NON-INVASIVE PREDICTORS OF PORTAL HYPERTENSION IN PATIENTS WITH HEPATITIS C VIRUS RELATED HEPATOCELLULAR CARCINOMA

By
ZAKARIA MOHRAN¹, MOHAMED SAKR¹, EMAN BARAKAT¹, AHMED ELBAZ²*, MOHAMED ABD AL-HAMID³, MOHAMED ABOU-ELMAATY²

Department of Tropical Medicine, Gastroenterology and Hepatology¹ and Department of Radiology², Faculty of Medicine, Ain Shams University, Cairo11566, Egypt
(*Correspondence email: ahmedelbaz75@gmail.com)

Abstract

The reference standard for portal venous pressure measurement which is clinically important for estimating the feasibility of resection of hepatocellular carcinoma is the hepatic venous pressure gradient, which is invasive and expensive. The present study evaluated the non-invasive parameters for assessment of portal hypertension in Child A patients with hepatocellular carcinoma on top of hepatitis C virus.

A total of 112 patients were subjected to clinical assessment, biochemical assay, ultrasonographic Doppler study, triphasic spiral abdominal computed tomography, upper gastrointestinal endoscopy and hepatic venous pressure gradient measurement. According to hepatic venous pressure gradient measurement, they were classified into groups: GI: 58 patients with hepatic venous pressure gradient <10 mmHg and GII: 54 patients with hepatic venous pressure gradient ≥ 10 mmHg. Significant variables in univariate analysis were included in a multivariate analysis to establish a model for prediction of clinically significant portal hypertension. Results showed that portal vein diameter ≥ 1.3 cm, mono or biphasic pattern of flow in hepatic veins and Giannini index ≤ 909 were independent risk factors for the clinically significant portal hypertension as indicated by HVPG ≥ 10 mmHg. A model with highest likelihood ratio and good fitness was created. This prediction model was displayed by the receiver operating characteristic curve and under the curve area was 0.969 (0.938-1).

Keywords Hepatocellular carcinoma, Hepatic venous pressure gradient, Portal vein diameter, Hepatic vein, Giannini index

Introduction

In the setting of cirrhosis, measurement of portal venous (PV) pressure is clinically important when diagnosing portal hypertension, estimating the likelihood of variceal bleeding, monitoring the progress of therapy (De Franchis et al, 2008) and also assesses feasibility of resection in patients with hepatocellular carcinoma (HCC) (Parikh, 2009). Normal bilirubin concentration and hepatic vein pressure gradient (HVPG) of less than 10 mmHg in Child A cirrhotic patients are the best predictors of excellent outcome after resection and are associated with almost no risk of postoperative liver failure with 70% 5-year survival (Llovet et al, 2008). The reference standard for measurement of portal venous pressure is HVPG calculated by subtracting the free hepatic venous pressure from the wedged hepatic venous pressure. Unfortunately, calculation of HVPG is invasive and expensive, and it cannot be used to monitor therapy. An accurate noninvasive technique that could be used to measure portal venous pressure would represent a major advance in the diagnosis and management of portal hypertension (Parikh, 2009). Several clinical, biochemical, and imaging parameters alone or together have good predictive power for non-invasive assessment of portal hypertension. Some parameters have been found to have a high specificity and sensitivity for the diagnosis of cirrhotic portal hypertension with ultrasound colour duplex Doppler examination such as coarse shrunken liver, dilated portal vein (diameter ≥ 13 mm), size of spleen, splenic vein (SV) diameter and ascites (Cotton et al, 1986), lack or reduced respiratory variations of splenic and superior mesenteric
vein diameter (Bolondi et al., 1982), reversal of portal blood flow, reduced portal vein velocity (Zoli et al., 1993), portal-systemic collateral circulation (van Leeuwen, 1990), altered hepatic venous Doppler pattern (Baik et al., 2006), increased intraparenchymal hepatic and splenic artery impedance (Sacerdoti et al., 1991; Bolognesi et al., 2001), increased intraparenchymal renal artery impedance (Berzigotti et al., 2006), increased congestion index of portal vein (Moriyasu et al., 1986) and reduced mesenteric artery impedance (Taourel et al., 1998).

The present study evaluated clinical, biochemical and ultrasonographic Doppler parameters with good predictive power for non-invasive assessment of portal hypertension in Child A patients with HCC on top of HCV related chronic liver disease so that to be excluded from hepatic resection list.

**Patients and Methods**

The present study was cross-sectional comparative conducted on 112 patients with HCC admitted from November 2010 to August 2013. The study was approved by the medical ethics committee of Ain Shams University and conducted in accordance with the principles of the declaration of Helsinki. All patients provided written informed consent before enrollment. Inclusion criteria were patients with HCV related chronic liver disease, Child class (A) with HCC which was diagnosed according to the following suggested alghorism shown in fig.1 for the diagnostic strategy after detection of hepatic nodule by ultrasound (Bruix and Sherman, 2005); absence of portal, splenic, hepatic vein thrombosis, any vascular invasions or arterio-venous fistula; absence of previously sclerosis or band ligation of oesophageal varices, transjugular intrahepatic portosystemic stent shunt, or surgery for portal hypertension; absence of drug intake for primary prophylaxis of variceal bleeding or previously any intervention for HCC.

Study Design and procedures

All patients were subjected to complete history taking, thorough clinical examination, laboratory investigations including complete blood count, liver profile, renal profile, hepatitis C virus antibody using third generation ELISA test and serum alpha-fetoprotein. Abdominal color Doppler ultrasonographic study by an ultrasound machine (Logic 9, General Electric, medical systems, Milwaukee, USA) was used, after 6 hours fasting, to assess the liver (size and echogenicity), portal vein (patency, diameter, portal vein cross sectional area, mean portal vein flow velocity and direction of flow), hepatic venous Doppler pattern, hepatic artery resistance index, spleen size, splenic vein (patency, diameter, splenic vein cross sectional area, mean splenic vein flow velocity), splenic artery resistance index, intraparenchymal renal artery resistive index (RARI), status of ascites and portosystemic collaterals. The portal vein cross sectional area (PV CSA) (cm²) was obtained assuming portal vein to be circular in cross section and calculated by the computer software of the machine up to 0.99 cm² in normal subjects (Moriyasu et al., 1986; Pozniak, 2002). The average mean portal vein flow velocity (mean PVV) (cm/sec) is above 19 cm/sec in normal subjects (Ozaki et al., 1988). Direction of flow was assessed so that if the flow is towards the transducer, it displays red color (hepatopetal), but if the flow is away from the transducer, it displays blue color (hepatofugal). In cases with both red and blue colors, the flow is bi-directional. The splenic vein cross sectional area (SV CSA) (cm²) and mean splenic vein flow velocity (mean SVV) (cm/sec) were calculated in the same way described with the portal vein. The normal SV CSA is up to 0.5 cm² and the average mean SVV is 19.9 ± 4.6 cm/sec in normal subjects (El Zeiny et al., 2002). Hepatic artery resistance index (HARI) was measured in the intrahepatic main branches. The resistance index (RI) was calculated...
over one cardiac cycle from the formula: 

\[ RI = \frac{\text{systolic velocity - end diastolic velocity}}{\text{systolic velocity}} \]

(this was calculated by machine software). Average value was 0.68 in normal one (Schneider et al., 1999). Splenic artery resistance index (SARI) was measured intra-parenchymally, near to the hilum. It was calculated like HARI, cutoff value is 0.60 in normal subjects (Sacerdoti et al., 1991). The reported values of the Doppler parameters were obtained by taking the average value of 3 consecutive measurements. Also the following indices were calculated; congestion index (CI) (cm/sec-1) which was calculated for portal and splenic veins as: 

\[ CI = \frac{\text{CSA}}{\text{mean velocity}} \]

The average PV CI in normal subjects is up to 0.07 cm/sec-1 and the average SV CI is up to 0.04 cm/sec-1 (Pozniak, 2002; El Zeiny et al., 2002). Modified liver vascular index (MLVI) (cm/sec) was calculated as: portal flow velocity/ hepatic artery RI (Piscaglia et al., 2001). Portal hypertension index (PH index) (m/sec-1) was calculated as: 

\[ [(\text{hepatic artery RI} \times 0.69) \times (\text{splenic artery RI} \times 0.87)]/ \text{portal vein mean velocity} \]

Portal-systemic collaterals e.g. left gastric vein, paraumbilical vein, porta hepatitis collaterals, lienorenal collaterals, splenic hilar collaterals and gastrorenal collaterals were also examined. Hepatic venous Doppler pattern was assessed either monophasic, biphasic or triphasic. Platelet count/spleen diameter ratio was calculated in millimeters by Giannini index (Giannini et al, 2003). Upper gastrointestinal (GIT) endoscopy Pentax EG-3440 videoscope system was used to evaluate the presence and degree of varices in addition to any relevant upper GIT lesions. Triphasic spiral abdominal computed tomography (CT) was done to diagnose HCC by typical vascular pattern and to assess tumor site, size, number and extension. HVP was measured with the patients under local anesthesia, a venous introducer was placed in the right internal jugular vein and a 5 French catheter with cobra head configuration was advanced under fluoroscopic control into the main right hepatic vein. Using an invasive monitor, pressure was measured while tip of catheter was floating in the middle of the hepatic vein (free hepatic venous pressure (FHVP)). The catheter is then pushed down in the hepatic vein until it cannot be advanced further, which results in a complete obstruction of flow (position of catheter was confirmed by using contrast material); the pressure recorded in the occluded position (using invasive monitor) is the wedged hepatic venous pressure (WHVP). HVPG was calculated by subtracting the FHVP from the WHVP. The HVPG is the difference between the portal vein and the inferior vena cava pressures (IVCP) and represents the real perfusion pressure within the portal and hepatic circulations. Normal HVPG is about 1-5 mmHg. When HVPG increases above 10-12 mmHg, a number of life-threatening complications can occur (Parikh, 2009).

Statistical analysis: Data were analyzed using SPSS for Windows (version 19.0). Continuous variables were expressed in term of mean and standard deviation (except for alpha-fetoprotein which was expressed in term of median and inter-quartile range) and ordinal and nominal categorical data were described as number and percentages (frequency). Chi-square test with Yates correction and Fisher-Exact were used to test association between two categorical variables. Student-t-test was used to test means' differences between groups (except for alpha-feto-protein where Mann Whitney test was used). Variables were significant at P<0.05. Logistic regression analysis was performed to identify variables independently associated with presence of clinically significant portal hypertension and established model for prediction significant portal hypertension in patients. As all significant variables in univariate analysis could not be included in the same regression model, different models
were generated. The best one was judged by likelihood ratio, significance of introduced predictors, odds ratio and confidence interval together with fitness and productivity of the model.

**Results**

As to HVPG measurement, patients were classified into two groups: GI included 58 patients (51.8%) with HVPG less than 10 mmHg. Mean HVPG was 5.5 +/- 1.8 mmHg. GII included 54 patients (48.2%) with HVPG equal to or more than 10 mmHg. Mean HVPG was 15.2 +/- 2.3 mmHg. Demographic profile and laboratory parameters were similar in both groups except a lower statistical significant difference in GI in comparison to GI regarding hemoglobin level, white blood cells and platelet counts. Patients in GI had statistically higher values of creatinine and alpha fetoprotein in comparison to GI. All patients had coarse echogenicity of liver with no detectable ascites on abdominal ultrasonography. Most of them had single hepatic focal lesion (HFL) in the right lobe of the liver. Patients in GI had larger spleen, more frequent to have collaterals and their Giannini index was significantly lower than patients in GI. As to upper GIT endoscopy findings, esophageal varices, fundal varices and portal hypertensive gastropathy (PHG) were significantly common in GII than GI (Tab. 1). All patients had patent portal vein with hepatopeda direction of flow and patent splenic vein. Doppler parameters were higher in GII compared to GI with a highly significant difference (Tab. 2).

Significant variables in univariate analysis were included into a binary logistic regression analysis stepwise method. The best predictive model gave the highest likelihood ratio; the relatively high predictivity meanwhile showed a good fitting using Hosmer & Lemshow Goodness of fit test. Portal vein diameter more than or equal to 1.3 cm, mono or biphasic pattern of flow in hepatic veins and Giannini index below or equal to 909 were found to be independent risk factors for presence of clinically significant portal hypertension as indicated by HVPG more than 10 in this study (Tab. 3). The performance of this prediction model is displayed by the receiver operating characteristic (ROC) curve. The area under the curve (AUC) was 0.969 (0.938-1.0), showed that this model gave a good discrimination between patients with HVPG more than 10 and those with lower HVPG (Fig. 2). A total of 37 patients fulfilled all parameters included in model (Predicted probability = .98260); only one had HVPG less than 10 and 20 had none of model parameters positives (Predicted probability=.00238); all had HPVG less then 10, an example of the general result that if log \[ P (Y=1) / P (Y=0) = b_0 + b_1 X_1 + .. + b_p X_p \text{ then } P (Y=1)=\exp (b_0 + b_1 X_1 + .. + b_p X_p)\] or \[ P (Y=1) =1/ (1 + \exp (\text{-} (b_0 + b_1 X_1 + .. + b_p X_p))) \text{ So, P (Predicted probability of High HVPG) = 1/1+exp \{- (constant (-6.039) + 4.51(when PV diameter 1.3 or more) + 3.55 (when mono- or biphasic HV Doppler pattern) + 2.01(when PLT/spleen ratio 909 or less))\} \]

![Fig. 1: ROC curve displaying discrimination ability of predictors model for HVPG (AUC 0.969 - 95% CI 0.938-1.0).](image)
ROC receiver operator characteristic, AUC area under curve.

Fig. 2: Algorithm to investigate nodule in ultrasound during screening or surveillance (Bruix and Sherman, 2005).

Table 1: Characteristics of study population

<table>
<thead>
<tr>
<th>Variable</th>
<th>GI (N=58)</th>
<th>GL (N=54)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Years)</td>
<td>55.97 ± 7.284</td>
<td>55.96 ± 5.956</td>
<td>0.998</td>
</tr>
<tr>
<td>Sex (Male/Female)</td>
<td>49/9</td>
<td>41/13</td>
<td>0.255</td>
</tr>
<tr>
<td>Hemoglobin (gm/dl)</td>
<td>13.410 ± 1.0327</td>
<td>12.902 ± 1.2369</td>
<td>0.020</td>
</tr>
<tr>
<td>White blood cells (10^9/L)</td>
<td>5.888 ± 1.9256</td>
<td>4.739 ± 1.4060</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Platelets (10^9/L)</td>
<td>154.52 ± 46.678</td>
<td>96.09 ± 37.913</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alanine transaminase (U/L)</td>
<td>62.74 ± 25.461</td>
<td>55.50 ± 18.137</td>
<td>0.108</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.856 ± 0.1456</td>
<td>0.999 ± 0.1708</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alpha fetoprotein (ng/dl)</td>
<td>44.50 (IQR=14.3-188.5)</td>
<td>102 (IQR=30.5-1004.5)</td>
<td>0.005</td>
</tr>
<tr>
<td>Liver size (shrunken/average/enlarged)</td>
<td>2/40/16</td>
<td>0/45/9</td>
<td>0.086</td>
</tr>
<tr>
<td>Collaterals</td>
<td>1</td>
<td>27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Splenic diameter (cm)</td>
<td>13.48 ± 1.78</td>
<td>16.63 ± 2.53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. of HFLs (1/2/3)</td>
<td>44/12/2</td>
<td>45/8/1</td>
<td>0.602</td>
</tr>
<tr>
<td>Site of largest HFL (cm)</td>
<td>4.866 ± 1.77</td>
<td>5.159 ± 2.0481</td>
<td>0.420</td>
</tr>
<tr>
<td>Oesophageal varices</td>
<td>10 (17%)</td>
<td>54 (100%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fundal varices</td>
<td>0 (0%)</td>
<td>13 (24.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PHG</td>
<td>7 (12.1%)</td>
<td>34 (63.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Giannini index (mm)</td>
<td>1159.82 ± 345.66</td>
<td>611.89 ± 305.04</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2: Independent factors predicting HVPG

<table>
<thead>
<tr>
<th>Variables</th>
<th>B^a</th>
<th>SE of B^a</th>
<th>P value</th>
<th>OR^95% CI)^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV Diameter ≥ 1.3 cm</td>
<td>4.51</td>
<td>0.88</td>
<td>&lt;0.001</td>
<td>90.9 (15.9 - 518.2)</td>
</tr>
<tr>
<td>Mono/Biphasic hepatic veins doppler pattern</td>
<td>3.55</td>
<td>1.10</td>
<td>0.001</td>
<td>34.8 (3.9 - 303.9)</td>
</tr>
<tr>
<td>Giannini Index ≤ 909</td>
<td>2.01</td>
<td>0.81</td>
<td>0.013</td>
<td>7.5 (1.5 - 36.3)</td>
</tr>
<tr>
<td>Constant</td>
<td>6.039</td>
<td>1.345</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

^aB=Regression Coefficient, ^bSE=Standard Error, ^cOR=Odds Ratio and ^dCI=Confidence Interval.
Table 3: Comparison between groups regarding Doppler parameters.

<table>
<thead>
<tr>
<th>Variable</th>
<th>GI (N=58)</th>
<th>GII (N=54)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PV diameter (cm)</td>
<td>1.033 ± 0.1559</td>
<td>1.559 ± 0.2469</td>
<td></td>
</tr>
<tr>
<td>PV CSA (cm²)</td>
<td>1.124 ± 0.2189</td>
<td>1.997 ± 0.5512</td>
<td></td>
</tr>
<tr>
<td>mean PVV (cm/sec)</td>
<td>21.68 ± 2.848</td>
<td>12.69 ± 2.360</td>
<td></td>
</tr>
<tr>
<td>PV CI (cm/sec-1)</td>
<td>0.06958 ± 0.086437</td>
<td>0.16984 ± 0.079771</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>SV diameter (cm)</td>
<td>0.658 ± 0.1003</td>
<td>0.985 ± 0.1951</td>
<td></td>
</tr>
<tr>
<td>SV CSA (cm²)</td>
<td>0.576 ± 0.0927</td>
<td>0.934 ± 0.2529</td>
<td></td>
</tr>
<tr>
<td>mean SVV (cm/sec)</td>
<td>19.72 ± 2.120</td>
<td>12.83 ± 2.309</td>
<td></td>
</tr>
<tr>
<td>SV CI (cm/sec-1)</td>
<td>0.03048 ± 0.007121</td>
<td>0.07704 ± 0.031416</td>
<td></td>
</tr>
<tr>
<td>HARI</td>
<td>0.6409 ± 0.04426</td>
<td>0.7050 ± 0.06737</td>
<td></td>
</tr>
<tr>
<td>SARI</td>
<td>0.6267 ± 0.03827</td>
<td>0.6726 ± 0.04020</td>
<td></td>
</tr>
<tr>
<td>RARI</td>
<td>0.6164 ± 0.04483</td>
<td>0.6757 ± 0.05256</td>
<td></td>
</tr>
<tr>
<td>MLVI (cm/sec)</td>
<td>33.974 ± 5.5116</td>
<td>18.251 ± 4.2253</td>
<td></td>
</tr>
<tr>
<td>PH index (m/sec-1)</td>
<td>0.01138 ± 0.002239</td>
<td>0.02350 ± 0.006442</td>
<td></td>
</tr>
<tr>
<td>Hepatic veins Doppler pattern</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monophasic</td>
<td>0 (0%)</td>
<td>14 (25.9%)</td>
<td></td>
</tr>
<tr>
<td>Biphasic</td>
<td>26 (48.3%)</td>
<td>37 (68.5%)</td>
<td></td>
</tr>
<tr>
<td>Triphasic</td>
<td>30 (51.7%)</td>
<td>3 (5.6%)</td>
<td></td>
</tr>
</tbody>
</table>

**Discussion**

In Egypt, there was a growing incidence of HCC (10-120/100,000), which represents the leading cause of death from all other cancer sites (El-Zayadi et al., 2010). Resection and transplantation achieve the best outcomes in well-selected candidates; 5-year survival of 60-80% (Llovet et al., 2012). The selection of optimal candidates for liver resection is usually based on the degree of portal hypertension (Llovet et al., 2008). The reference standard for measurement of portal venous pressure is the HVPG which is invasive and expensive (Parikh, 2009).

In the present study, both groups were age and sex matched without significant differences between them. Hemoglobin level, white blood cells and platelet counts showed significant lower differences in GI in comparison to GI agreed with others (Sharma et al., 2007; Qamar et al., 2008), also thrombocytopenia was correlated with clinically significant portal hypertension by HVPG more than 10 (Zaman et al., 1999; Berzigotti et al., 2013).

In the current study, no significant difference was detected between studied groups regarding alanine transaminase values. Other studies did not elicit association between liver enzymes values and clinically significant portal hypertension detected by presence of esophageal varices (Jeon et al., 2006; Sharma et al., 2007; Fagundes et al., 2008), but, one study established a predictive model for detecting patients with clinically significant portal hypertension using alanine transaminase, albumin and international normalized ratio (Berzigotti et al., 2008).

The present patients with clinically significant portal hypertension (CSPH) had statistical high creatinine values than the others (Woitas et al., 1997; Rendón Unceta et al., 2001) but disagreed by others (Zaman et al., 1999; Berzigotti et al., 2008; Abuel Makaarem et al., 2011) which found that portal hypertension in patients with cirrhosis was either compensated or not. Alpha fetoprotein was significantly higher in CSPH patients that agreed with Ripoll et al. (2009), who found that portal hypertension was an independent predictor of HCC development in patients with compensated cirrhosis due to structural abnormalities, fibrogenesis and neoangiogenesis processes. Significant differences were between groups as to presence of collaterals and longest axis diameter of spleen on ultrasound imaging in CSPH patients that agreed with authors (Sarangapani et al., 2010; Berzigotti et al., 2011; Cherian et al., 2011; Esmat et al., 2011). Also, no statistical difference was found between groups as to number, extension or size of largest hepatic focal lesion; as patients were selected with child A compensated cirrhosis with-
out vascular invasion or extrahepatic spread. Gastroesophageal varices was commonest in patients with CSPH with highly significant difference that agreed with others (Garcia-Tsao et al, 1985; Groszmann et al, 1990). Portal hypertensive gastropathy significantly higher in same patients agreed with others (Kim et al, 2010; Kumar et al, 2010).

In this study, Giannini index was significantly lower in patients with CSPH with high statistical significant difference which is consistent with other studies (Giannini et al, 2003; 2006; Sharma et al, 2007; Agha et al, 2009; Barrera et al, 2009; Sarangapani et al, 2010; Abu El Makarem et al, 2011; Ying et al, 2012). This went with other studies (Iwao et al, 1997; Plestina et al, 2005; Jeon et al, 2006; Tarzamni et al, 2008; Sarangapani et al, 2010; Cherian et al, 2011; Hong et al, 2011), the present study showed significant statistical differences between groups as to portal vein diameter, portal vein cross sectional area, portal vein mean flow velocity and portal vein congestion index. Others (Zaman et al, 1999; Choi et al, 2003) found no relation between Doppler parameters and HVPG due to significant variability in portosystemic collateral patterns (Merkel et al, 1998). The significant differences were between groups as to splenic vein diameter, splenic vein cross sectional area, splenic vein mean flow velocity and splenic vein congestion index agreed with others (Rodríguez et al, 1999; El Zeiny et al, 2002; Kayacetin et al, 2004), but differed due to lower sample sizes (De Bem et al, 2006) or due to liver disease with bleeding varices (Choi et al, 2003).

In the present study, HARI, SARI & RARI were highly significantly increased in CSPH patients compared to those without, who agreed with other studies (Piscaglia et al, 1997; Colli et al, 2001; Berzigotti et al, 2006; 20; Vizzutti et al, 2007; Zhang et al, 2007; Tarzamni et al, 2008); nut disagreed with Choi et al. (2003). Also, the present PHI were significantly higher in patients with portal hypertension while MLVI was significantly lower which agreed with others (Iwao et al, 1997; Amer et al, 2001; Piscaglia et al, 2001; Haktanir et al, 2005; Zhang et al, 2007; Tarzamni et al, 2008).

In the present study, loss of triphasic hepatic venous waveform was commonest in patients with CSPH, which agreed with two studies (Kim et al, 2007; Joseph et al, 2011), but disagreed with one study (Bhutto et al, 2012). Also, as all significant variables in univariate analysis could not be included in same regression model, different models were generated that gave highest likelihood ratio and good fitness. Portal vein diameter more than or equal to 1.3 cm, mono or bi- phasic pattern of flow in hepatic veins and Giannini index below or equal to 909 (Giannini et al, 2003) were independent risk factors for clinically significant portal hypertension by HVPG more than 10 mmHg. Performance of prediction model was displayed by ROC curve. AUC was 0.969 (0.938-1). The model gave a good discrimination between patients with HVPG more than 10 and those with lower HVPG.

The predictive models diagnoses CSPH in cirrhotic patients based on liver stiffness, platelet count and spleen size (Berzigotti et al, 2013), bilirubin (Park et al, 2009), palpable spleen, low platelet count, spleen size> 13.8 mm, portal vein> 13 mm and splenic vein> 11.5mm (Sarangapani et al, 2010), palpable spleen and thrombocytopenia (Sharma et al, 2007), prothrombin time, portal vein diameter and splenic width (Hong et al, 2011), low platelet count, Child-Pugh class B/C, spleen diameter and platelet spleen diameter ratio 909 (Cherian et al, 2011) or PH index and splenic diameter (Tarzamni et al, 2008) but none studied such models in HCC patients. Bilirubin level and prothrombin time showed no statistical different, as patients with Child class A compensated cirrhosis, and PH index significantly correlated
with HVPG gave accepted likelihood ratio or fitness.

**Conclusion**

Portal vein diameter \( \geq 1.3 \) cm, mono or biphasic pattern of flow in hepatic veins and Giannini index \( \leq 909 \) were 3 parameters in used model for non-invasive prediction of portal hypertension. This model in other patients' groups; cirrhotic without HCC, decompensated cirrhotic patients and cirrhotic patients due to etiologies other than HCV are strongly recommended.

The authors have no conflict of interest.

**References**


Hong, W, Dong, L, Jiang, Z, Jiang, Z, et al, 2011: Prediction of large esophageal varices in cirrhotic patients using classification & regress-


