



Doppler Ultrasonography as a Non-invasive Procedure for Diagnosis of Chronic Hepatitis: A Cross-sectional Study

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Authors' contributions

This work was carried out in collaboration between all authors. Author RNM involved with the patients during admission and ultrasonography and also involved with the writing of article. Author FE involved with the patients at time of ultrasonography and during admission and wrote the first draft of the manuscript.

Author NH involved with the patients during admission and read through the manuscript and made corrections. Author MBZ involved with the writing and revision of article and made language corrections.

Author SMT involved with the writing and revision of the article. Author MAT involved with the patients during liver biopsy and pathological examinations. All authors read and approved the final manuscript.

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ABSTRACT

Background: Viral hepatitis is a major public health problem in the world. Early recognition and treatment is crucial in order to avoid or decrease complications including cirrhosis and hepatocellular carcinoma. Liver biopsy is an invasive procedure for diagnosis of chronic hepatitis. The aim of this study was to evaluate Doppler ultrasound findings for diagnosis of chronic hepatitis.

Materials and Methods: Doppler studies of liver were performed in 110 patients who were admitted to the hospital. The patients were suspicious for chronic hepatitis, according to the physical examination and laboratory tests. Liver biopsy, ultrasonography of spleen and Doppler ultrasonography of liver were performed. The patients were divided into three groups: normal, chronic hepatitis and cirrhosis. The data were collected and analyzed using SPSS software.

Results: According to this study, there was a significant difference between IVC diameters in three groups during expiration. ($p < 0.001$). The difference between IVC diameters in three groups during inspiration was significant, too. ($p < 0.001$). In addition, there was a significant difference between hepatic arterial resistivity indexes in three groups. ($p < 0.001$).

Conclusion: Ultrasonography and Doppler ultrasonography provide valuable information for distinction of chronic hepatitis, cirrhosis and normal patients by measuring spleen size and IVC diameter during inspiration and expiration. Arterial resistivity index has limited value for detection of early stages of chronic hepatitis and cirrhosis.

Keywords: Doppler ultrasonography; liver; chronic hepatitis.

1. INTRODUCTION

Viral hepatitis is a common cause of liver fibrosis, as well as a major public health problem worldwide [1]. Viral hepatitis varies from mild to a severe infection such as fulminant hepatitis [2]. Chronic hepatitis is a spectrum of disease with different levels of severity, in which inflammation and liver necrosis are present for at least six months [3]. Chronic viral hepatitis may lead to cirrhosis and hepatocellular carcinoma. The gold standard method for diagnosis of chronic hepatitis is liver biopsy [1]. However, it is an invasive procedure that increases risk of various complications [4,5]. Doppler ultrasonography (DUS) is a non-invasive procedure. This modality is based on hemodynamic parameters [6]. Recently, DUS has been described for diagnosis of liver fibrosis and cirrhosis [2,6]. As the hepatic portion of IVC is connected to the liver, IVC diameter change is greatly dependent on the modification of parenchyma surrounding IVC. Arterial resistivity index can be measured by DUS. This index is dependent on liver fibrosis and stiffness [3].

In this study, we observed the role of DUS in detection of chronic hepatitis. The purpose of this study was to determine the important role of DUS in detection of chronic hepatitis and the role of Doppler parameters in diagnosis of chronic hepatitis.

2. MATERIALS AND METHODS

In this cross-sectional study, conducted from March 2010 to May 2013, 110 patients referring to the Shahid Sadoughi Hospital with suspicious of chronic hepatitis according to the physical examination and laboratory tests, who underwent liver biopsy, were enrolled according to the consecutive sampling technique, by which every individual meeting the criteria of inclusion was selected until the required sample size was achieved. Age, spleen size, IVC diameter, hepatic arterial resistivity index and gender were our variables. Ultrasonography of liver and spleen and DUS of hepatic vessels were performed. Hepatic arterial resistivity index was measured by DUS and the IVC diameter was recorded during inspiration and expiration. The procedure was performed using 3.5 Mhz probe by Piemedical ultrasound equipment. All patients were in the supine position and the IVC diameter was measured in the sagittal section near the site of hepatic veins' separation. DUS examinations were performed following a fasting period of a minimum of four hours. Afterwards, DUS of hepatic artery was performed. After finding the artery, the cursor was placed on the site of artery, and the angle between artery and ultrasound waves was set to less than 60. The characteristics of Doppler waves, including arterial resistivity index, were measured two times, and the average was recorded. After recording data, the patients underwent liver

biopsy under ultrasound guidance. The liver biopsy was performed by 18G Tru-Cut Biopsy Needle. The results of liver biopsy were recorded. Finally, the results of pathology, US and DUS were analyzed using SPSS for Windows (version 13.0, SPSS). The Mean \pm SD of hepatic arterial resistivity index was calculated for each group. The results were analyzed by Chi-square test.

3. RESULTS

In this study, 64.5% and 35.5% of patients were male and female respectively. (n=71 males, n=39 females). The youngest patient was 12-year old and the oldest one was 84-year old. (Average age 38.1 years old). The patients were divided into two groups: group 1) 12-34 year old (n=57) and group 2) 35-84 year old (n=53). There was not significant correlation between gender and liver pathological findings. (p= 0.463) (Table 1) Pathological evaluation of liver specimens revealed 19.1% of patients to have normal biopsy, 57.3% to have chronic hepatitis and 23.6% to have cirrhosis. In the group of normal patients, 14.3% had splenomegaly. Since pathological evaluation of liver specimens was normal in this group, splenomegaly could not be linked to be relevant to our study. Of patients with chronic hepatitis, 22.2% had splenomegaly whereas

84.6% of patients with cirrhosis had splenomegaly. In our investigated population, the prevalence of chronic hepatitis and cirrhosis in men was 55% and 22.5% respectively, whereas it was 61.6% and 25.6% in women, respectively. The prevalence of chronic hepatitis was 57.8% in group 1 and 56.6% in group 2.

21.1% of patients in group 2 suffered cirrhosis whereas 26.5% of 35-84 year old patients had cirrhosis. The most frequency of splenomegaly was in cirrhosis group (84.6%) followed by chronic hepatitis group (22.2%). The average IVC diameter during expiration, and the pathological features were investigated. Mean \pm SD of IVC diameter during expiration was 19.6 \pm 2.87 in normal group, 17.14 \pm 3.13 in chronic hepatitis group and 15.18 \pm 2.29 in cirrhosis group. The results were analyzed. There was a significant difference between IVC diameters in three groups during expiration. (p<0.001) (Table 2).

The average IVC diameter during inspiration, and the pathological features were investigated. Mean \pm SD of IVC diameter during inspiration was 10.96 \pm 4.16 in normal group, 8.04 \pm 3.73 in chronic hepatitis group and 3.44 \pm 1.32 in cirrhosis group. There was a significant difference between IVC diameters in three groups during inspiration. (p<0.001) (Table 3).

Table 1. Frequency of liver pathological findings according to gender in investigated population

Gender		Liver pathological findings			
		Normal	Chronic hepatitis	Cirrhosis	Total
Male	Number	16	39	16	71
	Percent	22.5	55	22.5	100
Female	Number	5	24	10	39
	Percent	12.8	61.6	25.6	100
Total	Number	21	63	26	110
	Percent	19.1	57.3	23.6	100

Table 2. Mean \pm SD of IVC diameter during expiration measured by Doppler ultrasonography according to the pathological features in investigated population

Pathological features	Numbers	Mean \pm SD of IVC diameter	Minimum of IVC diameter	Maximum of IVC diameter
Normal	21	19.6 \pm 2.78	14	25
Chronic hepatitis	63	17.14 \pm 3.13	9	27
Cirrhosis	26	15.18 \pm 2.29	10	19.6
All patients	110	17.15 \pm 3.2	9	27

Table 3. Mean \pm SD of IVC diameter during inspiration measured by Doppler ultrasonography according to the pathological features in investigated population

Pathological features	Numbers	Mean \pm SD of IVC diameter	Minimum of IVC diameter	Maximum of IVC diameter
Normal	21	10.96 \pm 4.16	4.9	19
Chronic hepatitis	63	8.04 \pm 3.73	1	19.5
Cirrhosis	26	3.44 \pm 1.32	0.4	6
All patients	110	7.5 \pm 4.32	0.4	19.5

Table 4. Mean \pm SD of hepatic arterial resistive index measured by Doppler ultrasonography according to the pathological features in investigated population

Pathological features	Numbers	Mean \pm SD of IVC diameter	Minimum of IVC diameter	Maximum of IVC diameter
Normal	21	0.69 \pm 0.027	0.63	0.76
Chronic hepatitis	63	0.70 \pm 0.051	0.56	0.82
Cirrhosis	26	0.76 \pm 0.034	0.69	0.83
All patients	110	0.71 \pm 0.052	0.56	0.83

Mean \pm SD of hepatic arterial resistivity index was 0.69 \pm 0.027 in normal group, 0.70 \pm 0.051 in chronic hepatitis group and 0.76 \pm 0.034 in cirrhosis group. There was a significant difference between hepatic arterial resistivity indexes in three groups ($p < 0.001$) (Table 4).

4. DISCUSSION

The degree of liver fibrosis or cirrhosis could be evaluated by ultrasonography. Diagnosis of cirrhosis in patients with chronic viral hepatitis requires the use of two or three ultrasound parameters. Spleen length is one of the most valuable parameters for early diagnosis of cirrhosis [7]. Ultrasonography and DUS have important role in detection of chronic hepatitis and other chronic liver disease as well as in screening of hepatocellular carcinoma [8]. In patients with chronic hepatitis or cirrhosis, IVC diameter changes with the increase in liver fibrosis and stiffness [9]. DUS is a sensitive modality for detecting hemodynamic changes following fibrosis and inflammation. In other words, DUS has a high diagnostic ability for diagnosis of chronic hepatitis and cirrhosis [6]. Ultrasound and serologic findings have pivotal role for diagnosis of liver fibrosis and cirrhosis [10]. In the present study, liver biopsy was performed in 110 patients with HBV or HCV infection as well as with suspicion of chronic hepatitis.

Spleen length has been considered as a major factor for diagnosis of cirrhosis. It has been

shown that spleen length measured by ultrasonography is one of the most important and valuable findings for diagnosis of liver cirrhosis [7]. There was a significant correlation between liver pathological findings and splenomegaly in our study, and spleen size was observed to be an important finding for diagnosis of liver cirrhosis. In our study, IVC diameter changes were also measured. Since the hepatic portion of IVC is connected to the liver, IVC diameter change is greatly dependent on the modification of parenchyma surrounding IVC. In general, an increase in parenchymal stiffness that occurs in liver fibrosis or cirrhosis, limits venous diameter changes. In this study, the average IVC diameter during expiration was 19.60, 17.14, 15.9 mm in normal, chronic hepatitis and cirrhosis groups respectively. The average IVC diameter during inspiration was 15.96 mm in normal group, 8.04 mm in chronic hepatitis group and 3.44 mm in cirrhosis group. There was a significant difference between the average IVC diameter in three groups during expiration and inspiration. The findings also exhibit that the expansibility of IVC decreases with the increase of liver fibrosis and stiffness in patients with chronic hepatitis and cirrhosis. Kitamura et al. [9] concluded that IVC diameter and its expansibility during respiration are reliable markers for assessment of liver condition. The results of our study are compatible with this conclusion. Hepatic arterial resistivity index is dependent on duration of fasting in patients. During fasting, hepatic arterial resistivity index decreases, while it increases with feeding. In addition, this index is dependent

on the liver stiffness and the degree of liver fibrosis. In patients suffering cirrhosis, hepatic arterial resistivity index increases. In the present study, hepatic arterial resistivity index was compared with pathological findings. The mean \pm SD of hepatic arterial resistivity index was 0.69 ± 0.027 in normal group, 0.70 ± 0.05 in chronic hepatitis group and 0.76 ± 0.034 in patients suffering cirrhosis. There was significant difference in normal and cirrhosis groups statistically but not in chronic hepatitis group. Although there is no exact cut off value for hepatic arterial resistivity index, in individuals who are fasting for at least 4 hours, this index is expected to be equal or less than 0.7. It is important to note that in the primary stage of chronic hepatitis, there is a mild liver fibrosis, or fibrosis can even be absent and in the higher stages, liver fibrosis is more severe than the lower stages, which in turn leads to the development of cirrhosis. IVC diameter and hepatic arterial resistivity index do not change significantly in primary stages of chronic hepatitis.

In conclusion, in the present study, there was a significant difference between the average IVC diameter in three groups during expiration and inspiration. The findings also exhibit that the expansibility of IVC decreases with the increase of liver fibrosis and stiffness in patients with chronic hepatitis and cirrhosis.

5. RECOMMENDATION

According to the results of this study, spleen size and IVC diameter can be used as diagnostic markers with high sensitivity in patient with suspicion of chronic hepatitis and cirrhosis. The authors recommend further investigations in patients with suspicion of chronic hepatitis regarding pathological features, to determine the role of ultrasonography in detection of low grade chronic hepatitis.

6. CONCLUSION

The diagnostic potential of DUS provides exciting new opportunities for detection of chronic hepatitis. Ultrasonography and DUS provide valuable information for distinction of chronic hepatitis, cirrhosis and normal patients by measurement of spleen size and IVC diameter during inspiration and expiration. Arterial resistivity index has limited value for detection of

early stages of chronic hepatitis and cirrhosis. However, further investigation is required to evaluation of ultrasound findings for diagnosis of chronic hepatitis.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Study projects such as our study should be approved by ethical committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran before performing, so this study was confirmed by ethical committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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