Non-Invasive Assessment and Evaluation of Portal Hypertension in Patients with Liver Cirrhosis

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ABSTRACT

Ultrasonography examination is one of examination that can be used to see the abnormality of portal vein system. The technology of ultrasonography examination has further developed especially after using of Doppler ultrasonography which could portray haemodynamic changes from portal vein in liver cirrhosis patient. From this examination we also could predict bleeding.

Key words: Liver cirrhosis, portal hypertension, doppler ultrasonography.

INTRODUCTION

Liver cirrhosis is a chronic liver disease signified by the presence of fibrosis and nodules. This disorder usually begins with inflammation, widespread liver necrosis, formation of connective tissues and regeneration nodules. Changes in the structure of the liver result in changes in the circulation. Functional liver cirrhosis is classified into two stadiums, compensation (early/latent cirrhosis) and decompensation (followed by liver failure and portal hypertension).1,2

Portal hypertension occurs due to an increase in the pressure of the portal vein system due to increased resistance of the blood vessels and/or increased portal vein blood flow.1,3,4

Liver cirrhosis accompanied with portal hypertension can cause bleeding of the upper gastrointestinal tract due to rupture of the esophageal varices. Seventy percent of patients with liver cirrhosis will eventually suffer from portal hypertension and esophageal varices. Djojoningrat reported a prevalence of gastrointestinal bleeding due to esophageal varices of 70.2% in RSCM in the year 1988. Soemarno, et al reported 93% prevalence of upper gastrointestinal bleeding due to esophageal varices and gastropathy.7 The prevalence on initial bleeding is 36%, and 70% on repeated bleeding.8

Sonography is a diagnostic tool that can be utilized to diagnose abnormalities of the portal vein system. Sonographic technology has further developed with the invention of Doppler combined analysis and standard color ultrasonography, which can portray haemodynamic changes in the portal vein in patients with liver cirrhosis and is currently the most un-invasive technique to evaluate the portal vein blood flow. The sensitivity and specificity of Doppler ultrasonography is 83% and 93% respectively.11,12

HEMODYNAMIC CHANGES OF THE PORTAL SYSTEM

Portal hypertension is mostly due to liver cirrhosis. In Indonesia, cirrhosis is most frequently caused by a virus, while cases abroad are more commonly due to alcohol. Other causes of portal hypertension include thrombosis, tumor, etc.1,2,3,4

The portal vein system consists of a venous network that begins at the superior mesenteric vein, goes through the portal vein and end at the hepatic vein. Before the portal vein enters the liver, it branches in two to supply the right and left hepatic lobe.

As we know, the portal pressure is attained from changes in the hepatic vein. It ranges between 5-10 mmHg measured using catheterization.1,5,6 Portal hypertension occurs due to an increase of pressure in the portal vein system due to an increase in blood vessel resistance and/or a pathologic increase in portal vein blood flow.
Changes that occur:\textsuperscript{1,2,3,4}

1. Increased blood vessel resistance
   Due to liver fibrosis because of the formation of collagen tissues due to liver sinusoid that hardens and causes mechanic obstruction
2. Increased portal vein blood flow
   Due to vasodilatation of the splanchnic artery because of humoral factors (glucagons, NO synthase), neurogenic factors, and local mechanisms
3. Portosystemic collateral formation
   Due to the mechanism of compensation because of pathologic portal blood flow to the heart and its resistance; This occurs as a mechanism to reduce the pressure of the portal system
4. Hyperdynamic condition
   Due to an increase in the level of endogen vasodilators which causes vasodilatation and an eventual increase in plasma volume
5. Splenomegaly

**PRINCIPLE OF MEASUREMENT USING THE DOPPLER ULTRASOUND DEVICE**

As we know, increase in the portal pressure occurs due to increased blood flow to the portal vein. Thus, we could indirectly measure pressure in the portal vein by measuring the portal vein blood flow using the Doppler echo.

Similar to the blood vessel system in general, changes in venous system pressure is a result of blood flow and blood vessel resistance, stated by Ohm’s Laws through

\[ P = Q \times R \]

\( P \) = Pressure changes
\( Q \) = Blood flow
\( R \) = Blood vessel resistance
Thus, the pressure will increase if there is an increase in blood vessel resistance and/or portal vein blood flow. On the other hand, the portal pressure will drop if there is a reduction in blood vessel resistance and/or portal vein blood flow.

Increased blood vessel resistance is caused by liver fibrosis that creates an obstruction/constriction, thus increasing the speed of blood flow, as stated in Pouseuille’s theorem, with the formula: $R = \frac{8 \pi L}{\pi r^4}$

$R =$ resistance  
$N =$ coefficient of viscosity  
$L =$ blood vessel length  
$r =$ blood vessel radius

**Figure 2. Scheme of the formation of portal hypertension**

**Figure 3. Doppler echo ultrasonography. Portrays increased blood flow through a narrowing tube**
N = coefficient of viscosity
L = blood vessel length
r = blood vessel radius

Using Doppler echo ultrasonography portrays not only the liver and the portal vein diameter, but also the characteristics of the blood vessel and blood flow, by measure-
Patients who suffered from bleeding of the esophageal varices and portal hypertension gastropathy was 14-18 Cm/sec. The velocity of flow in 14 patients with gastric bleeding was above 19 Cm/sec.

They concluded that a portal vein velocity above 8 Cm/sec signifies portal hypertension. A portal vein velocity above 9 Cm/sec signifies high risk of upper gastrointestinal bleeding. A portal vein velocity above 14 Cm/sec means upper gastrointestinal bleeding could result from esophageal varices or portal hypertension gastropathy. Thus, we could predict bleeding.

4. Diurnal variation

Alvarez et al conducted an experiment on diurnal fluctuation in 12 patients with liver cirrhosis, 10 men and 2 women ages 30-71 years. The patients were admitted to the hospital and the hemodynamic condition and blood flow was evaluated using Doppler ultrasound every 4 hours for 24 hours, and taken at least 2 hours after meals and after 30 minutes of rest in supine position. They found that the cardiac output and portal vein blood flow increased at midnight.

The mechanism of such increase in portal vein blood flow is still unknown. It is possible that this variation is due to humoral and neurogenic factors, which are an increase in the vasodilator component of VIP (vasoactive intestinal peptide), a strong endogenous vasodilator which peaks at midnight, or a reduction in sympathetic activity due to reduced secretion of catecholamine at midnight.

The variation of portal vein blood flow especially at midnight explains why the incidence of varicose bleeding is highest at night.
Patients with liver cirrhosis. Measurements were taken using Doppler ultrasonography first during fasting and the second time 60 minutes after taking a standard Italian meal (1100 calories = 18% protein, 39% fat, 43% carbohydrate).

This experiment showed an increase in portal vein blood flow in normal patients, patients with chronic hepatitis and those with cirrhosis, but the increase in cirrhosis patients was not very large.

Increase of blood flow, influenced by meals was due to both intrinsic mechanisms, which are increased transmural arteriole pressure and increased vasodilator agents, extrinsic mechanisms, such as the autonomic nervous system, as well as the influence of the gastrointestinal hormones gastrin and glucagon.

From this study, we conclude that meals can cause increased portal vein blood flow, consequently increasing portal pressure.

6. Evaluation of therapy

1. Experiment using pitressin and ranitidine:

Ohnishi et al studied 15 men and 4 women with portal hypertension. Measurements were taken using both angiography and Doppler ultrasound. The portal vein blood flow was measured before and after therapy. Several patients received intravenous pitressin 0.3 U/minute for 15 minutes, and the others received intravenous ranitidine 50 mg/30 minutes.

They found that there was a reduction in portal vein blood flow after administration of both pitressin and ranitidine. Similar results were obtained using angiography and Doppler ultrasound using the formula Y = 0.6 X – 1.723 (Y = angiography and X = Doppler ultrasound).

Doppler ultrasonography is sufficiently accu-

<table>
<thead>
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<th>Table 3. The effect of a standard meal on portal vein blood flow velocity</th>
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<td></td>
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<tr>
<td>NS(n = 12)</td>
</tr>
<tr>
<td>CAH (n = 11)</td>
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<tr>
<td>LC (n = 11)</td>
</tr>
</tbody>
</table>

NS = Normal patients; CAH = Chronic Active Hepatitis; LC = Liver Cirrhosis

<table>
<thead>
<tr>
<th>Table 4. Portal vein velocity in 12 patients with portal hypertension, before and after administration of pitresin and ranitidine</th>
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<tbody>
<tr>
<td>Patient Number</td>
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rate to measure portal vein flow and could also be utilized to observe hemodynamic changes of the portal pressure.

2. Experiment using propanolol.\textsuperscript{15}

Ohnishi et al studied 12 men and 3 women, aged 31-71 years, 13 with liver cirrhosis and 1 with hepatoma. Measurements were taken simultaneously using catheterization and Doppler ultrasound. Measurements were taken before and after administration of 5 mg of propanolol intravenously for 35 minutes. There was a decrease in pulse rate (-12.6\%), reduced cardiac output (-24.5\%) and reduced hepatic blood flow (-27.3\%).

Propanolol reduces the portal vein pressure by reducing portal vein blood flow. This is due to decreased cardiac output caused by a blockage of the B1 adrenergic receptor.

**CONCLUSION**

1. The Doppler ultrasound was used as a method to evaluate the presence of portal hypertension.
2. The Doppler ultrasound is currently the most un-invasive technique to assess portal vein blood flow.
3. The Doppler ultrasound could be used as a non-invasive method to evaluate changes in the hemodynamic condition of the portal vein due to medication or other causes.
4. Using Doppler ultrasound, we can predict bleeding.

**REFERENCES**


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**Table 5. The effect of propanolol on the systemic and splanic hemodynamic condition\textsuperscript{15}**

<table>
<thead>
<tr>
<th>Measurement</th>
<th>n</th>
<th>Base Value</th>
<th>After Propanol</th>
<th>p</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mmHg)</td>
<td>15</td>
<td>95±10</td>
<td>91±12</td>
<td>&lt;0,02</td>
<td>-3,6±5,1</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>15</td>
<td>68±7</td>
<td>61±7</td>
<td>&lt;0,001</td>
<td>-12,6±4,6</td>
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<tr>
<td>CO (/l/mnt)</td>
<td>10</td>
<td>6,03±1,18</td>
<td>4,48±0,88</td>
<td>&lt;0,005</td>
<td>-24,5±11,5</td>
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<tr>
<td>PVP (mmHg)</td>
<td>9</td>
<td>20,1±6,3</td>
<td>17,6±6,2</td>
<td>&lt;0,001</td>
<td>-13,3±6,7</td>
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<tr>
<td>WHVP (mmHg)</td>
<td>6</td>
<td>20,4±4,6</td>
<td>18,5±4,6</td>
<td>0,025</td>
<td>-9,6±5,6</td>
</tr>
<tr>
<td>FHVP (mmHg)</td>
<td>6</td>
<td>8,0±2,9</td>
<td>8,3±2,3</td>
<td>NS</td>
<td>+10,0±23,3</td>
</tr>
<tr>
<td>PVP-FHVP (mmHg)</td>
<td>6</td>
<td>11,5±3,7</td>
<td>9,0±4,4</td>
<td>&lt;0,02</td>
<td>-24,8±14,2</td>
</tr>
<tr>
<td>WHVP-FHVP (mmHg)</td>
<td>6</td>
<td>12,3±2,5</td>
<td>10,2±2,6</td>
<td>&lt;0,001</td>
<td>-18,2±5,9</td>
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<tr>
<td>EHBF (/l/mnt)</td>
<td>6</td>
<td>0,934±0,303</td>
<td>0,633±0,115</td>
<td>NS</td>
<td>-27,3±17,1</td>
</tr>
<tr>
<td>PVF (/l/mnt)</td>
<td>10</td>
<td>0,740±0,227</td>
<td>0,558±0,160</td>
<td>&lt;0,005</td>
<td>-22,3±14,4</td>
</tr>
</tbody>
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