The aim of this study is the assessment of the relative arterial and venous contribution to the total liver blood flow (hepatic perfusion index-HPI), with two methods (S1 and S2), and estimation of their value. With this correction, HPI nonsignificantly increases (p>0.05) in all the groups of patients, with a very high correlation between the HPI(S1) and HPI(S2) values (p<0.01). In comparison to the portal perfusion in controls, values were significantly (p<0.01) lower in chronic active hepatitis and liver cirrhosis and differed between themselves (p<0.01). In the groups of cirrhotic patients with esophageal varices, sclerosated esophageal varices, re-canalized umbilical vein, portal thrombosis and cavernous portal vein, portal perfusion was lower (p<0.01) than in controls, chronic active hepatitis and liver cirrhosis without collaterals.

Both angioscintigraphic methods are useful for the estimation of the disturbances in the portal system. Because of the more exact estimation of the liver perfusion, S2 is recommended.

Noninvasive methods, such as echoangiography of the large hepatic blood vessels, duplex-Doppler ultrasonography of the portal venous system and methods of nuclear medicine have been applied in hepatic perfusion studies. Angiography and other invasive methods follow. Computerized tomography and nuclear magnetic resonance, although used mainly for the morphological examination can also be performed in hepatic blood flow studies. Nuclear medicine methods are basically founded on the analysis of hepatic radionuclide angiogram (HRA), obtained after the "first pass" of the radioactive bolus and registered activity over liver and other abdominal organs after intravenous injection of $^{99m}$Tc. The technique of radionuclide angiography and determination of the hepatic perfusion index (HPI) proposed by Sarper et al. is noninvasive method supplying well reproducible information on portal blood flow.

Performing the different mathematical formulas, it is possible to estimate selectively arterial and venous liver perfusion. Sarper et al. proposed estimation of the hepatic perfusion index (HPI) using slopes of the arterial and venous phase of HRA (S1). Later, the same author, modified his method introducing the correction of HPI for the amount of the contribution of the arterial "washout" phase in the portal blood supply (S2).

The aim of the study is the estimation of various porto-hepatic circulation parameters using hepatic radionuclide angiography (HRA) in patients with portal vascular disorders and the hypertension syndrome. The other aim is the estimation of the validity of the correction of HPI obtained by Sarper’s method (S1), using the correction for the arterial hepatic "washout" phase (S2).

**INTRODUCTION**

Under physiological condition, liver receives approximately 70% of the portal and 30% of the arterial blood supply, but various pathological changes can disturb this ratio. Thus, studies of the liver blood flow are important in the evaluation of hemodynamic disorders in various hepatic diseases. The estimation of portal blood flow can provide the valuable information on the degree of portal flow restriction, the progress of pathophysiological changes and assessment of their extent, as well as for the appropriate choice of therapy (shunt surgery and its type).
with liver cirrhosis and sclerosed esophageal varices (LCSEV), in 12 with portal thrombosis, or the thrombosis of the portal venous branches (PVT), in 5 with recanalized umbilical vein (RUV) and in 8 with cavernous portal vein (CPV).

HRA was performed with bolus injection of 740 MBq $^{99m}$Tc-pertechnetate, (1 min, 1f/s), using ROTA scintillation camera. From the ROI over liver parenchyma, TA arterial-hepatic and portal-venous phase of the HRA, were separated at the moment when maximal activity over the left kidney ROI was registered. According to S1 method, on HRA, arterial slope (Ba) was estimated from the beginning of the activity in the liver region (T0), during 7s. Similarly, the portal slope (Bp) was estimated on the liver curve from the time point which reflects the maximal activity over the left kidney region (Tm), during 7s. HPI was calculated using formula: $HPI = Bp/(Ba+Bp)^9$. Thus, HPI reflects the value of the relative portal contribution to the liver blood flow. Improved (S2) method, demands calculation of the arterial ($A_s$ from T0 during 7 s) and venous (descendent - Ds, from kidney Tm during 7 s) slopes on the splenic curve. True portal slope (Pt) is obtained with the correction of Bp for the value of the arterial "washout" phase through hepatic veins (P0), using formulas: a) $Pt = Bp - P0$; b) $P0 = (DsxBa)/A_s$ and, finally, c) $HPI = Pt/(Ba+Pt)^{10}$.

The final diagnoses were based according to the clinical findings, results of the functional and laboratory analysis, ultrasound and Doppler ultrasound, angiography, biopsy with histopathology and other clinical examinations. Consent was obtained from each patient, and the study protocol conforms to the established ethical guidelines.

Besides the mean HPI values (X) and standard deviation (SD), statistical analysis included T test, U test, one and two way analysis of variance as well as Multiple range test.

For the estimation of the significances of differences of the HPI values obtained using two different methods inside the groups of the patients, U test was used. Paramet-

**RESULTS**

With this correction, HPI increases. However, significant differences between HPI values obtained with these two methods in the different groups of patients were not observed (Table 1). On the other hand, there was very high parametric correlation of the results obtained using these two methods in the C group ($r = 0.9139$, $p< 0.01$).
the groups of patients with higher standard deviation of the values, existed very high (p< 0.01) nonparametric correlation between the HPI results as follows: in CAH r =0.9683, in LC r=0.9545, in LCEV r=0.9183, in LCSEV r =0.9494, in PVT r=0.9193, in RUV r=0.9256 and in CPV r=0.9173.

With both methods, HPI values were decreased in all the groups of portal hypertensive patients in comparison to normal values (Tables 1 and 2).

**DISCUSSION**

Initially, Sarper, using the first (S1) method, Sarper et al. estimated the arterial phase slope during 7 s after the beginning of the liver activity, (because its shortest duration, obtained experimentally, lasted 7 s). Similarly, the initial slope of the portal phase was determined. The results, obtained with this method, showed very high correlation with angiographically determined degree of portal hypertension. However, at the same moment when portal component arrives in the liver, being late after arterial one because of the time needed to pass through the abdominal vessels, arterial blood, which previously arrived in the liver and passed through liver parenchyma outflows through hepatic veins, so, the portal phase slope of the liver curve is decreased for the value of the slope of the arterial washout phase. Because of that, Sarper, modified his method and suggested the correction of the portal slope for the slope of the arterial washout phase, supposing that the ratio of the ascendent, arterial phase of the spleen and its descendnent outflow phase is the same as the ratio between the arterial inflow of the spleen and splenic outflow phase. Using this, modified method, he obtained better correlation of the results with angiographic findings and the degree of portal hypertension in the patients with liver cirrhosis, especially in the most severe form.

According to our results, using Sarper’s modified method with correction of HPI, using correction of HPI for the value of the arterial "washout" component, obtained values are higher, pointing out higher participation of the portal blood in the total liver vascularization, in comparison to the results obtained by basic (S1) method. However, significant difference between HPI values obtained with these two methods (p<0.05) was not proved neither in the controls, nor in the groups of patients with portal hypertension. There is a high correlation between the HPI values obtained with this methods (p<0.01). Anyway, the absence of the significant differences between the HPI results obtained by Sarper’s basic and modified method, does not exclude the need for the correction of the slope of the portal component HRA because of the more exact estimation of the liver perfusion with S2 method.

In the patients with chronic active hepatitis, HPI was slightly, but significantly decreased (p<0.01) in comparison to C (Figure 1) and still significantly higher in comparison to other groups of portal hypertensive patients (LC, LCEV, LCSEV, RUV, PVT and CPV).

Venous liver perfusion is significantly (p) decreased in liver cirrhosis without and with esophageal varices, recanalisation of the umbilical vein (Figure 2) and portal occlusion (Figure 3). However, portal perfusion in the patients with liver cirrhosis without esophageal varices was still significantly (p<0.01) higher than in the groups of patients with portal hypertension. Whole values didn’t differ between themselves (p>0.05).

The literature data are similar to ours. The portal component of liver perfusion determined by scintigraphy was reduced in patients with liver cirrhosis and correlated to

### TABLE 1
VALUES AND SIGNIFICANCES OF THE DIFFERENCES OF HEPATIC PERFUSION INDEX OBTAINED BY SARPER’S BASIC (S1) AND SARPER’S MODIFIED (S2) METHOD IN THE DIFFERENT GROUPS OF PATIENTS STUDIED

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>HPIS1</th>
<th>HPIS2</th>
<th>SIGNIFICANCES</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>10</td>
<td>0.66 ±0.06</td>
<td>0.71±0.05</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>CAH</td>
<td>8</td>
<td>0.59 ±0.03</td>
<td>0.61±0.08</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>LC</td>
<td>13</td>
<td>0.49±0.13</td>
<td>0.53±0.12</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>LCEV</td>
<td>18</td>
<td>0.32±0.19</td>
<td>0.36±0.19</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>LCSEV</td>
<td>9</td>
<td>0.28±0.13</td>
<td>0.30±0.15</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>PVT</td>
<td>12</td>
<td>0.13±0.08</td>
<td>0.185±0.09</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>RUV</td>
<td>5</td>
<td>0.21±0.11</td>
<td>0.22±0.11</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>CPV</td>
<td>8</td>
<td>0.23±0.11</td>
<td>0.25±0.10</td>
<td>p&gt;0.05</td>
</tr>
</tbody>
</table>

C=control; CAH=chronic active hepatitis; LC=liver cirrhosis; LCEV=liver cirrhosis esophageal varices; LCSEV=liver cirrhosis sclerosated esophageal varices; RUV=recanaled umbilical vein; PVT=port vein thrombosis; CPV=cavernous portal vein
the development of cirrhosis and to portal-hepatic gradient pressure. Angioscintigraphy and Duplex Doppler appear to be complementary in the study and follow-up of portal hypertension. Gon et al. recommends the application of the assessment of the total liver blood flow, but relative portal inflow in the CAH and LC correspond to our values. The results of Takegoshi et al. correspond to our values. The ratio was proportionally decreased to the progression of the diseases (normal 74.5±7.3%, chronic hepatitis 58.8±9.2%, compensated liver cirrhosis 29.3±19.3%) and correlated well with the pathohistological findings. He recommended it as a noninvasive and simple method valuable in diagnosing the chronic liver disease, and in estimating its clinical course. Králík et al. obtained a decrease in the HPI which corresponded to the hemodynamical efficiency of collateral circulation. According to Dragoteanu et al., liver angioscintigraphy and per-rectal portal scintigraphy are related to the degree of portal hypertension, thus supporting disease staging and follow-up of evolution to cirrhosis and portal thromboses. Similarly, Miguel et al. claimed that the ratio of hepatic artery/portal flow in cirrhotic and alcoholic hepatitis was significantly different from normal controls (p<0.001) and recommended radionuclide methods as a noninvasive test in the study of chronic liver diseases. Santambrogio et al. obtained the mean HPI 0.42±0.24 in the LC group and 0.66±0.19 in the non-LC group (p<0.02), and claimed that HPI is useful factor in estimating hepatic blood flow and liver function. The results of other authors are also in accordance. Koranda et al. using HPI, confirmed that the net hepatic arterial blood flow is also increased in patients with cirrhosis. Fanfani et al. proved that HPI was reduced only in cirrhotic patients but not in those with chronic hepatitis, which is only partly in accordance to our findings. According to Sarper et al., abnormal values of HPI in spite of physiological values of liver function tests, proved this method to be a sensitive, noninvasive detector of early pathophysiological changes in the splanchnic organs of alcohol and drug abusers. The same author proved it to be correlated with the degree of portal hypertension established by angiography. The observations of Rypins et al. were similar: HPI in normal subjects was 66.0±3.4 and in cirrhotic patients with decreasing angiographic perfusion of grades 1 to 4 the index was 54±4.6, 37±2.6, 17±4.7% respectively which also proved high correlation with the angiographic grade of portal flow (p<0.001).

The results of Sauerbruch et al. show that while the portal venous fraction of hepatic blood flow is significantly reduced in patients with liver cirrhosis and esophageal varices (17±10%), it is not influenced by sclerotherapy (20±11%) but the values were significantly lower (56±9%, p<0.001) in comparison to the controls. The results of Gianpaolo et al., although not quite in accordance to our and the results of other authors, found increased arterial supply in liver cirrhosis and in shunted patients and in spite of some methodological limitations proved some clinical utility.

In the patients with portal thrombosis, HPI was significantly decreased (p<0.01) in comparison to C, CAH and LC. In a few patients with complete portal vein thrombosis, hepatic perfusion was exclusively arterial, which is similar to our findings. Also, MacMathuna et al. emphasized the importance of HRA as a safe and accurate screening method for evaluating portal vein patency or occlusion, particularly at a portal venous inflow of 20%, where the specificity was 100% and sensitivity 90%.

By performing echo-angiography and Duplex-Doppler echosonography, one can successfully determine the direction and rate of blood flow, the presence of the collateral circulation, the existence of thrombosis in blood vessels and detected other portal system vascular disorders, while hepatic radionuclide angiography enables the evaluation of relative liver perfusion. The results show that portal inflow was normal in control group and decreased in liver cirrhosis and portal hypertension, proportionally to the degree of portal hypertension. The lowest values for the participation of portal blood in the total liver vascularisation, were obtained in those with complete portal venous thrombosis. Angioscintigraphy is reasonably accurate, reproducible, safe and can be considered suitable for routine use in the assessment of liver hemodynamics.

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**TABLE 2**

**SIGNIFICANCES OF THE DIFFERENCES OF HEPATIC PERFUSION INDEX VALUES OBTAINED BY BOTH SARPER’S METHODS BETWEEN THE DIFFERENT GROUPS OF PATIENTS STUDIED**

<table>
<thead>
<tr>
<th>Group</th>
<th>CAH</th>
<th>LC</th>
<th>LCEV</th>
<th>LCSEV</th>
<th>RUV</th>
<th>PVT</th>
<th>CPV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>CAH</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>LC</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

C=control; CAH=chronic active hepatitis; LC=liver cirrhosis; LCEV=liver cirrhosis esophageal varices; LCSEV=liver cirrhosis sclerosated esophageal varices; RUV=recanalized umbilical vein; PVT=portal vein thrombosis; CPV=cavernous portal vein
CONCLUSION

Hepatic radionuclide angiography can be used, among other methods for the detection, evaluation, and follow-up of hemodynamic disturbances in the portal venous system. The HPI values obtained by both methods are proportional to the degree of portal hypertension.

However, because of the more exact estimation of the relative liver blood flow, S2 method is recommended.

REZIME

PROCENA RELATIVNE PERFUZIJE JETRE PRIMENOM DVE METODE RADIONUKLIDNE ANGIografije U BOLESNIKA SA POREMEČAJIMA PROTOKA KRVI U PORTNOM SISTEMU

Cilj rada je određivanie relativnog doprinosa arterijske i portne komponente u vaskularizaciji jetre (hepatički perfuzioni indeks - HPI) primenom dve metode (S1) i (S2), i procena njihove vrednosti.

U odnosu na S1, primenom S2 metode, HPI se povećava, ali ne značajno (p<0.05) u svim grupama ispitanih bolesnika, uz visoku korelaciju u vrednostima (p<0.01). U poredenju sa portnom perfuzijom u kontrolnoj grupi, vrednosti HPI su značajno niže (p<0.01) u grupama bolesnika sa hroničnim aktivnim hepatitisom i cirozom jetre, u kojima se i medjusobno razlikuju (p<0.01). U grupama bolesnika sa variksim jednjaka, skleroziromen variksim jednjaka, rekanalizovanim umibilikmalnom venom, trombozom vene porte i kavernoznom portnom venom, portna perfuzija je bila značajno niža (p<0.01) od vrednosti u kontrolnoj grupi, hroničnom aktivnom hepatitisu i cirozi jetre bez razvijene kolateralne cirkulacije.

Obe metode angioscintigrafije su korisne za procenu hemodinamskih poremećaja u portnom sistemu. Zbog egzaktnije procene relativne perfuzije jetre, preporučuje se S2 metoda.

The HPI values obtained by both methods are proportional to the degree of portal hypertension. However, because of the more exact estimation of the relative liver blood flow, S2 method is recommended.

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