The correlation between Doppler US measurement of hepatic arterial flow and the MELD score in patients with chronic liver disease

N.B. TOPAL¹, P. SARKUT², H.Z. DÜNDAR², A.U. ŞAHİN¹, İ. ERCAN³, T. AYYILDIZ⁴, R. IŞÇİMEN⁵, M. KIYICI⁴, E. KAYA², R. EMİROĞLU⁶

¹Department of Radiology, Faculty of Medicine, Uludag University, Uludag, Turkey
²Department of Surgery, Faculty of Medicine, Uludag University, Uludag, Turkey
³Department of Biostatistics, Faculty of Medicine, Uludag University, Uludag, Turkey
⁴Department of Gastroenterology, Faculty of Medicine, Ondokuzmayis University, Samsun, Turkey
⁵Department of Anesthesiology, Faculty of Medicine, Uludag University, Uludag, Turkey
⁶Acibadem University Atakent Hospital, Istanbul, Turkey

Abstract. – OBJECTIVE: The aim of the study was to determine the relationship between the Model for End-Stage Liver Disease (MELD) score and hepatic arterial hemodynamic parameters measured via Doppler US.

PATIENTS AND METHODS: Etiologic causes and hepatic artery hemodynamic parameters of 121 patients with chronic liver parenchymal disease were compared with MELD scores. Doppler ultrasonography (US) was used to assess flow velocity, pulsatility index (PI) and resistance index (RI) in the hepatic artery (HA). Each patient’s MELD scores were calculated at the time of Doppler ultrasound performed.

RESULTS: There was statistically significant difference between MELD score and hepatic artery RI value \(p<0.001, r=0.616\). This difference was statistically more significant in the group which consisted of multiple etiologic causes \(p<0.001, r=0.837\).

CONCLUSIONS: We found significant relation between MELD score and hepatic artery RI measurements in patients with chronic liver parenchymal disease.

Key Words: Doppler ultrasonography, Hepatic artery, MELD score.

Introduction

Estimating the degree of hepatic fibrosis is important for the diagnosis and therapeutic management of patients with chronic liver disease²⁴. Doppler ultrasonography (US) has been used more than 20 years for the assessment of arterial blood flow in patients with cirrhosis of the liver. The arterial resistance index (RI) is the most widely used Doppler US parameter for estimating intrahepatic vascular resistance in clinical studies. A hepatic artery RI > 0.70 is associated with liver fibrosis⁵⁹.

The Model for End-Stage Liver Disease (MELD) score was introduced in 2000 for predicting survival in patients with cirrhosis of the liver scheduled to undergo transjugular intrahepatic portosystemic shunt (TIPS)¹⁰. The MELD scoring system, which was developed to predict short-term mortality in patients with cirrhosis of the liver, is also used to determine the allocation of donated livers for transplantation²¹⁰⁻¹¹. The MELD score is based on 3 objective biochemical parameters that are easy to measure: serum bilirubin, serum creatinine, and the international normalized ratio of prothrombin time (INR). The MELD score is an excellent predictor of 3-month mortality in cirrhotic patients listed for orthotopic liver transplantation²⁰⁻¹¹.

The aim of the present retrospective study was to determine the relationship between the MELD score and hepatic arterial hemodynamic parameters measured via Doppler US.

Patients and Methods

Patients
The study included consecutive 121 patients (66 men, 55 women, the average age was 48.83 ± 11.67 years) that presented to Uludag University, School of Medicine Hospital, Organ Transplantation Center, that were diagnosed with chronic liver disease between May 2007 and January 2012. Patients with a documented hepatic parenchymal mass and those with cirrhosis due to Budd-Chiari syndrome were excluded.
The diagnosis of chronic liver disease in all patients was made based on serological test results, and fine needle biopsy or surgical biopsy findings. The MELD score was calculated for each patient and Doppler US findings were retrospectively evaluated. The study protocol was approved by the Uludag University School of Medicine Ethics Committee (28.09.2010, 2010-9/17). The subjects were previously informed about the adopted procedures, and gave their consent to the investigation.

**Study Protocol**

**MELD Score Calculation**

The MELD score was obtained by calculating the INR, and serum bilirubin and creatinine values using the following logarithmic formula: 

\[
\text{MELD} = 9.57 \times \log e (\text{creatinine} \ [\text{mg dL}^{-1}]) + 3.78 \times \log e (\text{bilirubin} \ [\text{mg dL}^{-1}]) + 11.20 \log e (\text{INR}) + 6.43.
\]

**Doppler US Techniques**

All the patients were examined by the same radiologist using B-mode and Doppler US after at fasting period of ≥ 4 h. Examinations were performed with patients in the supine, left decubitus, and right decubitus positions during 5-10 s of breath holding via the subcostal, intercostal, and subxyphoid transverse approaches. All examinations were performed using a color Doppler US device (Aplio SSA 770, Toshiba, Tokyo, Japan) equipped with 3.5-MHz convex probe. The common hepatic artery was evaluated via Doppler US. After evaluating the diameter and lumen of the vascular configuration via B-mode in the axial and longitudinal planes, Doppler US findings were evaluated following optimization of the flow rate interval, flow filter, and Doppler gain for minimizing noise and aliasing artifacts. The angle between the vascular configuration examined via Doppler US and the acoustic beam was maintained between 30° and 60°. The flow rate was adjusted specifically for each examination. The maximum velocity, minimum velocity, RI, and pulsatility index (PI) of the common hepatic artery (HA) were measured in the order listed via Doppler US.

**Statistical Analysis**

Statistical analysis was performed using SPSS v.13.0 for Windows (SPSS Inc., Chicago, IL, USA). The normality of the distribution of data was assessed via the Shapiro-Wilk test. The Mann-Whitney U test was used to compare paired independent groups, whereas the Kruskal-Wallis test (a non-parametric statistical test) was used to compare > 2 groups. Categorical variables were compared using Pearson’s chi-square test. Descriptive values for variables not normally distributed are presented as median (range), versus mean ± SD for variables with normal distribution. Categorical variables are presented as percentage. The level of statistical significance was set at \(\alpha = 0.05\).

**Results**

**Etiological Factors Are Presented in Table I**

The mean and standard deviation of HA maximum velocity, minimum velocity, RI and PI were 66.68 ± 16.31, 17.4 ± 6.2, 0.76 ± 0.07, 1.84 ± 0.32 respectively.

There weren’t any significant relationships between the etiological factors and the MELD score. Likewise, there weren’t any significant relationships between the etiological factors and

<table>
<thead>
<tr>
<th>Etiology</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatitis B</td>
<td>28</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>13</td>
</tr>
<tr>
<td>Delta hepatitis</td>
<td>8</td>
</tr>
<tr>
<td>Wilson’s disease</td>
<td>10</td>
</tr>
<tr>
<td>Primary sclerosing cholangitis</td>
<td>2</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>5</td>
</tr>
<tr>
<td>Primary biliary cirrhosis</td>
<td>6</td>
</tr>
<tr>
<td>Crigler-Najjar syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Congenital hepatic fibrosis</td>
<td>1</td>
</tr>
<tr>
<td>Portal hypertensive biliopathy</td>
<td>1</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>1</td>
</tr>
<tr>
<td>Hepatitis B + C</td>
<td>3</td>
</tr>
<tr>
<td>Hepatitis B + delta hepatitis</td>
<td>6</td>
</tr>
<tr>
<td>Alcoholic cirrhosis</td>
<td>14</td>
</tr>
<tr>
<td>Cryptogenic cirrhosis</td>
<td>17</td>
</tr>
<tr>
<td>Hepatitis B + alcohol</td>
<td>1</td>
</tr>
<tr>
<td>Hepatitis C + cryptogenic</td>
<td>1</td>
</tr>
<tr>
<td>Delta hepatitis</td>
<td>1</td>
</tr>
<tr>
<td>Alcohol + non-alcoholic steatohepatitis</td>
<td>1</td>
</tr>
<tr>
<td>Hepatitis B + hepatitis C + delta hepatitis</td>
<td>1</td>
</tr>
</tbody>
</table>
maximum velocity, minimum velocity, RI or PI of hepatic artery. Additionally, there were not significant relationships between MELD score and patient age with maximum and minimum velocity or the PI value of hepatic artery. In contrast, there was a significant relationship between the MELD score and hepatic artery RI value in the patients with 1 etiological factor \( (r = 0.616) \) and in the patients that had more than 1 etiological factor the significance of the relationship was greater \( (r = 0.837) \).

**Discussion**

Estimation of the degree of hepatic fibrosis is important for the diagnosis and therapeutic management of patients with chronic liver disease. Although percutaneous biopsy is the gold standard for diagnosing and determining the severity of cirrhosis and fibrosis, it is an invasive procedure and cannot be used for follow-up. Furthermore, histopathological analysis of liver biopsy specimens return false negative results due to sampling mistakes in 20%-30% of patients. As such, the importance of non-invasive methods of diagnosing liver fibrosis and cirrhosis is increasing.

Ultrasonography is commonly the first-line imaging method used for the clinical work-up of patients with chronic liver disease. Doppler US facilitates quantitative measurement of blood flow to the liver; therefore, many researchers have investigated the utility of Doppler US as a non-invasive method of assessing the degree of hepatic fibrosis, and measurement of the relative flow or velocity in the hepatic artery or vein, and in the portal vein has been the primary focus of such research.

Earlier studies on patients with chronic liver disease reported elevated hepatic artery RI values, which was thought to be related to the structural changes that occur in the liver as the severity of disease increases. A recent study by Piscaglia et al reported that an increase in the RI value is correlated with an increase in the histologic fibrosis score; however, the overall histologic score was not correlated with necrosis or inflammation. Generally, the RI value is affected by numerous variables, including patient age and the heart rate, and most studies have reported that there isn’t a correlation between the RI value and histological findings.

The MELD scoring system was developed to overcome the limitations of the Child-Pugh scoring in patients with end-stage liver disease. It was demonstrated that the MELD score more accurately estimates 3-month survival than the Child-Pugh score. Weisner et al investigated the 3-month mortality rate in 3437 patients with cirrhosis of the liver; the mortality rate was 1.9% in those with a MELD score < 9, versus 71.3% in those with a MELD score ≥ 40. Initially, the MELD score was used in patients with cirrhosis of the liver that underwent TIPS. Since it has been used to determine the prognosis in patients with different stages of cirrhosis of the liver. Observing that the MELD score yields more accurate prognostic results than the Child-Pugh score, United Network for Organ Sharing (UNOS) began to use it for listing patients for liver transplantation. Based on the MELD score, patients are listed for transplantation according to the rationale, “sickest first.” As the MELD score is based on standard laboratory tests and does not consider any subjective parameters or demographic factors such as age and race that could affect listing for organ transplantation, it is generally the preferred scoring system for listing patients for liver transplantation. Based on the current literature relevant to the MELD score, the present study aimed to determine the relationship between hepatic arterial hemodynamic flow and the MELD score in patients with chronic liver disease.

The literature includes only one study that compared the MELD score and etiological factors in patients with chronic liver disease. Angermayr et al compared the etiology-based MELD score and survival in patients with viral hepatitis-induced and alcohol-induced cirrhosis, and observed that there wasn’t a significant difference between the groups in 3-month period. However, in 12-month period, the MELD score was significantly higher and the survival rate was lower in the patients with viral hepatitis-induced cirrhosis. They explained these findings as follows: liver disease progresses in untreated viral hepatitis patients and in patients unresponsive to treatment, whereas the disease does not progress in patients with alcoholic-induced cirrhosis because the patients avoid consuming alcohol post diagnosis. Accordingly, the MELD score does not increase significantly over time in patients with alcoholic-induced cirrhosis, in contrast to those with hepatic cirrhosis. In the present study there wasn’t a significant relationship between the MELD score...
and etiological factors for cirrhosis of the liver; however, the MELD score wasn’t recalculated over time, it was calculated just once at the time Doppler US was performed.

In the present report there was a significant relationship between the MELD score and the hepatic artery RI value in the patients with only 1 etiological factor. Westra et al.24 conducted a study that included 38 children with end-stage liver disease and observed a significant increase in the hepatic artery RI value. Iwao et al.3, Sacerdoti et al.5 and Westra et al.24 also reported that hepatic artery RI and PI values were significantly higher in cirrhosis patients. Westra et al.24 explained this with the fact that the portal vein predominantly supplies hepatic sinusoids, and the hepatic artery predominantly supplies connective tissue and the biliary ducts of the portal triad. Progressive fibrosis causes an increase in peripheral resistance in the arterial microvascular bed and hepatic parenchymal compliance is lost during adaptation to the changes in pressure, which leads to an increase in arterial resistance and pulsatility.

In a similar study Yan et al.22 compared the MELD score and the degree of liver fibrosis in 53 liver cirrhosis patients, and reported that the 2 parameters were correlated. Similarly, in the present research patients with the highest MELD score had the highest hepatic artery RI value. The lack of any relationships between portal venous parameters, and hepatic arterial flow and PI despite there being a significant correlation between the hepatic artery RI value and MELD score was postied by Eipel et al.26 to be because in addition to intrinsic regulation by classical arterial autoregulation, hepatic arterial pressure has a second autoregulation system—hepatic artery buffer response (HABR). This system causes compensatory changes in the pressure in response to changes in the portal venous system. The hepatic artery dilates as portal venous flow decreases and constricts when portal venous flow increases. In non-cirrhotic patients 25%-60% of the decrease in portal venous flow can be buffered by an increase in hepatic arterial flow. This physiological response minimizes the likelihood of liver injury due to changes in portal venous flow and helps tissues meet oxygen need.

Iwao et al.25 observed that the Buffer capacity of the hepatic artery was significantly lower in cirrhotic patients than in healthy controls. Despite compensatory changes in portal venous flow, the portal vein cannot compensate for the differences in flow and pressure that occur in the hepatic artery. In addition, the portal vein cannot control its own flow, as it consists of total extrahepatic splanchnic blood flow. Therefore, changes in hepatic artery perfusion cannot be compensated for by changes in portal vascular flow or resistance.26

In the present work the relationship between the MELD score and hepatic artery RI value was stronger in the patients that had more than one etiological factor, which might have been because multiple etiological factors increased the degree of hepatic microlobular destruction. Sacerdoti et al.5 reported that the hepatic artery PI value is higher in cirrhotic patients than in healthy individuals. Iwao et al.25 referred that the hepatic artery PI value was higher in patients with cirrhosis and portal hypertension (PHT) than in healthy controls. In the present article the hepatic artery PI value in the patients increased, but it wasn’t significantly related to the MELD score.

There weren’t any significant relationships in the present paper between etiological factors, and the mean hepatic artery velocity or the hepatic artery RI and PI values, which is similar to earlier reports.23,5,7,9,14 Shabrawi et al.27 studied 25 children with chronic liver disease and reported that there wasn’t a significant relationship between etiological factors and US findings. This might be because of the reason that liver cirrhosis has similar histopathological features independent of the etiology.

Although providing new and potentially useful data, this work has some limitations. This was a retrospective study. Our population sample was heterogeneous, with hepatic cirrhosis of different stages and etiologies. Additional data would be necessary to assess systemic hemodynamics, because cardiac output is usually increased in cirrhotic patients with possible consequences on RI in peripheral arteries.

Use of the MELD scoring system for assessing the prognosis of hepatic parenchymal diseases is becoming more widespread. As the MELD score is an objective measure based on standard laboratory data that can accurately estimate prognosis, it generally preferred to other scoring systems.

Conclusions

We observed a significant relationship between the MELD score and the hepatic artery RI
value in patients with chronic liver disease. Furthermore, the present findings indicate that Doppler US can provide valuable data for estimating the prognosis in patients with chronic liver disease.

**Conflict of Interest**
The Authors declare that there are no conflicts of interest.

**References**

1. **LIM AK, PATEL N, ECKERSLEY RJ, KUO YT, GOLDIN RD, THOMAS HC, COSGROVE DO, TAYLOR-ROBINSON SD, BLOOMEY MJ.** Can Doppler sonography grade the severity of hepatitis C-related liver disease? AJR 2005; 184: 1848-1853.


8. **LIU CH, LIN JW, TSAI FC, YANG PM, LAI MY, CHEN JH, KAO JH, CHEN DS.** Non-invasive tests for the prediction of significant hepatic fibrosis in hepatitis C virus carriers with persistently normal alanine aminotransferases. Liver Int 2006; 26: 1087-1094.


