EUS-guided portal pressure gradient measurement with a simple novel device: a human pilot study

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Background and Aims: Portal hypertension (PH) is a serious adverse event of liver cirrhosis. The hepatic venous pressure gradient or portal pressure gradient (PPG) accurately reflects the degree of PH and is the single best prognostic indicator in liver disease. This is usually obtained by interventional radiology (IR), although it is not routinely performed. Recently, we developed a simple novel technique for EUS-guided PPG measurement (PPGM). Our animal studies showed excellent correlation between EUS-PPGM and IR-PPGM. We present the first human pilot study of EUS-PPGM in patients with liver disease.

Methods: EUS-PPGM was performed by experienced endosonographers using a linear echoendoscope, a 25-gauge fine-needle aspiration needle, and a novel compact manometer. The portal vein and hepatic vein (or inferior vena cava) were targeted using a transgastric–transduodenal approach. Clinical parameters of PH were evaluated in each patient. Feasibility was defined as successful PPGM in each patient. Safety was based on adverse events captured in a postprocedural interview.

Results: Twenty-eight patients underwent EUS-PPGM with 100% technical success and no adverse events. PPG ranged from 1.5 to 19 mm Hg and had excellent correlation with clinical parameters of portal hypertension including the presence of varices ($P = .0002$), PH gastropathy ($P = .007$), and thrombocytopenia ($P = .036$). PPG was increased in patients with high clinical evidence of cirrhosis ($P = .005$).

Conclusion: This novel technique of EUS-PPGM using a 25-gauge needle and compact manometer is feasible and appears safe. Given the availability of EUS and the simplicity of the manometry setup, EUS-guided PPG may represent a promising breakthrough for procuring indispensable information in the management of patients with liver disease. (Gastrointest Endosc 2017;85:996-1001.)

Portal hypertension (PH) is a severe adverse event of liver cirrhosis. Clinical manifestations may include the formation of varices with associated GI bleeding, ascites, encephalopathy, or hepatorenal syndrome.[1,2] Therefore, the diagnosis and quantification of portal hypertension by measuring portal pressure holds tremendous therapeutic and prognostic implications[1,3,4]

Abbreviations: CSPH, clinically significant portal hypertension; FNA, fine-needle aspiration; HV, hepatic vein; HVPG, hepatic venous pressure gradient; IR, interventional radiology; IVC, inferior vena cava; PH, portal hypertension; PHG, portal hypertensive gastropathy; PPG, portal pressure gradient; PPGM, portal pressure gradient measurement; PV, portal vein; WHVP, wedged hepatic venous pressure.

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The portal pressure gradient (PPG) is the difference between the portal vein pressure and the pressure within the hepatic vein (or inferior vena cava). It reflects the hepatic perfusion pressure. In patients with cirrhosis, portal pressure increases because of increased intrahepatic vascular resistance and increased portal blood flow.[1]

PPG is derived from subtracting the hepatic vein (HV) pressure from the portal vein (PV) pressure. These pressures ideally should be obtained through direct venous puncture. However, currently, the PV pressure is not routinely measured and is indirectly estimated and based on the wedged hepatic venous pressure (WHVP), and only the hepatic venous pressure is a true direct measure. In the cirrhotic liver, the WHVP is similar to the PV pressure. This gradient is termed the hepatic venous pressure gradient (HVPG), which accurately reflects the degree of PH in all forms of sinusoidal and postsinusoidal causes of portal hypertension.[2,5,6]

The definition of portal hypertension is an HVPG > 5 mm Hg. An HVPG > 10 mm Hg represents clinically significant portal hypertension (CSPH), and it is usually a prerequisite to the development of ascites and variceal bleeding. Monitoring HVPG may be useful in guiding pharmacologic prophylaxis of variceal bleeding. The risk of variceal bleeding is dramatically lowered if HVPG is reduced by 20% from baseline or an absolute value < 12 mm Hg is achieved.[2,7-9] Furthermore, the severity of portal hypertension is an independent factor for survival in patients with liver cirrhosis.[5]

The most common approach to quantifying portal hypertension in clinical practice is the transjugular route. This method is invasive, it involves radiation exposure, it requires the use of intravenous contrast, and it provides only indirect measurements of the PV pressure. The technique involves placement of a radiopaque catheter into the right HV via the jugular vein under fluoroscopic guidance. A free HV pressure and a WHVP are obtained, and HVPG is calculated.[5] Other methods, such as surgical and transhepatic percutaneous approaches, can be used for obtaining direct measurements; however, these are more invasive and are not performed in clinical practice.

We have recently presented EUS-guided portal pressure gradient measurement using a 25-gauge needle and a novel compact manometer in an animal model[10] demonstrating excellent accuracy and strong correlation with pressure values obtained by the criterion standard transjugular wedged and free hepatic venous pressure measurements by interventional radiology. We present the first pilot study in humans demonstrating safe and accurate direct portal pressure gradient measurements without the need for ionizing radiation, transhepatic catheter placement, or surgery.

Figure 1. Compact manometer.

METHODS

EUS-PPG was performed at a single tertiary academic center by experienced endosonographers. All cases were performed with the patient under moderate sedation or general anesthesia in the supine position. Patients between the age of 18 and 75 years with a history of liver disease or suspected cirrhosis were considered for PPG measurement. Exclusion criteria included pregnancy, significant bleeding risk (international normalized ratio > 1.5, platelet count < 50 $\times 10^9$/L), active GI bleeding, and postsinusoidal portal hypertension. Feasibility was measured and based on technical success, which was defined as a successful PPG measurement in each patient. Safety was assessed on the basis of adverse events that were captured in a postprocedural interview of all patients in person in recovery and by telephone within the subsequent 48 hours. Medical records including patient demographics, imaging studies, laboratory, EUS, and manometry results were retrospectively reviewed and analyzed. Full written informed consent was obtained from all patients. The study was approved by the Institutional Review Board for Human Research at the University of California, Irvine.

Endoscopic procedure

Before EUS-guided pressure measurement, a forward-viewing endoscope (Olympus, Tokyo, Japan) was used to