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Hepatic Venous Pressure Gradient - A review

KEYWORDS

Dr Rahul Jain
Dep of Gastroenterology, Army hospital R and R, New Delhi

Dr Kalpana Jain
Columbia Asia hospital, Gurgaon, Haryana

Lt col (Dr) Atul Jha
Dep of Gastroenterology, Army hospital R and R, New Delhi

Portal Hypertension

Portal hypertension is a clinical syndrome defined by increased portal venous pressure gradient above 5 mmHg due to raised pre-, intra-, or post-hepatic resistance. In liver cirrhosis (LC), portal hypertension develops in a case with fibrotic change in sinusoidal liver architecture and is a severe complication of chronic liver disease that severely affects mortality. Portal hypertension may lead major complications of LC, including variceal bleeding, ascites, or hepatic encephalopathy.[1]

Causes of portal hypertension (PH)[2]

1. Gastroesophageal (GE) Varices

GE area is the main site of formation of varices. Esophageal varices (EV) form when the HVPG exceeds 10 mm Hg. In the lower 2 to 3 cm of the esophagus, the varices in the sub-mucosa are very superficial and thus have thinner wall. In addition, these varices do not communicate with the periesophageal veins and therefore cannot easily be decompressed. These are the reasons why EV bleeds only at this site. GV are less common than EV and are present in 5%–30% of patients with PH with a reported incidence of bleeding of about 25% in 2 years, with a higher bleeding incidence for fundal varices.

2. Portal Hypertensive Intestinal Vasculopathies

Mucosal changes in the stomach in patients with PH include portal hypertensive gastropathy (PHG) and gastric vascular ectasia. PHG describes the endoscopic appearance of gastric mucosa with a characteristic mosaic, or snake-skin-like appearance with or without red spots. It is a common finding in patients with PH. The prevalence of PHG parallels the severity of PH and it is considered mild when only a mosaic-like pattern is present and severe when superimposed discrete red spots are also seen.

Portal hypertensive colopathy (PHC) refers to mucosal edema, erythema, granularity, friability, and vascular lesions of the colon in PH. PHC may be confused with colitis. Although they are found in up to 70% of patients with PH and are more common in patients with EV and PHG, they rarely cause bleeding.

3. Ascites and Spontaneous Bacterial Peritonitis (SBP)

Ascites is defined as the accumulation of free fluid in the peritoneal cavity. Cirrhotic PH is the most common cause of ascites, which accounts for approximately 75% patients with ascites. About 60% of patients with cirrhosis develop ascites during 10 years of observation. The development of ascites is an important event in cirrhosis as the mortality is approximately 50% at 2 years without a liver transplantation. The formation of ascites in cirrhosis is due to a combination of abnormalities in both renal function and portal and splanchnic circulation. The main pathogenic factor is sodium retention.

Patients with cirrhosis and ascites are also at risk of developing infections, particularly spontaneous bacterial peritonitis (SBP). SBP occurs in approximately 10% of hospitalized cirrhotic patients, with an associated mortality of 20–40% if untreated. Many patients are asymptomatic, but clinical signs can include abdominal pain, fever, and diarrhea. The diagnosis of SBP is based on neutrophil count >250 cells/mm in the ascitic fluid.

4. Hepatic Hydrothorax

Hepatic hydrothorax is an uncommon complication of end-stage liver disease. It is defined as a pleural effusion greater than 500 mL in patients with cirrhosis in absence of primary cardiac, pulmonary, or pleural disease. The underlying pathogenesis of hepatic hydrothorax is incompletely understood. Patients with cirrhosis and PH have abnormal extracellular fluid volume regulation resulting in passage of ascites from the peritoneal space to the pleural cavity via diaphragmatic defects generally in the tendinous portion of the diaphragm. Negative intra-thoracic pressure during inspiration pulls the fluid from the intra-abdominal cavity into the pleural cavity. Hydrothorax develops when the pleural absorptive capacity is surpassed, leading to accumulation of fluid in the pleural space.

Importance of HVPG

- Measurement of the hepatic venous pressure gradient (HVPG) is the gold standard technique for evaluation of portal hypertension in liver disease[3]
- In patients with cirrhosis, HVPG measurement provides independent prognostic information on survival and the risk of decompensation
- The HVPG response to pharmacological therapy enables the identification of patients with portal hypertension who are most likely to benefit from treatment
- Measurement of HVPG helps to assess the risk of liver failure and death after liver resection in patients with compensated chronic liver disease or hepatocarcinoma
- No noninvasive alternatives to HVPG measurement are currently available

Measurement of HVPG

Hepatic venous pressure gradient (HVPG) represents the gradient between the portal vein and the hepatic vein. HVPG measurement is the best available method to evaluate the presence and severity of portal hypertension. Clinically significant portal hypertension is defined as an increase in HVPG to >10 mmHg.[1] The HVPG is measured by liver vein catheterization and used to evaluate portal hypertension in clinical hepatology. The risk of bleeding from esophageal varices is taken to be negligible if HPVG is less than 12 mmHg, or if reduced by 20% or more during pharmaceutical treatment.[4]

The portal pressure gradient (measured as HVPG) is the difference between the wedged hepatic venous pressure (WHVP) and the free hepatic venous pressure (FHVP). The WHVP is measured by

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occluding the hepatic vein; stopping the blood flow causes the static column of blood so formed to equalize in pressure with the preceding vascular territory—in this case, the hepatic sinusoids (Figure 1).[4]

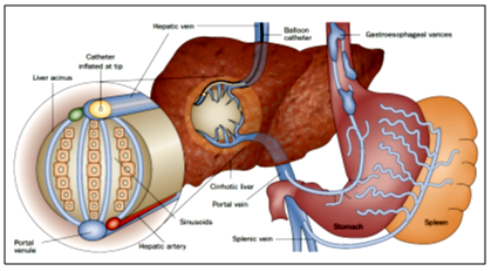

Figure 1: Measuring the portal pressure in the normal and cirrhotic liver.[3]

Thus, WHVP is a measure of hepatic sinusoidal pressure, not of portal pressure. WHVP is measured, either by 'wedging' the catheter into a small branch of a hepatic vein (Figure 2a) or by inflating a balloon at the tip of the catheter (Figure 2b). WHVP should be measured until the value remains stable (usually >40 s).[4]

- In the normal liver, WHVP is slightly lower (by ~1 mmHg) than portal pressure, owing to pressure equilibration through the interconnected sinusoids.
- In liver cirrhosis (LC), however, the static column of blood created by occluding the hepatic vein cannot be decompressed at the sinusoidal level because the connections between sinusoids are disrupted as a result of the presence of fibrous septa and nodule formation.
- In cirrhosis, therefore, WHVP gives an accurate estimate of portal pressure, as has been demonstrated both for alcoholic and viral cirrhosis.

FHVP is measured by maintaining the tip of the catheter 'free' in the hepatic vein, at 2–4 cm from its opening into the inferior vena cava. The FHVP should be similar in value to the inferior vena cava pressure; a difference of >2 mmHg signifies that the catheter is probably inadequately placed or that a hepatic vein obstruction exists.[4]

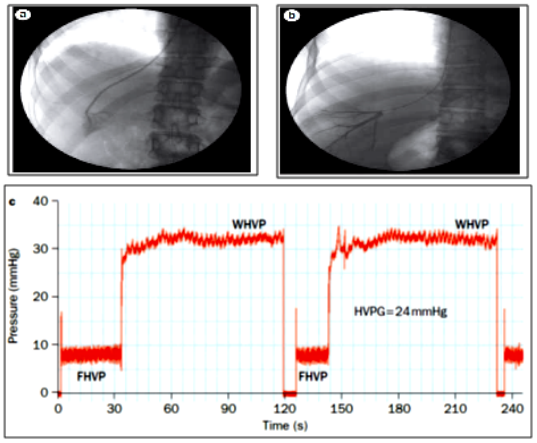

Figure 2: Measurement of wedged hepatic venous pressure (WHVP). WHVP can be measured by a; a. 'wedging' catheter or b. balloon occlusion. c. A typical HVPG tracing. Please note the slow speed of the recorder (1 mm/s), the range of pressures, and that equilibration of WHVP requires over 25 s.[4]

Clinical applications of HVPG[1]

Predicting liver fibrosis

In the diagnosis of stage 1 compensated LC, the sensitivity and specificity of HVPG for predicting stage 1 compensated LC were 78% and 81% in 6 mmHg of HVPG, respectively. Kumar et al also reported a positive correlation between HVPG and fibrosis score. The AUROC (Area under Receiver Operating Characteristic) of HVPG for predicting advanced fibrosis was 0.906. An HVPG value above 13.0 mmHg had 79% sensitivity and 89% specificity for predicting advanced fibrosis histologically. Patients with an HVPG <10 mmHg have a 90% probability of not developing LC.

In the study with post-liver transplant patients, there was a good correlation between liver stiffness measurement (LSM) and HVPG measurements in the overall population. In another study, HVPG predicted clinical decompensation in patients with compensated LC. Patients with an HVPG <10 mmHg were found to have a 90% probability of not developing clinical decompensation in a median follow-up of 4 years.

The most promising of the non-invasive tools to monitor fibrosis progression and associated portal hypertension is LSM by transient elastography. The correlation between liver stiffness and HVPG is excellent in patients with HVPG values below 10 mmHg. The AUROC for prediction of HVPG 10-12 mmHg ranges from 0.76 to 0.99 with a cut-off of 13.6 to 34.9 kPa. HVPG >6 mmHg and HVPG >10 mmHg were predicted by 8.7 kPa and 21 kPa cut-off, respectively

Predicting outcome of acute variceal bleeding

In patients with acute variceal bleeding, the HVPG measurement provides prognostic information and therapeutic efficacy on the evolution of the bleeding episode.

- Most studies described that patients with variceal bleeding almost have an HVPG of >12 mmHg.
- In other study, an initial HVPG of >20 mmHg was associated with a significantly longer hospital stay, greater transfusion requirements, and worse survival (1-year mortality: 64% vs. 20%, P<0.002).
- Another study suggested that a HVPG value of 11 mmHg is predictive of first variceal hemorrhage with a sensitivity of 92.4% and a specificity of 27.7%.
- Abraldes et al suggested that HVPG >20 mmHg independently predicted short-term prognosis in patients with acute variceal bleeding treated with a standard vasoactive, antibiotic and endoscopic regimen.

The early effects of endoscopic injection sclerotherapy (EIS) and endoscopic band ligation (EBL) on HVPG during acute bleeding have also been investigated. EIS was related with a sustained increase in HVPG compared with EVL. In a study with 50 cirrhotic patients, HVPG was measured before and immediately after endoscopic treatment (EBL and EIS) and every 24 hours, for a 5-day period. In the EBL and EIS groups, a significant increase (18.1 mmHg to 20.7 mmHg and 18.1 mmHg to 21.5 mmHg, P<0.0001) was observed in mean portal pressure immediately after treatment compared with pre-treatment. However, in the EBL group, HVPG returned to baseline values within 48 hours after treatment, while in the EIS group it remained high during the 5-day study period. Thus, during acute variceal bleeding EIS was associated with a sustained increase in HVPG.

Predicting effectiveness of beta blocker prophylaxis

The yearly incidence of variceal bleeding in cirrhosis patients is estimated at 4%, but this risk increases to 15% according to the size of varices. In the aspect of hemodynamic parameter, HVPG ≥10 mmHg is an excellent predictor of the development of varices. The haemodynamic response to pharmacological therapy for primary prophylaxis of variceal bleeding has only been evaluated in a few studies, because there is a low bleeding rate and as nonselective beta blockers are effective in primary prophylaxis.

Recent meta-analysis suggested that a reduction of HVPG below 12 mmHg or at least 20% from baseline reduced the risk of re-bleeding and death. Pharmacologic therapy has also been used in the

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prevention of re-bleeding in patients with varices. The likelihood of re-bleeding in untreated patients is 55-67%. Use of pharmacologic or endoscopic therapy or transjugular intrahepatic portosystemic shunt or other shunts all reduce the risk of bleeding. The likelihood of a failure to have a hemodynamic response varies from 45 to 63%.

Predicting postoperative outcomes in hepatocellular carcinoma

Preoperative portal pressure is an important predictor of hepatic decompensation in patients with cirrhosis after resection for HCC. Bruix et al evaluated that only HVPG was significantly associated with unresolved decompensation within 3 months after surgery (P=0.0001, odds ratio: 1.90). Another study suggested that high portal vein pressure was associated with poor long-term outcome after liver resection for HCC. Kim et al documented that in decompensated alcoholic cirrhosis, HVPG may be a useful predictive factor for the development of HCC and low serum sodium.

CONCLUSIONS

HVPG measurement is safe, simple, and reproducible method to measure portal pressure. The HVPG is the best surrogate marker in portal hypertension and should be measured in every trial involving pharmacologic therapy. In addition, patients with cirrhosis, the HVPG can predict the development of varices, ascites, encephalopathy, or other complications.

REFERENCE

1. Suk KT. Hepatic venous pressure gradient: clinical use in chronic liver disease. Clinical and Molecular Hepatology 2014;20:6-14.
2. Al-Busafi SA, McNabb-Baltar J, Farag A, and Hilzenrat N. Clinical Manifestations of Portal Hypertension. International Journal of Hepatology. (2012); Vol.2012, Article ID 203794:1-9.
3. Bosch J, Abraldes JG, Berzigotti A. The clinical use of HVPG measurements in chronic liver disease. Nat Rev GastroenterolHepatol 2009;6:576–82.
4. Keiding S, Vilstrup H. Intrahepatic heterogeneity of hepatic venous pressure gradient in human cirrhosis. Scand J Gastroenterol 2002;37:960– 964.