# Correlation of hepatic venous pressure gradient with varices, bleeding, ascites and Child's status in patients with Hepatitis B virus-related decompensated liver cirrhosis

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**Summary**

*Objective:* To investigate the relationship of hepatic venous pressure gradient (HVPG) with variceal size, ascites, Child-Pugh, and history of varice bleeding in decompensated liver cirrhosis patients due to hepatitis B virus (HBV). *Subject and method:* Patients with cirrhotic portal hypertension were enrolled in the study, who underwent clinical, paraclinical examination, include: Upper endoscopy, abdominal ultrasound, and HVPG measurement. *Result:* 51 liver cirrhosis patients (Male : female, 39 : 12; mean age 55.5 ± 9.58 years). The mean HVPG was lower in patients with no varices (11.94 ± 3.08mmHg) than in patients with varices (16.6 ± 3.58mmHg), p<0.001). The mean HVPG in bleeders was higher than in nonbleeders (17.23 ± 2.66 vs 14.42 ± 4.20mmHg; p<0.05). The mean HVPG was significantly higher in Child's B (16.28 ± 3.17mmHg) and C (22.00 ± 0.00mmHg) compared to Child's A cirrhotics (12.17 ± 3.71mmHg; p<0.01). There was no significant differences in HVPG between patients with ascites and those without ascites (16.07 ± 2.64 vs 14.16 ± 4.41mmHg; p=0.091). *Conclusion:* The hepatic venous pressure gradient clearly reflects portal pressure in cirrhotic portal hypertension. And its had a strong relation with variceal bleeding, Child's status, esophageal varices and size of varices.

*Keywords:* Hepatic venous pressure gradient, cirrhosis, esophageal varices.

## 1. Background

In the early stages of cirrhosis, the patient usually has a normal portal pressure (3 - 6mmHg). When liver disease progresses, HVPG gradually increases, which in turn leads to severe complications: Esophageal or gatric varices rupture, ascites, renal failure, and hepatic encephalopathy.

Portal hypertension is the leading cause of death in patients with cirrhosis. The presence of portal-systemic collaterals develops when HVPG > 10mmHg [1], according to Baveno III, which is the predictor of clinically significant portal hypertension [2] and the 12mmHg limit is the prediction of the risk of gastrointestinal bleeding from esophageal rupture [2], [3]. With a reduction in HVPG below 12mmHg or a reduction of 20% compared to the maximum would significantly reduce the risk of primary or secondary bleeding. In the post-TIPS study, when the HVPG was reduced to 0%, 25%, 50% reduced the bleeding rate by 18.7% and 1%, respectively [4]. Similarly,

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the formation of new nodules increases the risk of ascites, although the HVPG is about 10 - 12mmHg at risk for ascites, but the real association between HVPG and ascites has not been studied extensively. Although 8mmHg was suggested as the limit of HVPG in treatment of refractory ascites [5], the optimum level of HVPG remains unclear and controversial.

Child score in cirrhosis is a reliable basis for predicting the risk of varices bleeding. Any improvement in Child score will result in a reduction in HVPG. However, the link between the child's development and the Child's point has not been fully studied [5].

Direct measurement of portal pressure is an invasive procedure often causing many complications. In 1951, Myers and Taylor first used wedged hepatic venous pressure (WHVP), which was used to estimate portal pressure through complete occlusion catheter insertion in the liver. HVPG measurement is currently the best indicator of portal vein assessment; and HVPG is widely used in predicting complications of cirrhosis such as varices bleeding. HVPG is also used as an early predictor for cirrhosis and elevated HVPG associated with cancer risk, liver tumor. Continuous HVPG measurement also evaluates cirrhosis regardless of the cause.

Albilllos A and 2011 [6] have recently been linked to histopathology, clinical, hemodynamic and biological markers to give a classification system distinguishes between compensated cirrhosis and decompensated cirrhosis based on clinical outcomes. Therefore, the present study was performed to aim: *Assessment of portal pressure variability in patients with viral hepatitis B and related to varices, ascites, gastrointestinal bleeding and Child-Pugh score.*

## 2. Subject and method

51 HBsAg positive patients with liver cirrhosis admitted at the 108 Military Central Hospital from August 2016 to September 2018 who have been done clinical examination, laboratory examination, gastroscopy and ultrasound of the abdomen, HVPG measurement.

Exclusion criteria: The patient had one of the following complications: Hepatic encephalopathy; combined cardiopulmonary disease, Child score > 12, non-cirrhotic portal hypertension, treated with beta blockers/nitrates.

***Principle of measuring the door pressure difference***

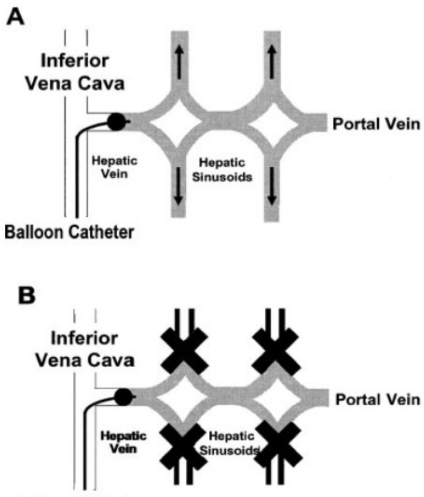



Figure A. In normal people, wedged hepatic venous pressures (WHVP) are balanced by the hepatic sinus. Thus WHVP is the pressure at the liver sinuses, lower than the portal vein pressure (about 1mmHg).

Figure B. In the fibrosis, the WHVP by the balloon injection can not be relieved at the level of the sinus due to the narrowing of the sinuses, the compression of the fibrosis and the nodules. Hence the WHVP corresponds to the portal pressure.

**Figure 1.** Measure WHVP in normal people and patients with cirrhosis [7]

*The processes steps*

Patients are fasting 6 hours before the procedure, ECG, blood pressure, $SpO_2$.

Sterilize, local anesthesia, a 5/7 French balloon catheter is placed in the right hepatic vein through a right jugular vein puncture under bright screen to right liver.

Check for a complete hepatic occlusion before the test (slowly pumping 5ml of contrast medium when the balloon is inflated gives complete imaging, until we see no reflux or washout of contrast medium into hepatic vein). Then deflate the balloon, measure free liver pressure (FHVP); then pumping the ball up to the original size, measuring the WHVP pressure.

Record the results: When stable, may be 2 minutes (usually upto 40 seconds). All numbers are score for 3 times if they are different more than 2mmHg, replace the catheter.

The measurement of WHVP will not be accurate if the hepatic vein is communicated to another vein.

HVPG is calculated by the formula: HVPG = WHVP - FHVP (Figure 2 illustrates HVPG measure which has done at the 108 Military Central Hospital).

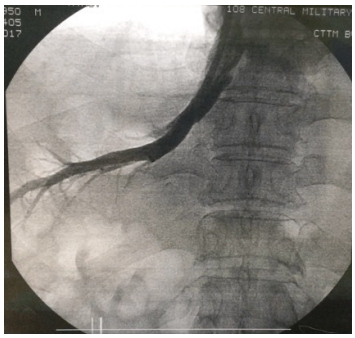
*Research criteria*

Degree of esophageal varices: Small dilated grade 1 - 2 (3mm); large grade 3 - 4 (> 3mm).

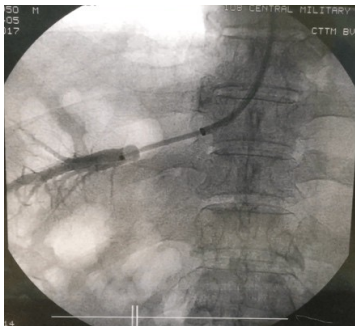
Bleeding due to Baveno VI standard diagnosis: Bleeding, white knot blood clot during endoscopy or gastric blood in patients with esophageal varices and unknown origin of bleeding.

Liver function is graded and classified by Child-Pugh: Child A 5 - 6 points, Child B from 7 - 9 points, Child C 10 points.

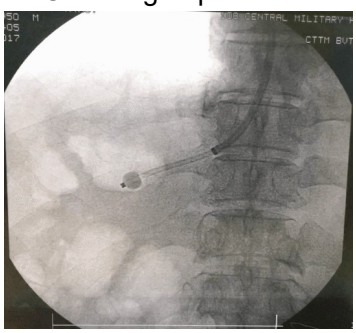
*Data analysis:* Calculate percentage and mean, standard deviation using Student t test to compare continuous variables.



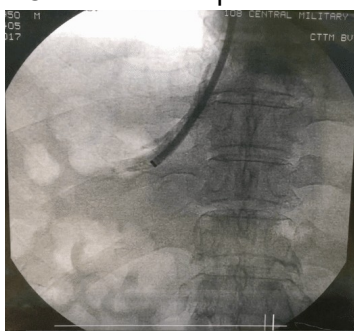
Checking hepatic vein



Occlusion of hepatic vein



WHVP measurement



FHVP measurement

**Figure 2.** Illustration of the HVPG measurement

## 3. Result and discussion

**Table 1. Characteristics of research subjects**

| Characteristics | Index |
|---|---|
| Age | 55.5 ± 9.58 (35 -73) |

| | |
|---|---|
| Gender<br>Male<br>Female | <br>39 (76.5%)<br>12 (23.5%) |
| Cause of cirrhosis virus B | 100% |
| Esophageal varices | 39 (76.5%) |

**Table 1. Characteristics of research subjects *(Next)***

| Characteristics | Index |
|---|---|
| Gastric varices | 7 (13.7%) |
| Bleeding due to varices | 12 (23.5%) |
| Child-Pugh classification<br>A<br>B<br>C | <br>17 (33.3%)<br>32 (62.7%)<br>2 (3.9%) |

Table 1 shown the age of the patients range from 35 to 73 years, the average age was 55.5 ± 9.58 years. Of those, 39 were male (76.5%), 12 were female (23.5%). There were 39 patients (76.5%) with esophageal varices, 7 patients with gastric varices, account for 13.7%, 12 patients (23.5%) had a history of bleeding. Concerning to Child-Pugh, there were 17 Child A patients, account for 33.3%; 32 patients with Child B, account for 62.7%; there were 2 patients with Child C, account for 3.9%.

**Table 2. Relationship between HVPG with status of varices**

| Esophageal varices | HVPG | p |
|---|---|---|
| Yes (n = 35)<br>No (n = 16) | 16.60 ± 3.58<br>11.94 ± 3.08 | <0.001 |
| Gastric varices<br>No (n = 44)<br>Yes (n = 7) | <br>15.43 ± 3.92<br>13.29 ± 4.61 | >0.05 |
| Grading of varices<br>No varices/grade I (n = 16)<br>Grade II (n = 20)<br>Grade III (n = 15) | <br>11.94 ± 3.09<br>17.65 ± 3.47<br>15.20 ± 3.34 | <0.01 |
| Bleeding due to varices<br>No (n = 38)<br>Yes (n = 13) | <br>14.42 ± 4.20<br>17.23 ± 2.68 | 0.029 |

Investigating the association of HVPG with the complications of portal hypertension, we found that there was a statistically significant difference (p<0.001) in HVPG between esophageal varices, the grade of varices, bleeding due to varices. The HVPG of esophageal varices patients was 16.6, meanwhile it was 11.95 in patients without esophageal varices. However, the difference of HVPG between gastric varices group was not statistically significant. The results of our study were in accordance with the study of Wadhawan M et al. In their study, the authors showed that the mean values of HVPG were higher in the large level of esophageal varices group than in the small group [7]. They also found a significantly HVPG elevation in patients with large varices (16.97 ± 6.99mmHg) compared with patients with small varices (11.55 ± 5.47mmHg) and no varices (8.29 ± 4.13mmHg), differences in the group were statistically significant. However, there was no difference in HVPG between the large and small TM groups.

The current study shown that HVPG in varices patient without bleeding was significantly lower than those with bleeding (14.42 vs 17.23, p=0.029). The low HVPG reducing bleeding in patients with varices was confirmed in several reports. Cirrhosis patients with HVPG less than 12mmHg are less likely to have varrices bleeding, and there was evidence that treatment HVPG below than 12mmHg can reduces the risk of bleeding [3]. The authors Al Mahtab M et al also found that average HVPG in patients with bleeding compared with no bleeding in the large varices group was 17.7 ± 5.5 and 14.9 ± 4.7mmHg, respectively with p=0.006 [8].

In the study by Wadhawan M et al, there was also a marked difference in HVPG between bleeding and no bleeding due to varices rupture [7]. Therefore, in order to reduce the risk of varices and bleeding due to varices rupture, treatment's aim is to reduce HVPG.

**Table 3. Relationship of Child-Pugh score with HVPG**

| Child-Pugh score | HVPG | p |
|---|---|---|
| A (n = 17) | 12.17 ± 3.71 | <0.001 |
| B (n = 32) | 16.28 ± 3.17 | |
| C (n = 2) | 22.00 ± 0.00 | |

The Table 3 shown that the difference in HVPG in Child A versus Child B and C was statistically significant, with p<0.001. This indicated that when elevated HVPG levels corresponded to the severity of cirrhosis. Patients with Child C had higher HVPG level than Child A. Wadhawan M et al also reported similar results [7]. In another report Al Mahtab M et al. found that HVPG was significantly higher in both Child B and C patients (14.10 ± 7.56 and 13.64 ± 7.17 mm Hg) than Child A (10.15 ± 5.63mmHg). The HVPG level between Child A and B, and Child A and C were statistically significant (p=0.01 and 0.041, respectively) [8]. In spite of HVPG values for Child C were lower than for Child B, the difference was not statistically significant.

In order to evaluate the relationship between HVPG with ascites, we divided the study cohort into two groups as patient with and without ascites.

**Table 4. Relationship of HVPG with ascites status**

| Ascites status | HVPG | p |
|---|---|---|
| No (n = 25) | 14.16 ± 4.41 | 0.091 |
| Yes (n = 26) | 16.07 ± 2.64 | |
| Total (n = 51) | | |

In general, the increase of pressure at the sinus level leading to ascites and the lower limit of HVPG values from 10 to 12mmHg is predictive value for ascites. However, in our study the difference in HVPG between patients with and without ascites was not statistically significant, with p>0.05 (16.07 vs 14.16). Wadhawan M et al compared HVPG with and without ascites showed that HVPG in patients with ascites 18.3 ± 7.8mmHg, without ascites 16.6 ± 5.7mmHg, the difference was statistically significant [7]. Our results may be due to the inclusion of heterogeneous patients, mainly with Child-Pugh B patients; the use of diuretics may affect the outcome. In addition, other factors that influence the level of ascites, such as liver function, should also be taken into account when analyzing.

## 4. Conclusion

Investigating 51 liver cirrhosis patients infected with HBV we found that: There was a statistically significant difference (p<0.001) in HVPG between esophageal varices, the grade of varices, bleeding due to varices. The difference of HVPG between gastric varices group was not statistically significant. The difference in HVPG in Child A versus Child B and C was statistically significant, with p<0.001. The difference in HVPG between patients with and without ascites was not statistically significant, with p>0.05 (16.07 vs 14.16).

## References