# Dopplerographic hemodynamic predictive parameters for portal hypertension associated with hepatic cirrhosis

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**Abstract**

**Background:** Early diagnosis of diffuse chronic liver pathologies greatly improves the treatment and pathology evolution prior to the installing of the irreversible fibrosis and cirrhosis. Color duplex Doppler ultrasonography appears to offer a number of advantages (accessibility, repeatability, etc.) in identifying asymptomatic patients and a satisfactory accuracy in assessing liver morphology and hepato-lien system hemodynamics. In order to identify hemodynamic indicators with acceptable significance estimating portal hypertension associated with liver cirrhosis in the study a detailed analysis of changes in hepatic vascular flow examined by color duplex Doppler ultrasound is performed.

**Material and methods:** The research group included 155 patients with varying degrees of fibrosis. Quantification of the fibrosis degree was based on the results of transient Fibroscan elastography, according to the Metavir score (1-4). Evaluation of portal hemodynamics in all patients was done using duplex Doppler ultrasound, hemodynamic indices estimation was performed on arterial and venous side.

**Results:** Reducing time-weighted average velocity in the portal vein, increasing the flow volume in the lien vein basin, vascular resistance increase at the level of lien artery, offers significant predictive values in identifying portal hypertension associated with liver cirrhosis.

**Conclusions:** Colored duplex Doppler ultrasound comprehensive approach of splenoportal hemodynamics showed hemodynamic indicators of unimportant significance for the prediction of cirrogene portal hypertension.

**Key words:** fibrosis, hepatic cirrhosis, hemodynamic indicators, duplex Doppler ultrasound.

## Introduction

Diffuse chronic liver diseases play an important role in the morbidity and mortality of the population in many countries economically developed and less developed countries, including the Republic of Moldova. Viral infection, alcohol abuse, metabolic disorders are the primary causes of these liver diseases. The accuracy of laboratory tests and diagnostic imaging methods in identifying asymptomatic patients or with slight expression in a population at high risk is a primary necessity [2,7.8]. Chronic liver disease often has an insidious onset and a slow and progressive evolution. Chronic inflammations are gradually progressing towards hepatic fibrosis potentially reversible at certain stages, eventually resulting in irreversible cirrhosis. Recommended therapeutic algorithms are to reduce the early portal hypertension, which usually has a progressive evolution as they advance and reverse fibrosis treatment stages. Early diagnosis significantly improves the therapeutic behavior benefits prior to irreversible fibrosis and hepatic cirrhosis installation, often associated with fatal complications: depression of liver function, esophageal variceal bleeding, hepatic encephalopathy, hepatocellular carcinoma [3,4,8].

The golden standard for estimating the portal hypertension still remains the catheterization of the hepatic veins with measurement of the pression gradient. Unfortunetly this method is laborious and invasive, with multiple complications and restrictions in use, both technical and often due to serious condition of hepatic patients [1]. Therefore,

this method has not found a desired application in everyday practice, with preponderant use in scientific research studies. The morphological diagnosis also has an important place in the estimating degree of liver tissue damage in chronic diseases, the results of which play a determining role in shaping the conduct of optimal treatment for each patient. However, although the morphological diagnosis is considered competent, liver biopsy remains an invasive method, with well-known complications, filled with difficulties, often common for obtaining the bioptate from the area of interest, such as the need for adequate ultrasound guidance, patients' obesity, and the uncooperative ones. So again, the method can not be widely used [1, 6, 10, 12].

In recent decades, thanks to advances in diagnostic imaging technology, numerous global multicenter studies have shown promising results in the non-invasive assessment of normal liver structure, identification and assessment of morphologically circumscribed and diffuse liver changes, but also in the evaluation of portal hypertension syndrome. Alternative non-invasive diagnostic methods become a vital necessity in monitoring patients with chronic liver diseases, both in accessibility (price/access to equipment) and repeatability.

Non-invasive diagnosis of liver fibrosis and cirrhosis is based mainly on biochemical laboratory tests and transient elastography (Fibroscan) being used successfully in predicting liver elasticity, providing a quantitative assessment of the degree of fibrosis. The degree of liver fibrosis determined by using elastography does not always correlate with the pressure gradient in the hepatic veins, which denotes a special involvement of hemodynamic changes and often it is not only due to advanced fibrosis [5, 9, 11]. Biphasic helical CT with contrasting dynamic magnetic resonance elastography are new methods to assess the stiffness of liver parenchyma. To assess the complications of cirrhosis, portal-systemic collaterals aggravated with bleeding or hepatocellular carcinoma computed tomography angiography with contrast and MRI are used [12, 13, 14]. In the series of diagnostic methods, conventional ultrasound (2D) and duplex Doppler color scheme has a number of advantages as an accessible, non-irradiated, repeatable method, which can be carried out even at the patient's bedside. The method has an acceptable accuracy in liver morphological assessment, favoring more information on hepato-lienal system hemodynamics [2, 3, 4, 10]. However, despite clear progress, noninvasive diagnosis of fibrosis and portal associated hypertension remains a complex issue and requires further studies.

The aim of the study was to make a detailed analysis of changes in hepatic vascular flow assessed by color duplex Doppler ultrasonography in order to identify the hemodynamic indicators with acceptable significance in estimation of portal hypertension associated with liver cirrhosis.

## Material and methods

During 2012-2014 years in the Department of Clinical Hepatology at the Republican University Hospital were investigated 155 patients with various degrees of fibrosis. The entire research group was subdivided into group determined with cirrhosis (fibrosis stage 4) – 111 and precirrhotic group, which included patients with various degrees of fibrosis (1-3) – 44. The mean age of selected patients was 48.4 years. Gender distribution was 55 males (35%), women – 100 (65%). Study methods of the group included both traditional analyses made in a patient with liver pathology and modern imaging techniques. Quantification of the fibrosis grade was based on the results of transient elastography Fibroscan according to the Metavir score (1-4). To assess liver structure by conventional echocardiography (2D) were used the following parameters: liver measurements – right lobe, left lobe, caudate lobe, spleen size; contour of the liver was assessed using linear probe. Evaluation of portal hemodynamics was performed in all patients by duplex Doppler ultrasound, estimating hemodynamic indices which were performed on arterial and venous side. Subsequently indicators used in the estimation of portal cirrhogene hypertension were calculated.

## Results and discussions

Evaluation of hemodynamic parameters in the portal vein in cirrhotic patients group revealed: dilatation of portal vein in 95 patients (85%), in precirrhotic group in 19 (43%) cases; decrease of time-weighted average velocity (TWAV) in the group of patients with cirrhosis was present in 90 (81%) cases versus to the precirrhotic group – 8 (18%). The increased flow in the portal vein in patients with cirrhosis occurred in 69 (62%) cases, in patients with fibrosis precirrhotic stages in 12 (27%). The values of the statistical indicators used to predict portal hypertension associated with liver cirrhosis are shown in tab. 1.

**Table 1**

**Predictive statistical indicators in portal vein**

| Indicators | Se | Sp | PPV | NPV | LR+ | LR- |
|---|---|---|---|---|---|---|
| Diameter of portal vein (mm) | 86% | 57% | 83% | 61% | 2 | 0,24 |
| TWAV (cm/sec) | 81% | 82% | 92% | 63% | 4,5 | 0,23 |
| Volume of flow ( ml/min) | 62% | 72% | 85% | 43% | 2,2 | 0,52 |

**Legend**: Se – sensitivity, Sp – specificity, PPV – positive predictive value, NPV – negative predictive value, LR+ – positive likelihood ratio, LR- – negative likelihood ratio.

The evaluation of these parameters in the portal vein showed a very good prediction time-weighted average velocity with a likelihood ratio of 4.5 times compared to only measuring the diameter and volume of vascular flow in the portal vein (fig. 1).

The appreciation of similar dopplerographic parameters at the level of lienal vein settled a dilatation of the lieanal vein in 87 (90%) in group of patients with hepatic cirrhosis compared with 13 (29%) in the group with different stages of fibrosis. Blood flow velocity assessed at this level was characterized by the increase in 83 (86%) in the cirrhotic group and 15 (34%)

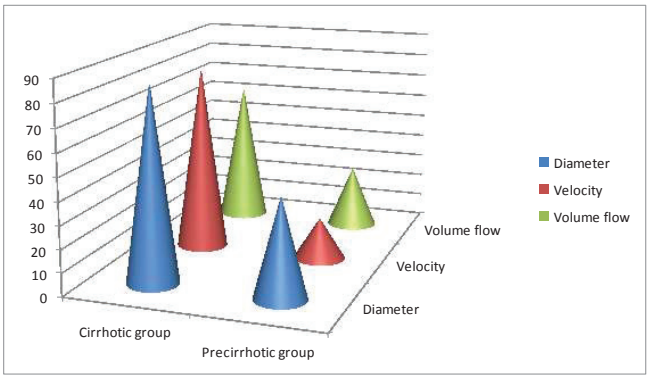


**Fig. 1. Comparative analysis of haemodynamic parameters in portal vein.**

in the precirrhotic group. Increased volume of the vascular flow in the lienal vein was constant in 92 (96%) in the group with cirrhosis and only 10 (22%) in the other group. Statistically obtained indicators values are shown in tab. 2.

**Table 2**

**Predictive statistical indicators in lienal vein**

| Indicators | Se | Sp | PPV | NPV | LR+ | LR- |
|---|---|---|---|---|---|---|
| Diameter of lienal vein (mm) | 90% | 70% | 87% | 77% | 3 | 0,14 |
| TWAV (cm/sec) | 86% | 65% | 85% | 69% | 2,5 | 0,21 |
| Volume of flow ( ml/min) | 95% | 77% | 90% | 89% | 4,1 | 0,064 |

We can see that practically all the indicators used to assess hemodynamics showed a satisfactory predictive value, especially blood flow volume in lienal vein, values which allow to increase the predicted values by 4,1 times in the diagnosis of disease (fig. 2).

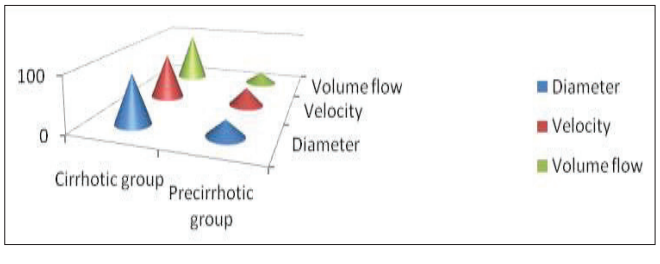


**Fig. 2. Comparative analysis of hemodynamic parameters in lienal vein.**

Assessing arterial hemodynamics slope impedance the indicators were analyzed: pulsatility index (PI) and resistivity index (RI) at the level of lien and hepatic artery. The obtained statistical indicators values are shown in table 3.

**Table 3**

**Predictive statistical indicators in hepatic and lienal artery**

| Indicators | Se | Sp | PPV | NPV | LR+ | LR- |
|---|---|---|---|---|---|---|
| Hepatic artery (PI) | 87% | 50% | 81% | 61% | 1,74 | 0,26 |
| Hepatic artery (RI) | 95% | 50% | 83% | 81% | 1,9 | 0,21 |
| Lienal artery (PI) | 53% | 95% | 96% | 48% | 10,6 | 0.1 |
| Lienal artery (RI) | 83% | 95% | 97 | 72 | 16,6 | 0,17 |

So, due to a comparative analysis of isolated hemodynamics of hepatic artery and the lienal artery we can notice a significant increase (16.6 times) of the probability of portal hypertension associated with cirrhosis in the presence of circulatory lien artery disorders (fig. 3).

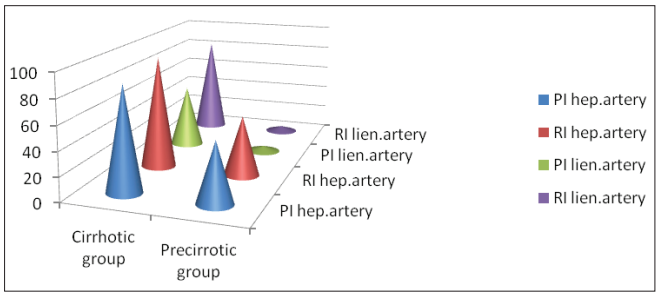


**Fig. 3. Comparative analysis of hemodynamic parameters in hepatic and lienal artery.**

Also, in this study other utility indicators known in assessing the portal hypertension were evaluated: congestion index (CI), splenoportal index (SPI), portal vascular index (PVI), the index of portal hypertension (IPH), which showed specificity and important positive likelihood ratio. Maximum values were found in CI, with a specificity of 93% and + 11.4 RP. Just PVI – Sp 87%, RP + 5.8.

Splenomegaly, is a mandatory criterion to quantify portal hypertension being analyzed in both groups of patients. It was confirmed that the known experience represents a test of a very high sensitivity, being present in 100 (97%) patients, the cirrhotic group, but a low specificity being present in 19 (43%) patients in group with various degrees of fibrosis (Se 98%, SP 57%). In identifying a more specific criterion we assessed the presence of portosystemic collaterals in both groups of patients, obtaining a positive test in 100 (90%) patients from cirrhosis group and only 2 (4.5%) patients in the precirrhotic group. Thus RP + 18, is an important predictive parameter for portal hypertension associated with cirrhosis (fig. 4.)

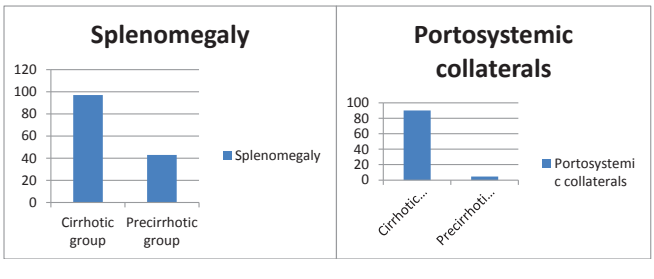


**Fig. 4. Comparative analysis of splenomegaly and portosistemic collaterals.**

In this research very high predictive indicators for the presence of cirrhosis were revealed, realized by color duplex Doppler ultrasound obtaining ROC curves. Thus, the area under the (AUC) curve for time-weighted average velocity in the portal vein, splenoportal index, the IPH is 1, and the congestion index is 0.976, which shows a great accuracy of using these parameters (fig. 5).

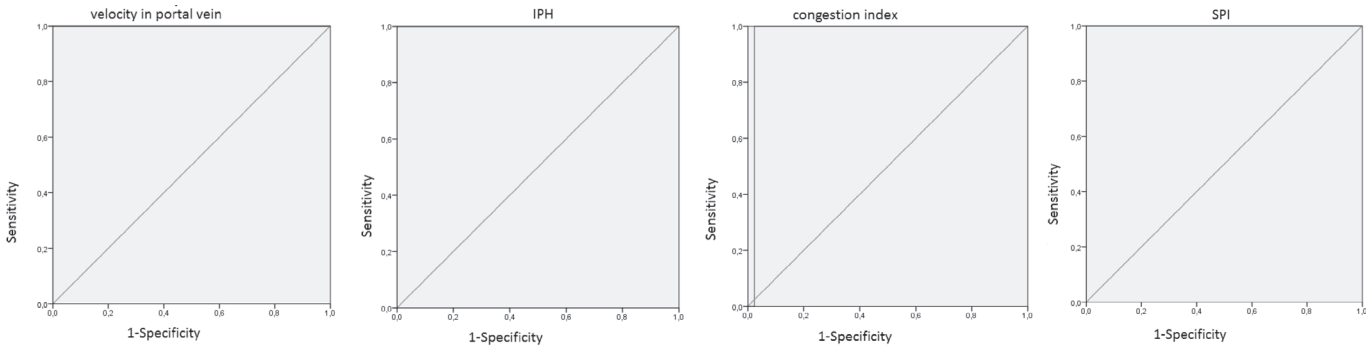


**Fig. 5. ROC curves for cirrhotic group.**

## Conclusions

1. The analysis of hemodynamic indexes by color duplex Doppler ultrasound revealed early emergence of circulatory changes associated with portal hypertension up to the irreversible morphological appearance.

2. Study of circulatory disorders in the portal vein side emphasized the importance of reducing time-weighted average velocity of the cirrhotic patients group.

3. Evaluation of the significance of flow in the lien vein basin determined the superiority of flow volume at this level compared to other indicators.

4. Hemodynamic evaluation of the arterial versant established a major importance of pulsatility and resistance indices at lien artery level predicting portal hypertension associated with liver cirrhosis.

5. Comprehensive approach by color duplex Doppler of splenoportal hemodynamics highlighted several circulatory aspects showing not only academic interest but also practical benefits for patients who can benefit from treatment at a very early stage of fibrosis.

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