



A STUDY ON USEFULNESS OF PLATELET COUNT TO SPLEEN BIPOLAR DIAMETER RATIO AS A NON-INVASIVE PREDICTOR OF OESOPHAGEAL VARICES IN PATIENTS WITH CIRRHOSIS OF LIVER

General Medicine

Dr. Anagha Raju	PG Resident, Department Of General Medicine, Jubilee Mission Medical College And Research Institute, Thrissur.
Dr. Anand M K	MD General Medicine, Associate Professor, Department Of General Medicine, Jubilee Mission Medical College And Research Institute, Thrissur.
Dr. Vinaya Ramesh	MD General Medicine, Associate Professor, Department Of General Medicine, Jubilee Mission Medical College And Research Institute, Thrissur.
Dr. Anil Kumar C R*	MD General Medicine, Professor, Department Of General Medicine, Jubilee Mission Medical College And Research Institute, Thrissur. *Corresponding Author
Dr. T K Joseph	Professor, Department Of Gastroenterology, Jubilee Mission Medical College And Research Institute, Thrissur

ABSTRACT

Background: Oesophageal varices are a direct result of portal hypertension and can lead on to serious consequences in patients with cirrhosis of the liver. This paper explores the usefulness of a non-invasive method (ratio of platelet count to spleen bipolar diameter) to predict oesophageal varices. **Objective:** To assess whether the platelet count to spleen bipolar diameter ratio can predict the presence of oesophageal varices. **Methods:** A cross-sectional study was conducted among 82 patients with cirrhosis of the liver who had no previous history of upper gastrointestinal bleeding. Maximum spleen bipolar diameter (in millimetres) was calculated by means of an ultrasound scan. Upper gastrointestinal endoscopy was done to confirm the presence of varices. The platelet count to spleen bipolar diameter ratio was calculated. **Results:** The cut off values of platelet count was less than 97,000 per mm³ and spleen bipolar diameter was more than 120 mm to predict varices. Patients with varices had significantly larger mean spleen bipolar diameters. The platelet count to spleen bipolar diameter ratio cut-off was less than 838 in predicting varices. Among the patients with a platelet count to spleen bipolar diameter ratio less than 838, 91.3% had oesophageal varices. In patients with a platelet count to spleen bipolar diameter ratio greater than 838, 77.78% of patients had no oesophageal varices, which was statistically significant (p value 0.0001). **Conclusion:** The new diagnostic tests, like the platelet count to spleen bipolar diameter ratio, can be incorporated into clinical practice to predict the incidence of varices in cirrhotic patients. Apart from being non-invasive, the platelet count to spleen bipolar diameter ratio is a relatively inexpensive test, as platelet counts and abdominal ultrasound would be obtained on all cirrhotic patients routinely as part of their clinical workup.

KEYWORDS

liver cirrhosis, oesophageal varices, platelet count to spleen bipolar diameter ratio, non-invasive prediction.

INTRODUCTION

Cirrhosis of the liver may lead to many serious consequences, one of which is portal hypertension. Those with progressing liver cirrhosis often have a portal venous pressure of more than 12 mmHg. Portal hypertension results from increased splanchnic blood flow because of vasodilation as well as increased resistance to blood flow in liver cirrhosis¹. Oesophageal varices are a direct result of portal hypertension². Bleeding gastroesophageal varices are the cause of death for one-third of people who are diagnosed with gastroesophageal varices³.

In 1996, the American Association for the Study of Liver Disease recommended screening for oesophageal varices in all patients with liver cirrhosis who had also been diagnosed with portal hypertension⁴. Endoscopy screenings should be repeated every two to three years, even for people who don't have varices. It is advised that individuals with modest varices should have a follow-up endoscopy every one to two years to monitor for the emergence or worsening of varices⁵.

Endoscopy is a risky procedure, and it is questionable whether or not it is worth the money⁶. It may thus be more efficient to regularly test people at high risk for the development of oesophageal varices by using non-invasive predictors. As a result, it may reduce the pressure on endoscopy centres and lower the expenses associated with procedures. And thus, it is important to determine which patients should have an upper gastrointestinal endoscopy, based on non-invasive predictors.

One non-invasive method to predict oesophageal varices in persons with cirrhosis is the ratio of platelet count to spleen bipolar diameter. It identifies the subset of the population that would benefit most from endoscopic screening for oesophageal varices. The ratio of platelet count to spleen bipolar diameter is non-invasive, easily reproducible, and of low cost.

METHODS

It is a cross-sectional study conducted among 82 patients with cirrhosis of the liver and no previous history of upper gastrointestinal bleeding.

Maximum spleen bipolar diameter was calculated by means of an ultrasound scan and was expressed in millimetres (mm). Upper gastrointestinal endoscopy was done to confirm the presence of varices. The platelet count to spleen bipolar diameter ratio was calculated.

Statistical Analysis

The receiver operating characteristic curve (ROC curve) was used to obtain the platelet count to spleen bipolar diameter ratio cut off with the best sensitivity and specificity.

RESULTS

Table 1: Mean Age Distribution Among Two Groups

Group	Mean age (years)	Standard deviation (years)	Range	P value
No Oesophageal varices group (NOV)	52.65	8.81	37 – 69	0.2214
Oesophageal varices (OV)	55.34	8.46	40 – 70	

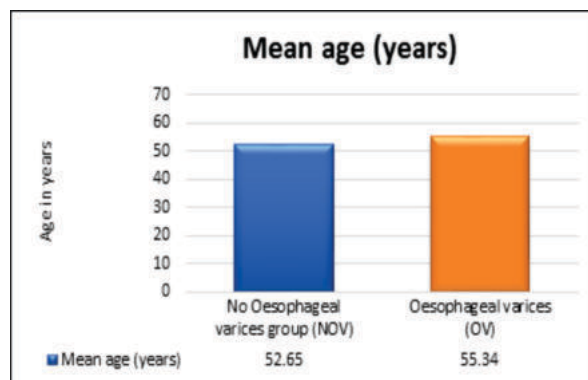


Figure 1: Mean Age Distribution Among Two Groups

The mean age in No Oesophageal varices group was 52.65 ± 8.81 years and in Oesophageal varices was 55.34 ± 8.46 years (Fig. 1) which was statistically not significant (p value = 0.22) as shown in Table 1.

Table 2: Gender Distribution Among Two Groups

Group	Female		Male		Total
	Number	%	Number	%	
No Oesophageal varices group (NOV)	8	25%	24	75%	32
Oesophageal varices (OV)	13	26%	37	74%	50
Total	21	25.61%	61	74.39%	82

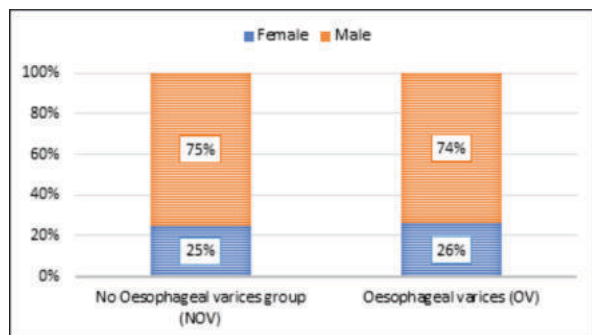


Figure 2: Gender Distribution Among Two Groups

The percentage distribution of male and female patients (Fig. 2) in No Oesophageal varices group were 75% and 25% respectively and in Oesophageal varices group were 74% and 26% respectively (Table 2).

Table 3: Platelet Count Correlation Among Study Groups

Group	Mean (n/mm ²)	Standard deviation	P value
No Oesophageal varices group (NOV)	127781.25	30207.59	0.0001
Oesophageal varices (OV)	69666	24245.92	

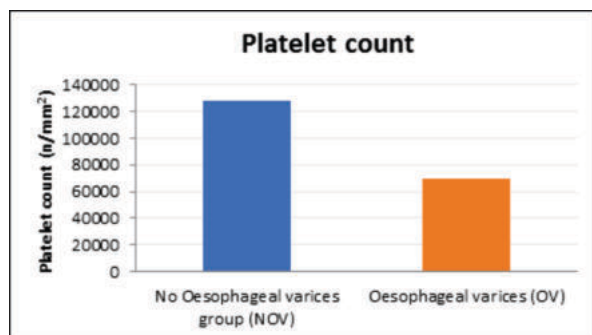


Figure 3: Platelet Count Correlation Among Study Groups

The mean platelet count (Fig. 3) in No Oesophageal varices group was 127781.25 ± 30207 n/mm² and in Oesophageal varices group was 69666 ± 24245 n/mm² (Table 3) which was statistically significant (p = 0.0001).

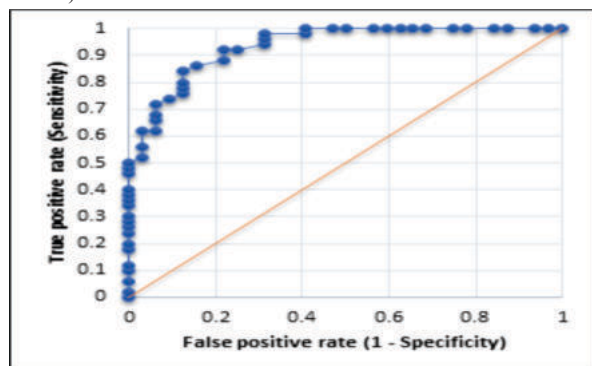


Figure 4: ROC Curve For Platelet Count (auroc: 0.935)

ROC curves (Fig. 4) to assess the platelet count cut off with the best sensitivity and specificity for diagnosis of Oesophageal varices (cut off = 97000, sensitivity = 84% (95% CI 71.1%–91.8%); specificity = 87.5% (95% CI 71.2–95.5).

The prevalence adjusted positive predictive values (PPV) and negative predictive values (NPV) for a platelet count less than 97000 were 91.3% and 77.8%, respectively. The Area under ROC curve (AUROC) for this platelet count cut off was 0.935 (95% CI 0.886–0.984).

Table 4: Spleen Bipolar Diameter Correlation Among Study Groups

Group	Mean (mm)	Standard deviation	P value
No Oesophageal varices group (NOV)	92.5	18.18	0.0001
Oesophageal varices (OV)	127.94	16.41	

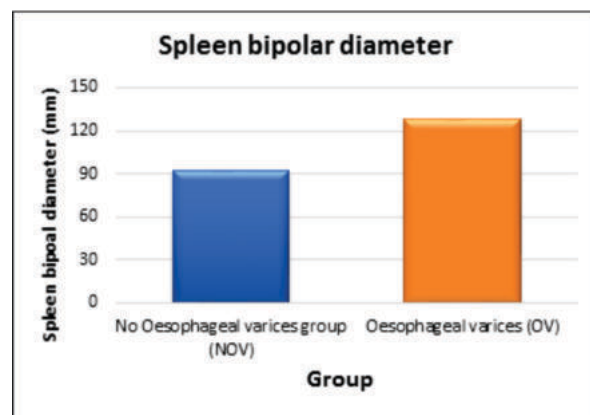


Figure 5: Spleen Bipolar Diameter Correlation Among Study Groups

The mean Spleen bipolar diameter (Fig. 5) in No Oesophageal varices group was 92.5 ± 18.18 mm and in Oesophageal varices group was 127.94 ± 16.41 mm (Table 4) which was statistically significant (p value: 0.0001).

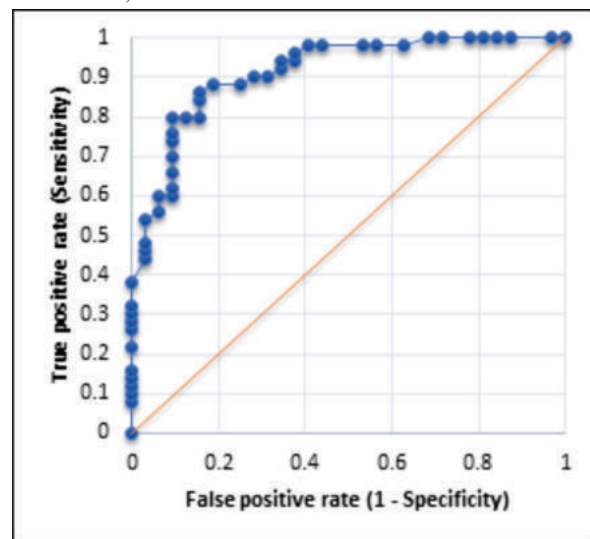


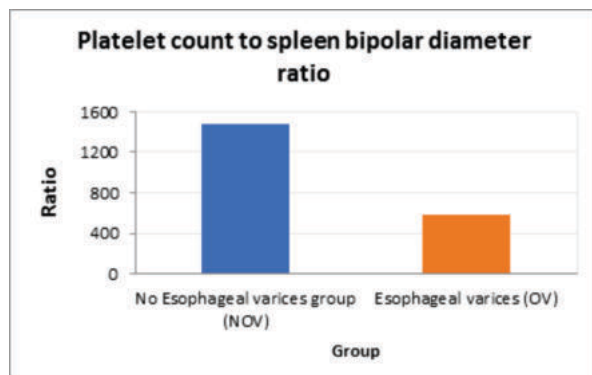
Figure 6: ROC Curve For Spleen Bipolar Diameter In Mm (auroc: 0.914)

ROC curve (Fig. 6) to assess the spleen diameter cut off with the best sensitivity and specificity for a diagnosis of OV (cut off = 120, sensitivity=80% (95% CI 66.7 – 88.9); specificity = 90.6% (95% CI 74.8–97.4)).

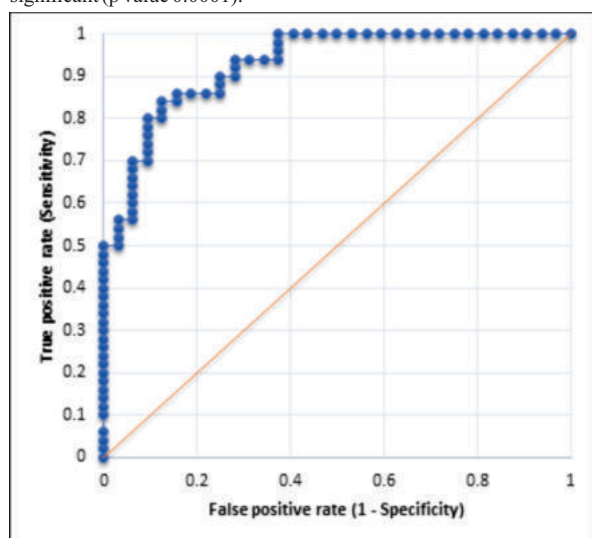
The prevalence adjusted positive and negative predictive values for a spleen diameter more than 120 were 93% and 74.4%, respectively. The AUROC for spleen diameter cut off was 0.914 (95% CI 0.853–0.975). Correlation of Platelet count to spleen bipolar diameter ratio among the study groups

Table 5: Platelet Count To Spleen Bipolar Diameter Ratio Among Study Groups

Group	Mean	Standard deviation	P value
No Oesophageal varices group (NOV)	1472.26	535.9	0.0001
Oesophageal varices (OV)	577.52	277.52	

**Figure 7: Platelet Count To Spleen Bipolar Diameter Ratio Among Study Groups**

The mean Platelet count to spleen bipolar diameter ratio (Fig. 7) in No Oesophageal varices group was 1472.26 ± 535 and in Oesophageal varices group was 577.52 ± 277 (Table 5) which was statistically significant (p value 0.0001).

**Figure 8: ROC Curve For Platelet Count To Spleen Bipolar Diameter In MM (auroc: 0.928)**

ROC curve (Fig. 8) to assess the platelet count to spleen diameter ratio cut off with the best sensitivity and specificity for a diagnosis of oesophageal varices (cut off = 838, sensitivity = 84% (95% CI 71.1 – 91.8); specificity = 87.5% (95% CI 71.2–95.5)).

The prevalence adjusted positive and negative predictive values for a platelet count to spleen diameter ratio less than 838 were 91.3% and 77.8%, respectively. The AUROC was 0.928 (95% CI 0.875–0.981)

In our study, both spleen diameter and platelet count cut offs with the best sensitivity and specificity for the diagnosis of oesophageal varices were identified by means of ROC curves, which had prevalence adjusted positive and negative predictive values and accuracies that were slightly lower than those of the platelet count to spleen diameter ratio.

DISCUSSION

About forty percent of individuals diagnosed with the early illness and about sixty percent of those diagnosed with portal hypertension have oesophageal varices¹⁸. The annual incidence of bleeding in the digestive tract ranges from 1 to 2 percent in patients without oesophageal varices, 5 percent in those who have small varices, and 15

to 20 percent in patients with large varices⁷. Endoscopy is now suggested at least once every two to three years in patients who do not have varices, and at least once every one to two years in patients who have small varices⁹.

The most common mortality cause in patients with cirrhosis is still bleeding from ruptured varices. The identification of individuals who are at risk of bleeding from varices is essential in prevention. Endoscopy can be avoided if varices could be diagnosed noninvasively, since this will identify people with high likelihood of developing varices.

Many investigators^{9, 10, 11} have shown a strong relationship between presence of oesophageal varices and values of platelet count as well as spleen size. Even though portal hypertension is a major contributor to low platelets in individuals with chronic liver disease, other variables, like a shorter mean platelet lifespan, reduced thrombopoietin synthesis, and the myelotoxic effects of alcohol or hepatitis viruses may also play a role. Splenomegaly is most often seen in cirrhotic individuals due to associated portal hypertension. Several studies^{12,13,14} have been conducted to test the viability of platelet count to spleen diameter ratio as a noninvasive screening tool for oesophageal varices. Intriguing findings emerged when the platelet count to spleen bipolar diameter ratio was used in Giannini et al¹⁵ (100 % sensitivity and 77 % specificity)

There had been 82 patients in our study, 61 men and 21 women (Table 2). The average age of those who had oesophageal varices was 52.65 ± 8.8 . The average age of those without oesophageal varices was 55.34 ± 8.44 . (Table 1).

There were more men than women across all age ranges. Oesophageal varices were seen in 13 of the 21 female and 37 of the 61 male cirrhotic patients and in 60.9% of all patients.

From our data, we found that, the average platelet count without varices was 127781.25 ± 30207.59 and with varices was 69666.97 ± 24245.384 . Statistically significant difference has been found (p < 0.05) in platelet count between the two patient groups.

ROC curve used for evaluating the platelet count cut off was 97,000 per mm³, which had 84 percent sensitivity and 87.5 percent specificity. Positive predictions were accurate in 91.3% of the time, while negative predictions were accurate in 77.8% of the time.

Other researchers, including Sharma et al.¹⁶, Tafarel et al.¹⁷, Abu El Makeram¹⁸ Baig et al.¹³, Schwarzenberger¹⁹, Barrera, et al.¹⁴, Cherian et al.²⁰, Sarangapani et al.²¹, Giannini et al.^{12,15}, all came to similar conclusions in their respective investigations. Platelet cut offs ranging from 68000 to 160000 have been demonstrated to have sensitivities as well as specificities that range from 71 to 90 percent and 36 to 73 percent, respectively, according to cross sectional studies.

Qamar et al.²² came to a conclusion that cross-sectional or longitudinal evaluation of platelet count is not an adequate noninvasive marker for gastroesophageal varices, after conducting a prospective, randomized, and double-blind trial on 213 patients. Therefore, guidelines that are currently in place for endoscopic screening for varices should be maintained.

According to the findings of our research, the average spleen diameter has been substantially different between the two groups (p < 0.01), having mean value of 127.94 ± 16.41 in patients with varices and 92.5 ± 18.18 in patients without varices. The receiver operating characteristic (ROC curve) showed that the splenic diameter cut off value of 120, which had an 80% sensitivity and a 90.6 % specificity. Predictive accuracy was calculated to be 74.4 percent positive and 93.1 percent negative.

Many researchers^{23,24,25} showed that platelet count to spleen diameter ratio is significantly correlated with the existence of varices. This novel parameter was tested by many other investigators^{12,14,18,19}.

The mean platelet count to spleen bipolar diameter ratio was significantly different for patients with and without oesophageal varices (p < 0.01). Using ROC curve, we determined that a platelet count to spleen bipolar diameter ratio cut off value of 838 for oesophageal varices would provide 84% sensitivity and 87.5 % specificity.

We followed the work of Giannini et al.¹⁵ and used a cut off value of 909, which they found to be highly sensitive (100%) and specific (93%).

Table 6: Studies With Platelet Count To Splenic Diameter Ratio As 909

Study	Platelet count/ Spleen diameter ratio	Sensitivity	Specificity	PPV	NPV
Baig et al13	909	80%	89%		
Giannini et al15	909	100%	93%		
Sarangapani et al21	909	88.5%	83%		
Schwarzenberger et al 19	909	80%	40%	74%	
Mattos et al26	909	77%	45.5%	79.5%	42.6%

The platelet count to spleen bipolar diameter ratio of 909 was first studied in a thorough review as well as a meta-analysis by Chawla S et al²⁷, who found it to be a reliable noninvasive predictor of oesophageal varices. They could extrapolate 89% sensitivity and 74% specificity from all of the meta-analyses. In general, the quality of the evidence has been poor, indicating that these findings would not generalize to other clinical contexts.

Acceptable test features for the platelet count to spleen bipolar diameter ratio of 909 were obtained from a pooled analysis by Chawla S et al²⁷, but the quality of the available data was not sufficient to support its use as a viable noninvasive screening tool for oesophageal varices. According to him, the platelet count to spleen bipolar diameter ratio is an elegant, straightforward, and low-cost alternative to conventional noninvasive prediction methods.

On evaluation of other studies in comparison to ours, we concluded that a platelet count to spleen bipolar diameter ratio of 838 was showing the highest levels of sensitivity and specificity. The sensitivity was 87.5% and the specificity was 84% when using cut off value of 838. The positive predictive value was found to be 91.3%, and the negative predictive value to be 77.8% when compared to prior studies. Using a cut off value of 909 resulted in an 86% sensitivity, 81% specificity, and 87% positive predictive value, along with a 78% negative predictive value. Our results have been mostly consistent with this. So far, no randomized controlled studies have been published that evaluate the impact of the platelet count to spleen bipolar diameter ratio on important patient results. The lack of randomized, controlled research does not preclude the use of research findings of test accuracy in clinical practice for a new diagnostic test like platelet count to spleen bipolar diameter ratio. This ratio is not only non-invasive but also extremely cost-effective method, since platelet counts and abdominal ultrasounds are routinely gathered on all cirrhotic patients.

CONCLUSION

This study was conducted to check whether platelet count to spleen bipolar diameter ratio can be used as a non-invasive predictor of oesophageal varices in patients with liver cirrhosis. A total of 82 patients with cirrhosis were included in this study after obtaining written informed consent.

In this study there was an increased incidence of oesophageal varices in male population. The cut off values of platelet count was less than 97,000 per mm³ and spleen bipolar diameter was more than 120 mm to predict varices. Mean splenic bipolar diameter was significantly more in patients with varices. Platelet count to spleen bipolar diameter ratio cut off was less than 838 to predict varices. Among the patients with platelet count to spleen bipolar diameter ratio less than 838, 91.3% had oesophageal varices. In patients with platelet count to spleen bipolar diameter ratio more than 838, 77.78% patients had no oesophageal varices, which was statistically significant (p value 0.0001).

The new diagnostic tests like platelet count to spleen bipolar diameter ratio can be incorporated into clinical practice to predict the incidence of varices in cirrhotic patients. Apart from being noninvasive, the platelet count to spleen bipolar diameter ratio is a relatively inexpensive test, as platelet counts and abdominal ultrasound would be obtained on all cirrhotic patients routinely as part of their clinical workup.

REFERENCES

1. Gupta, TK, Chen L, Groszmann RJ. Pathophysiology of portal hypertension. Clin. Liver

Dis. 1997; 1:1-12.

- De Franchis R, Primignani M. Natural history of portal hypertension inpatients with cirrhosis. Clin. Liver Disease 2001; 5: 645-63.
- Rigo GP, Merghi A, Chalen NJ, Mastronardi M, Codoluppi PL, Ferrari A et al. A prospective study of the ability of the three endoscopic classifications to predict hemorrhage from oesophageal varices. Gastrointest Endos. 1992; 38: 425-9.
- D'Amico G, Garcia-Isao G, Cales P. Diagnosis of portal hypertension; Howand When. Proceedings of the third Baveno International consensus workshop on definitions, methodology and therapeutic strategies. Oxford: Black well science 2001: 36-63.
- D'Amico G, Pagliano L, Bosch J, The treatment of portal hypertension, a meta-analysis review. Hepatology 1995; 22: 332-54.
- Brenna MRS, Targowhik L, Gareti SD, Hetal AK, Ian MG. Endoscopic screening for oesophageal varices in cirrhosis. Is it ever cost effective? Hepatology 2003; 37: 366-77.
- Ong J, Younossi ZM. Clinical predictors of large esophageal varices: how accurate are they? American Journal Of Gastroenterology 1999; 94: 3103-5.
- González-Ojeda A, Cervantes-Guevara G, Chávez-Sánchez M, Dávalos-Cobián C, Ornelas-Cázares S, Macías-Amezcu MD, Chávez-Tostado M, Ramírez-Campos KM, del Rocio Ramírez-Arce A, Fuentes-Orozco C. Platelet count/spleen diameter ratio to predict esophageal varices in Mexican patients with hepatic cirrhosis. World Journal of Gastroenterology: WJG. 2014 Feb 2;20(8):2079.
- Sheila Sherlock, James Dooley. Hepatic Cirrhosis. Chapter 21. Diseases of the liver and biliary system. 11th edition.
- Harrison's principles of Internal Medicine 18th edition. McGraw- Hill. 2012
- Vijay H. Shah, Patrick S. Kamath. Portal Hypertension and Gastrointestinal Bleeding. Sleisenger and Fordtran Gastrointestinal and Liver Disease. 9th edition. Chapter 84 and 90.
- E.G. Giannini, F. Botta, P. Borro et al. „Application of the platelet count/spleen diameter ratio to rule out the presence of esophageal varices in patients with cirrhosis: A validation study based on follow-up. Digestive and Liver Disease 2005; 37 779-785.
- WW Baig, MV Nagaraja, M Varma, R Prabhu et al. „Platelet count to spleen diameter ratio for the diagnosis of esophageal varices: Is it feasible? Can J Gastroenterol 2008; 22(10): 825-828.
- Barrera F, Riquelme A, Soza A. „Platelet count/spleen diameter ratio for non- invasive prediction of high risk esophageal varices in cirrhotic patients. Ann Hepatol. Oct-Dec 2009; 8(4): 325-30.
- Giannini E, Botta F, Borro P, Rizzo D, Romagnoli P, Fasoli A, Mele M R, Testa E, Mansi C, Savarino V, Testa R. Platelet count/spleen diameter ratio: proposal and validation of a non-invasive parameter to predict the presence of esophageal varices in patients with liver cirrhosis. Gut 2003; 52: 1200-1205.
- Sanjay Kumar Sharma and Rakesh Aggarwal. Prediction of large esophageal Varices in patients with cirrhosis of the liver using clinical, laboratory and imaging parameters. J Gastroenterol Hepatol. Nov 2007; 22(11): 1909-15.
- Tafarel JR, Tolentino LH, Correa LM, Bonilha DR, Piaulino P, Martins FP, Rodrigues RA, Nakao FS, Libera ED, Ferrari AP, da Silveira Röhr MR. Prediction of esophageal varices in hepatic cirrhosis by noninvasive markers. Eur J Gastroenterol Hepatol. Sep 2011; 23(9): 754-8.
- Abu El Makarem MA, Shatat ME, Shaker Y, Abdel Aleem AA, El Sherif AM, Moaty MA, Abdel Ghany HS, Elakad A, Kamal Eldeen AM. Platelet count/bipolar spleen diameter ratio for the prediction of esophageal varices: The special Egyptian situation: Noninvasive prediction of esophageal varices. Hepat Mon. Apr 1, 2011; 11(4): 278-84.
- Elliot Schwarzenberger, MD, Trinh Meyer, MD, w Vidushi Golla, MD, w Nicole Pena Sahdala, MD, and Albert D. Min, MDw et al. „Utilization of Platelet Count Spleen Diameter Ratio in Predicting the Presence of Esophageal Varices in Patients With Cirrhosis. □ J Clin Gastroenterol 2010; 44: 146-150
- Cherian JV, Deepak N, Ponnusamy RP, et al. Non-invasive predictors of esophageal varices. Saudi J Gastroenterol 2011; 17(1): 64-8
- Sarangapani A, Shanmugam C, Kalyanasundaram M, et al. Non-invasive prediction of large esophageal varices in chronic liver disease patients. Saudi J Gastroenterol 2010; 16(1): 38-42.
- Amir A. Qamar, Norman D. Grace, Roberto J. Groszmann, Guadalupe Garcia- Tsao „Platelet Count Is Not a Predictor of the Presence or Development of Gastroesophageal Varices in Cirrhosis. □ Hepatology 2008; 47: 153-159.
- Assessment of the prognosis of cirrhosis: Child-Pugh versus MELD Journal of Hepatology 2005; 42: S100-S107.
- Groszmann RJ. Reassessing portal venous pressure measurements gastroenterology 1984; 86: 1611-1614.
- Bayer TD, Triger DR, Horisawa M. et al. Direct transhepatic measurementso f p o r t a l vein pressure using a thin needle. Comparison with wedged hepatic vein pressure. Gastroenterology 1977; 72: 584-589.
- Mattos AZ, Mattos AA, Vianna FF, Musskopf MI, Pereira-Lima JC, Maciel AC. Platelet count/spleen diameter ratio: analysis of its capacity as a predictor of the existence of esophageal varices. Arq Gastroenterol. Sep 2010; 47(3): 275-8.
- Chawla S, Katz A, Attar BM, Gupta A, Sandhu DS, Agarwal R. Platelet count/spleen diameter ratio to predict the presence of esophageal varices in patients with cirrhosis: a systematic review. Eur J Gastroenterol Hepatol. Apr 2012; 24(4): 431-6.