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Observational Study

Correlation of the pressure gradient in three hepatic veins with the portal pressure gradient

HVPG in three hepatic veins and PPG

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Abstract

BACKGROUND

Liver is one of the most important organs in the human body, with functions such as detoxification, digestion, and blood coagulation. In terms of vascular anatomy, the liver is divided into the left liver and the right liver by the main portal vein, and there are three hepatic efferent veins (right, middle and left) and two portal branches. Patients with impaired liver function have increased intrahepatic vascular resistance and splanchnic vasodilation, which may lead to an increase in the portal pressure gradient and cause portal hypertension (PHT). In order to measure the increased pressure gradient of the patient's portal vein, the hepatic venous pressure gradient (HVPG) can reflect the portal pressure in clinical practice. The accuracy of portal pressure gradient (PPG) measurements is directly related to patient prognosis.

AIM

To analyze the correlation between HVPG of three hepatic veins and PPG in patients with PHT.

METHODS

From January 2017 to December 2019, 102 patients with PHT who met the inclusion criteria were evaluated during the transjugular intrahepatic portosystemic shunt (TIPS) procedure and analyzed.

RESULTS

The mean HVPG of the middle hepatic vein was 17.47 ± 10.25 mmHg, and the mean HVPG of the right and left hepatic veins was 16.34 ± 7.60 and 16.52 ± 8.15 mmHg, respectively. The average PPG was 26.03 ± 9.24 mmHg. The correlation coefficient and coefficient of determination of the right hepatic vein, middle hepatic vein and left hepatic vein were 0.15 and 0.02 ($P = 0.164$); 0.25 and 0.05 ($P = 0.013$); 0.14 and 0.02 ($P = 0.013$), respectively. The mean wedged hepatic vein/venous pressure (WHVP) of the

middle and left hepatic veins was similar at 29.71 ± 12.48 and 29.1 ± 10.91 mmHg, respectively, and the mean WHVP of the right hepatic vein was slightly lower at 28.01 ± 8.95 mmHg. The mean portal vein pressure (PVP) was 34.11 ± 8.56 mmHg. The correlation coefficient and coefficient of determination of the right hepatic vein, middle hepatic vein and left hepatic vein were 0.26 and 0.07 ($P = 0.009$); 0.38 and 0.15 ($P < 0.001$); 0.26 and 0.07 ($P = 0.008$), respectively. The average free hepatic venous pressure (FHVP) of the right hepatic vein was lowest at 11.67 ± 5.34 mmHg, and the average FHVP of the middle and left hepatic veins was slightly higher at 12.19 ± 4.88 and 11.67 ± 5.34 mmHg, respectively. The average inferior vena cava pressure (IVCP) was 8.27 ± 4.04 mmHg. The correlation coefficient and coefficient of determination of the right hepatic vein, middle hepatic vein and left hepatic vein were 0.30 and 0.09 ($P = 0.002$); 0.18 and 0.03 ($P = 0.078$); 0.16 and 0.03 ($P = 0.111$), respectively.

CONCLUSION

Measurement of the middle hepatic vein HVPG could better represent PPG. Considering the high success rate of clinical measurement of the right hepatic vein, it can be the second choice.

Key Words: Portal hypertension; Portal pressure gradient; Hepatic venous pressure gradient

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Core Tip: Portal hypertension is a serious complication of various liver diseases, including cirrhosis, with a high mortality rate. To improve its prognosis, methods to accurately measure the magnitude of the increase in portal pressure are needed. This article compares and analyzes the relationship between HVPG of three hepatic veins

and PPG in 102 patients with portal hypertension, aiming to find out the hepatic vein pressure gradient branch that best represents the patients' actual portal vein pressure gradient in clinic.

INTRODUCTION

The elevated pressure in portal hypertension (PHT) refers to the pressure gradient between the portal vein and the systemic circulation, and is mainly characterized by increased intrahepatic vascular resistance, varicose veins and bleeding caused by splanchnic vasodilation. The main cause of PHT is liver cirrhosis, which has a high mortality rate as it is a serious complication. In addition, the increased venous pressure gradient in the absence of known liver disease is termed noncirrhotic PHT and is usually caused by vascular liver disease^[1]. The clinical symptoms and prognosis of PHT are directly related to the degree of portal pressure, but it is difficult and risky to measure portal pressure directly. ² The hepatic venous pressure gradient (HVPG= wedged hepatic vein/ venous pressure (WHVP)-free hepatic venous pressure (FHVP) is used in clinical studies as the "gold standard" for indirectly reflecting portal venous pressure (PVP) and is a simple and low-risk technique^[2]. Theoretically, HVPG indirectly represents the difference between portal vein pressure (PVP) and inferior vena cava pressure (IVCP) ($PPG = PVP - IVCP$). There are few reports on whether HVPG accurately represents PPG in real-world measurements. In this study, we carried out actual measurements of three hepatic veins related to this issue. From January 2017 to December 2019, 102 patients with PHT who met the enrollment criteria were included in this study and measurements of the three hepatic veins and various other pressures were carried out during the transjugular intrahepatic portosystemic shunt (TIPS) procedure and analyzed.

MATERIALS AND METHODS

Basic information

The pressure of three hepatic veins was measured during the TIPS procedure in 102 patients with PHT who met the inclusion criteria from January 2017 to December 2019 and analyzed. The mean age of the 102 cases was 54.42 ± 12.37 years, of which 67 (mean age 50.28 ± 11.63 years) were male (65.7%) and 35 (mean age 61.87 ± 10.07 years) were female (34.3%). The cause of PHT was hepatitis B cirrhosis in 43 cases, hepatitis C cirrhosis in 8 cases, hepatitis B+C cirrhosis in 1 case, alcoholic cirrhosis in 12 cases, autoimmune cirrhosis in 7 cases, cholestatic cirrhosis in 6 cases, drug-induced cirrhosis in 2 cases, idiopathic portal hypertension in 5 cases, small hepatic vein occlusion syndrome in 14 cases, and hepatic sinusoidal occlusion syndrome in 4 cases. There were 67 cases of gastrointestinal bleeding, accounting for 68.3%, intractable ascites / pleural ascites in 15 cases, accounting for 14.7%, and gastrointestinal bleeding complicated by intractable ascites in 6 cases (5.9%). Other conditions included 14 cases of bruising jaundice, severe liver bruising combined with ascites, hepatorenal syndrome, and severe esophagogastric varices. Child-P classification was grade A in 49 cases, grade B in 34 cases, and grade C in 19 cases.

Inclusion criteria

Inclusion criteria were: 1) patients eligible for TIPS surgery; 2) aged 18-75 years old; 3) TIPS patients scheduled for elective surgery; 4) normal anatomy of the hepatic vein and inferior vena cava; and 5) successful simultaneous measurement of pressure in three hepatic veins.

Exclusion criteria

Exclusion criteria were: 1) Patients with tumors; 2) Patients with portal vein thrombosis (generally more than 1/2 of the diameter of the main portal vein); 3) Application of drugs affecting portal vein pressure within the previous week; and 4) Intraoperative factors affecting the accuracy of manometry, *e.g.*, bile heart reflex, incomplete balloon closure, *etc.*

Pre-operative preparation

The following preoperative tests were conducted: routine blood, liver and kidney function, ICG-R15 (quantitative liver function test - indocyanine green 15-min retention

rate) blood ammonia, blood group, electrocardiogram, coagulation, liver vascular ultrasound, cardiac ultrasound and abdominal computed tomography and/or magnetic resonance enhancement, appropriate adjustment of coagulation function, platelet count, bilirubin, albumin, and hemoglobin for interventional procedures. The results and risks of the procedure were explained to the patient and their family, and signed consent for the operation protocol was obtained. Medications affecting portal pressure were discontinued for at least 1 wk prior to surgery.

Pressure measurement methods ^[3]

Local routine disinfection drapes were placed and under local anesthesia the right internal jugular vein was punctured and the RUPS-100 set (COOK, USA) was placed into the right atrium and inferior vena cava to measure pressure. A Fogarty balloon catheter (Edwards, USA) was inserted into the right, middle and left hepatic veins, respectively, and the balloon catheter tip was placed in the hepatic vein approximately 1-5 cm from the opening of the inferior vena cava. WHVP and FHVP were measured before and after the balloon was dilated to occlude the hepatic vein (5 mL of contrast agent was injected). When the pressure was stable the value was recorded, the pressure was measured 3 times, the average value was noted, and then the HVPG value was calculated (Figure 1A, B, C). After measurement, balloon-blocking compression hepatic venography was performed (the total amount of contrast agent was 15 mL, 5 mL/s, pressure 300 psi), and both WHVP and FHVP were measured again after administration of contrast. Occlusion of the balloon catheter was observed after the balloon was expanded and the balloon catheter position was adjusted for retesting and imaging if there was poor blockage. The liver parenchyma and portal vein were punctured through the inferior vena cava or hepatic vein. After successful puncture of the portal vein, the pigtail or end-to-side hole catheter was inserted into the splenic vein or superior mesenteric vein for intravenous angiography. Before shunting, pressure in the portal vein was measured (3 measurements, averaged), and the PPG value was calculated (Figure 1D). After that, liver tissue in the pre-shunt channel was obtained, the shunt channel was established, the post-shunt portal trunk pressure was measured

(3 measurements, averaged), and the PPG value was calculated. Postoperatively, an indwelling catheter was inserted into the portal vein for at least 48 h and the portal pressure was measured at least 3 times daily. The inferior vena cava pressure and right atrial pressure were measured three times during extubation, respectively, and the average value was taken.

Statistical analysis

SPSS 17.0 software was used for statistical analysis. The differences between PPG and HVPG, WHVP and PVP, and FHVP and IVCP were analyzed using paired t-tests, and the correlations between them were analyzed using Pearson correlation tests to estimate correlations and coefficients of determination. $P < 0.05$ was considered statistically significant.

RESULTS

Relationship between HVPG and PPG

The mean HVPG of the three hepatic veins (right, middle, and left) were 16.34 ± 7.60 , 17.47 ± 10.25 , and 16.52 ± 8.15 mmHg, respectively. Mean PPG was 26.03 ± 9.24 mmHg. By Pearson correlation analysis, the correlation coefficients and coefficients of determination between HVPG and PPG in the right, middle and left hepatic veins, were 0.15 and 0.02 ($P = 0.132$); 0.25 and 0.05 ($P = 0.013$); 0.14 and 0.02 ($P = 0.164$), respectively (Table 1-A).

The maximum HVPG was higher than PPG in the right, middle and left hepatic veins, which were 14 mmHg, 24 mmHg, and 37 mmHg, respectively, and the maximum PPG was higher than HVPG, which was 43.67 mmHg, 43 mmHg, and 44 mmHg, respectively. The difference between HVPG and PPG was within 5 mmHg in 38 cases (37.25%) on the right side of the liver, 33 cases (32.35%) in the middle of the liver, and 29 cases (28.43%) on the left side of the liver. The difference between HVPG and PPG was more than 5 mmHg in 64 cases on the right side of the liver, accounting for 62.75%, in 69 cases in the middle of the liver, accounting for 67.65%, and in 73 cases on the left side of the liver, accounting for 71.57% (Figure 2).

Relationship between WHVP and PVP

The average WHVP of the right hepatic vein was 28.01 ± 8.95 mmHg, the average WHVP of the middle hepatic vein was 29.71 ± 12.48 mmHg, and the average WHVP of the left hepatic vein was 29.1 ± 10.91 mmHg. The average PVP was 34.11 ± 8.56 mmHg. Following Pearson correlation analysis, the correlation coefficients and coefficients of determination between WHVP and PVP for the right, middle and left hepatic veins were 0.26 and 0.07 ($P = 0.009$); 0.38 and 0.15 ($P < 0.001$); 0.26 and 0.07 ($P = 0.008$) (Table 1-B).

The maximum WHVP was higher than PVP in the right liver, middle liver, and left liver and were 14 mmHg, 28 mmHg, and 40 mmHg, respectively, and the maximum PVP was higher than WHVP, which was 43.67 mmHg, 32 mmHg, and 40.67 mmHg, respectively. The difference between WHVP and PVP was within 5 mmHg in 48 cases on the right side of the liver, accounting for 47.06%, in 43 cases in the middle of the liver, accounting for 42.16%, and in 45 cases on the left side of the liver, accounting for 44.12%. The difference between WHVP and PVP was more than 5 mmHg in 54 cases on the right side of the liver, accounting for 52.94%, in 59 cases in the middle of the liver, accounting for 57.84%, and in 57 cases on the left side of the liver, accounting for 55.88% (Figure 3).

Relationship between FHVP and IVCP

The average FHVP was 11.67 ± 5.34 mmHg for the right hepatic vein, 12.19 ± 4.88 mmHg for the middle hepatic vein and 12.64 ± 4.99 mmHg for the left hepatic vein. Average IVCP was 8.27 ± 4.04 mmHg. The correlation coefficients and coefficients of determination between the right hepatic, middle hepatic and left hepatic venous FHVP and IVCP were 0.30 and 0.09 ($P = 0.002$); 0.18 and 0.03 ($P = 0.078$); 0.16 and 0.03 ($P = 0.111$), respectively (Table 1-C).

There were 16 cases (15.7%), 18 cases (17.6%), 22 cases (21.6%) with collaterals in the right, middle, and left hepatic vein angiography of the balloon blocked liver, respectively (Figure 4). The average HVP was (8.02 ± 6.58) mmHg, (14.36 ± 6.65) mmHg, and (12.09 ± 5.36) mmHg. The average PVP was (26.13 ± 9.97) mmHg, (29.67 ± 7.96) mmHg,

and (29.68±8.77) mmHg ($P < 0.001$); the average WHVP was (19.81±8.18) mmHg, (24.62±6.26) mmHg, and (23.26±6.77) mmHg. The average PVP was (35.56±9.86) mmHg, (37.72±7.79) mmHg, and (37.86±8.40) mmHg ($P < 0.001$). The average FHVP was (11.79±4.46) mmHg, (10.26±3.07) mmHg, and (11.17±4.20) mmHg, and the average IVCP was (9.44±2.68) mmHg, (8.06±3.23) mmHg, and (8.18±3.19) mmHg, respectively, and the differences were statistically significant ($P < 0.001$), (Table2).

Balloon occlusion of the right, middle and left hepatic veins without collaterals (Figure 5) was seen in 86 cases (84.3%), 84 cases (82.4%), 80 cases (78.4%), respectively. The average HVPg was (18.64±6.33) mmHg, (18.68±8.47) mmHg, and (18.34±7.21) mmHg. The average PPG was (25.33±8.90) mmHg, (24.55±9.03) mmHg, and (24.29±8.80) mmHg ($P < 0.001$); the average WHVP was (30.14±7.52) mmHg, (30.74±10.10) mmHg, and (30.75±9.45) mmHg. The average PVP was (33.60±8.06) mmHg, (33.10±8.28) mmHg, and (32.83±8.05) mmHg ($P < 0.001$); the average FHVP was (11.50±4.87) mmHg, (12.06±4.21) mmHg, and (12.40±4.29) mmHg, and the average IVCP was (8.28±3.93) mmHg, (8.55±3.90) mmHg, and (8.54±3.94) mmHg, respectively, and the differences were statistically significant ($P < 0.001$), (Table 3).

DISCUSSION

The liver has a dual blood supply, with blood from the hepatic artery and portal vein entering the hepatic sinusoids and returning to the hepatic vein. Under normal conditions, the hemodynamics are in equilibrium, and generally the PVP is higher than or equal to the hepatic sinusoidal pressure, and WHVP represents the hepatic sinusoidal pressure. Generally FHVP is 0.5~1.0 mmHg higher than IVCP

[4, 5]. Normally HVPg is approximately equal to PPG and indirectly represents the perfusion pressure in the portal vein. Patients with PHT, especially cirrhotic PHT, have significant changes in liver tissue, blood vessels and other structures, resulting in changes in local and body hemodynamics, the main features of which are visceral vasodilation and increased total blood volume^[6]. Therefore, whether the changes in various vascular pressures in patients with PHT are consistent with normal hepatic

vascular pressures has been shown to be controversial^[7]. Studies have suggested that PPG is more meaningful than PVP in predicting the prognosis of PHT^[4, 5, 7, 8]. The importance of HVPG in diagnosing the etiology of PHT^[9, 10], in predicting the prognosis of chronic liver disease^[10], in predicting gastrointestinal bleeding^[11], in determining patient prognosis^[8], in determining the efficacy of drugs^[12], in the development of primary hepatocellular carcinoma and in surgical prognosis^[13-15] has been reported in the literature, based on the theoretical HVPG as the "gold standard" indirectly representing PPG or separate studies on HVPG.

Limited reports show a correlation between WHVP and PVP in patients with hepatitis cirrhosis and alcoholic cirrhosis, with fewer national studies^[4, 7, 16, 17]. A poor correlation between WHVP and PVP has been reported for large nodular cirrhosis^[18]. The reasons for WHVP being lower than PVP are related to hepatic vein collateral shunts. The reason for the higher WHVP than PVP is unclear and may be related to reverse hepatic flow, opening of the accessory umbilical vein, portal anastomotic branch^[16, 17] and gastrosplenic shunt^[19]. The above study focused on data measured in a single hepatic vein (right hepatic vein). Non-cirrhotic PHT is generally acute or subacute, and is usually caused by vascular liver diseases such as hepatic sinusoidal obstruction syndrome^[20], idiopathic PHT^[1], and Budd-Chiari syndrome. The main clinical manifestations are ascites and variceal hemorrhage. Moreover, in contrast to cirrhotic PHT, the collateral circulation is not established^[20]. HVPG, as a standard for measuring portal pressure, can accurately measure sinus PHT; however, it has been reported that for patients with a presinusoidal type of PHT, ¹if the balloon is inflated below the vein-to-vein shunt, the measured HVPG can still accurately represent portal pressure^[1].

The present study measured three hepatic veins in the same patient and showed that the correlation between WHVP and PVP was poor in all three ⁴hepatic veins, the right hepatic vein was similar to the left hepatic vein, and the middle hepatic vein was slightly better. The correlation between HVPG and PPG was poor in all three hepatic veins, the middle hepatic vein was better than the other two types, and the right hepatic

vein and the left hepatic vein were similar. The mean WHVP with hepatic vein collateral branches was significantly lower than the mean PVP, suggesting that hepatic vein collateral branches severely affect and underestimate WHVP. The mean HVPG of the three hepatic veins was also significantly lower than the mean PPG. The mean WHVP without hepatic vein collateral branches and the mean PVP of the three hepatic veins were also lower than the mean PVP. The mean HVPG of the three hepatic veins was also lower than the mean PPG; the correlation between the FHVP and IVCP of the right hepatic vein was better, and the literature reported better stability of FHVP and IVCP

[16, 17, 19]. During the measurement of WHVP, FHVP, IVCP, PVP, HVPG and PPG, some drugs or measurement methods may affect the accuracy of monitoring results, such as non-selective beta-blockers, which have an effect on PVP^[21], propofol deep sedation has a huge effect on the patient's PPG^[22], the bile heart reflex during TIPS, the position and thickness of the measurement catheter may affect the accuracy of PVP, the position of the catheter and the thickness of the hepatic vein wall during the measurement of WHVP and FHVP may have some influence on the pressure measurement results^[4, 5]. The effects of the preoperative application of growth inhibitors and their analogs, posterior pituitary hormones, and terlipressin on manometry are unclear. In this study, the unity of subjective factors was particularly emphasized, including preoperative treatment, balloon occlusion method to determine WHVP, measurement site, patient's respiratory activity, drug application, *etc.*, to exclude various factors that affect the accuracy of pressure measurement.

CONCLUSION

In summary, there was a correlation between WHVP and PVP in hepatitis and alcoholic cirrhosis, but the number of cases was limited. There is very little research on the correlation between HVPG and PPG. The results of this study show that WHVP correlated poorly with PVP and HVPG correlated poorly with PPG in all three hepatic veins, with the former being highest in the hepatic middle vein with a basic compliance

rate (within 5 mmHg difference) of 47.06% and the latter being highest in the hepatic middle vein with a basic compliance rate (within 5 mmHg difference) of 37.25%. The measurement of pressure in the middle hepatic vein could better represent the pressure in the left and right hepatic veins. However, in practice, the right hepatic vein is relatively thicker in its course and has a higher success rate. Hepatic vein collateral branches are an important cause of inaccuracy, as WHVP correlates poorly with PVP and HVPG correlates poorly with PPG in patients without hepatic vein collateral branches, and the reasons for the generation of WHVP over PVP and HVPG over PPG are unclear. These issues need to be studied in depth.

ARTICLE HIGHLIGHTS

Research background

The prognosis of portal hypertension with high mortality is directly related to the accuracy of the measured portal pressure.

Research motivation

Improve prognosis of portal hypertension.

Research objectives

Comparing the three hepatic veins that can more accurately represent portal pressure.

Research methods

Measuring three hepatic veins in 102 patients with portal hypertension of different etiologies and comparing with their mean portal pressure.

Research results

Correlation of PPG and HVPG is higher in the middle hepatic vein.

Research conclusions

The measurement of pressure in the middle hepatic vein could better represent PPG than the pressure in the left and right hepatic veins.

Research perspectives

Considering the high success rate of clinical measurement of the right hepatic vein, it can be the second choice.

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