

EUS-Guided Portal Pressure Gradient Measurement in Patients with Portal Hypertension: Evidence-Based Case Report

Putra Nur Hidayat*, Juferdy Kurniawan**

*Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia/
Dr. Cipto Mangunkusumo General National Hospital, Jakarta

**Division of Hepatobiliary, Department of Internal Medicine, Faculty of Medicine,
Universitas Indonesia/Dr. Cipto Mangunkusumo General National Hospital, Jakarta

Corresponding author:

Juferdy Kurniawan. Division of Hepatobiliary, Dr. Cipto Mangunkusumo General National Hospital. Jl. Salemba 6 Jakarta Indonesia. Phone: +6221 31900924. E-mail: juferdy.k@gmail.com

ABSTRACT

Aim: This evidence-based case report aims to assess the accuracy of EUS-PPG measurement in patients with portal hypertension.

Method: A literature search was performed using PubMed, Cochrane, ProQuest, and EBSCO. A total of 2 articles were selected after meeting the inclusion and exclusion criteria. Critical study assessment was conducted to assess the validity, importance, and applicability of the study.

Results: As a result, the first study found higher EUS-PPG measurement values in patients with clinical parameters of portal hypertension and the second study found a good correlation between EUS-PPG measurement values with hepatic vein pressure gradient (HVPG) and transjugular intrahepatic portosystemic shunt (TIPS) portal pressure gradient (PPG).

Conclusion: From these two studies, it can be concluded that EUS-PPG measurement is a safe, effective, and feasible method to be performed on patients.

Keywords: portal hypertension, endoscopic ultrasound, hepatic venous pressure gradient

ABSTRAK

Tujuan: Laporan kasus berbasis bukti ini bertujuan untuk menilai akurasi EUS- PPG pada pasien dengan hipertensi porta.

Metode: Pencarian literatur dilakukan dengan menggunakan PubMed, Cochrane, ProQuest, dan EBSCO. Sebanyak 2 artikel dipilih setelah memenuhi kriteria inklusi dan eksklusi. Telaah kritis dilakukan menilai validitas, kepentingan, dan aplikabilitas studi.

Hasil: Hasilnya, studi pertama menemukan nilai EUS-PPG yang lebih tinggi pada pasien dengan klinis parameter hipertensi porta dan studi kedua menemukan korelasi yang baik antara nilai EUS-PPG dengan hepatic vein pressure gradient (HVPG) serta transjugular intrahepatic portosystemic shunt (TIPS) portal pressure gradient (PPG).

Simpulan: Dari kedua studi ini dapat disimpulkan bahwa EUS-PPG merupakan metode yang aman, efektif, dan feasible dilakukan pada pasien.

Kata kunci: hipertensi porta, endoscopic ultrasound, hepatic venous pressure gradient

INTRODUCTION

Portal hypertension (PH) is a severe complication of cirrhosis. Manifestations of PH include esophageal varices and its bleeding, ascites, hepatic encephalopathy, and the hepatorenal syndrome.¹ The diagnosis of PH and the measurement of portal pressure have major implications for the prognostic and therapeutic value of patients with PH.² Measurement of portal pressure can be performed both directly and indirectly. Direct measurement of portal pressure can be performed invasively in patients undergoing transjugular intrahepatic portosystemic shunt (TIPS).³ In this procedure, direct puncture of the portal vein and inferior vena cava was performed, which was then calculated the difference as the portal pressure gradient (PPG). A higher portal venous pressure difference > 5 mmHg indicated PH. While the indirect measurement of PH was to use the hepatic venous pressure gradient (HVPG).⁴

Currently HVPG is still used as the main measurement method to assess the presence of PH. In HVPG, a catheter is used to enter the hepatic vein and then two measurements are taken. The first measurement is of the hepatic venous pressure itself. The second measurement is taken when the balloon catheter is inflated. When the balloon is inflated, the hepatic vein is occluded and the measurement read represents the pressure in the sinusoids. The presence of an increasing difference (> 5 mmHg) in hepatic vein pressure and wedge pressure indicates the presence of PH.⁵

Measurement with HVPG has several drawbacks such as the method which still includes invasiveness, the presence of radiographic exposure and intravenous contrast, and the measurement is indirect.⁶ On the other hand, endoscopic ultrasound guided portal pressure gradient (EUS-PPG) measurement is the newest method to measure the presence of PH. In this procedure, measurements are initiated by inserting an endoscope with an ultrasound probe at the end. Visualization of the hepatic vein or inferior vena cava and portal vein was performed before a direct puncture was performed on both veins and the portal pressure gradient was measured. This measurement is direct but less invasive than the TIPS procedure.⁷ Not many studies have discussed the safety, accuracy, and feasibility of this procedure therefore additional studies are needed as a basis for using this procedure in the future. This evidence-based case report aims to assess the accuracy of EUS-PPG measurement in patients with portal hypertension.

CASE ILLUSTRATION

A 64-year-old male patient was sent to Dr. Cipto Mangunkusumo General National Hospital for esophagogastroduodenoscopy (EGD) ligation. The patient was with known history of liver cirrhosis and chronic hepatitis B since January 2016. Since then, the patient has undergone EGD five times and HVPG once at the beginning of treatment. There were no complaints of vomiting blood and black stool at this time. On physical examination the patient was in a compos mentis state with stable vital signs. Abdominal examination showed no enlargement of the liver and spleen. On follow-up examination, it was found Hb 10 mg/dL, platelets of 141.000 cells/mm³, prothrombin time (PT) 11.2 (11.5) second, activated partial thromboplastin time (APTT) 33.9 (33.1) second, AST 51 IU/mL, ALT 47 IU/mL, and total bilirubin 1.01 mg/dL.

On the last EGD examination we found obliterated esophageal varices. The HVPG result at the start of treatment for cirrhosis and chronic hepatitis B was 14.4 mmHg. The patient was advised to re-check for HVPG after 1 year of treatment but the patient was unable to because he had to work outside Jakarta where HVPG facilities were not available. Currently, the patient asked whether there was an alternative HVPG test that can be used to assess the course of the disease.

METHOD

The clinical question in this evidence-based case report was how is the EUS-PPG measurement in assessing portal hypertension? Literature search on November 22, 2021 using search engines from PubMed, Cochrane, ProQuest, and EBSCO (Figure 1). The keywords used were “endoscopic ultrasound portal pressure gradient”, “portal hypertension”, and “hepatic venous pressure gradient” along with synonyms and related terms. Two publications were included in this study. The inclusion criteria used were publications in the last 5 years, human studies, prospective or retrospective cohort designs, and literature in English or Indonesian. The search exclusion criteria were publications that was not accompanied by full text. After the selection, the validity was done using critical appraisal kit based Oxford University's center of evidence-based medicine (CEBBM) criteria.

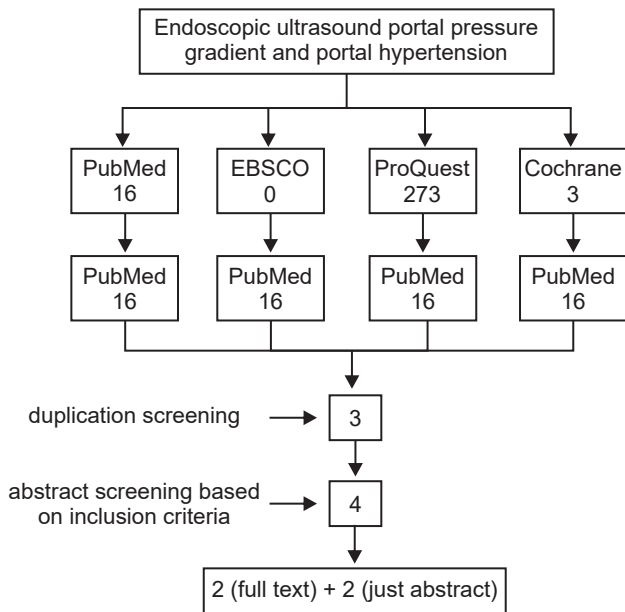


Figure 1. Flowchart of search strategy

RESULTS

This evidence based case report will review the accuracy, safety, and feasibility of EUS-PPG measurement in assessing portal hypertension. Primary endpoint is the correlation of EUS-PPG with portal hypertension parameter. After literature searching with mentioned criteria, we found 4 suitable studies with cohort design. Unfortunately, the 2 studies were not accompanied by full text. Both studies were excluded and the remaining two were included to this evidence based case report. A critical study was conducted to assess the validity, importance, and applicability of these 2 studies (Table 1). Summary of both studies can be seen in Table 2.

The first study by Huang et al (2017) assessed differences in EUS-PPG values between patients with and without clinical parameters of portal hypertension.⁸ A total of 28 participants were included in this study. The clinical parameters of portal hypertension that were correlated with the EUS-PPG value were the clinical signs of cirrhosis, varicose veins, gastropathy, and thrombocytopenia. Feasibility was assessed based on the success of PPG measurement. Safety was assessed from complications based on interviews up to 48 hours after the procedure. Medical record data, laboratory, imaging, and demographic data were collected and analyzed retrospectively. Prior to the EUS-PPG measurement, an endoscopy was performed to assess the presence of varicose veins or portal hypertensive gastropathy. A 25G fine needle aspiration (FNA) needle was used in this study.

In the study conducted by Huang et al, measurement of EUS-PPG was successfully performed in 28/28 patients (100%). The average PPG value was 8.2 mmHg (1.5-19 mmHg). In 9/28 patients the inferior vena cava was measured because of anatomic problems and there was no problem with accessing the portal vein measurements (using the transgastric or transduodenal route). There were no intra or postoperative complications such as bleeding, perforation, pain, and infectious complications.⁸

Portal pressure gradient (PPG) values were found to be elevated in patients with clinical cirrhosis ($p = 0.005$), varicose veins ($p = 0.0002$), portal hypertensive gastropathy ($p = 0.007$), and thrombocytopenia ($p = 0.036$) compared to patients without these conditions. The average PPG in patients with and without clinical cirrhosis was 10.33 vs 3.81 mmHg, with and without varicose veins was 14.37 vs 4.26, with and without portal hypertensive gastropathy was 12.76 vs 6.09, and with and without thrombocytopenia was 10.3 vs 5.48 in which all comparisons had significant difference in mean. The results of the calculation using logistic regression showed that patients with EUS-PPG > 5 mmHg had an 18.7 times higher probability of finding clinical cirrhosis than normal patients (< 5 mmHg) and a 6.1 times higher probability of thrombocytopenia with a negative correlation between PPG and platelet levels ($r = -0.473$).⁸

A second study by Zhang et al (2020) assessed the consistency of EUS-PPG with HVPG measurements in patients with acute and subacute portal hypertension. A total of 12 patients were included in this study.⁹ A 22G FNA needle was used to measure pressure in the portal vein and hepatic or inferior vena cava. If HVPG cannot be performed, then TIPS procedure is performed to assess the patient's PPG and correlate it with EUS-PPG. Feasibility, duration of action, and complications were also assessed in this study.

In the study conducted Zhang et al, measurement of EUS-PPG was successful in 11/12 patients (91.7%). Furthermore, the HVPG measurement failed to be carried out in 2 patients due to Budd Chiari syndrome hepatic vein subtype, so TIPS measurements were carried out in these 2 patients. In 1 patient who underwent HVPG, a shunt was found thus the HVPG assessment was declared inaccurate. The mean value of EUS-PPG was 18.07 ± 4.32 compared to HVPG/TIPS PPG which was 18.82 ± 3.34 mmHg, no significant difference was found. The correlation between the EUS-PPG assessment and HVPG or TIPS was assessed by Pearson correlation and obtained a value of 0.923

Table 1. Critically review all studies based on Oxford University's center of evidence-based medicine

Study	Representative patient spectrum	Comparative examination is carried out without looking at the results of the index test	Blinding	Easy for replication	Results are presented correctly
Huang JY, et al 2017 ⁸	+	+	-	+	+
Zhang W, et al 2021 ⁹	+	+	-	+	+

Table 2. Summary of all studies

Study	Study design	Subjects	Inclusion	Exclusion	Intervention/control	Outcome
Huang JY, et al 2017 ⁸	Cohort	28 patients. California, USA	<ul style="list-style-type: none"> 18-75 years old History of liver disease or suspected cirrhosis 	<ul style="list-style-type: none"> Pregnancy international normalized ratio (INR) > 1.5 Platelets < 50,000 Active gastrointestinal (GI) bleeding Post sinusoidal PH 	Clinical trials compared the endoscopic ultrasound guided portal pressure gradient (EUS-PPG) values of patients with and without clinical parameters of portal hypertension	The using of EUS-PPG technique was feasible and appeared safe
Zhang W, et al 2021 ⁹	Cohort	12 patients. Nanjing, Cina	<ul style="list-style-type: none"> Age 14-75 years old Diagnosed with acute and subacute PH 	<ul style="list-style-type: none"> Severe esophagogastric varices Active variceal bleeding INR > 1.5 Platelets < 50,000 HF NYHA II Critical illness condition Child Pugh > 10 Pregnancy Budd Chiari subtype inferior vena cava and mixed 	Clinical trials assessed the feasibility and safety of EUS-PPG (using a 22-gauge FNA needle) and calculated the correlation between the two measurements	EUS-PPG measurement was a safe and accurate method for evaluating the portal hypertension and also had the potential to be supplement for the measurement of HPVG in liver disease

($p < 0.001$). There was no difference in the duration of the procedure and complications such as bleeding, infection, and perforation.⁹

DISCUSSION

The EUS-PPG measurement is a new method that is direct and non-invasive compared to HVPG. Previous studies have shown that EUS-PPG has a good correlation with transjugular measurements in animal studies.⁷ However, measurement of EUS-PPG in humans has not been widely used as a diagnostic option because of the limited number of studies.

The study conducted by Huang et al showed that measurement of EUS-PPG with a 25G FNA needle proved safe and feasible in humans.⁸ No failures or complications were found. The EUS-PPG procedure also does not require iodine contrast or radiation. This measurement is direct therefore it is believed to be superior to the indirect measurement of HVPG. In patients with cirrhosis, thrombocytopenia, and coagulopathy, EUS-PPG remains safe in the presence of real time Doppler and hepatic parenchymal tamponade. EUS-PPG results correlate well with clinical portal hypertension and suspicion of cirrhosis. However, the weaknesses of this study are the small

sample size, no biopsy to confirm cirrhosis, and no HVPG examination.

The study conducted by Zhang et al was subsequently the first study to assess the application of EUS-PPG in acute and subacute PH.⁹ We found a good consistency of EUS-PPG with respect to HVPG testing. EUS-PPG with a 22G needle is also considered feasible, safe, and effective. There was no significant difference in duration between the two measurements. EUS-PPG can be used to assess pre-sinusoid PH whereas HVPG does not accurately assess this condition. Similar to the study conducted by Huang et al, the drawbacks of this study are the small sample size, and possible bias because HVPG was performed in conscious patients while EUS-PPG was performed in moderately sedated patients (patients with sedation were said to have lower pressure values).

Another study by Zhang et al shown that EUS-guided PPG with 22G needle was a direct, safe and accurate approach to assess PH in patients with hepatic sinusoidal obstructive syndrome. It might replace HVPG as the most used tool for portal pressure assessment.¹⁰ Study by Kolb et al also found that EUS-PPG shown high correlation with PH clinical parameters and histologic appearance in patients with advance liver disease.¹¹ Furthermore, EUS-PPG can be

performed at the same time during EUS-liver biopsy procedure which provide us some practical benefit in managing patients with advanced liver disease.¹²

CONCLUSION

In conclusion, measurement with EUS-PPG using either a 25G or 22G FNA needle is a safe, effective, and feasible method to perform on patients. This procedure has advantages over HVPG because it is direct, less invasive, and is able to assess portal hypertension in presinusoidal obstruction. Deficiencies in HVPG such as radiographic exposure and contrast exposure are also not used in the EUS-PPG procedure. Studies with a larger number of samples are highly recommended to be carried out in the future.

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