EDITORIAL

# Portal pressure measurement: Have we come full circle?

Portal hypertension develops during the natural history of cirrhosis and is responsible for its main clinical adverse events, including gastroesophageal variceal bleeding, ascites, hepatorenal syndrome, and hepatic encephalopathy. The degree of portal hypertension is an independent factor for survival among patients with cirrhosis.[1] The most common but indirect method of assessing the portal gradient is the hepatic venous pressure gradient (HVPG), which is calculated as the difference between free hepatic vein pressure and wedged hepatic vein pressure (WHVP). WHVP can be an accurate surrogate of portal venous pressure (PVP) in cirrhotic patients with sinusoidal causes of portal hypertension (Fig. 1).

The subject of portal pressures affords an interesting opportunity to review medical history. Over 40 years ago, the preeminent hepatologist Dr Sheila Sherlock[2] wrote that PVP should be recorded in any patient with portal hypertension. Recommended techniques for portal pressure measurement included intrasplenic puncture ("the most convenient technique"), operative portal pressure measurements, umbilical vein catheterization, and transhepatic portal catheterization. With regard to WHVP, she wrote, "This well-established technique of measuring sinusoidal pressure is now performed less often. It is time-consuming and is being replaced by the splenic and transhepatic techniques."

Although the technique for measuring WHVP as a surrogate for PVP was originally developed in the 1950s,[3] WHVP was considered a research tool for some time and was applied in a limited number of clinical situations. The re-evaluation of WHVP (and, in turn, HVPG) in the early 2000s as a clinical tool was tied to 2 developments: (1) the widespread use of transjugular intrahepatic portosystemic shunt for the treatment of patients with adverse events from portal hypertension[4] and (2) the observation that both baseline HVPG[5] and pharmacologic reduction in HVPG[6] correlated with risk of variceal bleeding. Indeed, HVPG has since been correlated with development of the myriad adverse events of portal hypertension. HVPG is now considered the criterion standard for assessing clinically significant portal hypertension.[7]

In this issue of *Gastrointestinal Endoscopy*, Zhang et al[8] present their study correlating EUS-guided portal pressure gradient (EUS-PPG) measurement and HVPG in patients with acute and subacute portal hypertension. EUS-PPG measurement with a 22-gauge FNA needle and central venous pressure monitor was successful in 11 of 12 patients (91.7%), and there were no procedural adverse events. Correlation between EUS-PPG and HVPG was ultimately performed on 9 patients (because HVPG was unsuccessful in 2 patients). The authors showed a strong association between the 2 variables, with a Pearson correlation coefficient of 0.923.

This particular study recalls older studies (many from the 1970s and 1980s) correlating WHVP with PVP, the criterion standard at the time.[9] Interestingly, we are now witnessing the inverse phenomenon of PVP, now measured through EUS guidance, being compared with the current criterion standard of WHVP (and, in turn, HVPG). Conceptually, it appears that we have come full circle.

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At first blush, such an observation may raise the question of why the current study is necessary. Some portal hypertension "purists" may argue that EUS-PPG is sufficiently different from the direct portal measurement techniques of old that it warrants a new study. We agree with this sentiment. In fact, we go further to argue that the new EUS-PPG technique represents an improvement on the old direct measurement techniques because it allows for measurement of both portal pressure and free hepatic vein pressure to allow for calculation of the portal pressure gradient (PPG) (Fig. 2), thereby eliminating the external zero reference point, another important source of potential error. PVP or WHVP by themselves can be falsely elevated in the presence of ascites and increased intra-abdominal pressure, but their difference (ie, the gradient) is not.[10] This is what makes HVPG conceptually attractive, and likewise PPG.


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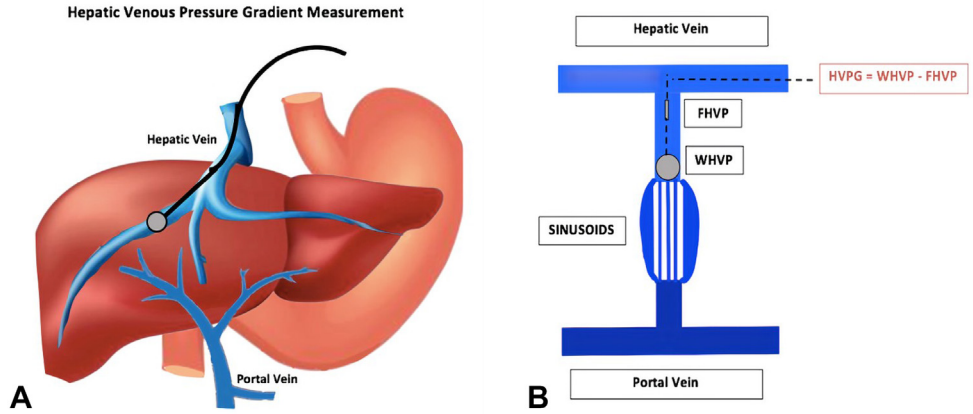


**Figure 1.** Hepatic venous pressure gradient (HVPG). **A,** Transjugular wedge balloon for measuring HVPG. **B,** HVPG is calculated as the difference between free hepatic vein pressure (FHVP) and wedged hepatic vein pressure (WHVP), which is a surrogate for portal vein pressure in sinusoidal causes of portal hypertension.

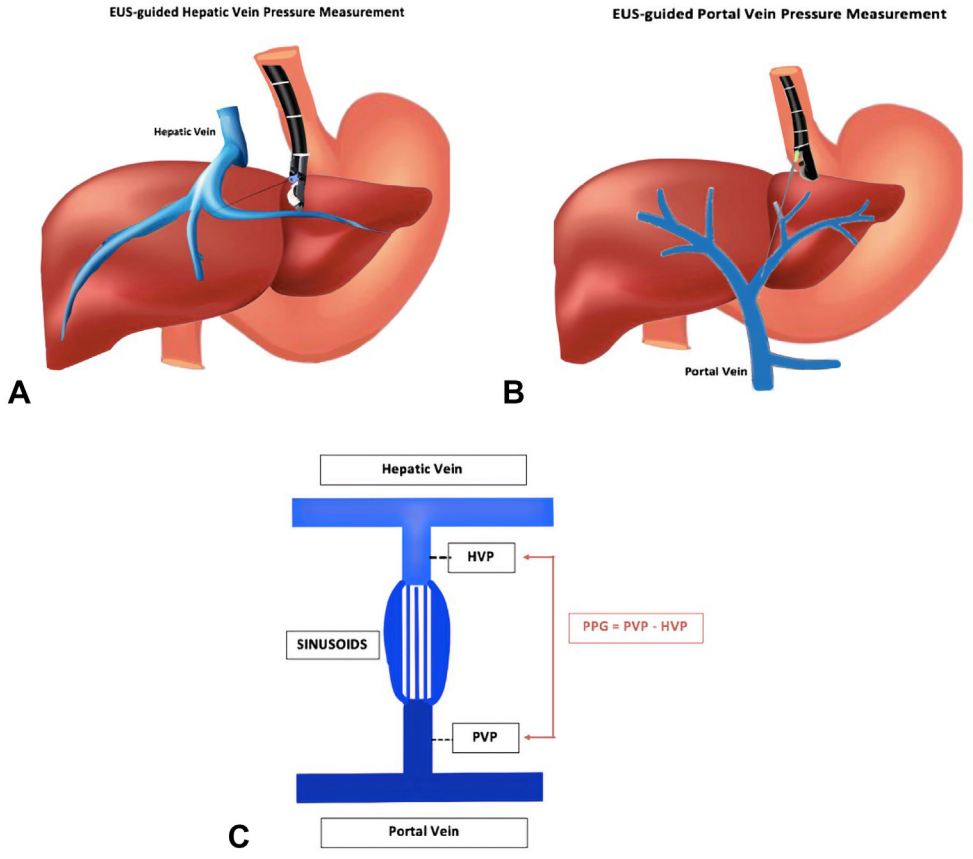


**Figure 2.** EUS-guided portal pressure gradient (PPG) measurement. **A,** Hepatic vein pressure (HVP) measurement. **B,** Portal vein pressure (PVP) measurement. **C,** Portal pressure gradient (PPG) is calculated as the difference between hepatic vein pressure (HVP) and direct portal vein pressure (PVP) and is theoretically accurate for presinusoidal, sinusoidal, and postsinusoidal causes of portal hypertension.

Several features of this study deserve particular mention. First, the patient cohort is both small and unique. Instead of patients with "typical" cirrhosis, 10 of 12 patients had an esoteric hepatic vascular disease called pyrrolizidine alkaloid-induced hepatic sinusoidal obstruction syndrome. In China, this disease is often associated with oral intake of plants that contain pyrrolidine alkaloids. Previously, existing guidelines were limited to hepatic portal pressure

gradient associated with hematopoietic stem cell transplantation in Western countries. As the authors cite, new expert consensus statements have emerged from the Chinese Society of Gastroenterology, including the Nanjing criteria for diagnosis and treatment, based on supportive care, anticoagulation, and transjugular intrahepatic portosystemic shunt for those who do not respond to medical treatment. Presumably, this was the clinical reason for determining PPG.

Second, there were methodologic differences compared with conventional HVPG that may have affected PPG measurement. For instance, EUS-PPG was calculated as the difference between portal pressure and inferior vena cava (IVC) pressure, instead of portal pressure and hepatic vein pressure. This technique varies somewhat from our approach to EUS-PPG measurement, which entails the use of a 25-gauge FNA needle and pressure measurement of the hepatic vein and portal vein. The authors explain that the reason for their approach was that hepatic veins were extremely thin and too small a target in pyrrolizidine alkaloid-induced hepatic sinusoidal obstruction syndrome. Although IVC pressures approximate hepatic vein pressures, this approach may have introduced a small but systematic error in PPG calculation. Additionally, as the authors point out, EUS-PPG was performed with patients under sedation, whereas HVPG was performed with the patients awake, and a prior study has shown that deep sedation can depress HVPG.[11]

Third, it is noteworthy that EUS-PPG succeeded in 2 cases where HVPG was not possible (both patients with Budd-Chiari syndrome) and in 1 case where HVPG was inaccurate owing to the presence of hepatic vein shunts. These cases suggest that EUS-PPG may succeed in scenarios (albeit rare) where the hepatic veins cannot be accessed by the transjugular catheter or an accurate WHVP cannot be obtained. Another category where EUS-PPG will theoretically be more accurate than HVPG is patients with presinusoidal portal hypertension (eg, schistosomiasis, nodular regenerative hyperplasia) because WHVP tends to underestimate PVP in these patients, but direct portal measurement circumvents this problem.

Fourth, the mechanism of the lone failure in the EUS-PPG case is instructive. One patient had an IVC that was too thin to be accessed. Are there are other clinical situations, such as in patients with advanced cirrhosis, in which the portal vein or hepatic vein/IVC are relatively inaccessible, rendering EUS-PPG impossible or inaccurate? Further experience in other patient populations with liver disease will shed light on this question. Additionally, it should be noted that all patients had ascites, and this was not a contraindication to transhepatic needle access.

The current report from the Nanjing group has timely relevance in the United States, with an EUS-PPG measurement device (25-gauge needle) recently obtaining approval from the U.S. Food and Drug Administration. Most of the published preclinical and clinical work using this device has come from Dr Kenneth Chang's group at University of California at Irvine. Incidentally, this group also published a preclinical PPG versus HVPG correlation study in the porcine model demonstrating excellent association (R 0.985-0.99) between the 2 measurements.[12]

Ultimately, the current study provides meaningful clinical information supporting an emerging EUS-guided procedure. The resurgence of a direct measurement for portal pressure instead of an indirect measurement is promising and carries significant potential to assist in the diagnosis and treatment of patients with portal hypertension. Near-term research goals for EUS-PPG will likely include the development of a standard methodology and a multicenter registry study to assess clinical effectiveness.

The diagnosis and management of portal hypertension should ideally use a measurement technique that is safe, easy, accurate, and noninvasive. We predict that further studies will show EUS-PPG to check the first 3 boxes. However, like HVPG, EUS-PPG will remain invasive. A key difference may be the "extras" provided during that endoscopic examination, such as variceal screening/surveillance, EUS-guided liver biopsy, EUS-based liver elastography, and general endoscopic foregut assessment. The degree of acceptance of an endoscopic "one-stop shop" for patients with chronic liver disease may ultimately determine the future scale of EUS-PPG.

## DISCLOSURE

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*Abbreviations: EUS-PPG, EUS-guided portal pressure gradient; IVC, inferior vena cava; HVPG, hepatic venous portal gradient; PPG, portal pressure gradient; PVP, portal vein pressure; WHVP, wedged hepatic vein pressure.*

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