Perendoscopic variceal pressure measurement: a reliable estimation of portal pressure in patients with cirrhosis?

SPAHR, Laurent François Joséph, et al.

Abstract
In patients with cirrhosis, the hepatic venous pressure gradient (HVPG) is the reference method for the assessment of portal hypertension (PHT). Variceal pressure (VP) may be measured at endoscopy, but its relationship to the HVPG remains controversial. The aim of the study was to retrospectively compare HVPG and VP values obtained in a cohort of patients with cirrhosis and PHT.

Reference

PMID : 17075452
Perendoscopic variceal pressure measurement

A reliable estimation of portal pressure in patients with cirrhosis?

Laurent SPAHR (1), Emile GIOSTRA (1), Isabelle MORARD (1), Gilles MENTHA (2), Antoine HADENGUE (1)

(1) Gastroenterology and Hepatology, (2) Transplantation Unit, Hôpitaux Universitaire de Genève.

SUMMARY

Objectives — In patients with cirrhosis, the hepatic venous pressure gradient (HVPG) is the reference method for the assessment of portal hypertension (PHT). Variceal pressure (VP) may be measured at endoscopy, but its relationship to the HVPG remains controversial. The aim of the study was to retrospectively compare HVPG and VP values obtained in a cohort of patients with cirrhosis and PHT.

Methods — Within 8 days (range: 6-10 days), 64 patients in a stable condition with biopsy-proven cirrhosis (alcoholic: 47; other 17; mean age: 56.5 yrs (35-70); mean Child-Pugh’s score: 9.4 ± 1.9; ascites: 37/64; previous variceal bleeding (="bleeders"): 24/64) and oesophageal varices (grade 2: 49; grade 3: 15) underwent both measurement of the HVPG during transjugular liver biopsy and VP at endoscopy using a “home made” pressure sensitive gauge in the absence of needle puncture of the varix. Alcoholic hepatitis was present in 28 patients with alcoholic cirrhosis.

Results — The pressure sensitive gauge was well tolerated. The mean HVPG and VP values were 18.5 ± 3.4 mmHg and 19 ± 3.7 mmHg, respectively. A significant difference was observed between “bleeders” (n = 24) and non “bleeders” (n = 40) in terms of VP values (21.4 ± 3.3 vs 17.2 ± 3.2 mmHg, P = 0.001), but not for HVPG values (19.4 ± 4.1 vs 17.9 ± 2.8 mmHg, P = 0.075). A positive correlation was observed between VP and HVPG values (r = 0.62, P < 0.0001).

Conclusions — In groups of patients with cirrhosis and oesophageal varices, a “home-made” pressure sensitive gauge allowed a non invasive perendoscopic measurement of VP. The positive correlation between VP and HVPG values suggests that measurement of VP may be a reliable estimate of portal pressure in these patients and may provide information on prognosis [5-8], treatment monitoring [9], as well as disease progression [10]. In spite of this, HVPG measurement is not routinely performed [3] for several reasons. First, the HVPG is a reliable indicator of portal pressure only in diffuse liver injury such as alcohol [11] and hepatitis C-related cirrhosis [12]. Second, the technique is invasive with potential neck vascular injury [13], and reported as disagreeable by some patients. Third, it requires adapted equipment and application using a standard technical, as recently stated [14].

RÉSUMÉ

La mesure de la pression des varices oesophagiennes par voie endoscopique : une estimation fiable de la pression portale chez des malades atteints de cirrhose ?

Laurent SPAHR, Emile GIOSTRA, Isabelle MORARD, Gilles MENTHA, Antoine HADENGUE

(Gastroenterol Clin Biol 2006;30:1012-1018)

Objectifs — Chez le malade atteint de cirrhose, le degré d’hypertension portale (HTP) est déterminé par la mesure du gradient de pression hépatique (GPH). La pression des varices (PV), influencée par la pression portale, peut être mesurée lors d’endoscopie, mais sa relation avec le GPH est controversée. Le but de ce travail était de comparer rétrospectivement les mesures de GPH et de PV obtenues dans un groupe de malades atteints de cirrhose compliquée d’HTP.

Méthodes — Dans un intervalle de 8 jours (6-10 jours), 64 malades avec cirrhose histologiquement prouvée [alcoolique : 47 ; autre 17 ; âge moyen : 56,5 ans (35-70) ; score de Child-Pugh moyen : 9,4 ± 1,9 ; ascite : 37/64 ; antécédent d’hémorragie : 24/64] et varices oesophagiennes (grade 2 : 49 ; grade 3 : 15) ont bénéficié d’une mesure du GPH et de la PV lors d’endoscopie. La mesure de la PV se faisait à l’aide d’un capteur endoscopique confectionné de façon artisanale, sans ponction de la varice. Une hépatite alcoolique était présente chez 28 malades.

Résultats — Le capteur de pression endoscopique était bien toléré. Les valeurs moyennes du GPH et de la PV étaient de 18,5 ± 3,4 mmHg et de 19 ± 3,7 mmHg, respectivement. On observait une différence statistiquement significative entre les patients ayant présenté une hémorragie (n = 24) et ceux qui n’avaient jamais saigné (n = 40) en terme de PV (21,4 ± 3,3 vs 17,2 ± 3,2 mmHg, P = 0,001), mais pas en terme de GPH (19,4 ± 4,1 vs 17,9 ± 2,8 mmHg, P = 0,075). Il existait une corrélation linéaire entre la PV et le GPH (r = 0,62, P < 0,0001).

Conclusion — dans ce groupe de malades atteints de cirrhose et de varices oesophagiennes, l’application endoscopique sur les varices d’un capteur de pression artisanal permettait d’estimer de façon fiable la pression.

Oesophageal varices are strongly influenced by portal pressure, but there is a non-linear relationship between the HVPG level and the risk of variceal bleeding [15, 16]. In patients with cirrhosis, the presence of OV at endoscopy is indicative of clinically significant PHT [17]. The risk of haemorrhage is higher in large as compared to small OV, in relation to an elevated intra-variceal pressure and wall tension according to Laplace’s equation [18]. Indeed, the size of OV, the presence of cherry red spots on the variceal wall and the severity of liver dysfunction, all influence the risk of variceal bleed [19]. In addition, the measurement of variceal pressure (VP) may provide information on the bleeding risk [20], and could be of value in predicting the response to pharmacological agents [9].

The methods developed to measure VP include the direct puncture of the varix [21] and the non-invasive application of a pressure sensitive device upon the OV. The latter technique may be performed non-selectively on the distal end of the oesophagus [22, 23], or selectively on an individual varix [20, 24-26] under endoscopic view. Intravariceal pressure measurements correlates to portal pressure in patients with cirrhosis [21], but is potentially associated with an elevated bleeding risk unless immediately followed by sclerotherapy [24]. When a non-selective manometry of OV is performed, VP correlated linearly to the HVPG values ($r = 0.64$) [23], and to portal pressure ($r = 0.68$) measured invasively during temporary TIPS occlusion [25]. Using an endoscopic device, which requires continuous gas perfusion through the system, investigators from the Barcelona group performed individual measurements of VP under direct visual control. They reported high VP values in patients with large OV [26, 27], but no linear correlation between VP and the HVPG ($r = 0.48$), which they hypothesized may be due to variations in resistance and blood flow in the collaterals.

In order to clarify this issue, we aimed to evaluate the value of a “home-made” pressure sensitive capsule to measure non-invasively VP at endoscopy, and to assess its relationship to the HVPG measured during transjugular liver biopsy in a large group of patients with cirrhosis and OV.

**Methods**

Between January 2001 and June 2002, 79 patients with cirrhosis were admitted to our hospital for decompensated cirrhosis, variceal haemorrhage, suspicion of alcoholic hepatitis, or as part of an evaluation for liver transplantation. Hepatic hemodynamic and endoscopic measurements, considered as a standard diagnostic work-up in patients with cirrhosis, included an upper gastrointestinal endoscopy, a transjugular liver biopsy with measurement of the HVPG. In addition VP measurement was performed at the time of upper gastrointestinal endoscopy.

Table I summarized the characteristics of the 64 patients in whom both hemodynamic and endoscopic data could be analyzed (see Results). All patients had clinically significant PHT with OV, and no portal vein thrombosis. The etiology of cirrhosis was alcoholic in the majority of the cases (47 out of 62 patients). Ascites was clinically present in 37 patients. Both transjugular liver biopsy and VP measurement were performed within a median time interval of 8 days (range: 6-10 days). Twenty four patients reported an episode of previous bleeding from OV. For 12 out of these 24 patients, time from bleeding to haemodynamic measurements (VP and HVPG) was 11 days (range: 5 to 21 days). These patients were all treated as follows: after initial fluid resuscitation, endoscopic treatment, IV octreotide infusion for 72 hours, and blood transfusions (if needed, to reach haemoglobin level of 80-100 gr/dL), patients received a fixed dose of propranolol 80 mg per day, starting 24-48 hours after the index bleed. During this time period, patients remained in a stable haemodynamic condition.

### Endoscopic assessment

Endoscopy was performed using an Olympus (Olympus Optical Co., Tokyo, Japan) videobescope. Patients in a fasting state were examined under conscious sedation using intravenous meperidine (25-50 mg). The size of the varices was graded from 1 to 3 [19].

### Variceal pressure measurement

We used a “home-made” pressure capsule to measure VP. The device was tested in an artificial varix system, as illustrated and detailed in figure 1, and a linear correlation ($r=0.92$) was observed (data not shown).

The VP was measured at endoscopy using the pressure sensitive gauge attached to the tip of the endoscope, as schematically represented and illustrated in figure 2. Briefly, a hollow plastic capsule measuring 8 mm in dia-

| Table I – Characteristics of 64 patients for whom hemodynamic and endoscopic measurements were analyzable. |
| Caractéristiques des 64 malades pour lesquels les mesures héodynamiques et endoscopiques étaient analysables. |

<table>
<thead>
<tr>
<th></th>
<th>All patients (n = 64)</th>
<th>Bleeders (n = 24)</th>
<th>Non bleeders (n = 40)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs, range)</td>
<td>56.5 (35-73)</td>
<td>56.4 (35-68)</td>
<td>56.6 (40-73)</td>
<td>0.68</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>45/19</td>
<td>18/6</td>
<td>27/13</td>
<td>0.11</td>
</tr>
<tr>
<td>Alcoholic cirrhosis</td>
<td>47/64</td>
<td>19/24</td>
<td>28/40</td>
<td>0.27</td>
</tr>
<tr>
<td>ASH on liver biopsy</td>
<td>28/47</td>
<td>10/24</td>
<td>18/23</td>
<td>0.18</td>
</tr>
<tr>
<td>Pugh’s score</td>
<td>9.4±1.9</td>
<td>8.9±2.1</td>
<td>9.6±1.8</td>
<td>0.33</td>
</tr>
<tr>
<td>Child class (A/B/C)</td>
<td>3/32/29</td>
<td>3/11/10</td>
<td>0/21/19</td>
<td>0.37</td>
</tr>
<tr>
<td>Ascites</td>
<td>37/64</td>
<td>10/24</td>
<td>27/40</td>
<td>0.08</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>19/64</td>
<td>8/24</td>
<td>11/40</td>
<td>0.11</td>
</tr>
<tr>
<td>Size of OV (II/III)</td>
<td>49/15</td>
<td>19/5</td>
<td>30/10</td>
<td>0.15</td>
</tr>
</tbody>
</table>

**OV:** oesophageal varices; **ASH:** alcoholic steatohepatitis.

**ABBREVIATIONS**:

- **HVPG**: hepatic venous pressure gradient
- **PHT**: portal hypertension
- **OV**: oesophageal varices
- **VP**: variceal pressure
meter was connected to a Teflon catheter and introduced into the operating channel of the endoscope. The whole system was carefully filled with saline, and sealed with a rubber membrane. Particular attention was paid to the absence of air bubble in the system. This system was then connected to a pressure transducer (Millar Instr, Houston, TX, USA) and the pressure recorded simultaneously on a PC screen using a data acquisition software (Perimed, Stockholm, Sweden). After a careful intubation of the oesophageal varix, the free pressure (i.e., the pressure in the oesophageal lumen in the absence of contact with the oesophageal wall) was recorded. Then, the endoscopic capsule was gently applied selectively on the varix under direct visual control. Care was taken not to elicit oesophageal contractions. The same physician (L.S) performed all measurements. A second physician (E.G or I.M) was in charge of setting the zero pressure prior to the application of the gauge on the varix, and assessing the quality and stability of the tracing. He was unaware of the endoscopic aspects of the OV, nor of the HVPG value. In addition to meperidine, all patients received IV 40 mg N-butyl scopolamine at the time of measurement of the free pressure in the oesophagus, to reduce as much as possible large oesophageal contractions that influence VP [28]. The criteria required for an acceptable measure included a zero pressure tracing and a VP recording with stable venous fluctuations for at least 10 seconds, with the gauge maintained on the varix under endoscopic view, in the absence of major oesophageal contractions. Both the procedure and a typical VP tracing are illustrated in figure 3. The mean value of two acceptable measurements determined the VP.

The patients with recent haemorrhage and bands visible on strangled varices had VP measurement performed on a native residual varix.

### Hepatic venous pressure measurement

Transjugular liver biopsy was performed in a fasting state and under sedation (meperidine 25-50 mg IV). A 8F curved catheter (Cordis Europa, Amsterdam, The Netherlands) was introduced into the right hepatic vein under fluoroscopic guidance. The wedged hepatic venous pressure (WHVP) was recorded when the tip of the catheter was wedged in a small hepatic vein, while the free hepatic venous pressure (FHVP) was measured when the tip of the catheter floated in the hepatic vein at the junction with the inferior vena cava. To ensure that the catheter was in a proper wedged position, radiological contrast was injected to visualize small portal branches. The HVPG resulted from the difference between WHVP and FHVP. We used the mid-chest as the external zero reference. Pressure tracings had to remain stable during at least 30 seconds to be considered interpretable. We performed 2 HVPG measurements in two different vascular territories, and the mean value was kept for analysis. For technical reasons, we could not keep paper records of the tracings and we used instant pressure reading on the monitor screen.

### Histological analysis

Liver biopsy was interpreted by a senior histopathologist expert in liver diseases. The presence of five histologic lesions (liver cell necrosis, Mallory bodies, neutrophilic infiltrate, fibrosis, and fatty infiltration) was required for the diagnosis of alcoholic hepatitis [29].

### Statistical analysis

Data were expressed as mean ± SD, and median and range (for time intervals). The non-parametric Wilcoxon signed rank test was used to compare hemodynamic data. Correlation analysis was performed using the non-parametric Spearman rank test. A P < 0.05 was considered statistically significant. All calculations were made using the Statview 5.0 Program (SAS Institute Inc., USA).

### Ethical considerations

The Institutional Review Board of the Hôpitaux Universitaires de Genève allowed us to retrospectively review the endoscopic, hemodynamic and clinical data of the patients. In addition, all patients gave a written informed consent for endoscopic procedures.

### Results

#### Haemodynamic data

In 15 patients, VP measurements were rejected due to artefacts related to residual air bubbles in the system (n = 4), large
Variceal pressure and portal hypertension

oesophageal contractions (n = 5) or difficulties in positioning the pressure gauge on the varix (n = 6). Thus, we present in table II the results of hemodynamic and endoscopic measures obtained in 64 patients. The mean HVPG value was 18.5 ± 3.4 mmHg, consistent with clinically significant PHT [17]. There was a trend (P = 0.075) towards higher HVPG values in the 24 patients who previously bled from OV (“bleeders”) as compared to the 40 patients who never bled (“non bleeders”). The mean VP value was 19 ± 3.7 mmHg. The intra-observer difference in VP measurement was 5.8%. Variceal pressure values were higher in “bleeders” as compared to “non bleeders” (P < 0.001). Figure 4 illustrates both HVPG and VP values in the 64 patients. The portal-variceal pressure gradient, calculated as the difference between VP and the HVPG and thought to reflect vascular resistance along the collaterals [27], was 3.7 ± 2.9 mmHg. Values were similar in “bleeders” and “non bleeders”.

Correlations

There was a linear correlation between VP and HVPG values (r = 0.62, P < 0.0001, see figure 5), but not with WHVP (r = 0.2).

Discussion

In this group of patients with cirrhosis and clinically significant PHT, we demonstrate that, i) the non invasive measurement of VP using a “home-made” pressure sensitive gauge is feasible and reproducible, ii) values of VP are elevated, iii) VP values are higher in patients who experienced a previous variceal bleeding episode as compared to those who never bled, and iii) there is a positive correlation (r = 0.62) between VP and HVPG. Our findings are in line with results obtained with the continuous gas perfusion endoscopic capsule [26, 27], and we report additional information on the relationship between VP and HVPG values.

Variceal pressure plays a central role in the pathogenesis of variceal haemorrhage [2]. VP is modified following pharmacological intervention [9] and may estimate portal pressure [23, 25]. The non invasive devices (balloon manometry and endoscopic capsule) developed to measure VP rely on the principle that the pressure necessary to compress the varix equals the pressure inside the lumen. The value is expressed as VP. According to Laplace’s law, intravariceal pressure is more elevated in large as compared to small OV, and this is associated with an
increased risk of rupture. Indeed, in our patients, VP values ranged from 12 to 26 mmHg, with highest values in patients with large OV. We also report higher VP in bleeders as compared to non-bleeders, consistent with previous results [27].

In our study, the “home-made” endoscopic pressure capsule was filled with saline in a close circuit and did not require a continuous gas perfusion [26]. The 19% unsatisfactory VP measurements were both related to technical limitations (such as air bubbles in the system), and to patient’s characteristics. Accordingly, persistent large oesophageal contractions in spite of anti-spasmodic agent, and small grade 2 OV proved to be the main limitations of VP in our patients. These problems have also been reported by others [9, 26].

In the present study, we observed a positive correlation between HVPG and VP, with mean values of 18.5 and 19 mmHg, respectively. These results of VP in our patients differ from those published by Rigau et al. [27], who reported less elevated VP values, in the range of 15 mmHg. These findings deserve comments and thus we put forward a number of hypotheses to explain our results. First, could liver failure affect VP? Azygos blood flow [30], which directly influences VP [26], increases in parallel with liver failure. Since the mean Pugh’s score was higher in our patients as compared to those in the study by Rigau (9.4 vs 7.4), a role for this parameter may be considered. Second, what is the role of ascites? By increasing intra-abdominal pressure [18], ascites raises VP[31]. In our study, 58% of patients had clinically evident ascites. In these patients, there was a trend towards higher VP values as compared to those without ascites (18.7 ± 3 vs 17.2 ± 4.1, P = 0.23). Third, may variceal bleeding affect VP? High VP is associated with elevated variceal wall tension which may eventually lead to rupture, according to Laplace’s law. This concept is supported by our results and those by Rigau et al. [27].

In our study, the “home-made” endoscopic pressure capsule was filled with saline in a close circuit and did not require a continuous gas perfusion [26]. The 19% unsatisfactory VP measurements were both related to technical limitations (such as air bubbles in the system), and to patient’s characteristics. Accordingly, persistent large oesophageal contractions in spite of anti-spasmodic agent, and small grade 2 OV proved to be the main limitations of VP in our patients. These problems have also been reported by others [9, 26].

In the present study, we observed a positive correlation between HVPG and VP, with mean values of 18.5 and 19 mmHg, respectively. These results of VP in our patients differ from those published by Rigau et al. [27], who reported less elevated VP values, in the range of 15 mmHg. These findings deserve comments and thus we put forward a number of hypotheses to explain our results. First, could liver failure affect VP? Azygos blood flow [30], which directly influences VP [26], increases in parallel with liver failure. Since the mean Pugh’s score was higher in our patients as compared to those in the study by Rigau (9.4 vs 7.4), a role for this parameter may be considered. Second, what is the role of ascites? By increasing intra-abdominal pressure [18], ascites raises VP[31]. In our study, 58% of patients had clinically evident ascites. In these patients, there was a trend towards higher VP values as compared to those without ascites (18.7 ± 3 vs 17.2 ± 4.1, P = 0.23). Third, may variceal bleeding affect VP? High VP is associated with elevated variceal wall tension which may eventually lead to rupture, according to Laplace’s law. This concept is supported by our results and those by Rigau et al. [27].

In our study, the “home-made” endoscopic pressure capsule was filled with saline in a close circuit and did not require a continuous gas perfusion [26]. The 19% unsatisfactory VP measurements were both related to technical limitations (such as air bubbles in the system), and to patient’s characteristics. Accordingly, persistent large oesophageal contractions in spite of anti-spasmodic agent, and small grade 2 OV proved to be the main limitations of VP in our patients. These problems have also been reported by others [9, 26].
study, 37% of the patients had a previous variceal bleed, which in 12 out of 24 of the cases was a recent event. It is at present unclear whether endoscopic therapy influences portal haemodynamics [32, 33], or if VP may vary early after bleeding from OV. Finally, in our group of patients in whom alcoholic cirrhosis predominates, could alcoholic steatohepatitis influence VP? Acute administration of alcohol to patients with cirrhosis increases portal pressure and collateral blood flow [34], but this effect is relatively short-lived and presumed to be absent several days after hospital admission. Alcoholic steatohepatitis, however, may increase portal pressure [35], and could have participated in the splanchic and collateral vessels hemodynamic alterations.

In conclusion, in this group of patients with PHT and OV, measurement of VP using a “home-made” endoscopic pressure sensitive capsule proved feasible and may provide a reliable estimate of portal pressure. Variceal pressure measurement, but not the HVPG, allowed to discriminate patients who had a previous variceal bleed from those who never bled. The possible role of factors such as ascites, degree of liver failure, recent hemorrhage and concomitant alcoholic steatohepatitis remains to be established.

Given the fact that VP measurement is technically demanding and potentially affected by artefacts in relation to either the device itself or the patient’s characteristics, its use cannot be recommended in routine clinical practice. If determination of portal pressure is clinically indicated, it should still be performed invasively by performing a hepatic venous catheterization using the technical standard [14] until further studies are available.

ACKNOWLEDGMENT - This work was supported by Funding HUG PRD-0006.

REFERENCES


