Research Article

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Application of Real-Time Shear Wave Elastography in The Evaluation of Acute Hepatitis After Treatment

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Abstract

Purpose: *To evaluate the elasticity modulus value of different stages and types of acute liver hepatitis after treatment by real-time shear wave elastography (SWE) technology.*

Methods: *Patients with a clinical diagnosis of acute hepatitis undergoing ultrasonography (US) and SWE were selected for the study, including those with drug-induced hepatitis, autoimmune hepatitis, and viral hepatitis. The elastic modulus values of three groups were measured before treatment and 1 month and 3 months after treatment, separately, and were statistically analyzed.*

Results: *A total of 45 patients were selected for the study, including those with drug-induced hepatitis (n = 17), autoimmune hepatitis (n = 8), and viral hepatitis (n = 20). The average elastic modulus values of three groups before treatment were 26.248 ± 7.837kPa, 14.670 ± 3.945kPa, and 23.860 ± 6.928kPa, respectively. After treatment for 1 month and 3 months, the mean modulus values of three groups decreased and have a statistically difference compared with that before treatment ($P < 0.05$). The mean elastic modulus value in autoimmune hepatitis group was statistically significant from those before treatment in the other two groups, respectively ($P < 0.05$). The mean elastic modulus value in viral hepatitis group was statistically significant from that 1 month after treatment in the other two groups, respectively ($P < 0.05$). The mean elastic modulus value in three groups after 3 months of treatment was not statistically significant ($P > 0.05$).*

Conclusion: *SWE can be used to differentiate between different stages and types of acute hepatitis before and after treatment.*

Keywords: Autoimmune Hepatitis; Drug-Induced Hepatitis; Elastic Modulus; Real-Time Shear Wave Elastography; Viral Hepatitis

Introduction

Real-time shear wave elastography (SWE) technology is a new ultrasound diagnostic technology. The elasticity of tissue is expressed by the elastic modulus, which makes up for the shortcomings of conventional ultrasonography (US) and computed tomography (CT) in measuring tissue elasticity. It is widely used to diagnose breast, thyroid, prostate, vascular wall, and superficial lymph node diseases, among others [1]. At present, many scholars have discussed the value of SWE technology in ascertaining normal liver elastic modulus values and for staging of chronic hepatitis and liver fibrosis [2-3]. However, there are few reports on the elasticity measurements of liver tissue in individuals who have received a diagnosis of acute hepatitis from various etiologies.

Acute hepatitis is one of the common liver diseases in gastroenterology. It is characterized by rapid onset, rapid progress, and high mortality, and its pathogens are diverse. Each pathogen affects the liver differently and requires a different treatment regimen. Therefore, early diagnosis is critical [4-5]. This study applies the SWE technique to the diagnosis and treatment of acute hepatitis, and it proposes a theoretical foundation for clinicians to choose a reasonable treatment.

Materials and Methods

Subjects

Between January 2015 and December 2018, 45 patients with a clinical diagnosis of acute hepatitis undergoing US and SWE in the First Affiliated Hospital of China Medical University were selected for study. The patients' ages ranged from 22 to 68 years (mean ± SD, 38.89 ± 6.23 years), and 21 of the patients were women. The patients in this study were diagnosed with drug-induced hepatitis, autoimmune hepatitis, or viral hepatitis. Each diagnosis was pathologically confirmed. No patient had contraindications to liver biopsy. This study was approved by the Ethics Committee of China Medical University. Informed consent was obtained from all patients enrolled after full explanation of the purpose and nature of all procedures performed.

Entry criteria for this study included patients with symptom onset within 14 days accompanied by elevated transaminases. Exclusion criteria included patients with a history of cirrhosis, any other cause of chronic liver disease, or malignancy. Patients were also excluded if they had obstructive cholestasis and/or jaundice as well as severe heart failure, as these diseases can lead to significantly increased liver stiffness values that do not correspond to proportionally advanced liver fibrosis.

Equipment and Methods

An Explorer color Doppler ultrasonic diagnosis system (Supersonic Medical Systems, France) with a probe frequency of 1 to 6 MHz was used. First, we performed routine US of the liver, then switched to SWE mode. The patients were in the supine position, and the sampling frame was placed at S6 of the liver. A scan of the right lobe of the liver at the junction of the right midclavicular line and the 6th intercostal space was performed. The measuring depth was approximately 4 cm the elastic range was 70 kPa, and the diameter of the region of interest (ROI) was 1 cm [7-9]. During the measurement, the patient was asked to hold their breath for 3 to 5 seconds. The color in the sampling frame was full, uniform, and stored after the image was stable. We determined the location of the selected area of the ROI and calculated the elastic modulus value of the ROI, including average, minimum, and maximum values (unit: kPa). We repeated the measurement three times for each ROI to calculate the average value of the elastic modulus of each group. Each patient was examined using the same method, and all examinations were completed jointly by two associate professors. When there was a dispute, an agreement was reached after discussion.

Follow-Up

Each patient was treated symptomatically after diagnosis. Before treatment and at 1 month and 3 months after treatment, routine US and SWE examinations were performed on each patient, and the liver elastic modulus value of each patient in each group at different time periods was obtained.

Statistical Analysis

Data were expressed as mean ± SD. Statistical analysis was performed using a one-way analysis of variance to see if the elastic modulus of the liver of the three patient groups came from the same population. Between-group comparisons were performed using the Bonferroni method for statistical analysis, and a value of $P < .05$ was considered statistically significant. All data handling relied on standard software (SPSS v21.0; IBM, Armonk, NY, United States).

Results

A total of 45 patients were selected for the study and included the drug-induced hepatitis group (n = 17), autoimmune hepatitis group (n = 8), and viral hepatitis group (n = 20). The clinical data are shown in Table 1; there is no statistical difference among sex or age of the three groups of patients ($P > .05$).

Table 1 Clinical data of drug-induced hepatitis, autoimmune hepatitis, and viral hepatitis

	Drug-induced hepatitis	Autoimmune hepatitis	Viral hepatitis
Gender			
male	7	3	9
female	10	5	11
Age			
≥60	11	5	13
<60	6	3	7

*$P < .05$, statistically significant; $P > .05$, not statistically significant.

Before treatment, color Doppler ultrasound shows hypoechoic or isoechoic livers in drug-induced hepatitis, autoimmune hepatitis, and viral hepatitis. Lymph nodes can be found in the hilar region, and the color Doppler flow images are normal. After treatment, there was no specific difference in the liver images, and they were still isoechoic. However, the SWE images showed that the liver of drug-induced hepatitis is uneven, with a mix of red, yellow, and blue colors on imaging. Autoimmune hepatitis liver images are evenly blue, and viral hepatitis liver images are a yellow-blue mix. After treatment, the elastic image of the livers turned blue, which was significantly different from that before treatment. (Fig. 1-3)

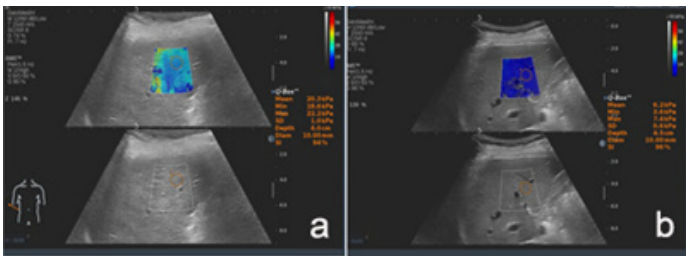

Figure 1: (a) The elastic modulus value of drug-induced hepatitis before treatment was 32.3 kPa. (b) The elastic modulus value of drug-induced hepatitis 3 months after treatment was 7.2 kPa.

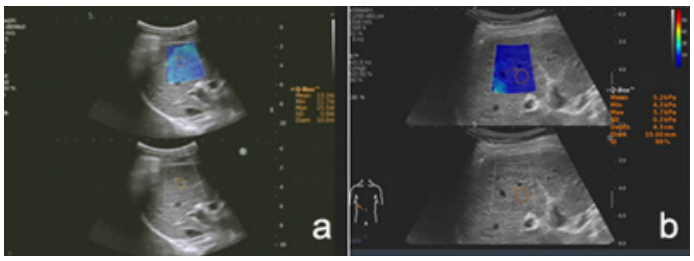

Figure 2: (a) The elastic modulus value of autoimmune hepatitis before treatment was 13.3 kPa. (b) The elastic modulus value of autoimmune hepatitis 3 months after treatment was 5.2 kPa.

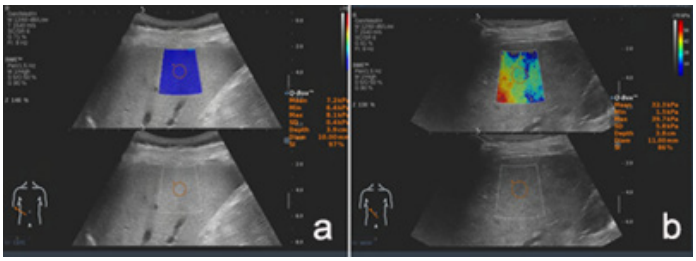

Figure 3: (a) The elastic modulus value of viral hepatitis before treatment was 20.3 kPa. (b) The elastic modulus value of viral hepatitis 3 months after treatment was 6.2 kPa.

The mean elastic modulus values of the three groups before treatment (mean ± SD) were 26.248 ± 7.837 kPa, 14.670 ± 3.945 kPa, and 23.860 ± 6.928 kPa, respectively. After 1 month of treatment, these values were 6.818 ± 2.657 kPa, 7.670 ± 2.235 kPa, and 13.750 ± 2.675 kPa, respectively. After 3 months of treatment, these values were 6.218 ± 1.447 kPa, 6.390 ± 1.314 kPa, and 6.830 ± 1.426 kPa, respectively (Table 2).

Table 2: Comparison of mean liver elastic modulus value of three groups patients (kPa)

Group	No.	The mean liver elastic modulus value before treatment (Pa)	The mean liver elastic modulus value 1 month after treatment (Pa)	The mean liver elastic modulus value 3 months after treatment (Pa)
Drug-induced hepatitis	17	26.248±7.837	6.818±2.657*	6.218±1.447
Autoimmune hepatitis	8	14.670±3.945#*	7.670±2.235*	6.390±1.314
Viral hepatitis	20	23.860±6.928	13.750±2.675	6.830±1.426

#Compared with drug-induced hepatitis, $P < .05$; *Compared with viral hepatitis, $P < .05$.

The mean liver elastic modulus value after 1 month of treatment in the drug-induced hepatitis group was statistically significant from that before treatment (P < .05). The mean liver elastic modulus value after 1 month of treatment in the drug-induced hepatitis group was not statistically significant from that after 3 months of treatment (P > .05). The mean liver elastic modulus value after 1 month of treatment in the autoimmune hepatitis group was statistically significant from that before treatment (P < .05). The mean liver elastic modulus value after 1 month of treatment in the autoimmune hepatitis group was not statistically significant from that after 3 months of treatment (P > .05). The mean liver elastic modulus value after 1 month of treatment in the viral hepatitis group was statistically significant from that before treatment (P < .05). The mean liver elastic modulus value after 1 month of treatment in the viral hepatitis group was statistically significant from that after 3 months of treatment (P < .05) (Table 2).

Before treatment, the mean liver elastic modulus value of the autoimmune hepatitis group was statistically significant from that of the drug-induced hepatitis group and the viral hepatitis group, respectively (P < .05). There was no statistical significance in the mean liver elastic modulus value of the drug-induced hepatitis group and the viral hepatitis group (P > .05). One month after treatment, the mean liver elastic modulus value of the viral hepatitis group was statistically significant from that of the autoimmune hepatitis group and the drug-induced hepatitis group, respectively (P < .05). There was no statistical significance in the mean liver elastic modulus value between the drug-induced hepatitis group and the autoimmune hepatitis group (P > .05). The mean value of the liver elastic modulus value of the three groups after 3 months of treatment was not statistically significant (P > .05). This is shown in Table 3.

Table 3 Comparison of mean liver elastic modulus value of three groups patients (kPa)

Group	No.	The mean liver elastic modulus value before treatment (Pa)	The mean liver elastic modulus value 1 month after treatment (Pa)	The mean liver elastic modulus value 3 months after treatment (Pa)
Drug-induced hepatitis	17	26.248±7.837	6.818±2.657*	6.218±1.447
Autoimmune hepatitis	8	14.670±3.945#*	7.670±2.235*	6.390±1.314
Viral hepatitis	20	23.860±6.928	13.750±2.675	6.830±1.426

#Compared with drug-induced hepatitis, *P* < .05; *Compared with viral hepatitis, *P* < .05

Discussion

The pathogenesis of drug-induced hepatitis is direct liver cell damage and damage from the immune response, which is easily confused with viral hepatitis and autoimmune hepatitis in clinical diagnosis [10-12]. Autoimmune hepatitis as a disease of unknown pathogenesis is associated with many diseases, and because the initial clinical symptoms are similar to those of viral hepatitis, clinical diagnosis is difficult [13]. Viral hepatitis is a liver disease with a higher incidence and a high degree of genetic susceptibility; therefore, it is a greater threat to long-term liver health [14]. Because the clinical symptoms of the three types of hepatitis are similar, they can easily be misdiagnosed by clinicians. Therefore, the ability to clarify the diagnosis among the three types of hepatitis is of important clinical value, particularly in regard to treatment. This study used SWE technology to evaluate the elastic value of acute hepatitis and then analyzed the severity and recovery of livers afflicted with different types of hepatitis.

Issa R found that during the development of drug-induced hepatitis, liver elasticity decreases and hardness increases. Yan et al. believed that viral hepatitis also increases liver stiffness due to degeneration, necrosis, and lymphocyte infiltration of liver cells during development. It was shown in this study that the elasticity modulus value of drug-induced and viral hepatitis increases greatly, and the elasticity modulus value of autoimmune hepatitis increases slightly. The reasons are as follows: first, the elasticity of the liver is related to liver stiffness and the bilirubin in liver [15-18]. Drug-induced hepatitis and viral hepatitis result in livers that are generally severely damaged, and bilirubin is significantly increased. Autoimmune hepatitis has weak liver cells, and the increase in bilirubin is small. Second, drug-induced hepatitis and virus hepatitis are usually acute, and autoimmune hepatitis generally results in chronic liver disease, which is relatively mild and can manifest as clinical symptoms of acute hepatitis.

This study shows that there is a statistical difference in the comparison among the mean liver elastic modulus values of the three groups both after and before treatment. This indicates that real-time SWE can be applied to clinically evaluate the treatment effects of the three types of hepatitis and give clinicians certain guidance. Since two-dimensional color Doppler US cannot distinguish between the image changes of the three types of hepatitis, real-time SWE technology can distinguish between the three types of hepatitis. It provides a theoretical basis for clinicians to diagnose each of the three types of hepatitis. SWE can precisely reflect the changes before and after treatment of each of the three types, mainly because SWE is related to the hardness of the tissue [19]. Changes in hardness and transaminase levels of the three types of hepatitis will affect the liver elastic modulus value.

Conclusion

The results of this study have shown that drug-induced hepatitis has a short recovery time, viral hepatitis has a long recovery time, and autoimmune hepatitis is somewhere in between. The main reason for this difference is related to their disease course and pathogenesis. The pathogenesis of drug-induced hepatitis is clear [20]. The duration of symptomatic treatment is fast and the recovery time is short. The pathogenesis of acute viral hepatitis is mainly direct liver cell damage with a total course of 2 to 4 months and has a slow recovery. Autoimmune hepatitis is an acute attack of chronic hepatitis, which gradually recovers after symptomatic treatment [21-22].

Study Limitations

All patients who were entered into the study groups had clinical symptoms of acute hepatitis. The pathogenesis of drug-induced hepatitis and viral hepatitis is not specifically subdivided, and interfering factors cannot be ruled out. In addition, this study excluded patients with severe disease; further, our study has a small number of cases. In future studies, we need to increase the sample size to further verify the results of this study.

In short, the elasticity modulus value of drug-induced hepatitis is significantly increased, and the course of disease is short. The elasticity modulus value of viral hepatitis is significantly increased, and the long course of disease requires antiviral treatment. The

elasticity modulus value of autoimmune hepatitis is not increased significantly, and its course falls in between that of drug-induced and viral hepatitis. Treatment generally consists of hormone therapy.

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