EVALUATION BY MRI OF CHANGES IN LIVER AND SPLEEN VOLUME IN PATIENTS WITH CHRONIC VIRAL HEPATITIS

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ABSTRACT

Objectives. This study aimed to examine the role played in the evaluation of hepatic fibrosis by the changes in liver and spleen volume in patients with chronic viral hepatitis.

Material and Methods. The study comprised 47 chronic viral hepatitis patients and 30 healthy control subjects. T2-weighted images were used to measure volume. The liver and spleen borders were marked on each slice and the volume was calculated by combining these borders on a computer. A biopsy was performed on the 47 patients. The fibrosis stages of the patients were defined according to the METAVIR scoring system. SPSS for Windows 11.5 statistical package program was used for the data evaluation.

Results. The liver volume of the patients was found to be lower than that of the control group whereas the spleen volume of the patient group was higher than control group one. When liver volume was evaluated according to stages, it was seen that the more the level of fibrosis increased, as the liver volume decreased. In the evaluation of spleen volume according to stages, the more the level of fibrosis increased, as spleen volume was seen to increase. When spleen volume to liver volume ratio was examined, a statistically significant increase was seen in the patient group compared to the control group.

Conclusions. It is considered that the measurements of liver and spleen volume can be a guide in the definition of the level of fibrosis in chronic liver diseases.

Key words: Liver, magnetic resonance imaging, organ size, spleen.

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Introduction

In chronic liver diseases, while liver volume decreases, spleen volume increases. Reduced liver volume may be associated with a decrease in hepatocytes due to hepatocyte damage and the extracellular matrix increase in the liver sinusoids and the matrix becoming thick, hard and collagen rich (particularly collagen Type I, III and IV) in place of the original matrix1,2. Increased spleen volume may be associated with portal hypertension. Regeneration nodules which develop associated with fibrosis lead to compression of the hepatic venous branches. This results in impaired liver blood drainage and an increase in flow resistance in the portal venous system. Thus, an increase in volume occurs due to venous pooling in the spleen3,5.

Some studies have reported that the measurements of liver and spleen volume can be used in the diagnosis of chronic liver diseases3,6,7. These studies reported that the ratios between total and segmental volume of the liver and total volume of the spleen can be used in the prediction of the level of liver fibrosis and patient monitoring9.

This current study aimed to research the role played by the changes in liver and spleen volume in the evaluation of hepatic fibrosis in patients with chronic viral hepatitis.
Materials and methods

Patients

The study included 47 patients who presented at our hospital between October 2009 and September 2010 and were diagnosed with chronic viral hepatitis from the clinical and laboratory findings, and a control group of 30 healthy volunteers. The patients included in the study were determined as 33 with chronic hepatitis B, 13 with chronic hepatitis C and 1 with chronic hepatitis B+C.

MRI Examination

A 1.5 Tesla Magnetom Symphony A Tim System (Siemens, Erlagen, Germany) was used for the imaging, which was performed without any need for sedation, in a supine position with a 16-channel body coil over the liver. T2-weighted images were used for the volume measurements. Axial T2 images directed at the upper abdomen were acquired in all patients and control group subjects. The T2-weighted images were taken in the form of TR 3440, TE 87 and NEX 1. The images were transferred to the clinic workstation (Syngo VIA console, Siemens). Measurements were made on this workstation by the contour interpolation technique. The liver and spleen borders were marked on each slice and the volume was calculated by combining these borders on the computer (Figure 1a, 1b, 2a and 2b).

Histopathology

Biopsy was performed on the 47 patients with chronic viral hepatitis using an automatic tru-cut biopsy needle with 16-18 gauge x 16cm trigger, under ultrasonography by a radiology specialist experienced in this area. No biopsy was performed on the control group. After staining with HE and Masson Tri Kom, the pathology specimens were evaluated by pathologists blinded to the research. The fibrosis stages of the patients were defined according to the META VIR scoring system. Liver fibrosis was staged on an F0-F4 scale: F0, no fibrosis; F1, portal fibrosis without septa; F2, portal fibrosis with few septa; F3, numerous septa without cirrhosis; and F4, cirrhosis(8). Those in the patient group were allocated to two groups of mild fibrosis (F1, F2) and advanced fibrosis (F3, F4).

Statistical Analysis

SPSS for Windows 11.5 statistical package program (SPSS 11.5, IL, USA) was used for the data evaluation. Pearson chi-square test was used in the comparison of gender distributions between the patient groups and the control group. Differences were considered to be statistically significant at P <0.05. The Fisher’s exact test was used instead of a chi-square test when one or more of the cells have an expected frequency of five or less.

Independent samples t-test was used in the comparison of mean ages, liver and spleen volumes between the patient group and the control group. Differences were considered to be statistically significant at P <0.05.

Kruskal-Wallis test was performed in the multiple comparisons of median volumes of the patients at different stages and the control group. Differences were considered to be statistically significant at P <0.05.

Mann-Whitney U Test with Bonferroni adjustment was performed in the pairwise comparison of median volumes of the patients at different stages and the control group. Differences were considered to be statistically significant at P <0.05/group number.

Results

The patients with chronic viral hepatitis comprised 18 (38%) females and 29 (62%) males of mean age 38.8 years (range, 18-65 yrs). The participants in the control group were 12 (40%) females and 18 (60%) males of mean age 38 years (range 21-60 yrs). There was no statistically significant...
difference between the patient group and the control group in terms of age or gender (Table 1).

<table>
<thead>
<tr>
<th></th>
<th>Patient group (n=47)</th>
<th>Control group (n=30)</th>
<th>Significant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, F/M</td>
<td>18/29</td>
<td>12/18</td>
<td>0.881</td>
</tr>
<tr>
<td>Age, years</td>
<td>38.8±13.5</td>
<td>38.0±11.9</td>
<td>0.795</td>
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<tr>
<td>Liver volume</td>
<td>1440.9±292.5</td>
<td>1573.3±167.1</td>
<td>0.014*</td>
</tr>
<tr>
<td>Spleen volume</td>
<td>354.8±168.9</td>
<td>250.5±72.1</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Spleen/Liver volume ratio (S/L)</td>
<td>0.27±0.19</td>
<td>0.16±0.04</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

Table 1. Distribution of age and gender between the groups, A comparison of the mean liver and spleen volumes of the patients and control group.

Data are n of participants, mean ± SD.

*P < 0.05, independent samples t-test.

A statistically significant difference was observed between the liver and spleen volumes of the patient and control group (P = 0.014, P < 0.001, respectively). The liver volume of patients with chronic viral hepatitis was found to be lower than that of the control group whereas the spleen volume was higher. A statistically significant increase was seen in the patient group compared to the control group when the ratio of spleen volume to liver volume was examined (P < 0.001) (Table 1).

In the evaluation of liver volume according to the staging, it was seen that the more increase fibrosis degree, so the liver volume decreased. In the F2 group, the liver volume was slightly reduced compared to the control group, whereas the F1 group showed a slight increase compared to the control group, although this was not statistically significant (P = 0.957, P = 0.806, respectively).

F3 group showed a significant difference compared to control F1 and F2 groups in terms of the liver volume (P < 0.001, P < 0.001, P = 0.001, respectively). F4 group showed a significant difference compared to control, F1, F2 and F3 group in terms of the liver volume (P < 0.001, P = 0.001, P = 0.003, P = 0.009, respectively).

The spleen/liver volume ratio was seen to increase the more the degree of fibrosis increased. When spleen volume was evaluated according to staging, it was seen that spleen volume increased with an increase in the degree of fibrosis (Table 2).

The liver volume of the mild fibrosis group did not show a significant difference compared to the control group (P = 0.826). However in the advanced stage fibrosis group, a statistically significant reduction in volume was observed compared to both the mild fibrosis and the control groups (P < 0.001, P < 0.001, respectively). The spleen volume showed a statistically significant increase in the advanced fibrosis group compared to the mild fibrosis and the control groups (P < 0.001, P < 0.001, respectively). No evident difference in volume was determined between the mild fibrosis group and the control group (P = 0.234). A statistically significant increase was seen in spleen volume to liver volume ratio in the advanced fibrosis group compared to the mild fibrosis and the control ones (P < 0.001, P < 0.001, respectively).

A statistically significant increase compared to control, F1, F2, F3 and F4 group in terms of the liver volume (P < 0.001, P = 0.001, P = 0.003, P = 0.009, respectively). Honda et al stated that the ratios of caudate lobe/left+right liver lobe and spleen/left+right liver lobe could be used in the diagnosis of cirrhosis and chronic active hepatitis. In a study of patients with viral hepatitis using MDCT, Li et al

Discussion

Published studies have reported that liver and spleen volume measurements in the definition of the level of fibrosis can be used in the diagnosis and monitoring of chronic liver diseases. However, there are not yet enough studies on this subject. US, CT, MRI and radionuclide imaging can be used in the measurement of liver and spleen volume. Although there are studies on liver and spleen volume measurement by CT in chronic liver disease, most of these have been conducted on patients with non-viral hepatitis. The most significant disadvantage of volume measurements taken by BT imaging is the use of ionizing radiation. USG may be inadequate for abdominal examination, especially in the obese as it is dependent on the operator. MRI, which has the best soft tissue resolution, does not contain ionizing radiation.

In a study by Zhou et al of patients with viral cirrhosis, the liver volume of Child-Pugh C class patients was determined to be significantly low compared to that of Child-Pugh A and B class patients. In a study by Lin et al, when the liver volume of patients with chronic viral hepatitis was compared with that of the control group, a significant reduction was determined in the Child-Pugh A, B and C classes. Honda et al stated that the ratios of caudate lobe/left+right liver lobe and spleen/left+right liver lobe could be used in the diagnosis of cirrhosis and chronic active hepatitis. In a study of patients with viral hepatitis using MDCT, Li et al...
reported a decrease in total liver volume of chronic liver disease patients compared to the control group and an increase in the spleen volume (3).

Similarly in the current study, the liver volume in chronic liver disease was found to be reduced compared to the control group whereas the spleen volume was found to be increased compared to the control group. The spleen volume to liver volume ratio was found to be increased compared to the control group.

Li et al. also reported that the stages of fibrosis increased so liver volume decreased. A statistically significant difference was reported between the patient group and the healthy control group in respect of liver volume; however the difference between the mild fibrosis group and the advanced fibrosis group was not statistically significant (3). Similarly in the current study, no significant difference was observed between the mild fibrosis group and the control group (P >0.017). However, there was a statistically significant difference between the advanced fibrosis group and both the mild fibrosis group and the control group.

Li et al. also reported that spleen volume increased with an increase in the level of fibrosis. This increase was not statistically significant between the control group and the mild fibrosis group and the advanced fibrosis group, but there was a significant difference between all these groups and the cirrhosis group (3). In the current

### Table 2: Age and gender distribution of fibrosis groups and control group, a comparison of the median liver and spleen volumes of fibrosis groups and control group.

<table>
<thead>
<tr>
<th></th>
<th>F1 (n=25)</th>
<th>F2 (n=8)</th>
<th>F3 (n=9)</th>
<th>F4 (n=5)</th>
<th>Control (n=30)</th>
<th>Significant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>18/7</td>
<td>3/5</td>
<td>5/4</td>
<td>3/2</td>
<td>18/12</td>
<td>&gt;0.05*</td>
</tr>
<tr>
<td>Age, years</td>
<td>33.0 (18-63)</td>
<td>36.5 (19-62)</td>
<td>41 (20-48)</td>
<td>45 (33-65)</td>
<td>37 (20-63)</td>
<td>0.523</td>
</tr>
<tr>
<td>Liver volume</td>
<td>1610 (1250-1950)</td>
<td>1584 (1260-1850)</td>
<td>1150 (1050-1256)</td>
<td>1030 (924-1125)</td>
<td>1156 (1294-1965)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Spleen volume</td>
<td>269 (164-456)</td>
<td>294 (163-369)</td>
<td>568 (185-685)</td>
<td>658 (512-810)</td>
<td>246.5 (134-410)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>S/L</td>
<td>0.16 (0.09-0.30)</td>
<td>0.18 (0.10-0.25)</td>
<td>0.50 (0.16-0.55)</td>
<td>0.61 (0.49-0.88)</td>
<td>0.15 (0.10-0.23)</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

* 2x2 Crosstab comparisons were performed and Fisher's exact test was used.

* P < 0.05 was considered statistically significant (Kruskal Wallis Test)

* P < 0.01 was considered statistically significant (Mann-Whitney U Test, with Bonferroni adjustment)
study, while no significant difference was observed between the mild fibrosis group and the control group, a significant difference was determined between the advanced fibrosis group and the mild fibrosis group.

In the study by Li et al, the spleen/liver volume ratio was significantly raised in the liver fibrosis and cirrhosis groups compared to the control group\(^3\). Murata et al stated that a high spleen/liver volume ratio was a significant factor in the prognosis of primary biliary cirrhosis and the prediction of symptom development\(^16\).

In the current study, the ratio of spleen volume to liver volume showed an increase with the increase in the level of fibrosis. While this increase was not significant between the mild fibrosis group and the control group, it was significant between the advanced fibrosis group and both the mild fibrosis and the control ones. As spleen volume to liver volume ratio was associated with both the increased volume which develops in the spleen and the decreased volume of the liver, the F3 and F4 groups in particular showed a statistically significant difference compared to the control, F1 and F2 groups. However, no significant difference was observed between the F3 and F4 groups.

The main limiting factor of the current study was the low number of patients at stages F2, F3 and F4. Further studies would be improved by a sufficient number of patients at the different stages of fibrosis.

### Conclusion

As MRI is a non-invasive imaging technique which does not contain ionizing radiation, measurements of liver and spleen volume made by this technique can be considered as a guide in the determination of the level of fibrosis in chronic liver disease and for patient monitoring.

### References


### Table 3: Age and gender distribution of mild and advanced fibrosis groups and control group, a comparison of the median liver and spleen volumes of mild and advanced fibrosis groups and control group.

Data are n of participants, median (minimum-maximum)

<table>
<thead>
<tr>
<th></th>
<th>Mild fibrosis group (n=33)</th>
<th>Advanced fibrosis group (n=14)</th>
<th>Control group (n=30)</th>
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<tr>
<td>Gender, F/M</td>
<td>12/21</td>
<td>6/8</td>
<td>12/18</td>
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<td>Age, years</td>
<td>33 (18-63)</td>
<td>42 (20-65)</td>
<td>37 (20-63)</td>
<td>0.389</td>
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<tr>
<td>Liver volume</td>
<td>(1250-1590)</td>
<td>(924-1256)</td>
<td>(1294-1965)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Spleen volume</td>
<td>281 (163-456)</td>
<td>582 (185-810)</td>
<td>134-410</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>S/L</td>
<td>0.16 (0.09-0.30)</td>
<td>0.52 (0.16-0.88)</td>
<td>0.15 (0.10-0.23)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

\(^a\) P < 0.05 was considered statistically significant (Kruskal Wallis Test)

\(^b\) P < 0.017 was considered statistically significant (Mann-Whitney U Test, with Bonferroni adjustment)


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