

Reliability of testicular stiffness measurement by shear wave elastography to predict testicular atrophy in patients with chronic liver disease

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Abstract

Aim: Chronic liver disease is one of the most important public health problems in both developed and developing countries. It has been reported that testicular atrophy may occur in these patients. The aim of this study is to demonstrate changes in testicular structure and elasticity due to hypogonadism secondary to chronic liver disease (CLD) by shear wave elastography (SWE).

Material and Methods: Eighteen patients aged 22-50 years were included in the study. The control group consisted of 16 participants aged 17-52 years. In all patients and in the control group; first scrotal gray scale and doppler US examination were performed to determine the presence of focal lesions and structural anomalies in both testicles, then the mean testicular shear wave velocity values (SWVV) in the parenchyma was calculated. Testicular volumes and testicular arterial flow indices (Vmax, RI) were recorded.

Results: The results of 34 participants (patient and control groups) were examined; There was no significant difference between volumetric measurements, flow indices and SWVQ values between the two groups. In addition, right testicular arterial Vmax values were lower in the patient group than in the control group ($p < 0.005$).

Conclusion: A decrease in right testicular arterial Vmax indicates that CLD may play an acceptable role in the development of testicular atrophy. However, the duration of the disease and the drugs used can have an impact on our findings. Prospective studies with larger cohorts may be useful in revealing this relationship.

Keywords: Chronic liver disease; shear wave elastography; testicular atrophy

INTRODUCTION

Cases with CLD often develop clinical signs of hypogonadism and feminization symptoms due to hypogonadism. As a result of hypogonadism, testosterone production is reduced, but biologically potent estrogens appear to have an increase in the circulation of men with cirrhosis. For all clinical and biochemical features found in men with cirrhosis, there is no enough single hypothesis to provide sufficient explanation. The pathogenesis of endocrine changes in men with cirrhosis may include multifactorial causes such as decreased hepatic clearance of estrogenic compounds or a combination of autoimmune-mediated primary testicular defect and alcohol effect (1).

Many studies have been conducted regarding the relation between sexual dysfunction and chronic liver diseases (2-

4). In patients with advanced parenchymal liver diseases, we usually observe hypogonadism symptoms such as erectile dysfunction (ED), infertility and decreased libido (5). Testicular atrophy is accompanying finding with decreased body hair and other feminization findings and it is a more prominent finding in alcoholic cirrhosis and hemochromatosis cases. It has been shown that there is a correlation between the severity of liver cirrhosis and ED degree (6).

Ultrasound (US) elastography is an advanced, noninvasive, real-time imaging modality that facilitates the evaluation of parenchymal viscoelasticity.

The most common US elastography techniques are compressive or strain elastography and shear-wave elastography (SWE). However, they are different in terms of the forces being measured and in their imaging

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methods. In strain elastography, stress is applied by repeated manual compression of the transducer, and the amount of lesion deformation relative to surrounding normal tissue is measured. Thus, with this technique, data acquisition and interpretation of elasticity images are more dependent on the user's experience, and significant interobserver variability has been observed (7). In contrary to strain elastography, SWE uses an acoustic radiation force impulse (ARFI) created by a focused US beam, which allows to measuring propagation speed of shear waves within the tissue to be able to locally quantify its stiffness. SWE has been reported to be highly reproducible and had high interobserver reliability (7,8).

A few studies have been published in the literature about the efficacy of the SWE on testicular pathologies. These pathologies are limited to neoplastic processes (9-12), infarction (9,13,14), torsion (15) and orchitis (12,14,16,17).

In clinical practice, testicular elastography examinations are mostly focused on the neoplastic processes. Stiffness increases due to neoplastic testicular lesions (9-11).

On the contrary in benign testicular processes such as orchitis and infarction stiffness have been decreased.

However, in the literature, there is no data about the testicular atrophy in hepatitis B virus (HBV) related liver disease, chronic hepatitis or early-stage liver cirrhosis patients.

In this study, we aimed to investigate the predictive value and the reliability of testicular stiffness (SWE) in chronic hepatitis B patients by comparing testicular volumetric measurements.

MATERIAL and METHODS

Between April 2019 and July 2019, 18 patients with hepatitis B (mean age 37.11 ± 7.53 years) with hepatitis B were included in this retrospective study. In addition, 16 patients aged 17-52 years (mean age 31.56 ± 10.15) in the same age group with no complaints of infertility were included in the study and a control group was formed. Testicular mass, orchitis, infarction and malignancy patients were not included in the study. Control group considered as reference.

In both groups, two radiologists with at least 11 years' experience conducted the US examinations and scrotal gray scale, Doppler US and SWE were performed. The ultrasound examination was performed in each subject in the same session with SWE measurements, using RS-80A (S-Shearwave; Samsung Medison, Hongcheon, Korea), with a linear probe of LA2-9A and L3-12A. Testicular volumes, testicular artery flow indices (V_{max} , RI,) and mean shear wave velocity values (SWVVs) of each testis and an average testicular SWVV for each patient were calculated (Figure 1-2).

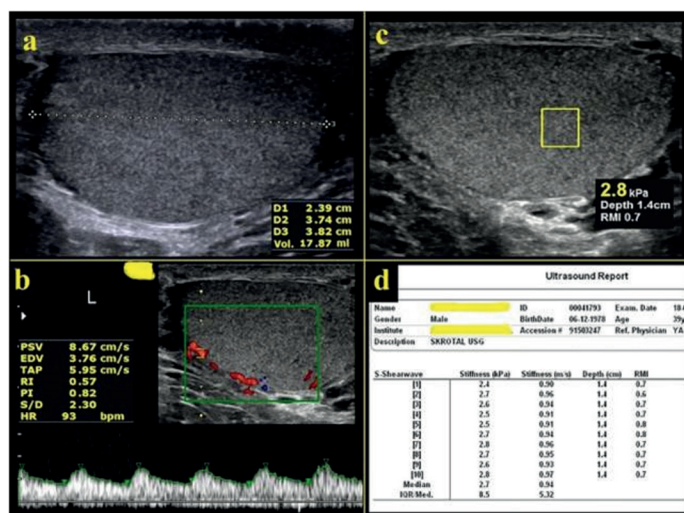


Figure 1. 40 year male patient with chronic liver disease; right testes volume measurement in gray-scale US (a), testicular stiffness measurement with Shear Wave Elastography (b), testicular artery flow indices with Doppler Ultrasound (c), and the summary of Shear Wave Elastography measurements (d)

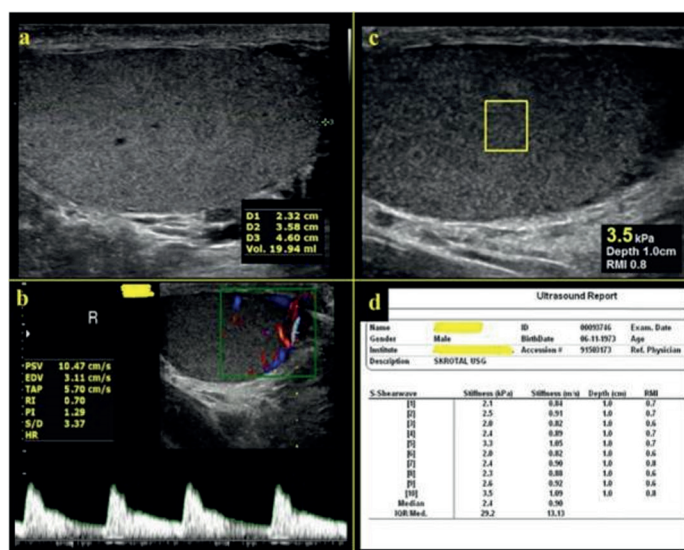


Figure 2. 38 year male in control group; right testes volume measurement in gray-scale US (a), testes rigidity measurement with Shear Wave Elastography (b), testicular artery flow indices with Doppler US (c), and the summary of Shear Wave Elastography measurements (d)

Statistical Analysis

Shapiro-Wilk test was used to determine the consistency of continuous variables to normal distribution. Descriptive statistics were shown as mean \pm standard deviation since all of the variables were normally distributed. In the comparison of groups, independent samples t-test was used. $p < 0.05$ was considered significant.

RESULTS

There was no significant difference between the patient and control groups SWVV values ($p = 0.680$). There was no significant difference between left and right SWVV values of the patient and control groups ($p = 0.577$). A significant

difference was found between the right testis Arterial Vmax values of the patient and control groups (p = 0.001).

No significant difference was found between the left testicular arterial and Vmax values of the patient and control groups (p = 0.527). There was no significant difference between the right testis arterial RI values of the patient and control groups (p = 0.296).

There was no significant difference between the left testicular arterial RI values of the patient and control

groups (p = 0.462). There was no significant difference between the right testicular volume of the patient and control groups (p = 0.117). There was no significant difference between the left testicular volume and the control group (p = 0.271).

In the patient group, right testicular arterial Vmax values were lower than the control group (p <0.005). In addition, there were no significant differences in volumetric measurements, flow indices and SWVQ values between the two groups.

Table 1. Shear wave velocity values, testicular volumes, testicular artery flow indices (Vmax, RI) in patient and control groups

	Patient group (n=18)	Control group (n=16)	P value
Age (year)	37.11 ± 7.53	31.56 ±10.15	0.078
Right Testicular SWV (kPa)	2.49±0.38	2.53±0.29	0.680
Right Testicular Artery Vmax (cm/sec)	8.7±2.39	11.79±2.56	0.001*
Right Testicular Artery RI value	22(20) 0.69±0.12	18(15) 0.74±0.16	0.62 0.296
Right Testicular Volume (cm ³)	15.17±4.66	18.07±5.83	0.117
Left Testicular SWV (kPa)	2.55±0.36	2.63±0.41	0.577
Left Testicular Artery Vmax (cm/sec)	85(78) 10.44±3.49	84(69) 11.13±2.70	0.77 0.527
Left Testicular Artery RI value	20(19) 0.70±0.12	18(15) 0.73±0.17	0.66 0.462
Left Testicular Volume (cm ³)	14.28±4.53	16.37±6.29	0.271

Vmax: maximum velocity; RI: resistivity index; SWV: shear wave velocity values; kPa: kiloPascal; cm/sec: centimeters/second; cm3: cubic centimeter
*: statistically significant at 0.05

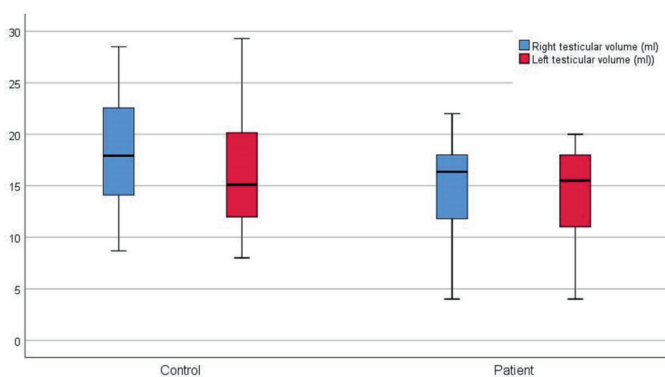


Figure 3. Comparison of right and left testicular volumes according to groups

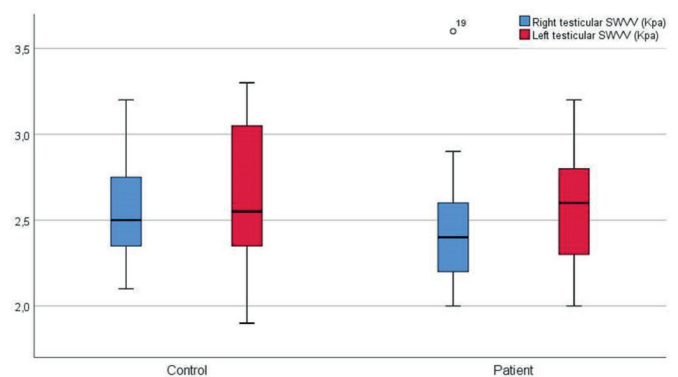


Figure 4. Comparison of SWV values of right and left testis according to groups

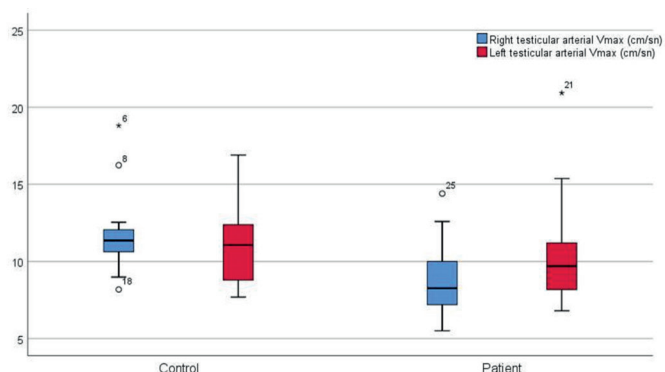


Figure 5. Comparison of right and left testicular arterial Vmax values by groups

DISCUSSION

As testosterone is an effective anabolic hormone, its deficiency not only causes problems with libido, but also causes cardio-metabolic problems. These problems include impaired cognitive function, decreased muscle mass, endothelial dysfunction, high incidence of cardiovascular events, and an increased risk of death (19-22). Many studies have been conducted about relation with CLD and sexual dysfunction in patients with decompensates cirrhosis, liver transplantation and alcoholic liver cirrhosis (2-4). Patients with advance liver disease have hypogonadism symptoms such as erectile dysfunction (ED), infertility, decreased libido and testicular atrophy (5). Testicular atrophy is associated with decreased body hair and other feminization findings. These findings are more prominent especially in alcoholic cirrhosis and hemochromatosis cases. In addition, it has been shown that there is a correlation between the severity of liver cirrhosis and the degree of ED (6).

Testicular atrophy can be observed in patients with CLD. Oxidative stress is known to cause male infertility with peroxidative injury to sperm and testes (17-18).

Ultrasonography is the primary imaging modality used to evaluate the scrotum (23). Besides ease of access, it is a tolerable examination method for patients. The Grayscale US is usually sufficient to measure testicular volumes and to determine parenchymal echogenicity (24). SWE is a noninvasive method that quantitatively measures the elasticity of soft tissue (25). SWE has been used in many studies of focal testicular lesions (26).

Although a small change in the echogenicity of a testis shows a decrease in testicular function, it is not easy to detect (24). Sakamoto et al. demonstrated a strong correlation between testicular function and testicular volume in patients with chronic renal failure (CRF) (27). However, there is no scientific study showing a significant decrease in testicular volume in patients with CLD.

In SWE elasticity is measured by a shear wave which is perpendicular to 1000 times weakened axial displacement caused by US pulse (22). SWE is an advantageous method because tissue compression is not required and tissue

elasticity can be quantitatively measured in kilopascals (16). In this study using SWE, both testicular volumes and parenchymal elasticity were measured in CLD patients and in the control group. There was no significant difference in testicular volumes and parenchymal stiffness between CHD and control groups. Only the right testicular arterial Vmax was found to be decreased compared to the left testis.

We believe that a decrease in testicular volume and parenchymal fibrosis can be detected by SWE in long-term CLD patients. However, there is still a need for controlled randomized prospective trials with a bigger cohort due to the variability of treatment duration attributable to a limited number of patients with a large limitation of our study, considering the mean testicular volume or parenchymal SWE values and arterial flow indices.

CONCLUSION

Testicular SWVQ using the average SWV technique is a reliable, noninvasive and acceptable stable method. However, the duration of the disease and the medication administered may have an impact on the findings. Therefore, we think that there is a need for studies with longer and more cases.

Conflict of interest: The authors declare that they have no competing interest.

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional committee at which the studies were conducted (IRB approval number 2019/72) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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