig. 1. pSWE of liver (right) and spleen (left) with data on normal parenchyma stiffness with a fixed field of interest. The values of the ten measurements are displayed in sequence on the left side of the screen

The stiffness of the liver and spleen is determined sequentially. The patient is instructed to take a deep breath and hold it until the values are calculated. The field of interest is of fixed size (Fig. 1).

The measurements of the density of both organs are performed by the same software and are calculated in m/s.

Liver biopsy. Single use biopsy guns with a Tru-cut 16Ga needle, 22 mm biopsy length (TSK Laboratory, Japan) were used to perform the liver biopsy. The biopsy contains up to 11 portal spaces in compliance with all safety criteria.

Statistical analysis. The data analysis was performed with the statistical program IBM SPSS, v. 26 (2018), the specialized program for medical analysis MedCalc v. 19.4.1 (2020) and the statistical program Minitab v. 19 (2020). Spearman's rank correlation, Cohen's correlation coefficients, and Kolmogorov–Smirnov test were used.

Results. Demographic data. The study groups were similar in terms of number of patients, distribution by sex and age. Mean age 46.20 ± 14.55 years with an age range between 20 and 83 years, without significant difference in the relative parts of the two sexes, $p = 0.633$.

In healthy controls the values for SS (spleen stiffness) are 2.46 ± 0.22 m/s, and for LS (liver stiffness) – 1.69 ± 0.34 m/s, and in patients with liver cirrhosis the values are, respectively: SS 3.76 ± 0.36 m/s, LS 3.21 ± 0.45 m/s.

Of the two parameters – SS and LS, the second one showed a significant dependence on body mass index, with higher BMI values being associated with higher liver stiffness. Spleen stiffness is not affected by BMI. The results of the correlation analysis show no significant relationship between BMI and spleen stiffness ($r_s = 0.083$, $p = 0.637$) and a high positive relationship between BMI and liver stiffness ($r_s = 0.571$, $p = 0.011$) (Fig. 2).

Correlation between spleen and liver stiffness and histological evaluation. High positive correlations were found between SS and LS and histological

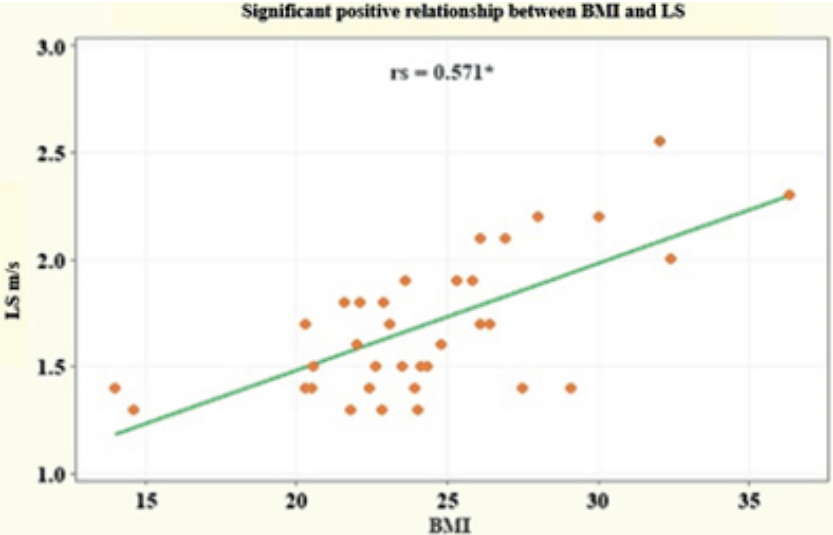


Fig. 2. Relationship between liver stiffness and body mass index

evaluation, but a higher degree of consistency was observed between SS and histological evaluation ($rs = 0.838$, 95% CI: 0.749–0.898, $p < 0.001$) compared to that between LS and histological evaluation ($rs = 0.769$, 95% CI: 0.652–0.850, $p < 0.001$) (Fig. 3).

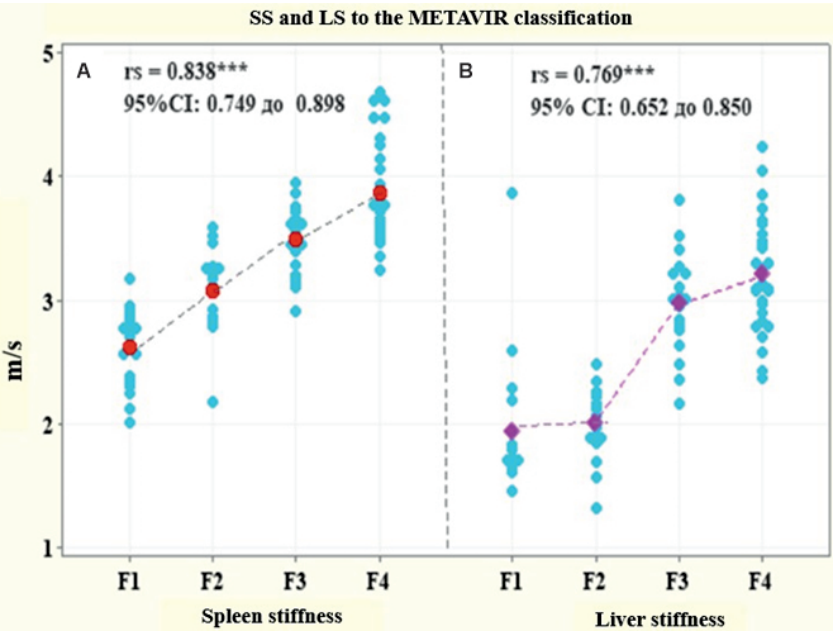


Fig. 3. The degree of consistency between SS and LS and histological evaluation

It can be seen that the values of SS (Panel A) increase systematically with increasing histological stage from F1 to F4, while in LS (Panel B) the difference between the first two levels (F1 to F2) and between the last two (F3 to F4) is not so clear. Based on the present results, we can conclude that the individual values of SS are more indicative of the histological level of the disease compared to those of LS. If we also include the influence of BMI on LS, the diagnostic potential of LS decreases further.

Distinguishing between patients with stage F2 fibrosis from F1 on the basis of SS and LS. Both values showed significant diagnostic potential in distinguishing F2 cases from F1 cases ($p < 0.001$ for both parameters), with SS emerging as a more reliable indicator with an accuracy of 86.40% (AUC = 0.864) compared to 78.60% LS accuracy (AUC = 0.786), but the difference in AUC = 0.078 did not reach statistical significance, $p = 0.422$. The optimal criterion value of SS, distinguishing histological stage F2 from F1 is > 2.95 m/s, with sensitivity 70% and specificity 94.44%, positive predictive value 93.32% and negative predictive value 73.94%. The optimal criterion value of LS (> 1.86 m/s) is characterized by sensitivity 80%, specificity 83.33%, positive predictive value 84.14% and negative predictive value 78.97% (Table 1).

T a b l e 1

Results for the diagnostic accuracy of SS and LS regarding the differentiation of histological stage F2 from F1

Parameters	SS	LS	Difference
AUC	0.864	0.786	0.078
95% CI	0.714–0.953	0.623–0.902	–0.112–0.268
SE	0.057	0.080	0.097
p	0.000***	0.000***	0.422
Optimal criterion value (95% CI)	> 2.95 m/s (> 2.92 m/s to > 3.17 m/s)	> 1.86 m/s (> 1.83 to > 1.94 m/s)	
Sensitivity	70.00%	80.00%	
Specificity	94.44%	83.33%	
PPV	93.32%	84.19%	
NPV	73.94%	78.97%	

AUC – Area under the curve; SE – standard error; PPV – positive predictive value; NPV – Negative predictive value; *** – Statistical significance at $p < 0.001$

Discussion. For decades, the staging of liver fibrosis in patients with chronic viral hepatitis has been performed by liver biopsy. At present, non-invasive diagnostic methods have significantly replaced liver biopsy to determine the extent of liver involvement in chronic liver conditions. Several are those that have the potential to detect early and moderate liver fibrosis: transient elastography (TE) and point shear wave elastography [6–8]. TE has a high diagnostic value in the diagnosis of advanced liver fibrosis [9]. In the present study, we show that liver pSWE can diagnose liver fibrosis in the intermediate stages of development and

distinguish between F2 and F1 with a cut-off value of 1.86 m/s, characterized by a sensitivity of 80%, and specificity of 83.33%. Stage F2 marks the beginning of the progression of liver damage and is associated with a stronger need to start treatment. The development of liver fibrosis is associated with inflammation of the parenchyma, which affects LS levels [10, 11]. On the other hand, LS is highly dependent on obesity. BOTA et al. [12] indicate that obesity, old age and male gender additionally negatively affect the level of successful studies and the accuracy of pSWE in determining liver stiffness.

The last two – obesity and inflammation in the liver parenchyma, do not affect the spleen. In the intermediate stages of liver fibrosis, SS distinguishes between F2 and F1 with a cut-off value > 2.95 m/s, with a sensitivity of 70% and a specificity of 94.44%.

The diagnostic potential of SS and LS is similar according to our statistical data, but LS depends on additional factors that further reduce the diagnostic potential.

Conclusion. Ultrasound elastography of the spleen is not widely used, but it proves clinically useful. In patients with chronic viral hepatitis, the stiffness of the spleen is a more accurate indicator than the stiffness of the liver in the intermediate stages of liver fibrosis, when the changes are reversible, so it can be introduced into routine diagnostic practice.

REFERENCES

- [1] SANAI F. M., E. B. KEEFFE (2010) Liver biopsy for histological assessment: The case against, *Saudi J. Gastroenterol.*, **16**, 124–132.
- [2] MCGILL D. B., J. RAKELA, A. R. ZINSMEISTER, B. J. OTT (1990) A 21-year experience with major hemorrhage after percutaneous liver biopsy, *Gastroenterology*, **99**, 1396–1400.
- [3] PICCININO F., E. SAGNELLI, G. PASQUALE, G. GIUSTI (1986) Complications following percutaneous liver biopsy. A multicentre retrospective study on 68,276 biopsies, *J. Hepatol.*, **2**, 165–173.
- [4] DIETRICH C. F., J. BAMBER, A. BERZIGOTTI et al. (2017) EFSUMB guidelines and recommendations on the clinical use of liver ultrasound elastography, update 2017 (long version), *Ultraschall Med.*, **38**(4), e16–e47.
- [5] European Association for Study of Liver (2015) EASL-ALEH Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis, *J. Hepatol.*, **63**, 237–264.
- [6] ROCKEY D. C. (2008) Noninvasive assessment of liver fibrosis and portal hypertension with transient elastography, *Gastroenterology*, **134**(1), 8–14.
- [7] YONEDA M., K. SUZUKI, S. KATO et al. (2010) Nonalcoholic fatty liver disease: US-based acoustic radiation force impulse elastography, *Radiology*, **256**(2), 640–647.

- [8] KARLAS T., C. PFREPPER, J. WIEGAND et al. (2011) Acoustic radiation force impulse imaging (ARFI) for non-invasive detection of liver fbrosis: examination standards and evaluation of interlobe differences in healthy subjects and chronic liver disease, *Scand. J. Gastroenterol.*, **12**, 1458–1467.
- [9] WONG V. W. S., J. VERGNIOL, G. L. H. WONG et al. (2010) Diagnosis of fbrosis and cirrhosis using liver stiffness measurement in nonalcoholic fatty liver disease, *Hepatology*, **51**(2), 454–462.
- [10] ARENA U., F. VIZZUTTI, G. CORTI et al. (2008) Acute viral hepatitis increases liver stiffness values measured by transient elastography, *Hepatology*, **47**, 380–384.
- [11] FUNG J., C. L. LAI, D. BUT et al. (2010) Reduction of liver stiffness following resolution of acute flares of chronic hepatitis B, *Hepatology*, **4**, 716–722.
- [12] BOTA S., I. SPOREA, R. SIRLI et al. (2014) 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 1,031 subjects, *Eur. J. Radiol.*, **83**, 268–272.

¹*Department of Diagnostic Imaging, Medical University-Plovdiv,
15-A Vasil Aprilov Blvd, 4002 Plovdiv, Bulgaria
e-mails: katia_doykova@abv.bg, sts2001@abv.bg*

²*II Department of Internal Diseases, Medical University-Plovdiv,
15-A Vasil Aprilov Blvd, 4002 Plovdiv, Bulgaria
e-mails: daniel_doykov@abv.bg, vladkoandonov@abv.bg*