

Association of Portal Vein Indices with Upper Gastrointestinal Endoscopic Findings in Patients with Cirrhosis of Liver

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ABSTRACT

Introduction: Upper Gastrointestinal (UGI) bleed is major cause of mortality and admissions in cirrhotics. Timely initiation of prophylaxis reduces the burden of disease. Few endoscopists at periphery are compelled to look at other options to identify at risk patients. This study explores Portal Vein Diameter (PVD) as an option while taking clues and corrections from past studies.

Aim: To identify any association between increase in portal pressure with appearance of oesophageal varices.

Materials and Methods: This was an observational cross-sectional study on 75 patients of cirrhosis of liver, from November 2018 to June 2019. Baseline characteristics were noted and assessment of the severity of disease was done. Endoscopy and Portal Vein (PV) Doppler was performed in same time frame. Analysis of Variance (ANOVA) and unpaired t-tests were used for analysis of the collected data. A p-value <0.05 was considered significant in both the tests.

Results: Grade of varices was found to have a direct relationship with portal diameter and a statistically significant inverse relationship with Portal Venous flow Velocity (PVV) (p-value 0.037). Total 28 patients had active bleed or history of UGI bleed and showed higher mean portal diameter and lower average portal velocity compared to patients without any history of variceal bleeding. A statistically significant relation was found between diameter of Portal Vein (PV) and Child-Turcotte-Pugh (CTP) grade from A to C. Patients with grade C had on an average, the biggest portal diameter and lowest PVV. Patients with Model for End-Stage Liver Disease (MELD) scores values higher than 14 and had higher mean PV diameter and a lower mean PVV. Also, hepato-fugal flow was recorded with advanced cirrhosis.

Conclusion: In advanced cirrhosis, the PV Doppler can be thought of as a substitute to endoscopy in starting primary medical prophylaxis, though more extensive study is needed to arrive at a definitive conclusion.

Keywords: Gastroesophageal varices, Portal vein diameter, Portal vein flow velocity

INTRODUCTION

The UGI bleed is one of the most commonly encountered medical emergencies and a major cause of mortality and hospital admissions in cirrhotics. The most common reason is the bleeding gastroesophageal varices; a potentially lethal complication unless rapidly controlled, arising by virtue of portal hypertension, an inexorable side effect of liver cirrhosis [1,2]. Portal hypertension is defined when the pressure gradient between portal vein and inferior vena cava is increased to more than 5 mmHg [3,4]. But to measure this gradient, the tests available are invasive and not readily available in peripheral areas [3,5].

Almost 35 to 80% of patients with cirrhosis have oesophageal varices, more so in patients with CTP grade C cirrhosis (up to 85%) out of these almost one-third patients experience episodes of variceal bleeding [1,6]. The first bleeding episode can cause mortality in up to 40% of patients. Outcome of the bleeding is usually related to the severity of the underlying cirrhosis [7]. Ranging from 0% in CTP grade A to almost 40% in grade C [8]. Endoscopy is the gold standard in diagnosis of varices but is an invasive procedure requiring a lot of expertise and still carries some risk of bleeding [3,4]. Besides its diagnostic value, ability to perform preventive or emergency treatment through endoscopy provides an added benefit [9]. Periodic screening by endoscopy is required to assess the progression of portal hypertension or varices thus making it unpleasant as well as expensive for the patients. Also, it is important to note that half of the patients with portal hypertension may not develop varices even in 10 years therefore will be undergoing unnecessary screening. Moreover, lesser availability of endoscopy units as well as limited number of

expert Endoscopists, in the peripheral region compels to look at other options for early identification of the patients at risk [10,11]. Timely initiation of prophylaxis carried before onset of index bleed, either medical in form of Non-Selective Beta Blockers (NSBB) or intervention like Endoscopic Variceal Ligation (EVL), reduces the burden of disease, and can be life-saving at times. So, assessment of bleeding risk by screening and triaging of the patients that either needs further investigation or immediate prophylaxis at the earliest, can significantly improve the prognosis [12].

In recent years, multiple researchers have come forward with various studies exploring several non-invasive procedures in evaluating various facets of portal hypertension in cirrhotics, although their clinical value is still not proven [3,5,13,14]. Colour Doppler ultrasonography is one such alternative that has been brought to notice. It can be used to correlate the portal vein indices (portal vein diameter and portal vein velocity) and presence or absence of oesophageal varices [3,5-7]. Large varices are mostly associated with higher ultrasonographic portal venous diameter [15]. Other parameters including splenic enlargement, ascitis, presence of collateral vessels and changes in splenic and hepatic arterial resistance can also be identified using colour Doppler [1,7]. Its availability even at the peripheral regions and absence of any side effects due to the procedure tilts the scale in its favour [5-7].

This study aimed to identify any significant association between increases in portal pressure with appearance of oesophageal varices. It explored the possibility of establishing PV Doppler as a screening tool to start primary prophylaxis for UGI bleed in cases of cirrhosis and also for long term monitoring.

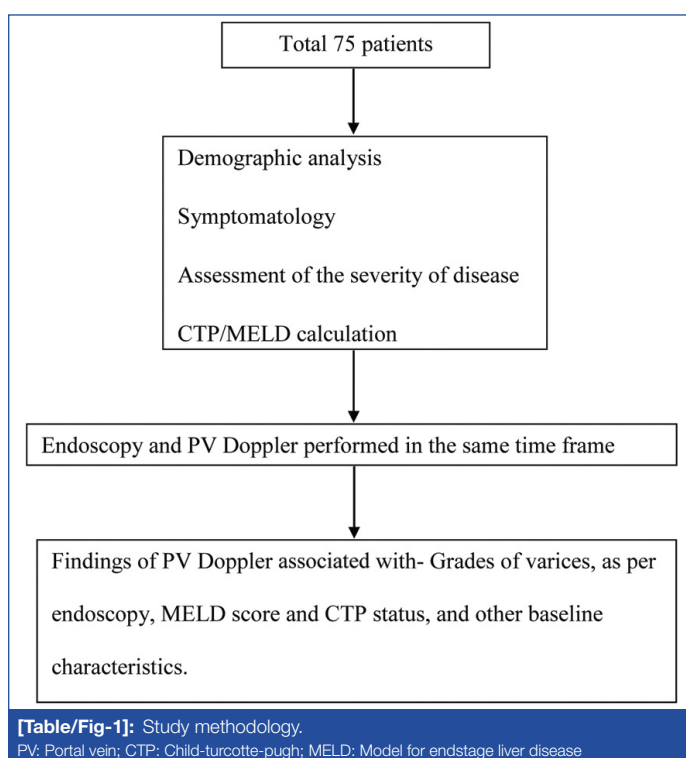
MATERIALS AND METHODS

A cross-sectional observational study was conducted over a period of eight months on patients of cirrhosis of liver with varied CTP status. Total 75 patients, admitted between November 2018 and June 2019, were included in the study using a convenient sampling method. The study was conducted in a tertiary care hospital, Stanley Medical College, Chennai, Tamil Nadu, India. The Institutional Ethical Committee approved the study (meeting held on 3rd April 2019).

Inclusion criteria: Patients of any gender 18 to 75 years of age having a confirmed diagnosis of cirrhosis of liver and presenting for the first time were enrolled in the study.

Exclusion criteria: Patients with bleeding disorders of any kind, immunocompromised status and those patients on any treatment or those who have undergone endoscopic or surgical treatment for varices in the past were excluded from the study.

Baseline characteristics were noted as per performa. Assessment of the severity of disease was done using CTP and MELD scores. The endoscopy and PV Doppler were performed in same time frame. The process has been summarised in [Table/Fig-1].



Varices	Number	PVD (mm)	Statistical outcome	PVV (cm/sec)	Statistical outcome
Grade 1	12	9.225±3.146	One-way ANOVA: f-ratio=0.9361 p-value=0.399825.	12.834±5.638	One-way ANOVA: f-ratio=3.53818. p-value=0.037594.
Grade 2	24	10.371±2.722		9.895±5.219	
Grade 3	11	11±4.123		7.182±4.094	
Active bleeding/history of bleeding	28	10.36±2.873	Unpaired t-test: p-value >0.05	10.2±6.0	Unpaired t-test: p-value >0.05
No Active bleeding/history of bleeding	47	9.98±2.70		10.43±4.2266	

[Table/Fig-2]: Association of varices with Portal Vein Diameter (PVD) and Portal Vein flow Velocity (PVV).

CTP grade	N	PVD (mm)	Statistical outcome	PVV (cm/sec)	Statistical outcome
A	9	6.43±2.07	One-way ANOVA: f-ratio=9.43361. p-value=0.00027.	11.86±5.34	One-way ANOVA: f-ratio=1.00365. p-value=0.37
B	28	9.04±2.51		11.29±4.69	
C	38	10.6±2.42		9.60±5.47	

[Table/Fig-3]: Association of CTP status with Portal Vein Diameter (PVD) and Portal Vein flow Velocity (PVV).
CTP: Child-turcotte-pugh grading

STATISTICAL ANALYSIS

The findings of PV Doppler were assessed for any association with grades of varices, MELD score and CTP status, and also with other baseline characteristics using ANOVA and unpaired t-tests

for analysis of the collected data. A p-value <0.05 was considered significant in both the tests. The cut-off of 14 MELD score was selected by applying the Youden's Index after plotting the Receiver Operating Characteristic (ROC) curve. Statistical analysis was conducted using graph pad and Microsoft excel.

RESULTS

Out of the 75 patients included in the study, 60 were males. The mean±SD portal diameter of 11±4.12 mm and mean portal velocity 7.18±4.09 cm/sec was recorded. Twelve patients were found to have grade 1 varices. Grades of varices had an inverse relationship with portal venous velocity, which was found to be statistically significant on assessment using one-way ANOVA (p-value=0.037) and a direct relationship with the diameter of Hilum, but it was not statistically significant. Twenty-eight patients were found to have presented with or had history of UGI bleed. These patients had a mean portal diameter of 10.36±2.873 mm and a mean portal velocity of 10.2±6.0 cm/sec. Patients presenting with, or those who have been treated for UGI bleed were observed to have higher mean portal vein diameter and lower mean PVV, compared to those presenting without UGI bleed but these relations were found to be statistically non-significant [Table/Fig-2].

On categorising as per Child Pugh criteria, 38 patients had grade C cirrhosis and mean portal diameter of 10.6±2.42 mm and Portal velocity of 9.60±5.47 cm/sec. Twenty-eight patients presented with grade B cirrhosis having a mean portal diameter of 9.04±2.51 mm and mean portal velocity of 11.29±4.69 cm/sec. Nine patients were recorded to have grade A cirrhosis with mean portal diameter 6.43±2.07 mm and portal velocity of 11.86±5.34 cm/sec. A significant relationship was found between diameter of PV and CTP grade from A to C, patients with grade C had on an average the biggest portal diameter (p-value=0.00027). Although the mean PVV was seen to fall with the increase in CTP grade from A to C, it was not statistically significant [Table/Fig-3].

On comparing portal values with corresponding MELD scores, it was observed that patients with MELD values higher than 14 had higher mean PV diameter and lower mean PVV. On assessment of MELD scores 15 patients were found to have scores higher than 14, these patients had a mean portal diameter of 8.09±2.77 mm and a mean portal velocity of 11.73±4.74 cm/sec. The relationship between MELD Score and PV diameter was found to be statistically significant (p-value=0.0089 using unpaired t-test) [Table/Fig-4]. Another finding observed was that, the advanced disease with higher CTP grade and MELD scores more than 14 were more likely to have hepato-fugal flow.

MELD score	Number	PVD (mm)	Statistical outcome	PVV (cm/sec)	Statistical outcome
>14	15	8.09±2.77	Unpaired t-test: p-value=0.0089.	11.73±4.74	Unpaired t-test: p-value=0.039
<14	50	11.734±4.74		10.360±5.61	

[Table/Fig-4]: Association of MELD score with Portal Vein Diameter (PVD) and Portal Vein flow Velocity (PVV).

DISCUSSION

All chronic liver disease patients do not have varices and all varices do not bleed. This fact envisages whether routine endoscopy in all cirrhotics is justified. In the present study, 63% patients of cirrhosis of liver had varices. The relationship between the grade of varices and portal velocity was found to be statistically significant. A total of

16% patients with grade 3 varices had a lower mean portal velocity and a higher mean portal diameter. Similar results were reported in a study by Li FH et al., [1]. Even the patients with active UGI bleed or history of the same were noted to be having higher mean portal diameter, and a lower mean portal velocity, strengthening the findings of this study of a probable relationship between Doppler findings and variceal bleed.

Upon assessment of the relationship of Doppler and the grade of cirrhosis, 51% patients had CTP grade C. A statistically significant relationship was found between PV diameter and CTP grade from A to C. The mean PVV was seen to fall with the increase in CTP grade from A to C, it was not statistically significant as depicted in [Table/Fig-4]. Another finding was a statistically significant relationship, between higher MELD score, especially more than 14 and high PV diameter as well as a low PV velocity. Similar results were found in a study by Ali WI et al., and Yan G et al., [16,17]; although there were a few studies that claim this relation to be untrue [5,18,19]. Another finding observed was that, the advanced disease with higher CTP grade and MELD scores more than 14 were more likely to have hepato-fugal flow (no data shown), this finding is supported by findings from the study by Gaiani S et al., [18].

Although PV Doppler is not in any way equivalent to the gold standard i.e., endoscopy, several other studies like this, also believe PV Doppler to be a good alternative to endoscopy for assessment of varices and portal vein size and portal velocity to be an indicator of bleeding oesophageal varices [20-23].

Limitation(s)

Nevertheless, the study does have several limitations. The sample size was relatively small as it was restricted by no. of patients presenting to the hospital over the duration of the study. Also PV Doppler has its own limitations by being a subjective investigation.

CONCLUSION(S)

In advanced cirrhosis, the PV Doppler can be thought of as a substitute to endoscopy in starting primary medical prophylaxis. This has more importance for cirrhotic patients in a developing country like India where to assess the disease progression; repeated screening by endoscopy is not always available or affordable, especially in the resource constricted settings. And as we know that, timely initiation of prophylaxis has proven benefits for outcome of the patients, using Doppler as a substitute can have a significant impact. Hence, we are justified in starting primary medical prophylaxis in cirrhotic patients on the basis of the PV Doppler and general condition of the patient. A multicentre, well-designed more extensive study with larger group of patient is recommended, for further development and research in this area so as to arrive at a definitive conclusion.

REFERENCES

- [1] Li FH, Hao J, Xia JG, Li HL, Fang H. Hemodynamic analysis of esophageal varices in patients with liver cirrhosis using color Doppler ultrasound. *World J Gastroenterol*. 2005;11(29):4560-65.
- [2] Bhasin DK, Malhi NJ. Variceal bleeding and portal hypertension: Much to learn, much to explore. *Endoscopy*. 2002;34(2):119-28.
- [3] Vaishnav B, Bamanikar A, Chatterjee L, Grewal G, Kakrani AL. Comparative study for the prediction of large oesophageal varices by ultrasound doppler and serum markers in portal hypertension due to liver cirrhosis. *The Journal of Medical Research*. 2018;4(1):48-52.
- [4] Vanbiervliet G, Pomier-Layrargues G, Huet PM. Invasive diagnosis of portal hypertension in cirrhosis: A critical evaluation of the hepatic venous pressure gradient measurement. *Gastroenterol Clin Biol*. 2005;29(10):988-96.
- [5] Achim CA, Bordei P, Dumitru E. The role of ultrasonography in the evaluation of portal hemodynamics in healthy adults and pathologic conditions. *ARS Medica Tomitana*. 2016;2(22):128-34.
- [6] Nemichandra, Salam KS, Kanse VY, Shiakh N, Singh D, Singh K. Non endoscopic predictors of esophageal varices in patients with cirrhosis of liver. *IOSR Journal of Dental and Medical Sciences*. 2015;14(1):65-68.
- [7] Masoud S, Elzeftazy WM, Elnaggar A, Saleh OI, Ibrahim A. Color Doppler ultrasonography changes of portal circulation after band ligation of esophageal varices in Egyptian patients with chronic liver disease. *American Journal of Medicine and Medical Sciences*. 2018;8(7):145-54.
- [8] Cremers I, Ribeiro S. Management of variceal and nonvariceal upper gastrointestinal bleeding in patients with cirrhosis. *Ther Adv Gastroenterol*. 2014;7(5):206-16.
- [9] Akhavan Rezayat K, Mansour Ghanaei F, Alizadeh A, Shafaghhi A, Babaei Jandaghi A. Doppler surrogate endoscopy for screening esophageal varices in patients with cirrhosis. *Hepat Mon*. 2014;14(1):e11237.
- [10] Zhang CX, Xu JM, Li JB, Kong DR, Wang L, Xu XY, et al. Predict esophageal varices via routine trans-abdominal ultrasound: A design of classification analysis model. *J Gastroenterol Hepatol*. 2016;31(1):194-99. Doi: 10.1111/jgh.13045.
- [11] Shastri M, Kulkarni S, Patell R, Jasdandwala S. Portal vein doppler: A tool for noninvasive prediction of esophageal varices in cirrhosis. *J Clin Diagn Res*. 2014;8(7):MC12-15.
- [12] Ekenawy YN, Elarabawy RA, Ahmed LM, Elsayy AA. Portal vein flow velocity as a possible fast noninvasive screening tool for esophageal varices in cirrhotic patients. *JGH Open*. 2020;4(4):589-94.
- [13] Uppalapati S, Lokesh S. Correlation of portal vein diameter with the presence of oesophageal varices in chronic liver disease: A prospective study. *Int J Adv Med*. 2018;5(4):859-64.
- [14] Shanker R, Banerjee S, Anshul, Ganguly S, Bansal S, Uppal A, et al. A study of association of portal vein diameter and splenic size with gastro-esophageal varices in liver cirrhosis patients. *IOSR Journal of Dental and Medical Sciences*. 2016;15(9):125-29.
- [15] D'Amico G, Pagliaro L, Bosch J. The treatment of portal hypertension: A meta-analytic review. *Hepatology*. 1995;22(1):332-54.
- [16] Ali WI, Hammad MI, Abu AMZ, Heikal IA. Association between portal vein colored doppler ultrasound findings and severity of liver disease in cirrhotic patients with portal hypertension. *AIMJ*. 2020 March. Doi: 10.21608/aimj.2020.22659.1095.
- [17] Yan G, Duan Y, Ruan L, Chao T, Yang Y. A study on the relationship between ultrasonographic score and clinical score (MELD, CPT) in cirrhosis. *Hepatogastroenterology*. 2005;52(65):1329-33.
- [18] Gaiani S, Bolondi L, Bassi SL, Zironi G, Siringo S, Barbara L. Prevalence of spontaneous hepatofugal portal flow in liver cirrhosis. Clinical and endoscopic correlation in 228 patients. *Gastroenterology*. 1991;100(1):160-67.
- [19] Dib N, Konate A, Oberti F, Calès P. Noninvasive diagnosis of portal hypertension in cirrhosis. Application to the primary prevention of varices. *Gastroenterol Clin Biol*. 2005;29(10):975-87. Article in French.
- [20] Plestina S, Pulanic R, Kralik M, Plestina S, Samarzija M. Colour Doppler ultrasonography is reliable in assessing the risk of esophageal variceal bleeding in patients with liver cirrhosis. *Wien Klin Wochenschr*. 2005;20(19-20):711-17.
- [21] Bhattarai S, Gyawali M, Dewan K, Shrestha G, Patowary B, Sharma P. Study of portal vein diameter and spleen size by ultrasonography and their association with gastro-esophageal varices. *Nepalese Journal of Radiology*. 2017;4(2):06-14.
- [22] Bosch J, Groszmann RJ, Shah VH. Evolution in the understanding of the pathophysiological basis of portal hypertension: How changes in paradigm are leading to successful new treatments. *J Hepatol*. 2015;62(1 Suppl):S121-30.
- [23] Zaman A, Becker T, Lapidus J, Benner K. Risk factors for the presence of varices in cirrhotic patients without a history of variceal hemorrhage. *Arch Intern Med*. 2001;161(21):2564-70.

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