International Journal of Research in Medical Sciences
Kumar S et al. Int J Res Med Sci. 2023 May;11(5):1721-1726
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20231343

Original Research Article

Comparison of diagnostic accuracy of APRI and Transient Elastography for prediction of esophageal variceal bleed in liver cirrhosis

Shailesh Kumar*, Vinay Kumar, Richa Giri, S. K. Gautam

Department of medicine, GSVM Medical College, Kanpur, Uttar Pradesh, India

Received: 16 March 2023
Revised: 15 April 2023
Accepted: 19 April 2023

***Correspondence:**
Dr. Shailesh Kumar,
E-mail: drsk2013@gmail.com

ABSTRACT

Background: Liver Cirrhosis is the end-stage for chronic liver disease. Repeated course of endoscopy is recommended, as this intervention is expensive and often poorly accepted by patients, there is a need for non-invasive methods to predicts the progression of portal hypertension as well as the presence and size of esophageal varices. This study was aimed to assess the APRI and Transient Elastography for predicting esophageal variceal bleed in cirrhotic patients. Objectives of the study were to study Diagnostic accuracy of APRI for Prediction of esophageal variceal bleed in liver cirrhosis, diagnostic accuracy of Transient Elastography for Prediction of esophageal variceal bleed in liver cirrhosis, comparison of diagnostic accuracy of APRI and Transient Elastography for Prediction of esophageal variceal bleed in liver cirrhosis.
Methods: It was a Single centre, observational study in 35 patients of chronic liver disease. Patients were included in the study after fulfilling inclusion and exclusion criteria. CBC, LFT, KFT, SE, viral marker, USG whole abdomen, UGIE, Transient Elastography was done. APRI was calculated for every patient.
Results: The APRI and Transient Elastography showed moderate diagnostic accuracy in predicting the presence of esophageal variceal bleed. Transient Elastography performed better for prediction of esophageal variceal bleed.
Conclusions: The APRI and Transient Elastography showed moderate diagnostic accuracy in predicting the presence of esophageal variceal bleed. They help in starting prophylactic therapy earlier to prevent the bleeding and other complications of varices. These non-invasive parameters can also play an effective role in conjunction with endoscopy in predicting the presence of esophageal varices.

Keywords: APRI, CLD, Liver cirrhosis, Transient Elastography

INTRODUCTION

Liver Cirrhosis is the end-stage for chronic liver disease and is the leading cause of liver-related death globally.[1] Cirrhosis is frequently compensated. The development of complications of portal hypertension and/or liver dysfunction is decompensated cirrhosis. It is defined by the presence of variceal haemorrhage, ascites, encephalopathy, hepatorenal syndrome, jaundice or hepatocellular carcinoma. The transition from a compensated to a decompensated stage occurs at a rate of 5 to 7% per year.[2] Esophageal variceal bleeding is a life-threatening portal hypertension-related complication in liver cirrhosis.[3] Esophageal varices are present at

diagnosis in approximately 50% of cirrhotic patients and the rate of development of new varices and increase in grades of varices is 8% per year.[4] The mortality is 3.4% per year in patients with non-bleeding varices. By comparison, the mortality rises to 57% per year in patients with variceal bleeding.

About 80% of patients with cirrhosis of liver will eventually develop varices.[5] In cirrhotic patients who do not have esophageal varices at initial endoscopy, new varices will develop at a rate of approximately 5% per year. Up to 25% of patients with newly diagnosed varices will experience variceal bleeding within two years. In patients with cirrhosis who are being followed chronically, the development of portal hypertension is usually revealed by the presence of thrombocytopenia, the appearance of an enlarged spleen, or the development of ascites, and/or esophageal varices with or without bleeding. Thus, early diagnosis of varices and primary prophylaxis of variceal bleeding in high-risk patients with liver cirrhosis is important in improving survival.[6] Esophagogastroduodenoscopy (EGD) is the gold standard for diagnosing varices in liver cirrhosis. However, because of its invasiveness and discomfort, most patients are reluctant to undergo this procedure. The progression of fibrosis parallels the increase in portal pressure, as liver fibrosis contributes to the increased hepatic resistance.[7]

Endoscopy is the only means to directly visualize varices which are a consequence of poral hypertension.[8] The predisposing factors of bleeding are large size of the varices, endoscopic variceal features such as red spots and stripes, high portal pressure and liver failure. Drugs capable of causing mucosal erosion, such as salicylates and NSAIDs can also precipitate bleeding.[9] Current practice guidelines recommend endoscopic screening for the presence of esophageal varices in all patients with cirrhosis. If varices are not present, screening endoscopy should be repeated 2-3 years or sooner if there is evidence of hepatic decompensation.

Paquet classification of grade of varices

Grade I: Varices extending just above the mucosal level.

Grade II: Varices projecting by one - third of the luminal diameter that can-not be compressed with air insufflation.

Grade III: Varices projecting up to 50% of the luminal diameter and in contact with each other.

During the course of cirrhosis repeated course of endoscopy is recommended. As this intervention is expensive and often poorly accepted by patients who may refuse further follow up, there is a need for non-invasive methods to predict the progression of portal hypertension as well as the presence and size of esophageal varices. Several studies have recently attempted to identify non-invasive predictors of esophageal varices. They are platelet count, AST-to-ALT ratio, AST-to-platelet ratio index (APRI), Platelet count/ spleen diameter ratio, Lok index, Forn index, Fib-4 and fibro index. Of these Transient Elastogram, APRI, and Platelet count/spleen ratio are promising predictors.[10] It was suggested that liver stiffness measured by transient elastography, a novel non-invasive technology may reflect not only fibrosis and portal pressure but it may even predict the presence or absence of large esophageal varices, in patient with cirrhosis. Liver stiffness values significantly correlates with the grade of esophageal varices. The liver stiffness value of 19.2 kPa was highly predictive for the presence of esophageal varices. This study was aimed to assess the APRI and Transient Elastography for predicting esophageal varices in cirrhotic patients

APRI was calculated by the following formula:

$$APRI = \frac{\text{AST (IU/L)/AST (Upper Limit of Normal) (IU/L)}}{\text{Platelets (109/L)}} \times 100$$

The aims and objectives of the present study was to do prediction of esophageal variceal bleed in liver cirrhosis by APRI, prediction of esophageal variceal bleed in liver cirrhosis by Transient Elastography and Comparison of APRI and Transient Elastography for Prediction of esophageal variceal bleed in liver cirrhosis.

METHODS

It was a Single centre, Observational study carried out in KPS Post Graduate institute of Medicine, G.S.V.M. Medical College, Kanpur from January 2021 to October 2022. 35 patients of chronic liver disease were included in the study after fulfilling inclusion and exclusion criteria. CBC, LFT, KFT, SE, viral marker, USG whole abdomen, UGIE, Transient Elastography was done for all patients.

Inclusion criteria includes patients willing to give written signed informed consent to participate in the study, >18 to <65 years of age, of either sex (Male/Female), alcoholics, HBV+, HCV+, cirrhotic patients undergoing screening endoscopy at the time of cirrhosis diagnosis, patients with a known diagnosis of liver cirrhosis but who had never under gone screening endoscopy for esophageal varices (EV).

Exclusion criteria includes patients with active bleeding, previous endoscopic sclerosis for band ligation of EV, previous surgery of portal hypertension or trans – jugular intrahepatic porto-systemic stent shunt, patients not willing to give consent, pregnancy and psychiatric illness.

Statistical analysis

Statistical analysis of the obtained data was performed using Jamovi (v2.3.18) software. P value <0.05 was taken as statistically significant.

RESULTS

Incidence of cirrhosis was maximum in the age group 31-50 years (51%). Over all mean age was 44.54±11.27. Youngest patient in our study was 24 years old and oldest was 65 years. In our study 9 were in the age group 31-40 years and also 9 were in the age group 41-50 years (Table 2).

Our study population consisted of 35 patients of whom 23 were male and 12 were female. Males constituted 65.7% of the study population (Table 3). Among 35 patients studied cause of cirrhosis was found to be alcoholism in 52% followed by HBV+ in 23%, Cryptogenic in 14% and HCV+ in 11% (Figure 1).

Among 35 patients studied 85.7% patients were found to have varices. Based on endoscopic grading, the grading of the varices in the study population was done. Incidence of grade II and grade III predominated and were 28% and 40% respectively, however the incidence of grade I varices accounting for 17% and varices were absent in 15% of cases.

On correlation of the age of the patients with the grade of varices it did not show any statistical significance by according to a P=0.619. On correlation of grade of varices with gender, there was no statistical significance associated with gender P=0.366. In our study the area under the ROC curve (AUROC) for APRI for prediction of esophageal variceal bleed is 0.753 (Figure 2).

In our study the area under the ROC curve (AUROC) for Transient Elastography for prediction of esophageal variceal bleed is 0.882 (Figure 3).

At a cut off of APRI 1.95, it predicts variceal bleed with a sensitivity of 81.3% and specificity of 63.2%. At a cut off of Transient Elastography 49.00 it predicts variceal bleed with a sensitivity of 87.5% and a specificity of 78.9%. (Table 1 and Figure 4).

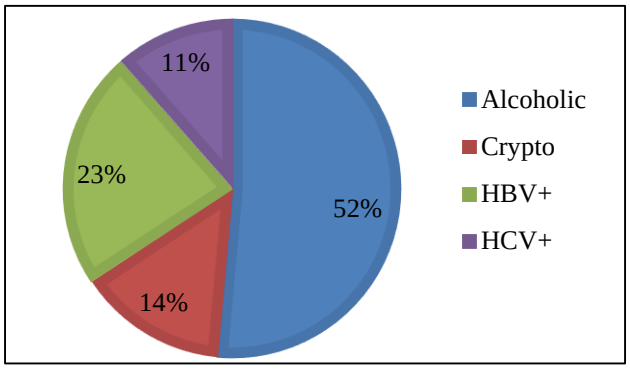

Figure 1: Distribution of cases according to etiology of liver cirrhosis (n = 35).

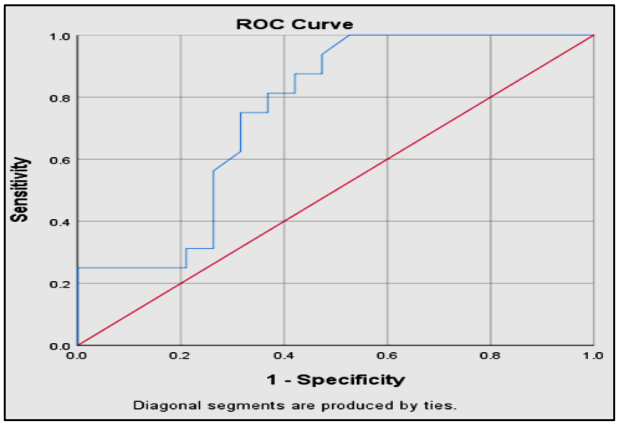

Figure 2: ROC curve analysis showing diagnostic performance of APRI score in predicting variceal bleed present vs variceal bleed absent (n = 35).

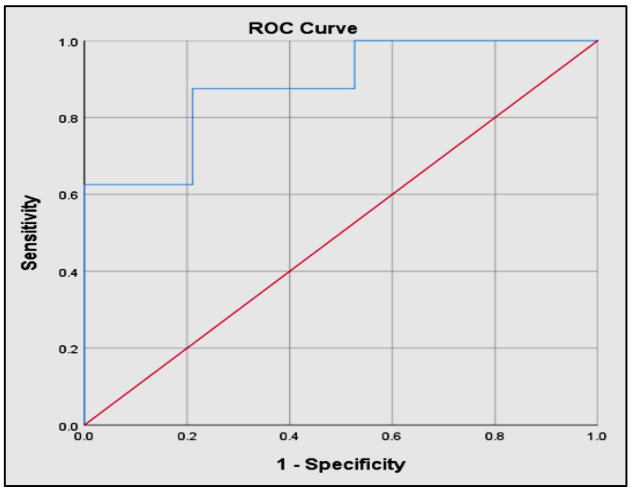

Figure 3: ROC curve analysis showing diagnostic performance of transient elastography in predicting variceal bleed present vs variceal bleed absent (n=35).

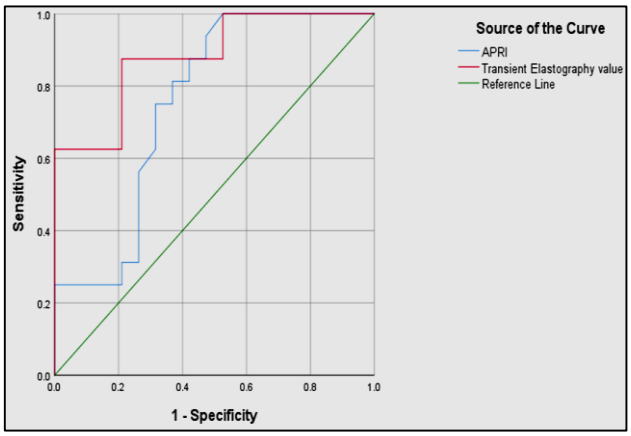

Figure 4: ROC curve analysis comparing diagnostic performance of apri and Transient Elastography in predicting variceal bleed present vs variceal bleed absent (n=35).

Table 1: Comparison of the diagnostic performance of various predictors in predicting variceal bleed present vs variceal bleed absent.

Predictor	AUROC	P value	Sn	Sp	PPV	NPV
APRI	0.753	0.011	81.3%	63.2%	65.0%	80.0%
Transient elastography	0.882	<0.001	87.5%	78.9%	77.7%	88.2%

Table 2: Distribution of cases according to age of the patient (n=35).

Age of the patient	Number of cases
30 years or below	6 (17.14%)
31 – 40 years	9 (25.71%)
41 – 50 years	9 (25.71%)
51 – 65 years	11 (31.42%)
Mean age of the patient in years (SD)	44.54 (11.27%)

Table 3: Distribution of cases according to sex of the patient (n=35).

Sex of the patient	Number of cases
Male	23 (65.71%)
Female	12 (34.28%)

DISCUSSION

In 2007, the American Association for the Study of Liver Diseases stated that screening esophago-gastroduodenoscopy (EGD) for the diagnosis of esophageal and gastric varices is recommended when the diagnosis of cirrhosis of liver is made according to the AASLD guidelines.

Therefore, there is a particular need for a non-invasive predictor for the presence of EVs to ease the medical and economic burden of the disease. Previous studies have documented good predictive value of various non-endoscopic methods for the presence or absence of varices. In our study we used only simple, commonly available, reproducible parameters.

Our study sample consisted of 35 patients of whom 23 were male and 12 were female. Males constituted about 65.7% of the study population. Incidence of cirrhosis was maximum in the age group 31-50 years (51%). Over all mean age was 43.78±11.78. However mean age was 51 (range 20-80) in study by Baig et al, mean age was 42 (range 17-73) in a study by Cherian et al and in study by Sarangapani's et al median age was 45 (range 18-74).[11]

Youngest patient in our study was 24 years old and oldest was 65 years. In our study 9 were in the age group 31-40 years and also 9 were in the age group 41-50 years. Males predominated in each of the age group studied. Among 35 patients studied cause of cirrhosis was found to be alcoholism in 52% followed by HBV+ in 23%, Cryptogenic in 14% and HCV+ in 11%. Among 35 patients studied 85.7% patients were found to have varices. Based on endoscopic grading, the grading of the varices in the study population was done. Incidence of grade II and grade III predominated and were 28% and 40% respectively, however the incidence of grade I varices accounting for 17% and varices were absent in 15% of cases.

On correlation of the age of the patients with the grade of varices it did not show any statistical significance by according to a P=0.619. On correlation of grade of varices with gender, there was no statistical significance associated with gender P=0.366. In our study Cut off value for APRI as a predictor of EV bleed is >1.95 whereas in Deng et al, Hassan et al. and Morishita et al it was >0.85, >1.22 and >1.62 respectively.[12-14] In our study, when a cut off 1.95 was used it was found moderate sensitivity 81.3%, a specificity 63.2%, PPV 65%, and NPV 80%.

Castera proposed the cutoff of 1.3 for APRI as a predictor of EV, where they found sensitivity 68%, specificity 64%, PPV 51%, NPP 78%, which is dissimilar from our study.[15] That study was only on hepatitis C positive patient and Child A grade were included. In our study all etiologies and all grade including compensated and decompensated cirrhosis were included.

Tafarel studied at a higher cut of point (1.64) and found it is significant. Here in this study higher cutoff value also tested, though good specificity and positive predictive value were found, sensitivity and NPV were disappointing.[16] Wang proposed lower cut of value 0.77 as the optimal one to predict EVs with a better sensitivity 71% & NPV 79%, but in our study in lower value, specificity & NPV were disappointing.[17]

In current study the diagnostic performance of Transient elastography (TE) was tested, as a noninvasive tool for prediction of EV. In our study, when a cut off 49 was used it was found moderate sensitivity 87.5%, a specificity 78.9%, PPV 77.7%, and NPV 88.2% were observed indicating moderately high level of significance. Hassan showed that TE could diagnose the EV at a cutoff value of 18.2 Kpa. Its sensitivity 80%, specificity 72%, PPV 84%, and NPV 67%.19. Liu showed cutoff value at 18 with 91% sensitivity and 63% specificity.[13]

Kitson showed the lower cutoff value of 25Kpa to predict EVs with a sensitivity 71.9%, specificity 58.1%, PPV 88%, NPV 88%.[11] Qu show a meta-analysis with a good sensitivity 84%, specificity 68%, positive likelihood ratio 2.58, and negative likelihood ratio 0.24, which is also comparable to our study.[18]

In our study Cut off value for Transient Elastography as a predictor of EV bleed is 49 Kpa whereas in Debashis Kumar Sarkar et al, Hassan et al. and Kitson it was 18 Kpa, 18.2 Kpa and 25 Kpa respectively.[19,13,18] In our study, when a cut off 49 was used it was found moderate sensitivity 87.5%, a specificity 78.9%, PPV 77.7%, and NPV 88.2%.

Limitation

The study was single centered with small study population. Further multicentric study with large sample size with prospective cohort studies are needed to validate its efficacy.

CONCLUSION

The APRI and Transient Elastography shows moderate diagnostic accuracy in predicting the presence of esophageal varices; Thus these parameters mentioned above play effective role in predicting esophageal variceal bleed non-invasively and would help in starting prophylactic therapy earlier to prevent the bleeding and other complications of varices. Although endoscopy remains the primary modality for diagnosis of esophageal varices.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980- 2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1736-88.
2. D'Amico G, Garcia TG, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. J Hepatol. 2006;44(1):217-31.
3. Biecker E. Portal hypertension and gastrointestinal bleeding: diagnosis, prevention and management. World J Gastroenterol. 2013;19(31):5035-50.
4. Groszmann RJ, Garcia TG, Bosch J. Beta-blockers to prevent gastroesophageal varices in patients with cirrhosis. N Engl J Med. 2005;353(21):2254-61.
5. Grace ND, Minor MA. Portal hypertension and esophageal variceal hemorrhage. In: Greenberger NJ, Blumer RS, Burakoff R (eds), Current diagnosis and treatment,Mc Grew Hill, New York. 2012:55-59.
6. Franchis R. Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertension. J Hepatol. 2010;53(4):762-8.
7. Kumar M, Kumar A, Hissar S. Hepatic venous pressure gradient as a predictor of fibrosis in chronic liver disease because of hepatitis B virus. Liver Int. 2008;28(5):690-8.
8. Par G, Trosits A, Pakidi F, Szabo I, Czimer J. Transient elastography as a predictor of esophageal varices in patients with liver cirrhosis. J Orv Hetil. 2014;155(7):270-6.
9. Walker BR Colledge NR, Ralston SR, Penman ID. Devidson's principle and practice of medicine. 22nd edition. Edinburgh, Elsevier. 2014;942-3.
10. Sebastiani G, Tempesta D, Fattovich G, Laurent C, Halfon P. Prediction of esophageal varices in hepatic cirrhosis by simple non-invasive markers: Results of a multicenter, large scale study. J Hepatol. 2010;53:630-8.
11. Sarangapani A, Shanmugam C, Kalyanasundaram M. Noninvasive prediction of large esophageal varices in chronic liver disease patients: platelet spleen diameter ratio 909 had a sensitivity and specificity of 88.5%, 83% respectively. J Hepatol. 2010;53:630-8.
12. Deng H, Qi X, Peng Y. Diagnostic accuracy of apri, aar, fib-4, fi, and king scores for diagnosis of esophageal varices in liver cirrhosis: a retrospective study. Med Sci Monit. 2015;21:3961-77.
13. Hassan E, El-Din S, Sharaf A. Noninvasive fibrosis scores as prognostic markers for varices needing treatment in advanced compensated liver cirrhosis. Open J Gastroenterol. 2017;7:230-42.
14. Morishita N, Hiramatsu N, Oze T, et al. Liver stiffness measurement by acoustic radiation force impulse is useful in predicting the presence of esophageal varices or highrisk esophageal varices among patients with HCV-related cirrhosis. J Gastroenterol. 2014;49(7):1175-82.
15. Castera L, Vergniol J, Fouchar J, Le-Bail B, Chanteloup E, Haaser M. Prospective comparison of ransientelastography, fibrotest, APRI and liver biopsy for assessment of fibrosis in chronic hepatitis C. Gastroenterol. 2013;128:343-50.
16. Tafarel JR, Tolentino LH, Correa LM, Bonita DR, Matin FS. Prediction of esophageal varices in hepatic cirrhosis by noninvasive markers. Eur J Gastroenterol Hepatol. 2011;23:754-8.
17. Wang JH, Cruah SK, Lu SN, Hung CH, Chen CH. Transient elastography and simple blood markers in the diagnosis of esophageal varices for compensated patients with hepatitis B virus related cirrhosis. J Gastroenterol Hepatol. 2012;27:1213-8.
18. Kitson MT, Robert SK, Colman JC, Paul E, Button P. Liver stiffness and the prediction of clinically significant portal hypertension and portal

hypertensive complications. Scandinavian J Gastroenterol. 2015;50:462-9.
19. Sarkar DK. Prediction of esophageal varices in liver cirrhosis by transient elastography and aspartate aminotransferase - to - platelet ratio index (APRI). Bangladesh Crit Care J March. 2018;6(1):16-21.

Cite this article as: Kumar S, Kumar V, Giri R, Gautam SK. Comparison of diagnostic accuracy of APRI and Transient Elastography for prediction of esophageal variceal bleed in liver cirrhosis. Int J Res Med Sci 2023;11:1721-6.