Portal and Hepatic Artery Hemodynamics in Cirrhotic Patiens: Relationship with the Severity of Portal Hypertension and Hepatic Failure

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The **aim** of our study was to investigate the value of Doppler ultrasonography of the portal vein and hepatic artery in liver cirrhosis and to detect any relationship between the ultrasonographic changes and the severity of the portal hypertension and hepatic failure.
Methods: The study comprised 112 patients diagnosed with cirrhosis who had different degrees of esophageal varices, no ascites and who had been divided into groups according to Child-Pugh score. We evaluated the portal vein and hepatic artery velocities and we calculated the hepatic artery resistance and pulsatility index.
Results: Our data suggest that in patients with cirrhosis there is a significant correlation between the pulsatility index and the size of esophageal varices ($p < 0.0001$) and between the portal velocity and the size of esophageal varices ($p < 0.0001$). We found a significant inverse correlation between the portal velocity and the pulsatility index ($r = -0.63$) and a negative correlation between the portal velocity and the resistance index ($r = -0.23$).There was no correlation between the portal velocity and the peak systolic arterial flow ($r = 0.017$). There were no statistical differences of the studied portal vein and hepatic artery hemodinamics to different stages of liver disease.
Conclusion: Portal vein and hepatic artery hemodinamics are unrelated to the degree of hepatic failure. In patients with cirrhosis the hepatic artery pulsatility index is correlated with the severity of the portal hypertension respectively with the degree of esophageal varices. Doppler ultrasound determination of these indices may contribute to a non-invasive evaluation of varices.

Keywords: liver cirrhosis, portal hypertension, esophageal varices, hepatic artery pulsatility index

Introduction

Portal hypertension leads to serious complications and is responsible for significant morbidity and mortality in patients with liver cirrhosis. Precise assessment of the severity of portal hypertension is useful in the management of this patients.

Even though measurement of the hepatic venous pressure gradient is accepted as the gold standard for assessing the degree of portal hypertension this invasive technique is not routinely performed in all centers and it is not suitable for widespred routine clinical use [1,2,3].

On the other hand even if esophagogastroduodenoscopy (EGD) is the standard method to diagnose the presence of esophago-gastric varices repeated endoscopic examinations are unpleasant for patients, and have cost impact on health care insurance. In recent years a wealth of new methods have been proposed as alternatives to conventional EGD for the non-invasive or minimally invasive diagnosis of esophageal varices(EV). Despite all the research, non-invasive techniques that identify patients with clinically significant portal hypertension steel require further study [4].

In spite of being evaluated since 1983, the accuracy, sensitivity and specificity of duplex Doppler imaging as a non-invasive diagnostic and prognostic modality for liver cirrhosis, and its correlation to the degree of functional impairment of the liver, remains controversial and is still debated by many investigators. Adding duplex Doppler to the standard grayscale ultrasonography evaluation has clarified the role of this modality in the evaluation of portal hypertension, presence or absence of EV and the degree of the varices [5,6]. The present study aims to identify non-invasive parameters based on ultrasonographic measurements that have a potential in assessment of presence and size of esophageal varices in patients with liver cirrhosis. Also, we intend to show behavior among studied parameters to the degree of liver failure, with respect to the Child-Pugh clinical score.

Material and methods

The study was performed on 112 patients represented by 62 males and 50 females admitted in the Department of gastroenterology from the University of Medicine and Pharmacy Tg-Mureş or seen as outpatients between november 2008 and december 2010. Eligible patients were diagnosed with liver cirrhosis and had different degrees of esophageal varices, assessed with endoscopy. Diagnosis of cirrhosis was based on the combination of typical clinical, biochemical and ultrasonographic findings or on the results of liver histologic examination. Exclusion criteria included ascites (in order to avoid the interferences of the fluid with the Doppler measurements), portal vein thrombosis, evidence of hepatocellular carcinoma on ultrasonography and splenectomy. Patients who have received surgical intervention for portal hypertension previously were also excluded from the study.

Table I. Clinical characteristics of patients

Sex (M/F)	62/50
Age (yr; mean ± SD)	55.43 ± 9.31
Age range (yr)	22-77
Aetiology of liver cirrhosis	
Alcohol	63
Hepatitis B virus	6
Hepatitis C virus	29
Hepatitis B+D virus	1
Alcohol and hepatitis C virus	5
Wilson disease	2
Primary biliary cirrhosis	2
Autoimmune cirrhosis	3
Cryptogenic	1
Oesophageal varices grade (I/II/III/IV)	32/43/31/6
Child-Pugh classification (A/B/C)	75/31/6
Mean speed of flow in portal vein (cm/sec)	9.44±1.81
Mean speed of flow in hepatic artery (cm/sec)	65.08±19.76
Mean HARI	0.8±0.09
Mean HAPI	1.53±0.26

The following information was collected for each patient: age, gender, etiology of cirrhosis, presence and degree of esophageal varices, results of laboratory investigation. Two experienced endoscopist who used the grade I–IV classification did the endoscopies [7]. Further, patients were classified dichotomously either as having large EV (grade III-IV) or as having small EV (grade I-II). Laboratory investigations included serum levels of total bilirubin, albumin, prothrombin time. The degree of liver failure was assessed according to the Child classification modified by Pugh assigning patients into three categories [8].

All patients underwent a gray-scale US and Doppler US assessed with ultrasound device Philips HD 11 XE serially equipped with curvilinear transducer of 3.5 MHz and software for calculation of the hemodinynamic parameters based on the spectral Doppler waveform. Patients were examined the morning after an overnight fast in peacefully lying supine position for portal vein and hepatic artery flow evaluation, mean portal vein velocity (PVV), portal vein dimension, peak systolic (PSFV), end diastolic and mean hepatic artery velocity, resistance index of hepatic artery (HARI) and pulsatility index of hepatic artery (HAPI). HARI was calculated as the ratio of the difference of peak systolic minus end diastolic velocity to peak systolic velocity. HAPI was calculated as the ratio of the difference of peak systolic minus end diastolic velocity to mean velocity. Diameter was measured in milimeters (mm) and the speed of flow in the portal vein and hepatic artery in centimeters per second (cm/s). Due to anatomical and procedural difficulties in assessing proper anatomical structures we performed hepatic artery hemodynamic evaluation only on 76 patients.

Statistical analysis was performed using the Fisher's exact test and p values < 0.05 were considered significant. To study the correlations between the speed of flow in the portal vein and the hepatic artery hemodynamics we used Pearson's correlation coefficient, calculated using Microsoft Office Excel. Patient characteristics were expressed as mean values +/- standard deviations and as percentages as appropriate.

Results

Selected clinical and demographic characteristics of the patients enrolled in this study are presented in Table I.

Most patients had alcoholic associated cirrhosis (56.25%) followed by viral hepatitis associated cirrhosis (25.89% hepatitis C associated cirrhosis and 5.36% hepatitis B associated cirrhosis, respectively). The incidense is higher in men (62 men versus 50 women). 75 (66.96%) patients were allocated into Child-Pugh class A, 31 (27.68%) into class B and 6 (5.36%) into class C, where class C represents the most pronounced liver dysfunction.

All the 112 patients presented low portal vein velocity, with speed of flow in portal vein between 5.06 and 14.8 cm/s. The mean speed was 9.44 cm/s. The data from our study suggest that in patients with liver cirrhosis the reduction of the speed of flow in the portal vein is correlated with the degree of esophageal varices ($p < 0.0001$) (Table II).

Due to anatomical and procedural difficulties from the 112 patients enrolled in our study we performed hepatic artery hemodynamic evaluation only on 76 patients. Mean PSFV in the studied sample was 65.08 cm/sec, the mean HARI was 0.8 and the mean HAPI was 1.53. There was no correlation between the PVV and the PSFV ($r = 0.017$), a negative correlation between the PVV and the HARI ($r = -0.23$) and a significant inverse correlation between the PVV and the HAPI ($r = -0.63$). In our study sample there was a significant correlation between the HAPI and the size of EV ($p < 0.0001$). However the PSFV and the HARI did not correlate with the degree of the EV (Table II).

There were no statistical differences of the studied portal vein and hepatic artery hemodynamics to different stages of liver disease with respect to the Child-Pugh class. (Table III).

Table II. Correlation between the degree of the EV and the portal vein and hepatic artery hemodynamics

	Small grade EV	Large grade EV	p value
PVV	10.55 ± 1.21	7.18 ± 1.04	< 0.0001
Portal Vein Diameter	1.42 ± 0.16	1.54 ± 0.18	NS
PSFV	68.64 ± 22.07	62.76 ± 18.32	NS
HARI	0.84 ± 0.09	0.78 ± 0.08	NS
HAPI	1.76 ± 0.17	1.38 ± 0.17	< 0.0001

Table III. Correlation between the Child-Pugh class and the portal vein and hepatic artery hemodynamics

	Child A	Child B	Child C	p value
PVV	9.49 ± 1.77	9.22 ± 1.95	9.81 ± 1.38	NS
Portal Vein Diameter	1.45 ± 0.18	1.48 ± 0.17	1.42 ± 0.08	NS
PSFV	65.18 ± 19.73	67.68 ± 20.13	50.18 ± 10.26	NS
HARI	0.8 ± 0.1	0.82 ± 0.09	0.78 ± 0.02	NS
HAPI	1.55 ± 0.29	1.51 ± 0.19	1.36 ± 0.15	NS

Discussion

With the availability of Doppler ultrasound attempts have been made to study various blood flow characteristics in patients with liver cirrhosis and portal hypertension, using simple and non-invasive techniques.

In the present study we tried to correlate the hemodynamic parameters of the portal vein and hepatic artery with the severity of the portal hypertension, respectivly with the degree of EV and with the severity of the hepatic affection evaluated by Child-Pugh's classification of cirrhosis.

As variceal bleeding in cirrhotic patients is associated mainly with fatal outcome a regular pursuit and evaluation of esophageal varices plays an important role in the management of this patients. EGD remains the standard method to diagnose the presence of esophago-gastric varices but endoscopy is an invasive, unpleasant and costly diagnostic procedure. Therefore and in order to reduce the increasing burden that endoscopy units have to bear, introduction of non-invasive parameters for assessment of presence and size of EV is becoming a major goal that some studies have attempted to identify.

In concordance with other studies our study results show that the reduction of the speed of flow in the portal vein is correlated with the degree of esophageal varices [5]. We also found that in patients with liver cirrhosis the HAPI is correlated with the severity of the portal hypertension respectively with the degree of EV. We also obtained a negative correlation between the PVV and the HARI. Thus we found no correlation between the HARI, the peak systolic velocity and the degree of EV. It is already known that HAPI is significantly higher in patients with cirrhosis than in controls and directly correlated with the hepatic venous pressure gradient [9]. An increase of HARI was observed among patients with cirrhosis. Iwao reported a 1.1 best cut-off value of HAPI, showing a sensitivity and specificity of 84% and 81%, a significantly higher HAPI in patients with EV and a correlation between the resistivity index and the degree of portal hypertension [10]. However, other studies have reported that the resistivity index in the hepatic artery did not correlate with the hepatic venous pressure gradient, nor with portal hypertension [3, 11, 12]. This results are due to the fact that HAPI is superior to HARI when arterial resistance is extremely high that the end diastolic velocity is very low.

Regarding the correlation of the hemodynamic parameters of the portal vein and hepatic artery with the severity of the hepatic impairment evaluated by Child-Pugh's classification conflicting results have been reported. We found no statistical differences of the studied portal vein and hepatic artery hemodinamics to different stages of liver disease with respect to the Child-Pugh class. El-Shabrawi et al investigated the value of Doppler ultrasound in the assessment of the hemodynamics of the portal vein in children with chronic liver disease and concluded that duplex Doppler added to grayscale US can detect significant morphologic and portal hemodynamic changes that correlate with the severity of chronic liver disease, but not with etiology [13]. Zecanovic et al demonstrated that in patients with liver cirrhosis there is an inversely reciprocal relationship of conjugated HARI with PVFV, correlating to disease grade [14]. Kayacetin et al found that portal flow velocity was decreased in cirrhotic patients with Child's C cirrhosis, as compared to those with Child's A cirrhosis [15]. Furthermore Schneider et al reported a weak correlations between HAPI and Child-Pugh score [9]. The results in our study may we olso owed to the fact that, in order to have accurate measurements of the investigated parameters, none of the patients had ascites. On the whole ultrasonography is a modern imaging modality which plays an important role in the first-line diagnosis of liver cirrhosis and portal hypertension. Ultrasound examination is a safe, non-invasive method, easy to access, confortable for the patients and and a cost effective method. Further validation of the results will be achieved through long-term follow-up of the patients and a larger number of studied subjects.

Conclusion

There is no correlation between the cirrhosis clinical grade and the alteration of portal and hepatic artery hemodinamics.

In patients with cirrhosis the hepatic artery pulsatility index is correlated with the severity of the portal hypertension respectively with the degree of esophageal varices.

The pulsatility index may be useful for diagnosing large esophageal varices in liver cirrhosis. Doppler ultrasound determination of these indices may contribute to a non-invasive evaluation of varices.

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