Original Article

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Portal Vein Doppler: A Tool for Non-Invasive Prediction of Esophageal Varices in Cirrhosis

Internal Medicine Section

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ABSTRACT

Background and Objectives: Esophageal varices (EV), a major complication of liver cirrhosis, can lead to life threatening gastrointestinal (GI) bleeding. Esophagogastroduodenoscopy (EGD) is the gold standard for diagnosis and management of esophageal varices. However, it is not always available in resource-constrained settings.This study was aimed at evaluating portal vein indices (PVI) using Doppler on ultrasound abdomen, which is more widely available, as tools to predict the presence of EV.

Methods: A total of 50 adult patients with cirrhosis were included in the study. All subjects underwent a percutaneous liver biopsy, abdominal ultrasound and EGD along with other tests as part of the work up for cirrhosis. The portal vein indices that were studied included hepatic congestion index (HCI), portal vein diameter (PVD) and portal vein velocity (PVV). Their sensitivity, specificity and predictive values were calculated using EGD as a gold standard.

Results: Association of PVD, PVV and HCI with presence of EV was statistically significant (p-value <0.01). PVV had the highest sensitivity 84% (95% CI 66.45%- 94.10%) for detecting the presence of EV. PVD and HCI had the highest specificity of 55% (95% CI 0.31-0.77) and the highest negative predictive value of 38%(95% CI 0.24-0.52). Positive predictive value was highest PVV at 76%. (95% CI 0.61-0.86)

Conclusion: In resources- constricted settings where EGD is not available, PVI (PVV, PVD and HCI) on ultrasound abdomen can be used as non-invasive parameters to predict the presence of EV. Although EGD remains the gold standard for the diagnosis and management of EV, when this is not possible due to scarcity of resources, PVV may be used a tool to triage patients for referral for an EGD as it has the highest sensitivity of 84% (95% CI 66.45%-94.10%) and positive predictive value of 76% (95% CI 61.51%-86.47%) amongst the PVI studied for detecting the presence of EV.

Keywords: Esophagogastroduodenoscopy, Hepatic congestion index, Portal vein indices, Portal vein diameter, Portal vein velocity

INTRODUCTION

Portal hypertension (PHT), a progressive complication of liver cirrhosis, is defined as a pathological increase in the portal venous pressure between the portal vein and the inferior vena cava to higher than the normal (Normal range is ≤ 5 mmHg [1]. Clinically significant PHT (Hepatic venous pressure gradient ≥ 10 mmHg) is necessary for the development of EV and variceal bleeding along with the development of decompensation [2-4]. Variceal bleeding occurs in 25-40% of patients with cirrhosis. Each episode of variceal bleeding is associated with approximately 20% mortality rate [5,6]. One in four patients with EV, will likely suffer an episode of variceal bleeding over a period of two years [5].

The gold standard for the diagnosis of EV and management of its complications is EGD. A screening EGD is recommended in all patients at the time of initial diagnosis of cirrhosis to screen for the presence of EV [7,8]. On screening EGD,9-36% patients with cirrhosis are found to have esophageal varices [9,10].

EGD, however, is not consistently available in resources constrained settings in developing and under developed countries. Non-invasive modalities like ultrasound of the abdomen are significantly less resource intensive and are often available in settings where EGD is not consistently available. This study is aimed at evaluating various PVI on portal vein Doppler during abdominal ultrasound as markers for detecting the presence of EV.

METHODS

This was cross-sectional study conducted at Sir Sayajirao General Hospital-Vadodara, a regional tertiary care hospital situated in Gujarat; India. Fifty adult patients with cirrhosis of liver were included in the study. Patients having hepatic encephalopathy, hepatorenal syndrome, hepatopulmonary syndrome, coagulopathy, hepatocellular carcinoma or metastasis in liver were excluded. Patients already on prophylaxis for portal hypertension with Beta-blockers or those who had undergone endoscopic or surgical treatment for esophageal varices were also excluded.

Complete history and physical examination along with complete blood count, metabolic profile, electrocardiogram (EKG), viral hepatitis panel, erythrocyte sedimentation rate (ESR) and prothrombin time (PT/INR) were done for all the study participants. Ascitic fluid analysis, Echocardiogram, Anti Liver Kidney Microsomal 1(LKM 1) antibody, Anti Mitochondrial Antibody (AMA) and Anti Smooth Muscle Antibody (ASMA) were done as clinically indicated.

All study participants also underwent an ultrasound of the abdomen, per-cutaneous liver biopsy and EGD.

On ultrasound evaluation performed during inspiration; liverspan along with echogenicity, nodularity of surface, and size of the spleen were noted. Splenomegaly was defined as spleen size > 12 cm along the long axis. Ascites if present was graded.

The following PVI were used to document PHT on ultrasound Doppler:

1. Portal vein diameter > 13 mm
2. Portal vein velocity <16 cm/ sec
3. Congestion Index, calculated as ratio of cross sectional area of portal vein and portal vein velocity > 0.1

Sex (male/ female)	34 / 16 (68% / 32%)
Mean Age (years)	41.9 ± 10.9
Etiology of cirrhosis:	
HCV	1 (2%)
HBV	2 (4%)
Autoimmune	4 (8%)
Congestive Heart Failure	1 (2%)
Alcohol	26 (52%)
Mean duration of alcohol consumption in years	17 ± 4.34
Cryptogenic	16 (32%)
Child Pugh Classification:	
A	2 (4%)
B	13 (26%)
C	35 (70%)
Mean score	10.12 ± 2.04
Ascites	40 (80%)
Splenomegaly(> 12 cm)	40 (80%)
Hemoglobin (gm%)	8.37 ± 3.0
Platelet count/ cu.mm.	113260 ± 76299
Serum bilirubin (mg%)	4.38 ± 5.4
Serum albumin (gm%)	2.44 ± 0.64
Prothrombin time(seconds)	18.1 ± 5.49
Upper GI Endoscopy:	
No varices	18 (36%)
Grade 1 varices	2 (4%)
Grade 2 varices	13 (26%)
Grade 3 varices	17 (34%)
Total patients with varices	32 (64%)

[Table/Fig-1]: Clinical, laboratory, sonographic and endoscopic features of cirrhotic patients included in study (n=50)

Varices on EGD	PV Diameter >13	PV Diameter <13	Total
Presence	23	9	32
Absence	8	10	18
Total	31	19	50
p-value= 0.001568(<0.05)			
	Estimated Value	95% Confidence Interval	
		Lower Limit	Upper Limit
Prevalence of varices	0.64	0.49143	0.76715
Sensitivity	0.71875	0.530204	0.856014
Specificity	0.555556	0.31347	0.775952
Positive predictive value	0.62	0.471633	0.750019
Negative predictive value	0.38	0.249981	0.528367

[Table/Fig-2]: Correlation of portal vein diameter and esophageal varices

A single operator with training and 10 years of experience performed all the EGDs in gastroenterology using Olympus Evis 140 digital video-endoscope system with 91 F Q140 gastroduodenoscope. A three size classification system was used for grading esophageal varices: Grade1- varices obliterating < 1/3rd of the esophageal lumen, Grade2- varices obliterating > 1/3rd of the esophageal lumen, Grade3- varices obliterating > 2/3rd of the esophageal lumen.

STATISTICAL ANALYSIS

Patients were divided into two groups - patients with EV (n=32) and patients without EV (n=18) on EGD. Ultrasound based PVI including PVV, PVD and HCI were compared to EGD, which was used as the gold standard, to calculate their sensitivity, specificity, positive and negative predictive value for detecting presence or absence of EV. Fisher t-test was used for statistical analysis.

Varices on EGD	PV Velocity <16	PV Velocity >16	Total
Presence	27	5	32
Absence	11	7	18
Total	38	12	50
p-value = 0.00468 (< 0.05)			
	Estimated Value	95% Confidence Interval	
		Lower Limit	Upper Limit
Prevalence of varices	0.64	0.49143	0.76715
Sensitivity	0.84375	0.664536	0.941008
Specificity	0.388889	0.182626	0.638599
Positive predictive value	0.76	0.615134	0.864783
Negative predictive value	0.24	0.135217	0.384866

[Table/Fig-3]: Correlation of portal vein velocity and esophageal varices

Varices on EGD	Congestion index >0.1	Congestion Index <0.1	Total
Presence	23	9	32
Absence	8	10	18
Total	31	19	50
p-value = 0.001568(< 0.05)			
	Estimated Value	95% Confidence Interval	
		Lower Limit	Upper Limit
Prevalence	0.64	0.49143	0.76715
Sensitivity	0.71875	0.530204	0.856014
Specificity	0.555556	0.31347	0.775952
Positive predictive value	0.62	0.471633	0.750019
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[Table/Fig-4]: Correlation of hepatic congestion index with varices

RESULTS

Thirty two out of the 50 patients included in the study had EV on EGD. Male to female ratio was 2.1:1. Mean age was 41 (±10.9) years. Alcoholism, defined as alcohol consumption of >50 gm a day for more than five years, was the most common aetiology of cirrhosis in the study patients (52%) with mean duration of alcohol ingestion of 17 ± 4.34 years. These, and other baseline characteristics of the study population are summarized in [Table/Fig-1]. The association of PVI with EV detected on EGD is summarized in [Table/Fig-2-4] respectively.

As evident from the tables above, all the portal vein indices under study correlated significantly with the presence of EV on EGD (p <0.05). Among these parameters, PVV had the highest sensitivity of 84%. PVD and HCI had the highest specificity of 55% and highest negative predictive value of 38%. Positive predictive value was highest for PVV at 76%.

DISCUSSION

Occurrence of portal hypertension and esophageal varices is one of the major complications of cirrhosis [11]. Numerous methods to detect portal hypertension non-invasively are in use but none are perfect [12]. Several studies have been done in the past to develop non-invasive markers to predict the occurrence of EV in order cut down on cost and complications associated with EGD. It is now known that the presence of a palpable spleen and low platelet count are independent predictors of occurrence of lower esophageal varices in patients with cirrhosis [13]. In another study, it was shown that in patients who have at least two of the following three: ascites, splenomegaly, and alcoholism, there is an increased risk of having large esophageal varices [14]. It has been shown that in patients with splenomegaly or platelet count < 88,000/mm^3, the risk of large esophageal varices was 28% (p < 0.0001) [15].

Currently, endoscopic screening of EV in association with primary

prophylaxis is recommended in patients at high risk of bleeding from EV. Endoscopic screening besides being invasive may not be consistently available, especially in developing countries [11]. Hence, under certain situations, non-invasive diagnosis of portal hypertension may be useful. There are several non-invasive predictive factors of esophageal varices: prothrombin time, splenomegaly, spider naevi, Child-Pugh class, hyperbilirubinemia, and platelet count/spleen diameter ratio and blood markers of fibrosis [16]. But all these require validation. Ultrasonography is an established imaging modality of immense utility in the initial assessment for the diagnosis of cirrhosis and portal hypertension [17]. Color Doppler of the portal circulation has been shown to be useful to predict variceal bleeding in cirrhosis [18]. Currently; the only test that is useful in clinical practice is conventional endoscopy [11].

Indirect sonographic markers of PHT and EV include: ascites, portal vein diameter > or = 13 mm, spleen length, maximal and mean velocity of portal vein flow, respectively < 20 cm/sec and < 12 cm/sec [11]. Ultrasound has supplanted the invasiveness, discomfort and expense of contrast angiography in the evaluation of many patients with advanced liver disease [19].

In prior studies it has been suggested that hemodynamics of the left gastric vein appears to be superior to those of the portal vein in predicting patients with cirrhosis who are at a higher risk of bleeding [20]. However, it was not shown that it is superior to portal vein in detecting the presence of esophageal varices. Similarly, the ratio of splenic vein flow volume to portal trunk flow volume (SV/PT) may be valuable in predicting esophageal variceal bleed [21]. Liver vascular index, calculated as the ratio of portal venous velocity to hepatic artery pulsatility index, has also been shown to be useful in the diagnosis of portal hypertension [22]. Some recent studies evaluating non-invasive methods to predict the occurrence of EV and PHT failed to show any utility of PVI for detecting EV or PHT [23,24].

This study aimed to calculate the sensitivity, specificity, positive predictive value and negative predictive value of PVD, PVV and HCI with reference to conventional EGD as gold standard. Cottone M et al., found that among 215 patients with cirrhosis, PVD of > 13 mm had a positive predictive value and a negative predictive value of 0.34 and 0.96 respectively. In the absence of respiratory motion, PVD of > 13 mm precluded the need for endoscopy in 47 % of the cases [25]. In our study, the positive predictive value was higher, however the negative predictive value was lower. This variation could be due to inter-observer differences between the interpreting sonologists. This operator dependent variation is in fact, one of the major limitations of non-invasive parameters like portal vein indices when compared to EGD, which allows for direct visualization of portal veins [26].

In a study by Tarzamni et al., patients of cirrhosis having EV,PVD of 13.8± 2.42 had p-value <0.005 and PVV of 13.25± 3.66 had p-value <0.005 for the detection of varices. Also, for HCI of more than 0.1 p-value was < 0.002 [27]. Moriyasu F et al., in a study of 72 patients of cirrhosis, showed that a mean cross sectional area of portal vein was 1.49± 0.49 cm^2 with p-value of <0.001. The mean PVV was 9.7±2.6 cm/sec with p-value of <0.001. Patients of cirrhosis had mean HCI of 1.71± 0.075 with p-value of < 0.001 [28]. Findings of our study are consistent with these prior studies.

Limitations of the study include a relatively small sample size. This limits both the external validity of the study and the ability to perform an aetiology of cirrhosis specific correlation. This small sample size is also the reason for the 95% CI being so wide. Moreover, the exclusion of patients on prophylactic treatment and the presence of other complications prevent generalizations of the results. Larger studies to address these limitations are needed. Moreover, Doppler ultrasound of the portal vasculature has inherent pitfalls that make it important to refine the protocols for a more accurate assessment of portal hypertension [29].

It is clear from the result of the study that out of the various PVI, one is not clearly superior to the other. They are complementary to each other with respect to sensitivity, specificity, positive predictive value and negative predictive value and they should be used in conjunction with each other. If only one is being used as a tool to triage patients for referral for EGD, PVV should be used because of its highest sensitivity and positive predictive value amongst all the PVI.

Clearly, PVI are inferior to EGD, which remains the gold standard for diagnosis and management of EV in patients with PHT and cirrhosis

CONCLUSION

In resources constrained settings, ultrasound Doppler can be an easy, cheap and safe alternative, where EGD is not available, for triaging patients for referral for EGD. PVI that are useful for detecting EV include PVD, PVV and HCI. Amongst the PVI studied here, PVV has the highest sensitivity and may be useful as a marker to decide referrals. Ultrasound Doppler as a tool for predicting EV has several limitations and EGD still remains the gold standard for the diagnosis and management of EV. Further studies to evaluate the reproducibility of these PVI for the diagnosis of EV in independent cohorts of patients with different clinical backgrounds and aetiology of cirrhosis are recommended.

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