OPEN ACCESS

Saudi Journal of Medical and Pharmaceutical Sciences
Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) | ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article **Hepato-Gastroenterology**

The Usefulness of Non-Invasive Liver Stiffness Measurements by Fibroscan in Predicting Clinically Significant Portal Hypertension in Cirrhotic Patients

Fatiha Bouhamou[1*], Mouna Salihoun[1], Ilham Serraj[1], Nawal Kabbaj[1]

[1]Hepato-Gastroenterology Unit of Functional Digestive Explorations at University Hospital Ibn SINA in Rabat Morocco

DOI: 10.36348/sjmps.2024.v10i03.002 | **Received:** 02.01.2024 | **Accepted:** 08.02.2024 | **Published:** 06.03.2024

***Corresponding author:** Fatiha Bouhamou
Hepato-Gastroenterology Unit of Functional Digestive Explorations at University Hospital Ibn SINA in Rabat Morocco

Abstract

Background: Liver stiffness measurement (LSM) has proposed as a non-invasive method for estimating the severity of fibrosis and the complications of cirrhosis. Measurement of the hepatic venous pressure gradient (HVPG) is the gold standard for assessing the presence of portal hypertension, but its invasiveness limits its clinical application. The aim of our study is to investigate if LSM could predict the size of Esophageal varices (EV) in patients with liver cirrhosis to limit upper endoscopic procedures only to those patients that really need it (patients with large EV or EV at risk for bleeding). ***Methods:*** Our retrospective study includes 46 cirrhotic patients over a period of 40 months between January 2019 and April 2022, at the Service of Digestive Functional Explorations of Hepato-gastroenterology of the University hospital Ibn-Sina of RABAT, all patients underwent a liver stiffness measurement by Transient elastography FibroScan. ***Results*:** Of the 46 cirrhotic patients included in this study, with a mean age of 58.5(21-90) years, 18 (39.1%) of patients were male and 28(60.9%) were female. the predominant etiology of cirrhosis was chronic viral hepatitis C 20 (43.5%). The area under the ROC curve of the diagnosis of large EVs (EV≥II) was 0.724 (95%CI). The optimal cut-off of elasticity was 20.5 for this purpose, with a sensitivity of 66.7%, specificity of 94.74%. ***Conclusions:*** these results indicate that Transient elastography FibroScan is a reliable, non-invasive method to assess portal hypertension and can be used for the screening and diagnosis of clinically significant portal hypertension.

Keywords: Cirrhosis- Portal hypertension- Transient Elastography- FibroScan- Esophageal varices.

INTRODUCTION

Portal hypertension is a major consequence of cirrhosis and is responsible for its most severe complications, including ascites, bleeding from gastro-oesophageal varices and encephalopathy. Direct portal pressure measurement is difficult as there is no direct connection between the portal and systemic circulations. In practice, the best surrogate for the true portal pressure is the hepatic vein pressure gradient (HVPG), which is considered the reference standard [1].

Portal hypertension is defined as portal venous pressure >5 mmHg. Clinically significant portal hypertension is defined as HVPG 10 mmHg and this incurs a risk of developing complications [2]. A HVPG>12 mmHg confers increased risk of esophageal variceal bleeding [3]. Despite such important prognostic information being provided by HVPG, it is rarely measured in clinical practice, due to its invasiveness, cost and expertise required [4]. Therefore, several non-invasive methods have been proposed in order to substitute HVPG for the evaluation of the severity of portal hypertension.

Over the last decade our understanding of the pathophysiology of portal hypertension has increased. Novel diagnostic technologies have facilitated and improved the diagnosis and treatment of hepatic fibrosis and cirrhosis. One of the most studied markers of portal hypertension is liver stiffness measured by transient elastography FibroScan. First, it was used as an alternative to liver biopsy for staging fibrosis in patients with viral liver disease, especially HCV. Later, it was demonstrated that FibroScan had a high accuracy on diagnosing cirrhosis. Nowadays, it is generally accepted that transient elastography measurements can also be correlated with the degree of portal pressure [5]. However, it has been documented that this correlation between LSM and HVPG weakens in HVPG values higher than 10–12 mmHg, which is the threshold for the

development of severe liver complications. In addition, clear association between LSM and the size of EVs has not been verified [6].

The aim of our study is to investigate if LSM could predict the size of EV in patients with liver cirrhosis to limit upper endoscopic procedures only to those patients that really need it (patients with large EV or EV at risk for bleeding).

METHODS

Participants

This study included 46 Patients diagnosed with cirrhosis of various etiologies; who performed a liver stiffness measurement LSM using transient elastography FibroScan during the study period. Exclusion criteria were any cirrhotic patient who did not have FOGD as part of their cirrhosis follow-up workup.

Study Design

This is a retrospective study including 46 cirrhotic patients. Our study covers the period from 01/01/2019 to 31/04/2022 in the Hepato-Gastroenterology Department of Functional Digestive Explorations at CHU Ibn Sina in RABAT.

We found 101 files of cirrhotic patients with 46 exploitable files having the complementary examinations necessary for our study.

A checklist was used to record the data. First demographic features and biological data of the patients. Then, all patients underwent FibroScan using the FibroScan compact 530 devices (Echosens, France). All FibroScans were performed according to the manual of the manufacturer.

Data Analysis

The application JAMOVI 2.2.5 was used for data analysis. Mean, standard deviation, median, interquartile range (IQR), frequency, and percentages were used to describe the results. Distribution normality of quantitative variables were determined using the Shapiro-Wilk normality and the Mann-Whitney test was used for comparison mean LSM values and medians between the different subgroups. The receiver operating characteristic (ROC) curves were drawn to determine the diagnostic value of transient elastography FibroScan for the differentiation of EV grade ≥II of EV grade <II. The area under the ROC (AUC) curve was calculated and the optimal cut-off was also determined for this purpose using the ROC curves. *p* values ≤ 0.05 were regarded as statistically significant.

RESULTS

Of the 46 cirrhotic patients included in this study, with a mean age of 58.5(21-90) years, 18 (39.1%) of patients were male and 28(60.9%) were female. the predominant etiology of cirrhosis was chronic viral hepatitis C 20 (43.5%). General characteristics of the study participants are shown in Table 1. Based on FibroScan results The LSM of our sample ranged from a minimum of 12 kPa to a maximum of 67.9 kPa with a median of 19.4(14.8 - 31.2). According to the results of the gastroscopy performed in the 6 months preceding or following the FibroScan: 8 (17.4%) patients had EV grade III, 18(39.1%) had EV grade II and 9(19.6%) had EV grade I and 11(23.9%) had no esophageal varices.

The Mann-Whitney test shows that the liver stiffness of the group "presence of EV" is higher than that of the "absence of EV" group (27 KPa and 14.9 KPa respectively) with a significant difference *p* value =0.02 **(**table2) and showed also a higher mean elasticity in the "EV grade > II" group than in the "EV grade < II" group (37 KPa and 16.8 KPa respectively) with a statistically significant difference between the 2 groups *p* = 0.01(table3).

Figure 1 demonstrates the ROC curves of liver stiffness for detection of EV>=II from the EV<II group. The area under the ROC curve was 0.724 (95%CI). The optimal cut-off was 20.5 for this purpose, with a sensitivity of 66.7%, specificity of 94.74%, the results are shown in Table 4.

Table 1: General characteristics of the study participants

Variables	Values (N=46)
Age(years) #	58.5(21-90)
Gender §	
Male	18 (39.1)
Female	28(60.9)
Etiology of cirrhosis §	
HCV	20(43.5)
Cryptogenic	12(26.1)
Autoimmune hepatitis	6(13)
HBV	4(8.7)
CBP	2(4.3)
Alcohol	1(2.2)
NASH	1(2.2)
LSM #	19.4(14.8 -31.2)
Esophageal varices §	
Grade III	8(17.4)
Grade II	18(39.1)
Grade I	9(19.6)
grade 0	11(23.9)

N number, **#** median and interquartile interval, **§** effective (percentage),
HBV, hepatitis B virus; HCV, hepatitis C virus; LSM, liver stiffness measurement.

Table 2: Comparison of liver stiffness by presence or absence of esophageal varices

Indices	Presence of EV	Absence of EV	*p* value
LSM	22(12-67.9)	14.4(12.5-27)	0.02

EV: Esophageal varices; LSM: liver stiffness measurement
*Analyzed by Mann–Whitney test

Table 3: Comparison of liver stiffness between the group grade VO< II vs VO≥ II group

Indices	EV>=II	EV<II	*p* value
LSM	37+/-10.4	16.8+/-3.09	0.01

EV: Esophageal varices; LSM: liver stiffness measurement
*Analyzed by Mann–Whitney test

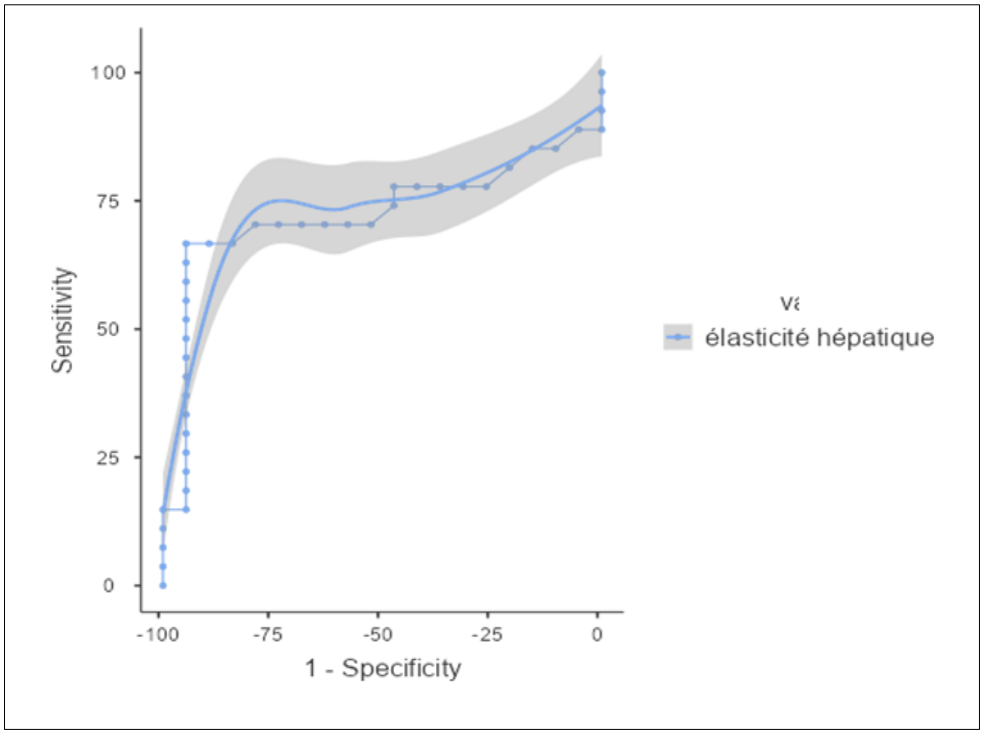

Figure 1: Liver stiffness measurement ROC curve for the diagnosis of large EVs (EV≥II)

Table 4: Diagnostic performance of liver stiffness for the differentiation of EV grade >=II from EV grade <II

Indices	AUC	CI 95%	Optimal cut-off	Sensitivity (%)	Specificity (%)
LSM	*0.724*	0.623-0.825	20.5	66.7	94.74

EV: Esophageal varices; LSM: liver stiffness measurement; CI confidence interval; AUC area under the curve

DISCUSSION

Patients with cirrhosis transition through different prognostic stages, the main ones being the compensated and decompensated stages. Transition from the compensated to the decompensated stage is clinically marked by the development of complications such as ascites, variceal hemorrhage and overt hepatic encephalopathy. The various disease stages are associated with differing outcomes, including risk of death, Therefore, the assessment of portal hypertension is one of the most important steps in the management of chronic liver disease. The best method to diagnose portal hypertension is the direct measurement of portal pressure. The hepatic venous pressure gradient (HVPG) is currently the gold standard for the diagnosis of intrahepatic portal hypertension. In healthy individuals, HVPG is below 5 mmHg. An HVPG greater than 5 mmHg is suggestive of the presence of portal hypertension, but the complications related to portal hypertension, such as ascites or variceal bleeding, tend to appear if HVPG ≥10 mmHg [7], therefore this threshold is known as clinically significant portal hypertension CSPH.

Test-retest reliability of HVPG measurement is excellent but influenced by the stage of liver disease (lower in decompensated patients) and its etiology (higher in patients with alcohol-related disease) [8], and it is also considered an invasive method. Therefore, the development of new non-invasive markers of portal hypertension is encouraged. From the initial report of the new technique to quantify the amount of liver fibrosis by liver stiffness measurement LSM using transient elastography FibroScan TE [9]. Many studies have

validated this method in the diagnosis of liver fibrosis and cirrhosis. After that, a series of studies focused on validating the feasibility and accuracy of LSM in different clinical settings, and a meta-analysis in 2017 showed that LSM with TE could detect CSPH with AUROC > 0.9 [10]. In this meta-analysis, the most critical issue used to calculate the summary estimates of diagnostic accuracy is the between-study heterogeneity due to the threshold effect. Various cut-off values were adopted among the 11 studies, and ranging from 8.74–25 KPa. These differences may be due to the heterogeneity of the studied population and different etiologies. Liver stiffness is more elevated in alcoholic liver disease compared to viral liver disease. The optimal cut-off values are higher in the alcoholic group than in the hepatitis C virus infected group (34.9 KPa vs. 20.5 KPa) [5] .Furthermore, liver stiffness is very well correlated with HVPG up to values of 10-12 mmHg, but above these values the correlation is lower, demonstrating that portal hypertension is only partially caused by the amount of fibrosis [11].

In our study, the AUC for the diagnosis of clinically significant portal hypertension (the presence of large esophageal varices EV) was 0.724 (95% CI). The optimal cut-off was 20.5 for this purpose, with a sensitivity of 66.7% and specificity of 94.74%. Our results were similar to those reported in the literature, and the sensitivity of the threshold could be optimized if combined with another criterion such as platelet count. Based on these data, we can say that FibroScan® is discriminative for the detection of large EV (AUC = 0.724).

The major limitations of this study are the small sample size, the various etiology and the fact that the cirrhosis has not been confirmed by liver biopsy in all the patients. Based on this study, further carefully designed studies will be conducted in the future.

In summary, these results indicate that Transient elastography FibroScan is a reliable, non-invasive method to assess portal hypertension and can be used for the screening and diagnosis of clinically significant portal hypertension.

REFERENCES

1. De Franchis, R., Bosch, J., Garcia-Tsao, G., Reiberger, T., Ripoll, C., Abraldes, J. G., ... & Yoshiji, H. (2022). Baveno VII–renewing consensus in portal hypertension. *Journal of hepatology*, *76*(4), 959-974.
2. Ripoll, C., Groszmann, R., Garcia–Tsao, G., Grace, N., Burroughs, A., Planas, R., ... & Portal Hypertension Collaborative Group. (2007). Hepatic venous pressure gradient predicts clinical decompensation in patients with compensated cirrhosis. *Gastroenterology*, *133*(2), 481-488.
3. Groszmann, R. J., Bosch, J., Grace, N. D., Conn, H. O., Garcia-Tsao, G., Navasa, M., ... & Lerner, E. (1990). Hemodynamic events in a prospective randomized trial of propranolol versus placebo in the prevention of a first variceal hemorrhage. *Gastroenterology*, *99*(5), 1401-1407.
4. Thalheimer, U., Bellis, L., Puoti, C., & Burroughs, A. K. (2011). Should we routinely measure portal pressure in patients with cirrhosis, using hepatic venous pressure gradient (HVPG) as a guide for prophylaxis and therapy of bleeding and rebleeding? No. *European Journal of Internal Medicine*, *22*(1), 5-7.
5. Lemoine, M., Katsahian, S., Ziol, M., Nahon, P., Ganne-Carrie, N., Kazemi, F., ... & Beaugrand, M. (2008). Liver stiffness measurement as a predictive tool of clinically significant portal hypertension in patients with compensated hepatitis C virus or alcohol-related cirrhosis. *Alimentary pharmacology & therapeutics*, *28*(9), 1102-1110.
6. Reiberger, T., Ferlitsch, A., Payer, B. A., Pinter, M., Schwabl, P., Stift, J., ... & Peck-Radosavljevic, M. (2012). Noninvasive screening for liver fibrosis and portal hypertension by transient elastography-a large single center experience. *Wiener klinische Wochenschrift*, *124*.
7. Groszmann, R. J., Garcia-Tsao, G., Bosch, J., Grace, N. D., Burroughs, A. K., Planas, R., ... & Makuch, R. (2005). Beta-blockers to prevent gastroesophageal varices in patients with cirrhosis. *New England Journal of Medicine*, *353*(21), 2254-2261.
8. De Franchis, R., Bosch, J., Garcia-Tsao, G., Reiberger, T., Ripoll, C., Abraldes, J. G., ... & Yoshiji, H. (2022). Baveno VII–renewing consensus in portal hypertension. *Journal of hepatology*, *76*(4), 959-974.
9. Sandrin, L., Fourquet, B., Hasquenoph, J. M., Yon, S., Fournier, C., Mal, F., ... & Palau, R. (2003). Transient elastography: a new noninvasive method for assessment of hepatic fibrosis. *Ultrasound in medicine & biology*, *29*(12), 1705-1713.
10. You, M. W., Kim, K. W., Pyo, J., Huh, J., Kim, H. J., Lee, S. J., & Park, S. H. (2017). A meta-analysis for the diagnostic performance of transient elastography for clinically significant portal hypertension. *Ultrasound in Medicine & Biology*, *43*(1), 59-68.
11. Castera, L., Pinzani, M., & Bosch, J. (2012). Non invasive evaluation of portal hypertension using transient elastography. *Journal of hepatology*, *56*(3), 696-703.