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EUS-guided portal pressure gradient measurement for evaluating the severity of portal hypertension: A retrospective analysis

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Abstract

Background and Objectives: EUS-guided portal pressure gradient (EUS-PPG) measurement has been proposed as a novel direct manometry to quantify portal hypertension. This study aimed to explore the ability of EUS-PPG measurements to evaluate the severity of portal hypertension.

Methods: The clinical features of patients with diagnosed cirrhosis or chronic liver disease who underwent EUS-PPG measurement at a single center were retrospectively analyzed. The correlations between the clinical features of portal hypertension and the EUS-PPG measurements were analyzed, and then receiver operating characteristic curves were used to evaluate the ability of the EUS-PPG measurements to evaluate disease severity.

Results: A total of 197 patients were included in this study. The EUS-PPG measurements varied significantly among patients categorized by gastroesophageal varices, red signs, variceal bleeding, ascites, hepatic encephalopathy, thrombocytopenia, hypoproteinemia, prothrombin time, international normalized ratio, or Child-Pugh grade ($P < 0.05$). The areas under the receiver operating characteristic curves for gastroesophageal varices, decompensated cirrhosis, ascites, and recent variceal bleeding were 0.919, 0.847, 0.813, and 0.804, respectively ($P < 0.001$). Furthermore, the optimal EUS-PPG cutoff values for gastroesophageal varices, decompensated cirrhosis, ascites, and recent variceal bleeding were 11.5 mm Hg (sensitivity = 80.3%, specificity = 89.5%), 12.75 mm Hg (sensitivity = 77.8%, specificity = 76.7%), 15.75 mm Hg (sensitivity = 66.7%, specificity = 83.1%), and 16.75 mm Hg (sensitivity = 76.2%, specificity = 70.1%), respectively.

Conclusions: EUS-PPG measurement seems to be an effective technique for assessing disease severity and risk of variceal bleeding in patients with diagnosed cirrhosis or chronic liver disease.

Keywords: Cirrhosis; Portal hypertension; Portal pressure gradient; EUS

Introduction

Portal hypertension is a serious complication of liver cirrhosis. It manifests as a series of clinical syndromes originated from increased pressure in the portal vein system and its tributaries.[1] With the aggravation of cirrhosis, various clinical manifestations may appear one after another, including gastroesophageal varices, variceal bleeding, ascites, hepatic encephalopathy, hepatorenal syndrome, spontaneous bacterial peritonitis, splenomegaly, and hypersplenism.[2] Therefore, accurate assessment of portal vein pressure is highly essential for the diagnosis, treatment, and prognosis of patients with portal hypertension.[3]

The latest Baveno VII workshop reported that the hepatic venous pressure gradient (HVPG) is still the gold standard for the evaluation of portal hypertension.[4] Under fluoroscopy, a balloon catheter is guided into the hepatic vein to measure the free hepatic venous pressure and wedged hepatic venous pressure (WHVP). The HVPG is the difference between the WHVP and the free hepatic venous pressure, which indirectly reflects the portal pressure gradient (PPG) to remove the effects of intra-abdominal pressure and hemodynamics.[5] Typically, the range of HVPG in the normal population is 3–5 mm Hg, and HVPG >5 mm Hg is defined as portal hypertension.[6] An HVPG ≥10 mm Hg indicates an increased risk of gastroesophageal varices and is also the gold standard for the diagnosis of clinically significant portal hypertension.[7–9] Previous research has demonstrated that an HVPG ≥12 mm Hg is necessary for the occurrence of variceal bleeding.[10,11] Cirrhotic patients who had an acute variceal bleeding with an HVPG ≥20 mm Hg are at risk of early rebleeding after emergency treatment.[12] In addition, with increasing HVPG, the risk of uncontrollable complications and mortality gradually increases.[13]

EUS-guided PPG (EUS-PPG) measurement is a novel technique that has shown excellent safety and feasibility in recent animal

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experiments and clinical trials.[14–17] Under the guidance of EUS, the portal vein, hepatic vein, or inferior vena cava is punctured with a 25- or 22-gauge aspiration needle attached to a pressure transducer. The pressure gradient between the portal vein and the hepatic vein or the inferior vena cava is used to evaluate portal hypertension. Previous prospective studies have demonstrated a strong correlation between EUS-PPG and HVPG in patients with acute or subacute portal hypertension and patients with chronic portal hypertension.[18,19] In addition, several other studies have demonstrated that simultaneous EUS-PPG and EUS-guided liver biopsy are safe and feasible.[20–22] Compared with HVPG, EUS-PPG is direct manometry and can be used to perform both EUS-guided liver biopsy and necessary endoscopic procedures simultaneously. Therefore, EUS-PPG is expected to replace HVPG as an effective means to evaluate portal hypertension. Although previous studies have shown a meaningful association between EUS-PPG measurements and the clinical features of patients with portal hypertension,[23] its thresholds for evaluating the severity of cirrhotic portal hypertension require further study.

In this study, we retrospectively analyzed the clinical features of patients with diagnosed cirrhosis or chronic liver disease who had undergone EUS-PPG measurement at our institution to explore the correlations between the different clinical features of portal hypertension and EUS-PPG and the ability of EUS-PPG to detect gastroesophageal varices, decompensated cirrhosis, ascites, and recent variceal bleeding.

Methods

Patients

This retrospective study included consecutive patients with diagnosed cirrhosis or chronic liver disease who underwent EUS-PPG at Xiangya Third Hospital of Central South University from March 2022 to July 2024. The exclusion criteria included patients who had undergone splenectomy, transjugular intrahepatic portosystemic shunt, or hepatectomy and patients whose complete clinical data were unavailable. The ethics review committee of our institution approved this study (approval No. 24789).

EUS-PPG measurement

EUS-PPG was measured similarly to previously described methods.[17,24] All patients were given intravenous moderate sedation, and then endoscopy and EUS-PPG were performed with the patients in the left lateral position. Before EUS-PPG measurement, endoscopic evidence of portal hypertension was evaluated by endoscopy (EPK-i7000A; Pentax, Japan). The pressure transducer was subsequently placed at the right atrial level and then connected to the central venous pressure module (BeneView T5; Mindray, China) and a 25-gauge aspiration needle (ECHO-25; Cook, USA) by a noncompressible tube. After that, heparinized saline was used to clear any bubbles from the entire manometric system, and it was zeroed for the subsequent procedure. Linear array EUS (EG-3870UTK; Pentax) was used to assess the anatomy of the portal vein system and the hepatic vein system and identify the optimal vascular branches. When hepatic vein puncture was difficult, the inferior vena cava was selected instead. Before puncture, we evaluated the degree of difficulty and prioritized puncturing difficult target vessels to reduce the impact of the puncture time interval. After ensuring that the puncture path had no blood flow signal, the target vessel was punctured by the transduodenal or transgastric path. One milliliter to 2 mL of heparinized saline was flushed, and water bubbles were observed to determine whether the needle had entered the lumen of the target vessels. When the reading had stabilized for 30 seconds, the fluctuations in 3 consecutive readings within 3 mm Hg were recorded. After the needle was withdrawn, color Doppler and 5 minutes of endoscopy for puncture points were performed to exclude active bleeding. The EUS-PPG measurement is derived by subtracting the mean hepatic vein pressure or the mean inferior vena cava pressure from the mean portal vein pressure. All operations were performed by 2 experienced endoscopists.

Data collection and definitions

The general medical history data and the laboratory examination and imaging data collected within 7 days before EUS-PPG measurement were retrospectively reviewed. The diagnosis of cirrhosis could be made by liver biopsy, history, physical examination, laboratory results, imaging, or endoscopy. The signs of decompensated cirrhotic patients are variceal bleeding, ascites, jaundice, or hepatic encephalopathy at present or in the past.[1] Patients who were admitted to the hospital due to signs of gastrointestinal bleeding and subsequently active variceal bleeding or the presence of blood clots attached to varices without other lesions were detected by endoscopy; the patients were defined as having experienced recent variceal bleeding. Thrombocytopenia was defined on the basis of a platelet count $<150 \times 10^9$/L.[25] The universal definition of hypoproteinemia (albumin <35 g/L) was utilized.[26]

Statistical analysis

This study used the statistical software R 4.2.1 (Ross Ihaka, NZ) and GraphPad Prism 8.4 (GraphPad Software, CA) for statistical analysis. Continuous variables are reported as the means ± SDs, and categorical variables are reported as frequencies (%). The *t* test or Wilcoxon test was used to compare the distributions of normally or non–normally distributed data in the different groups. One-way analysis of variance was used for multiple group comparisons, and the least significant difference test was used for pairwise comparisons. The χ^2 test was used to describe classification variables. Multiple linear regression analysis was used to identify the independent factors correlated with EUS-PPG. The diagnostic performance of EUS-PPG for predicting gastroesophageal varices, decompensated cirrhosis, ascites, or recent variceal bleeding was assessed by using receiver operating characteristic (ROC) curves. Optimal cutoff values were selected on the basis of Youden index. $P < 0.05$ was considered statistically significant.

Results

Patients

From March 2022 to July 2024, a total of 276 patients with diagnosed cirrhosis or chronic liver disease underwent EUS-PPG measurement at our center [Figure 1]. Ultimately, 79 patients were excluded (63 patients who had undergone splenectomy, 8 patients who had undergone hepatectomy, 1 patient who had undergone transjugular intrahepatic portosystemic shunt, and 7 patients without complete clinical data), and 197 patients were included in this study. As demonstrated in Table 1, the proportions of male and female patients were 66.5% and 33.5%, respectively, and the average age was 57.01 ± 11.59 years. Among the 197 patients, 190 patients were diagnosed with cirrhosis (96.4%), and 7 patients had highly suspected cirrhosis (3.6%), of which the most important

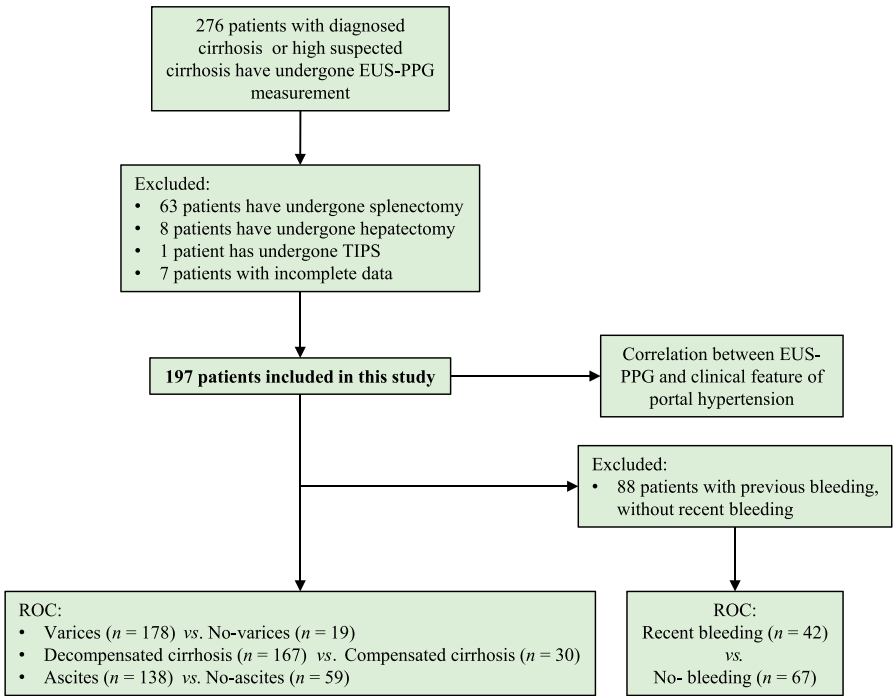

Figure 1. Flowchart for this study.

etiology was viral hepatitis (73.1%). Furthermore, 178 patients had gastroesophageal varices (90.4%), 167 patients had decompensated cirrhosis (84.8%), and 138 patients had ascites (70.1%). There were 42 patients with recent variceal bleeding (21.3%), 88 patients with a history of previous variceal bleeding but without recent variceal bleeding (44.7%), and 67 patients without a history of variceal bleeding (34.0%). The mean Model for End-Stage Liver Disease (MELD) score and EUS-PPG were 9.27 ± 3.50 and 15.30 ± 5.74 mm Hg, respectively, in 197 patients.

Correlation between EUS-PPG and clinical features

We subsequently analyzed the differences in EUS-PPG measurements according to different clinical features (Table S1, http://links.lww.com/ENUS/A371). As shown in Figures 2A–D and F–I, the EUS-PPG measurement was greater in patients with (*vs.* without) clinical features of gastroesophageal varices (16.23 ± 5.06 *vs.* 6.63 ± 4.32 mm Hg, $P < 0.001$), red signs (17.18 ± 4.82 *vs.* 13.07 ± 5.97 mm Hg, $P < 0.001$), ascites (17.15 ± 5.11 *vs.* 10.98 ± 4.75 mm Hg, $P < 0.001$), hepatic encephalopathy (22.00 ± 8.07 *vs.* 15.09 ± 5.55 mm Hg, $P = 0.003$), thrombocytopenia (15.98 ± 5.22 *vs.* 8.97 ± 6.61 mm Hg, $P < 0.001$), hypoproteinemia (16.31 ± 5.44 *vs.* 14.14 ± 5.88 mm Hg, $P = 0.008$), prolonged prothrombin time (PT) (16.47 ± 5.74 *vs.* 14.63 ± 5.65 mm Hg, $P = 0.03$), and prolonged international normalized ratio (INR) (16.78 ± 5.72 *vs.* 14.27 ± 5.55 mm Hg, $P = 0.002$). Furthermore, the EUS-PPG measurement was significantly lower in patients without variceal bleeding than in patients with previous variceal bleeding or patients with recent variceal bleeding (12.24 ± 5.93 *vs.* 15.93 ± 4.87 *vs.* 18.87 ± 4.62 mm Hg, $P < 0.001$), as shown in Figure 2E. In terms of the Child-Pugh grade, the EUS-PPG measurement in patients with Child-Pugh class A disease was significantly lower than that in patients with Child-Pugh classes B and C (13.39 ± 5.70 *vs.* 16.14 ± 5.27 *vs.* 18.58 ± 5.91 mm Hg, $P < 0.001$), as shown in Figure 2J.

To further explore the independent factors of EUS-PPG, the above clinical features were included in the multivariate linear regression analysis. The results are shown in Figure 2K. Hepatic encephalopathy ($\beta = 6.70$, $P < 0.001$), gastroesophageal varices ($\beta = 6.66$, $P < 0.001$), ascites ($\beta = 4.84$, $P < 0.001$), red signs ($\beta = 1.45$, $P = 0.024$), and variceal bleeding ($\beta = 1.41$, $P = 0.002$) were independently correlated with EUS-PPG measurements.

Assessment of EUS-PPG in gastroesophageal varices

As demonstrated in Table 2, compared with those in patients with gastroesophageal varices, the platelet counts (70.34 ± 41.90 *vs.* 182.68 ± 146.40 × 10^9/L, $P < 0.001$) and albumin levels (33.86 ± 6.18 *vs.* 37.55 ± 8.56 g/L, $P = 0.018$) in patients without gastroesophageal varices were significantly greater. Conversely, the EUS-PPG measurement was significantly lower in patients without gastroesophageal varices than in patients with gastroesophageal varices (16.23 ± 5.06 *vs.* 6.63 ± 4.32 mm Hg, $P < 0.001$). Figure 3A shows the ROC curve of EUS-PPG for the assessment of patients with gastroesophageal varices. The area under the ROC curve was 0.919, and the optimal EUS-PPG cutoff value was 11.5 mm Hg (sensitivity = 80.3%, specificity = 89.5%).

Assessment of EUS-PPG in decompensated cirrhosis

As demonstrated in Table 3, the average age (57.80 ± 11.34 *vs.* 52.60 ± 12.18 years, $P = 0.023$), PT (14.14 ± 2.10 *vs.* 13.-27 ± 1.71 seconds, $P = 0.033$), and EUS-PPG measurement (16.43 ± 5.12 *vs.* 9.02 ± 4.95 mm Hg, $P < 0.001$) of patients with decompensated cirrhosis were significantly greater. There was a significant difference in the proportion of Child-Pugh grades

Table 1

Basic characteristics and EUS-PPG measurements in 197 patients.

Characteristics (N = 197)	n (%) or Mean ± SD
Sex	
Male	131 (66.5%)
Female	66 (33.5%)
Age, yr	57.01 ± 11.59
Cirrhosis	
Highly suspected cirrhosis	7 (3.6%)
Diagnosed cirrhosis	190 (96.4%)
Etiology	
HBV/HCV	144 (73.1%)
Alcohol	20 (10.2%)
Cholestasis	4 (2.0%)
Schistosome	4 (2.0%)
Autoimmune	5 (2.5%)
Other	20 (10.2%)
Laboratory values	
Platelet, $\times 10^9$/L	81.17 ± 68.26
Total bilirubin, μmol/L	25.12 ± 23.14
Albumin, g/L	34.21 ± 6.51
Prothrombin time, s	14.01 ± 2.07
INR	1.22 ± 0.19
Clinical symptoms	
Varices	178 (90.4%)
Red signs	107 (54.3%)
Ascites	138 (70.1%)
Hepatic carcinoma	23 (11.7%)
hepatic encephalopathy	6 (3.0%)
Variceal bleeding	
No	67 (34.0%)
Previous	88 (44.7%)
Recent	42 (21.3%)
Child-Pugh grade	
A	78 (39.6%)
B	99 (50.3%)
C	20 (10.2%)
MELD score	9.27 ± 3.50
EUS-PPG, mm Hg	15.30 ± 5.74

EUS-PPG: EUS-guided portal pressure gradient; HBV: hepatitis B virus; HCV: hepatitis C virus; INR: international normalized ratio; MELD: Model for End-Stage Liver Disease.

between the 2 groups. Furthermore, compared with those in patients with decompensated cirrhosis, the platelet counts (73.80 ± 50.71 *vs.* 122.20 ± 121.31 × 10^9/L, $P < 0.001$) and albumin levels (33.47 ± 6.42 *vs.* 38.38 ± 5.42 g/L, $P < 0.001$) in patients with compensated cirrhosis were significantly greater. Figure 3B shows the ROC curve of EUS-PPG for the assessment of patients with decompensated cirrhosis. The area under the ROC curve was 0.847, and the optimal EUS-PPG cutoff value was 12.75 mm Hg (sensitivity = 77.8%, specificity = 76.7%).

Assessment of EUS-PPG in ascites

As demonstrated in Table 4, compared with those in patients with ascites, the platelet counts (73.76 ± 52.42 *vs.* 98.51 ± 93.90 × 10^9/L, $P = 0.019$) and albumin levels (33.22 ± 6.51 *vs.* 36.55 ± 5.95 g/L, $P = 0.001$) in patients without ascites were significantly greater. Conversely, the PT (14.24 ± 2.19 *vs.* 13.47 ± 1.64 seconds, $P = 0.017$), INR (1.24 ± 0.20 *vs.* 1.18 ± 0.15, $P = 0.036$), and EUS-PPG measurement (17.15 ± 5.11 *vs.* 10.98 ± 4.75 mm Hg, $P < 0.001$) in patients without ascites were significantly lower than those in patients with ascites. Figure 3C shows the ROC curve of EUS-PPG for the assessment of patients with ascites. The area under the ROC curve was 0.813, and the optimal EUS-PPG cutoff value was 15.75 mm Hg (sensitivity = 66.7%, specificity = 83.1%).

Assessment of EUS-PPG in recent variceal bleeding

To further explore the ability of EUS-PPG to assess variceal bleeding, we excluded 88 patients with a history of previous variceal bleeding but without recent variceal bleeding. As demonstrated in Table 5, the platelet counts (64.57 ± 37.14 *vs.* 107.67 ± 98.25 × 10^9/L, $P = 0.008$) and albumin levels (30.94 ± 5.37 *vs.* 36.09 ± 6.86 g/L, $P < 0.001$) in 67 patients without variceal bleeding were significantly greater than those in 42 patients with recent variceal bleeding. Conversely, the PT (14.48 ± 2.26 *vs.* 13.58 ± 1.59 seconds, $P = 0.017$), INR (1.26 ± 0.21 *vs.* 1.19 ± 0.15, $P = 0.029$), and EUS-PPG measurement (18.87 ± 4.62 *vs.* 12.24 ± 5.93 mm Hg, $P < 0.001$) were significantly lower in patients without variceal bleeding than in patients with recent variceal bleeding. Figure 3D shows the ROC curve of EUS-PPG for the assessment of patients with recent variceal bleeding. The area under the ROC curve was 0.804, and the optimal EUS-PPG cutoff value was 16.75 mm Hg (sensitivity = 76.2%, specificity = 70.1%).

Discussion

In this study, EUS-PPG measurements were significantly correlated with the clinical features of portal hypertension in the largest cohort reported thus far, and they were independently correlated with gastroesophageal varices, red signs, variceal bleeding, ascites, and hepatic encephalopathy. Furthermore, for the first time, we assessed the performance of EUS-PPG for assessing the severity of portal hypertension. The results showed that the performance of EUS-PPG in assessing gastroesophageal varices, decompensated cirrhosis, ascites, and recent variceal bleeding is excellent. The corresponding optimal EUS-PPG cutoff values for disease status assessment are 11.5, 12.75, 15.75, and 16.75 mm Hg, respectively.

Assessment of disease progression is critical and challenging at all stages of cirrhosis development. Accurate and reliable assessment of portal vein pressure is highly important for selecting follow-up treatment options, predicting complications, and evaluating patient prognosis.[4] Although the HVPG is the gold standard for evaluating portal hypertension, there are still many shortcomings. First, the HVPG indirectly reflects sinusoidal portal hypertension under radiation exposure. Second, HVPG measurement via the transjugular approach is associated with the risk of bile leakage, arteriovenous fistula formation, and intravenous contrast agent allergy.[27,28] Third, the existence of intrahepatic venovenous collateral shunts and the position of balloon catheter placement affect the accuracy of measuring the HVPG.[29] Compared with the HVPG, EUS-PPG reduces the above deficiencies to a certain extent and can be used to simultaneously perform endoscopy, EUS-guided liver biopsy, and necessary endoscopic treatment.[22] To date, the safety and feasibility of EUS-PPG have been verified in previous studies.[17–23] Compared with previous studies, our sample size is the largest reported thus far. We also found that EUS-PPG measurement is a direct pressure measurement technique with a high success rate and few complications. The Baveno VII consensus for portal hypertension released in 2021 included an evaluation of the effectiveness, safety, and accuracy of EUS-PPG on the

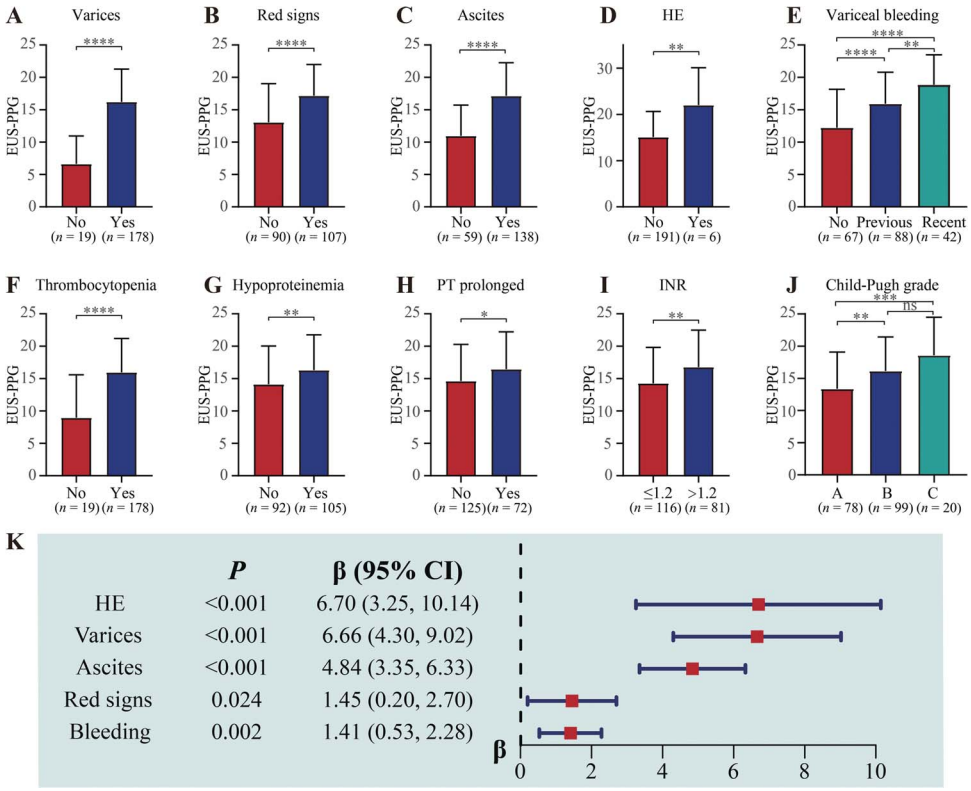

Figure 2. Association between EUS-PPG and the clinical features of patients with portal hypertension. A–J, Differences in EUS-PPG measurements between different groups categorized according to varices, red signs, ascites, hepatic encephalopathy, variceal bleeding, thrombocytopenia, hypoproteinemia, PT, INR, and Child-Pugh grade. K, Results of multiple linear regression analysis of EUS-PPG measurements. ns: $P > 0.05$, *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, ****$P < 0.0001$. EUS-PPG: EUS-guided portal pressure gradient; INR: International normalized ratio; ns: Not statistically significant; PT: Prothrombin time.

research agenda.[4] Therefore, it is necessary to explore the efficiency of EUS-PPG in evaluating the severity of portal hypertension.

EUS-PPG in this study (15.30 ± 5.74 mm Hg) was significantly greater than that reported in previous studies of 83 patients with chronic liver disease or suspected cirrhosis (7.06 ± 6.09 mm Hg).[23] This occurred because patients with decompensated cirrhosis (84.8%) were the main subjects in this study, which also reflects that EUS-PPG increases with the aggravation of cirrhosis. Ascites, gastroesophageal varices, and hepatic encephalopathy are common clinical manifestations of decompensated cirrhosis, and red signs are high-risk signals for variceal bleeding.[30] Previous clinical studies have also revealed that the HVPG is significantly increased in patients with these positive indicators.[31] Advanced cirrhosis is often accompanied by thrombocytopenia, and previous noninvasive predictive models regard the platelet count as a strong predictor.[4,32] Coagulation disorders are also integral components of advanced cirrhosis, which is often accompanied by prolonged PT and INR.[33] In terms of the Child-Pugh grade, the HVPG in patients with Child-Pugh class C disease was significantly increased.[34] Furthermore, this study is the first to propose that EUS-PPG is significantly higher in patients with recent variceal bleeding than in patients without variceal bleeding or previous variceal bleeding. These results show that an increase in EUS-PPG is closely related to aggravation of the disease.

In this study, the area under the ROC curve was 0.919, with a cutoff of EUS-PPG ≥11.5 mm Hg (sensitivity = 80.3%, specificity = 89.5%) for the diagnosis of gastroesophageal varices, which is relatively satisfactory. Notably, variceal screening can be performed simultaneously with EUS-PPG measurement, which may reduce the possibility of a missed diagnosis. Therefore, when the EUS-PPG reaches 12 mm Hg, even if gastroesophageal varices are not

Table 2

Characteristics of patients categorized by gastroesophageal varices.

Characteristics	Varices (n = 178)	No varices (n = 19)	P
Male (%)	118 (66.3)	13 (9.9)	0.852
Age, yr	57.22 ± 11.20	55.00 ± 14.99	0.428
Platelet, $\times 10^9$/L	70.34 ± 41.90	182.68 ± 146.40	**<0.001**
Albumin, g/L	33.86 ± 6.18	37.55 ± 8.56	**0.018**
Total bilirubin, μmol/L	25.73 ± 23.91	19.34 ± 12.96	0.254
Prothrombin time, s	14.05 ± 2.11	13.67 ± 1.59	0.449
INR	1.23 ± 0.20	1.19 ± 0.15	0.374
Child-Pugh grade (%)			
A	66 (37.1)	12 (63.1)	
B	93 (52.2)	6 (31.6)	
C	19 (10.7)	1 (5.3)	0.086
MELD score	9.39 ± 3.46	8.14 ± 3.75	0.141
EUS-PPG, mm Hg	16.23 ± 5.06	6.63 ± 4.32	**<0.001**

EUS-PPG: EUS-guided portal pressure gradient; INR: international normalized ratio; MELD: Model for End-Stage Liver Disease.

Boldface indicates $P < 0.05$.

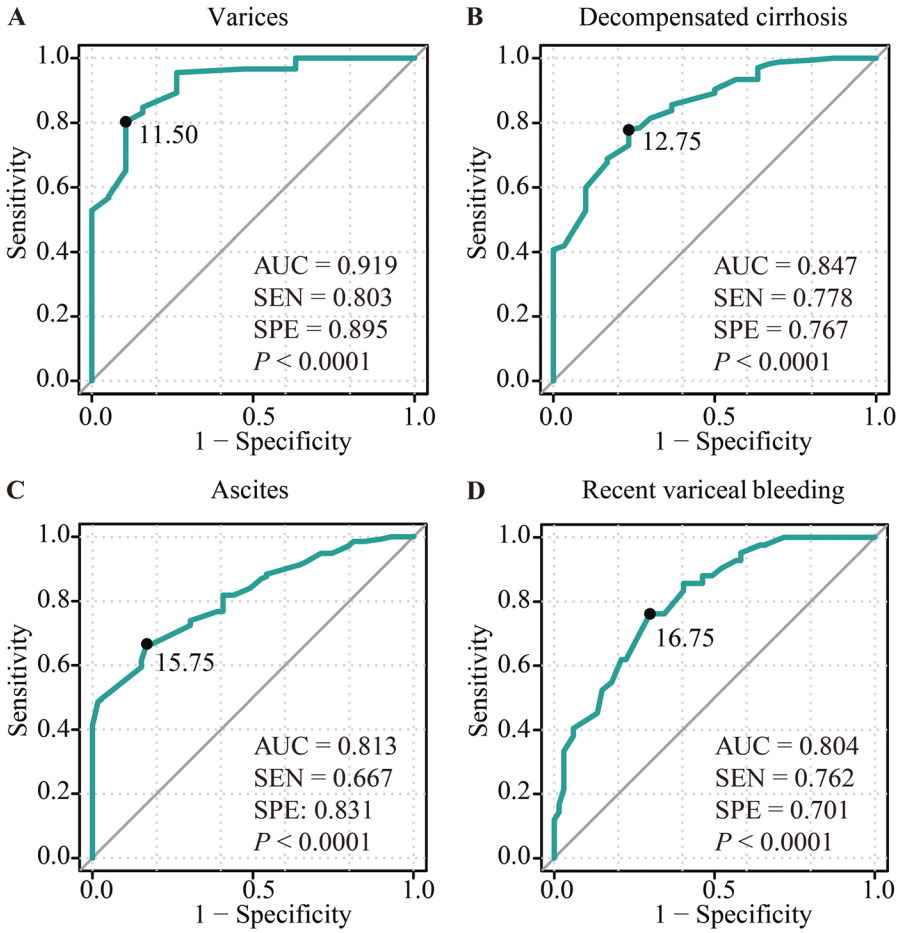

Figure 3. Diagnostic value of EUS-PPG. ROC analysis for (A) gastroesophageal varices, (B) decompensated cirrhosis, (C) ascites, and (D) variceal bleeding. EUS-PPG: EUS-guided portal pressure gradient; ROC: Receiver operating characteristic.

Table 3

Characteristics of patients categorized by decompensated cirrhosis.

Characteristics	Decompensated (n = 167)	Compensated (n = 30)	P
Male (%)	108 (64.7)	23 (76.7)	0.2
Age, yr	57.80 ± 11.34	52.60 ± 12.18	**0.023**
Platelet, $\times 10^9$/L	73.80 ± 50.71	122.20 ± 121.31	**<0.001**
Albumin, g/L	33.47 ± 6.42	38.38 ± 5.42	**<0.001**
Total bilirubin, μmol/L	25.66 ± 24.54	22.08 ± 12.60	0.436
Prothrombin time, s	14.14 ± 2.10	13.27 ± 1.71	**0.033**
INR	1.23 ± 0.20	1.17 ± 0.15	0.051
Child-Pugh grade (%)			
A	53 (31.7)	25 (83.3)	
B	94 (56.3)	5 (16.7)	
C	20 (12.0)	0 (0)	**<0.001**
MELD score	9.33 ± 3.67	8.90 ± 2.34	0.529
EUS-PPG, mm Hg	16.43 ± 5.12	9.02 ± 4.95	**<0.001**

EUS-PPG: EUS-guided portal pressure gradient; INR: international normalized ratio; MELD: Model for End-Stage Liver Disease.

Boldface indicates $P < 0.05$.

found by endoscopy, the doctor should strengthen the prevention of varices and variceal bleeding.

Decompensated cirrhosis usually occurs in the symptomatic stage of liver cirrhosis, which is often accompanied by variceal bleeding, ascites, jaundice, hepatic encephalopathy, and other symptoms.[1] A previous prospective study revealed that the HVPG is the most reliable predictor of decompensation in patients with compensated cirrhosis and that patients with an HVPG <10 mm Hg are less likely to convert to clinical decompensation in the next 4 years.[7] However, the purpose of that study was to evaluate the predictive value of the HVPG for disease progression. Our study was a practical assessment of the current situation of cirrhotic patients. Our finding of a cutoff of EUS-PPG ≥12.75 mm Hg (sensitivity = 77.8%, specificity = 76.7%) for the diagnosis of decompensated cirrhosis is roughly in agreement with the findings of a previous study.[7] Thus, a comprehensive treatment plan should be formulated for such patients to prevent further decompensation events.

Another important finding is that the area under the ROC curve was 0.813 for the presence of ascites. Nevertheless, the optimal EUS-PPG cutoff value for ascites is 15.75 mm Hg (sensitivity = 66.7%, specificity = 83.1%). Compared with an HVPG ≥12 mm Hg

Table 4

Characteristics of patients categorized by ascites.

Characteristics	Ascites (n = 138)	No-ascites (n = 59)	P
Male (%)	91 (65.9%)	40 (67.8%)	0.801
Age, yr	57.82 ± 10.69	55.12 ± 13.38	0.135
Platelet, $\times 10^9$/L	73.76 ± 52.42	98.51 ± 93.90	**0.019**
Albumin, g/L	33.22 ± 6.51	36.55 ± 5.95	**0.001**
Total bilirubin, μmol/L	26.63 ± 26.06	21.57 ± 13.68	0.161
Prothrombin time, s	14.24 ± 2.19	13.47 ± 1.64	**0.017**
INR	1.24 ± 0.20	1.18 ± 0.15	**0.036**
Child-Pugh grade (%)			
A	32 (23.2%)	46 (78.0%)	
B	86 (62.3%)	13 (22.0%)	
C	20 (14.5%)	0 (0%)	**<0.001**
MELD score	9.54 ± 3.77	8.64 ± 2.70	0.1
EUS-PPG, mm Hg	17.15 ± 5.11	10.98 ± 4.75	**<0.001**

EUS-PPG: EUS-guided portal pressure gradient; INR: international normalized ratio; MELD: Model for End-Stage Liver Disease.

Boldface indicates $P < 0.05$.

indicating that the risk of ascites will gradually increase,[7] EUS-PPG ≥15.75 mm Hg seems to be an acceptable result. However, this result seems to be influenced by individual differences, disease stages, or other factors. Thus, it is not advisable to suggest EUS-PPG ≥15.75 mm Hg as a threshold of ascites, and further prospective cohort studies are needed to explore the value of EUS-PPG in predicting ascites.

Furthermore, we found that the area under the ROC curve was 0.813, with a cutoff of EUS-PPG ≥16.75 mm Hg (sensitivity = 76.2%, specificity = 70.1%) for a diagnosis of recent variceal bleeding. This observation is in agreement with the notion that an HVPG ≥12 mm Hg is necessary for variceal bleeding. Although variceal bleeding is closely related to EUS-PPG, it is also affected by various factors, such as constipation and vomiting, which should be evaluated in subsequent studies. Even so, our results provide evidence that the prevention and treatment of variceal bleeding should be strengthened for patients with an EUS-PPG ≥16.75 mm Hg but without a bleeding event.

Table 5

Characteristics of patients categorized by recent variceal bleeding.

Characteristics	Recent bleeding (n = 42)	No bleeding (n = 67)	P
Male (%)	31 (73.8)	45 (67.2)	0.462
Age, yr	56.50 ± 10.11	56.27 ± 11.79	0.916
Platelet, $\times 10^9$/L	64.57 ± 37.14	107.67 ± 98.25	**0.008**
Albumin, g/L	30.94 ± 5.37	36.09 ± 6.86	**<0.001**
Total bilirubin, μmol/L	25.77 ± 15.95	22.30 ± 13.13	0.219
Prothrombin time, s	14.48 ± 2.26	13.58 ± 1.59	**0.017**
INR	1.26 ± 0.21	1.19 ± 0.15	**0.029**
Child-Pugh grade (%)			
A	7 (16.7)	39 (58.2)	
B	28 (66.7)	24 (35.8)	
C	7 (16.7)	4 (6.0)	**<0.001**
MELD score	9.48 ± 3.78	8.82 ± 3.00	0.315
EUS-PPG, mm Hg	18.87 ± 4.62	12.24 ± 5.93	**<0.001**

EUS-PPG: EUS-guided portal pressure gradient; INR: international normalized ratio; MELD: Model for End-Stage Liver Disease.

Boldface indicates $P < 0.05$.

Previous studies on the HVPG have shown that an HVPG ≥10 mm Hg indicates an increased risk of varices, and an HVPG ≥12 mm Hg is the threshold for the diagnosis of decompensated cirrhosis and is a necessary condition for the occurrence of variceal bleeding.[5,7,11] However, our data show that the threshold of EUS-PPG for gastroesophageal varices, decompensated cirrhosis, ascites, and recent variceal bleeding is greater than that of HVPG. A previous study revealed that approximately one-third (81/222) of patients had different degrees of intrahepatic venovenous collateral shunts, and the WHVP in patients with moderate and severe intrahepatic venovenous collateral shunts was significantly underestimated.[35] Furthermore, the WHVP also underestimates portal vein pressure in decompensated nonalcoholic fatty liver cirrhosis patients.[36] The accuracy of HVPG measurement is reduced when the catheter is inserted too shallowly into the hepatic vein or when the front end of the catheter is blocked.[37] Therefore, we speculate that EUS-PPG avoids the error caused by this factor, but this speculation still needs further exploration.

Undeniably, this is a single-center retrospective clinical analysis. A multicenter prospective study is necessary to validate our results in the future. Second, the subjects included only patients with diagnosed cirrhosis or chronic liver disease and could not represent all types of portal hypertension. Third, the total sample size of this study and the sample size of patients with early cirrhosis are insufficient, and more follow-up clinical data will be accumulated for further analysis.

Conclusion

In summary, EUS-PPG measurements were significantly correlated with the clinical features of patients with portal hypertension and were independently correlated with gastroesophageal varices, red signs, variceal bleeding, ascites, and hepatic encephalopathy. Furthermore, our data demonstrated that EUS-PPG showed significant efficiency in the evaluation of the severity of portal hypertension and revealed the thresholds of EUS-PPG for disease status assessment, including for gastroesophageal varices, decompensated cirrhosis, ascites, and recent variceal bleeding. Beyond the threshold, the corresponding positive symptoms changed considerably in our study cohort. These findings demonstrate that EUS-PPG measurement is an effective technique for assessing disease severity and the risk of variceal bleeding in patients with diagnosed cirrhosis or chronic liver disease.

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Ethical Approval

This study was approved by the ethics review committee of the Third Xiangya Hospital of Central South University (Approval No. 24789).

Informed Consent

Not applicable.

Conflicts of Interest

The authors declare that they have no financial conflict of interest with regard to the content of this report.

Author Contributions

Rongkun Luo: conceptualization, data curation, writing, project administration, methodology. Mingcong Chen: data curation, formal analysis, investigation, methodology. Huanyuan Lu: data curation, formal analysis, investigation, methodology. Rui Zhang: data curation, formal analysis, investigation. Hongwu Luo: formal analysis, methodology. Yinghong Liu: validation, software. Xunyang Liu: formal analysis, methodology. Feizhou Huang: formal analysis, methodology, supervision. Gang Deng: formal analysis, data curation, supervision. Zhao Lei: conceptualization, funding acquisition, supervision. All authors contributed to the article and approved the submitted version. All authors agreed to be accountable for all aspects of the manuscript.

Data availability statements

The datasets generated during the current study are available from the corresponding author on reasonable request.

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