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Use of Elastometry for Non-Invasive Screening and Staging of Esophageal Varices in Patients with Hepatitis C Virus -Related Liver Cirrhosis

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Abstract: Aim: *To evaluate liver stiffness measurement as a non-invasive predictor of presence and grade of esophageal varices (EV) in patients with hepatitis C virus infection(HCV)- related liver cirrhosis.*
Methods: *This is a prospective, single-center study that lasted 4 and a half years including all patients with HCV-related liver cirrhosis, compensated or not, and treated at Hassan II University Hospital in Fez, Morocco. Upper endoscopy associated with liver stiffness measurement by FibroScan® are performed by different operators.*
Results: *Forty-six patients were included in the study; the average age was 60.30 +/- 9.9 years with 52.2% of men. Cirrhosis was compensated in 84.8% of cases. Twenty-nine patients (63.0%) had EV (30.4% grade I, 26.1% grade II and 6.5% grade III). 67.4% of patients had large varices. The average of liver stiffness was 21.9 +/-18.7 kPa. The AUROC for the diagnosis of EV was 0.92 and the cut-off value was 13.75 kPa, with a sensitivity of 89.7% and a specificity of 82.4%, positive predictive value (PPV) of 89.66% and a negative predictive value (NPV) of 82.35%. The cut-off for prediction of large varices was 14, 45 Kpa with a sensitivity of 80%, a specificity of 61.3%, a PPV of 50%, an NPV of 86.4% and an AUROC = 0.782. Biological scores AAR, APRI and Fib-4 were also predictors of the presence of EV (Cut-offs respectively 0.95 ≥ - ≥1.59 - ≥3.72 and AUROC of 0.76 - 0.68 - 0.71 respectively) and even the presence of large EV (cut-off respectively of ≥1.15 - ≥1.67 - ≥5.39 and AUROCs respectively of 0.840 – 0.794 – 0.886).*
Conclusion: *Our study proves that liver stiffness measurement can predict the presence and grade of EV in patients with HCV-related liver cirrhosis. The applies to the biological scores AAR, APRI and Fib-4.*
Keywords: *Liver cirrhosis; hepatitis C virus infection; portal hypertension; liver stiffness; non-invasive tools; upper gastrointestinal endoscopy, screening for EV.*

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I. Introduction

Infection with the hepatitis C virus is a real global public health problem as it is one of the leading causes of chronic liver disease and cirrhosis worldwide. The overall number of people chronically infected is estimated at about 160 million. This infection is responsible for more than 360 000 deaths per year because of the various serious complications [1], including gastrointestinal bleeding associated with high mortality in the range of 30 to 50% in the absence of effective treatment at each bleeding episode. The most common cause is the rupture of esophageal varices (EV) that are present in approximately 50% of patients with cirrhosis. Their presence is correlated with the severity of chronic liver disease. While only 40% of Child-Pugh A patients have EV, they are present in 85% of Child-Pugh C patients. Patients without EV develop them at a rate of 8% per year. Similarly, patients with small varices develop large varices at an annual rate of 8% [2].

It has also been shown that 16% of patients with chronic hepatitis C with bridging fibrosis have EV [2].

The risk of bleeding by EV rupture is clearly related to their size; this risk varies from 7% for grade 1 EV to 30% for grade 2 or 3 EV [3-4].

Therefore, the primary prevention of EV rupture is essentially screening for their presence and especially their size. Given the high prevalence of EV in cirrhotic patients, ranging from 24 to 80% according to studies [2 - 5], and the need for periodic variceal screening varying from one to three years [2 -5-6-7]. This program of periodical upper tract endoscopy in these patients might result in a heavy economic burden even for developed countries [8]. In addition, repeated examinations; are often poorly accepted by patients who may refuse further follow-up [9].

For these reasons, the search for a non-invasive parameter such liver stiffness measurement as well as some biomarkers in predicting the presence and grade of EV in cirrhotic patients has become a necessity [1-10-11-12]. Our purpose is to attempt to establish a relationship between liver stiffness, some biomarkers, and the presence and grade of EV in patients with HCV-related liver cirrhosis.

Patients And Methods:

Inclusion And Collection Of Data:

It is a prospective, observational and monocentric study spread over a period of 4 years and a half, including 46 patients with compensated or not HCV-related liver cirrhosis, followed at Hassan II University Hospital in Fez. For all patients the following parameters were recorded: age, sex, cause of cirrhosis, clinical examination data, body mass index (BMI) and biological data (albumin levels, serum gammaglobulin, total bilirubin (TB) Prothrombin activity (PT), serum aspartate aminotransferase (AST), serum alanin aminotransferase (ALT), gammaglutamyl transpeptidase activity (GGT), platelet count and virological examination). From these serum parameters, some scores were calculated such as AAR score (AST/ALT ratio), APRI score (AST to platelet ratio index), and FIB-4 (fibrosis-4). The abdominal ultrasound was performed with a measurement of the size of spleen; we were thus able to calculate the platelet count / size spleen ratio [13]. It should be noted that the diagnosis of cirrhosis was retained either on the obvious signs of it (clinical, biological and radiological) or on the liver biopsy in case of non-obvious signs.

Upper tract endoscopy was performed by an endoscopist unaware of the results of FibroScan®. Different types of groups were then formed. On the one hand: " a group with presence of EV " and " a group without EV " and, on the other hand: " an EV grade <2 group " (= group without EV and EV of grade 1) and "an EV grade ≥ 2" group (= EV group of grade 2 and grade 3 "). Patients with large gastric varices (GV) (GOV and IGV) were included with "EV grade ≥2 group." Liver elasticity was performed with FibroScan® (EchoSens®; Paris, France) by an operator who does not know the results of the endoscopy. We excluded from the study non-cirrhotic intrahepatic portal hypertension, Budd Chiari syndrome, portal vein thrombosis, hepatocellular carcinoma, as well as all failed patients with FibroScan®.

Statistical analysis:

Quantitative variables were described in terms of averages and quartiles, and qualitative variables in terms of percentage. Then a univariate analysis was performed to find the association between the EV and some explanatory variables (age, sex, etc.). This univariate study investigated the association between liver stiffness, some biomarkers and the presence and grade of EV. When comparing the groups, we used classical parametric tests (Chi 2, ANOVA), as well as nonparametric tests in case of small numbers. p values less than 0.05 were considered statistically significant.

Then, the receiver-operating characteristics (ROC) curves were computed, (and areas under the curves as well as 95% confidence intervals (CI) were calculated) according to the sensitivity and the specificity allowing to define the thresholds on the one hand of presence of EV and on the other hand of presence of large EV. Statistical analysis was performed with SPSS (Statistical Package for the Social Science) software version 20.0.

II. Results

General characteristics:

Clinical data:

Forty-six patients were included. The average age of our patients was 60.30 +/- 9.9 years of which 24 men (52.2%) and 22 women (47.8%). The average BMI of all patients was 25,057 +/- 3,14 Kg / m2. Table 1 summarizes the clinical data of the patients.

Tablle 1: clinical data of patients (n= 46)

Physical examination	***Number***	***Percentage (%)***
Normal	41	89
Hepatomegaly	1	2,2
Splenomegaly	3	6,5
Ascites	1	2,2
State of cirrhosis :		
- Compensated	39	84,8
- Decompensated	7	15,2
** Isolated ascites*	3	6,52
** Isolated bleeding*	1	2,17
** Ascites + Bleeding*	3	6,52
Child-Pugh score:		
- A	37	80,4

- B	9	19,6
- C	0	0

Biological data of patients :
Table 2 summarizes the results of the biological parameters and scores of our patients:

Table 2 : Biological data of patients (n = 46)

Variable	***Effective (%)***	***Average***
Platelets (elt/mm)	46 (100%)	122.747,8 (+/- 53618,7)
PT (%)	46 (100%)	81,7 (+/- 16,2)
TB (mg/l)	46 (100%)	13,3 (+/- 9,6)
AST (UI/l)	46 (100%)	78,9 (+/- 46,6)
ALT (UI/l)	46 (100%)	79,0 (+/- 56,4)
AAR score	46 (100%)	1,1 (+/- 0,5)
APRI score	46 (100%)	1,8 (+/- 1,6)
FIB 4 score	46 (100%)	5,5 (+/- 4,1)

Ultrasound data:
The average splenic diameter was 121.3 +/- 29.4 mm. The average platelet count / splenic diameter ratio was 1133.9 +/- 623.
Table 3 summarizes the results of abdominal Doppler ultrasound in our patients:

Table 3: Abdominal Doppler ultrasound data:

Variable	***Effective***	***Perrcentage***
Dilated portal vein	08	17,4 %
Splenomegaly	15	32,6 %
Ascites,	06	13,0 %
Liver condition :		
- Heterogeneous	31	67,4 %
- Homogenous	10	21,7 %
- Steatosis	05	10,9 %
Doppler study of portal vein :		
- Normal	40	87,0 %
- Low flow velocity	06	13,0%

Liver biopsy:
Among our patients included in the study, the histological diagnosis of cirrhosis by liver biopsy was retained only in 09 cases (19.6%). In the other 37 patients (80.4%), the diagnosis of cirrhosis was based on clinical, biological and radiological criteria.
Results of digestive endoscopy:

Table 4: Results of upper gastrointestinal endoscopy:

Variable	***Effective***	***Percentage***
No EV	17	37,0 %
Presence of EV	29	63,0 %
- EV grade I	14	30,4 %
- EV grade II	12	26,1 %
- EV grade III	03	6,5 %
Red signs	06	13,0%
Portal hypertensive gastropathy	19	9,1 %
Gastric varices	02	4,3 %
Group ''EV grade < II''	31	67,4%
Group ''EV grade ≥ II''	15	32,6%

Liver stiffness measurement:
In our series the average liver stiffness was 21,9 +/- 18,7 Kpa, with an interquartile range average of 3,4 +/- 3 Kpa and a success rate of 89,7 +/- 12,4 %

Diagnosis of the presence of EV:
The clinical and paraclinical characteristics of the two groups " absence of EV " and " presence of EV " are summarized in Table 5:

Table 5: comparison between the group " presence of EV " versus " absence of EV " regarding clinical and paraclinical data (n = 46).

Parameter	***"Absence of EV " Group (n=17)***	***" Presence of EV " Group (n=29)***	***p***
Age (year)	62 +/- 9,6	59,3 +/-10,1	0,381
Male sex	5 (29,4%)	19 (65,5%)	**0,031**
BMI (kg/m2)	25,2 +/- 3	25 +/- 3,3	0,853
Decompensated cirrhosis	17 (43,6%)	22(56,4%)	**0,036**
Child score :			
A	17 (100%)	20 (69%)	-
B	0 (0 %)	9 (31 %)	-
C	0	0	-
PT	92,4 +/- 4,2	75,5 +/-15,8	**0,000**
TB	9,4 +/- 4,2	15,6 +/-11,2	**0,036**
AST (UI/l)	65,6 +/- 28	86,6 +/-53,6	0,141
ALT (UI/l)	92,9 +/-77	70,9 +/-39,2	0,205
Platelet count (/mm^3)	146118 +/-58604	109048+/- 46173	**0,022**
Spleen size (mm)	100,7 +/- 12,6	133,5 +/- 29,8	**0,000**
Platelet/spleen size ratio	1494,8 +/- 692,7	922,3 +/-473,5	**0,002**
AAR score	0,94 +/-0,56	1,31 +/- 0,60	**0,045**
APRI score	1,36 +/- 0,98	2,11 +/- 1,85	0,134
Fib-4 score	3,9 +/- 3	6,4 +/- 4,4	**0,045**
Stiffness (Kpa)	8,8 +/- 4,4	29,5 +/- 19,6	**0,000**
Splenomegaly	1(5,9%)	14(48,3%)	**0,003**

Comparing the groups " absence of EV " versus " presence of EV ", finding that the male sex, the decompensation of cirrhosis and the presence of splenomegaly are predictive factors of the presence of EV with values statistically significant (p value equal to 0.031, 0.036, 0.003, 0.000, respectively). We also found a significant difference between these two groups concerning the parameters: prothrombin time, platelet count, and total bilirubin, spleen size with p values equal to 0.000; 0.022; 0.036 and 0.000 respectively. Similarly, for AAR score, Fib-4 score (p = 0.045) and platelet count / spleen size (p = 0.002). Liver stiffness was higher in the EV group than in the non EV group with averages of 29.5 +/- 19.6 Kpa and 8.8 +/- 4.4 Kpa respectively and a very significant p-value (p = 0.000).
We studied the ROC curve for the diagnosis of EV by FibroScan® and the AAR, APRI, Fib-4 scores (Figure 1).

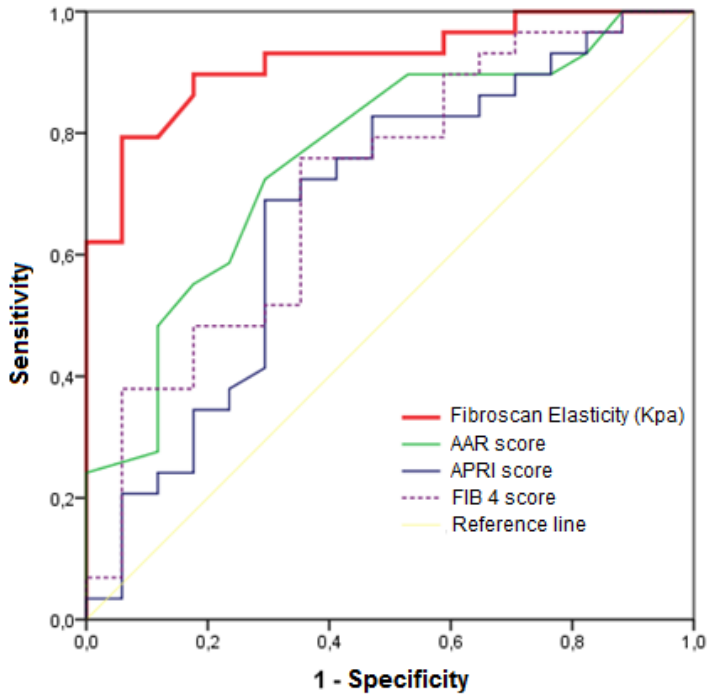

Figure 1: The ROC curve of the parameters: Elasticity, AAR, APRI, Fib-4 (criterion presence of EV versus absence of EV).

Thus, different threshold values were determined to maximize the sensitivity and specificity of these non-invasive parameters in the detection of EV (Table 6)

Table 6: Threshold values predictive of the presence of EV of the different non-invasive parameters studied. (PPV: positive predictive value. NPV: negative predictive value):

Parameter	*AUROC*	*Cut-off*	*Sensibility*	*Specificity*	*PPV*	*NPV*
AAR score	0,76	≥ 0,95	72,4%	70,6%	-	-
APRI score	0,68	≥1,59	69%	70,6%	-	-
Fib-4 score	0,71	≥3,72	75,9%	64,7%	-	-
Elasticity (Kpa)	0,92	≥13,75	89,7%	82,4%	89,66%	82%

Diagnosis of the presence of the grade of EV:

The main clinical and paraclinical characteristics of the two groups "EV grade <II" and "EV grade ≥ II" are summarized in Table 7.

Table 7: comparison between " EV grade < II " group versus " EV grade ≥ II " group regarding clinical and paraclinical data (n = 46).

Parameter	**''EV grade < II'' group (n= 15)**	**''EV grade ≥ II'' group (n= 31)**	***p***
Age (year)	60,3 +/- 9,4	60,3 +/- 11,2	0,986
Male sex	12 (38,7%)	12 (80,0%)	**0,012**
BMI (kg/m2)	25,4 +/- 2,8	24,3 +/- 3,7	0,260
Decompensated cirrhosis	2 (6,5%)	5 (33,3%)	**0,029**
Child score :			
A	30 (96,8 %)	7 (46,7%)	
B	1 (3,2 %)	8 (53,3 %)	
C	0	0	
PT	87,6 +/-13,5	69,60+/-14,7	**0,000**
TB	10+/- 4,2	20,1 +/-13,7	**0,000**
AST (UI/l)	69,5 +/- 32	98,2 +/-64,7	**0,049**
ALT (UI/l)	85,9+/- 64,9	64,8 +/-29,8	0,239
Platelet count (/mm^3)	138045 +/-52970	91133+/- 40490	**0,004**
Spleen size (mm)	108,7 +/- 22,5	147,3 +/- 24,9	**0,000**
Platelet/Spleen size Ratio	1361,5+/- 591,7 0,96+/- 0,36	663,7+/381,7	**0,000**
AAR score	1,36 +/- ,82 3,83+/- 2,42	1,53+/- 0,47	**0,000**
APRI score	16,1 +/- 13,7	2,81+/- 2,33	**0,003**
Fib-4 score		8,98 +/- 4,70	**0,000**
Elasticity (Kpa)		33,7+/- 22,2	**0,002**
Speénomegaly	4(12,9%)	11(73,3%)	**0,000**

Liver stiffness was significantly higher in the " EV grade ≥ II" group (33.7 +/- 22.2 Kpa) than in the " EV grade <II" group (16.1 +/- 13.7 Kpa) (p = 0.002).

The comparison between these two groups shows a significant difference in biological scores such as Platelet / Spleen Size Ratio, AAR, APRI, and Fib-4 scores (p = 0.000 - 0.000 - 0.003 - 0.000 respectively), as well as other clinical and biological parameters detailed in Table 7.

The study of the ROC curve relating to the diagnosis of large EV (Figure 2), allowed us to determine a threshold value of detection of large EV by FibroScan® of the order of 14.45 Kpa with a sensitivity of 80%, a specificity of 61.3%, a positive predictive value (PPV) of 50% and a negative predictive value (NPV) of 86.4%, with an AUROC of 0.782 (95% CI ranged 0-1) and p = 0.002.

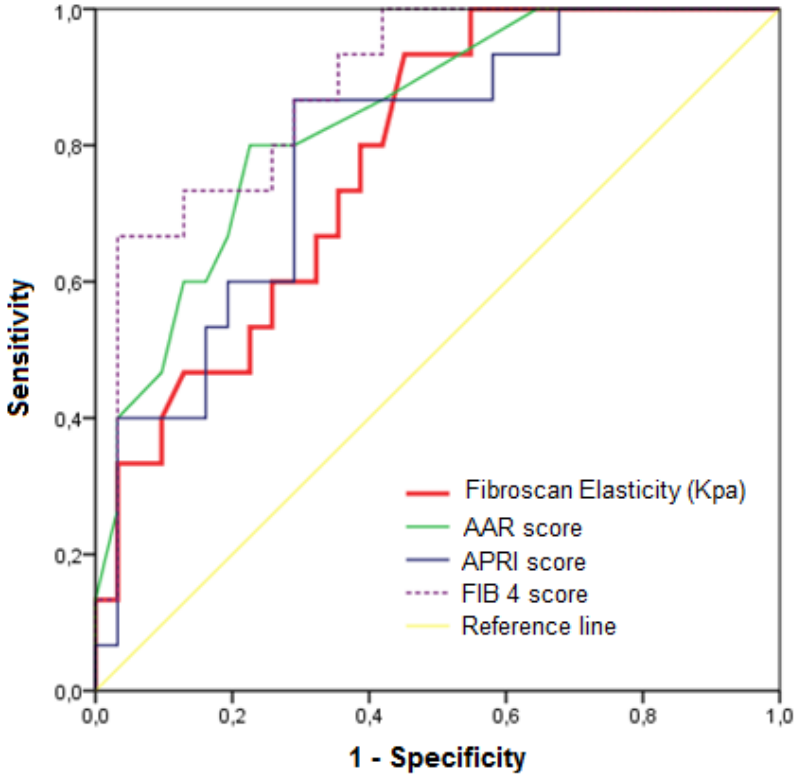

Figure 2: The ROC curve of the parameters: Elasticity, AAR, APRI, Fib-4 score (Criterion " EV grade ≥ II " versus' 'EV grade < II ").

The threshold values of the Fibroscan, AAR, APRI and Fib-4 scores in the detection of large EV are shown in Table 8.

Table 8: Threshold values predictive of the presence of large EV of the different non-invasive parameters studied.

Parameter	*AUROC*	*Cut-off*	*Sensibility*	*Specificity*	*PPV*	*NPV*
AAR score	**0,840**	≥ 1,15	80%	61%	-	-
APRI score	**0,794**	≥1,67	86,7%	71%	-	-
Fib-4 score	**0, 886**	≥5,39	73,3%	87,1%	-	-
Elasticity (Kpa)	0,782	≥14,45	80%	61%	50%	86,4%

III. Discussion

To date, several studies have been published concerning the non-invasive diagnosis of the presence of EV and large varices in cirrhotic patients [14-15-16-17-18-19-20-21-22-23- 24-25-26-27] and in particular in patients with viral cirrhosis C [10-11-22-28]. The reason for this effort is simple: the number of patients undergoing endoscopic screening for EV continues to increase due to the increasing mass of patients with chronic liver diseases [29-30].

This screening is repeated every 1 to 3 years, according to international recommendations, generates a huge cost with poor acceptability of patients sometimes leading to non-compliance with these screening protocols.

This is why there was a particular need for a parameter or a non-invasive tool allowing the diagnosis of EV but also the reduction of medical, social and economic costs.

The purpose of our prospective, monocentric study, carried out at the university hospital center in Fès, was to study in patients with viral cirrhosis C the relationship between the presence and the grade of EV, liver stiffness and certain biological parameters and scores of liver fibrosis.

In an EASL meta-analysis published in 2011 [31] and grouping 40 eligible studies concerning elastography performance for the diagnosis of fibrosis compared to liver biopsy, concluded that elastography theoretically has good sensitivity and specificity in the diagnosis of cirrhosis (but less for low degrees of fibrosis). However, it must be carefully applied in daily clinical practice because there is no validation of the elasticity threshold values corresponding to the different stages of fibrosis (F1 to F4 of METAVIR). Validation

of these threshold values is necessary before considering elastography sufficiently precise to determine the stage of liver fibrosis. Note that this meta-analysis included all the causes of liver cirrhosis.

However, in a study by Ziol M and Al. [32], liver stiffness has been shown to be strongly related to hepatic fibrosis assessed by liver biopsies. Realized in patients with chronic hepatitis C, it showed a strong correlation with the grade of fibrosis according to the METAVIR scoring system, and it allowed with high accuracy a non-invasive diagnosis of cirrhosis, these results were supported by the study realized by Castera L. and Al. [33].

Nevertheless, liver elastometry has limitations. The main one in practice is the impossibility of obtaining a measurement in about 5% of cases [12], especially in obese patients. In our series, we recorded a failure rate of 11.5%.

The study Kasemi and Al. [16] strongly suggested that liver stiffness measurement can predict the presence of EV especially large EV in cirrhotic patients. His study shows a threshold value of 13.9 Kpa (AUROC = 0.85, 95% CI = 0.78-0.90) for the diagnosis of the presence of EV with sensitivity = 95% and specificity = 43% and a threshold value of 19 Kpa (AUROC = 0.83, 95% CI = 0.76 - 0.89) for the diagnosis of EV grade ≥ II with sensitivity = 90% and

Specificity = 60%.

In the Vizzutti F and Al series [17], liver stiffness was correlated with the presence of EV (p = 0.002), however no correlation was found between EV size and liver stiffness. The AUROC for the prediction of the presence of the EV was 0.76 and the threshold value of the elasticity was 17.6 Kpa with a sensitivity of 90% and a NPV of 66%.

In the series of Pár G and Al. [26], liver stiffness values were significantly correlated with EV grade (r = 0.67, p <0.0001). The threshold value of 19.2 Kpa was highly predictive of the presence of EV (AUROC: 0.885, 95% CI: 0.81 - 0.96, sensitivity = 85%, specificity = 87%, PPV = 85%, NPV = 87%) and the presence of large varices (AUROC: 0.850, 95% CI: 0.754 - 0.94). In our serie, we also found a good correlation of liver stiffness compared to the results of endoscopy. Regarding the diagnosis of the presence of EV, the liver stiffness was higher in the group with EV than in the group without EV with averages of 29.5 +/- 19.6 Kpa and 8.8 +/- 4.4 Kpa respectively and a very significant p value (p = 0.000). The threshold value was 13.75 Kpa, with a sensitivity of 89.7%, a specificity of 82.4%, a PPV of 89.66% and a NPV of 82.35% ((AUROC = 0.92 95% CI: 0-1 and p = 0.000). The correlation was also good for the diagnosis of large varices, because the difference was statistically very significant between the "EV <II " group and "EV ≥ II" group (respectively 16.1 +/- 13.7 Kpa and 33.7 +/- 22.2 Kpa, p = 0.002). The threshold value greater than 14.45 Kpa was predictive of large varices with a sensitivity of 80%, a specificity of 61.3%, a PPV of 50% and a NPV of 86.4%, (AUROC = 0.782, 95% CI of 0-1 and p = 0.002). The cut-off values in our study were relatively low compared to previously reported studies (Table 9 and 10). This is probably due in part to the heterogeneity of the etiologies of cirrhosis in these studies, whereas in our study we only included patients with HCV-related liver cirrhosis.

Indeed, the difference in liver stiffness predictive of the presence of EV according to etiologies, was demonstrated by the study of I. Sporera [35] including 697 cirrhotic patients. The median elasticity values assessed by FibroScan® were significantly higher in cirrhotic patients with alcoholic etiology compared to those with a viral etiology: 41 Kpa vs 21.1 Kpa, p <0.0001. Any etiology combined, the value > 29.5 Kpa, had 77.5% sensitivity and 86.9% specificity to predict the presence of large varices (AUROC = 0.871). It amounts to 32.5 Kpa (AUROC = 0.836) in case of alcoholic cirrhosis, against 24.8 Kpa (AUROC = 0.867) for viral cirrhosis.

It is therefore necessary to compare our results with those of studies including HCV-related liver cirrhosis. Castera L. [20] in a study including 333 patients with HCV-related liver cirrhosis had determined a threshold value of 17.6 Kpa for the detection of EV (sensitivity (Ss) = 84%, specificity (Sp) = 61%, PPV = 57 % and NPV = 86%) and 21.5 Kpa for the diagnosis of large varices (Ss = 85%, Sp = 68%, PPV = 39% and NPV = 95%). The study of Y. SAAD and AL. [10] found threshold values of 29.7 Kpa for diagnosis of EV (Ss = 95% and Sp = 67%), and 38.2 Kpa for diagnosis of large EV (Ss = 100% and Sp = 77.3 %). Eman M. Hassan and Al. [11] selected a threshold value of 18.2 Kpa for the detection of EV (AUROC = 0.79, Ss = 82%, Sp = 73, PPV = 89% and NPV = 49%) and 22.4 Kpa for the diagnosis of large EV (AUROC = 0.801, Ss = 84%, Sp = 72%, PPV 84% and the NPV 72%).

In 2015, the consensus of Baveno VI [37] has stated that in patients with virus related compensated chronic liver diseases, non-invasive methods are sufficient to rule-in clinically significant portal hypertension, defining the group of patients at risk of having endoscopic signs of portal hypertension. The following can be used: liver stiffness by transient elastography ≥ 20-25 Kpa, at least two measurements on different days in fasting condition, alone or combined to platelets and spleen size. Our threshold values are still low, even when compared with studies of similar populations (Table 9 and 10). These are probably due to several reasons, including the willingness of previous authors to choose threshold values to maximize specificity at the expense

of sensitivity, the small number of patients included in our study and probably a peculiarity of Moroccan patients. Thus, studies with a large number of patients should be conducted to confirm or refute these results.

Table 9: Comparison between different studies in the diagnosis of the presence of EV by liver elastometry.

Study (year)	***N***	***Cause of cirrhosis***	***Cut off***	***AUROC (95% CI)***	***Ss (%)***	***Sp(%)***
Kasemi and AL. (2006) [17]	165	All causes	13,9	0,84 (0,78 – 0,90)	95	43
Vizzuti and Al. (2007) [19]	47	All causes	17,6	0,76 (0,60 – 0,87)	90	43
De Filippi and AL. (2011) [36]	127	All causes	14,3	0,80 (NA)	81 (PPV)	67 (NPV)
Castera and AL. (2009) [20]	333	Viral Cirrhosis C	17.6	0.84 (0.75–0.94)	84	61
Y. Saad and al (2013) [10]	32	Viral Cirrhosis C	29,7	NA	95%	67
Eman M. Hassan and al (2014) [11]	65	Viral Cirrhosis C	18,2	0.79 (NA)	82	73
Our study (2014)	***46***	viral Cirrhosis C	***13,75***	***0,92 (0,84- 0,99)***	***89,7***	***82,4***

NA: not available. PPV: positive predictive value. NPV: negative predictive value. Ss: sensibility. Sp: specificity.

Table 10: Comparison between different studies in the detection of large EV by liver elastometry.

Study (year)	***N***	***Cause of cirrhosis***	***Cut off***	***AUROC (95% CI)***	***Ss (%)***	***Sp (%)***
Kasemi and AL. (2006) [17]	165	All causes	19	0,83 (0,76 – 0,89)	90	60
Vizzuti and Al. (2007) [19]	47	All causes	17,6	NC	NC	NC
De Filippi and AL. (2011) [36]	127	All causes	22,1	0,72 (NA)	74 (PPV)	68 (NPV)
Castera and AL. (2009) [20]	333	Viral Cirrhosis C	21, 5	0.87 (0.77-0.97)	85	68
Y. Saad and al (2013) [10]	32	Viral Cirrhosis C	38,2	NA	100	77,3
Eman M. Hassan and al (2014) [11]	65	Viral Cirrhosis C	22,4	0,801 (NA)	84	72
Our study (2014)	**46**	Viral Cirrhosis C	**14,45**	**0,78 (0,65- 0,91)**	**80**	**61,3**

NA : not available. PPV : positive predictive value; NPV : negative predictive value, NC : no correlation. Ss ; sensibility. Sp : specificity.

IV. Conclusion

The results of our prospective study show that liver stiffness measurement by FibroScan® can predict the presence of EV in patients with HCV-related liver cirrhosis from a value of 13.75 Kpa and the presence of large EV from 14.5 Kpa. It may help in selecting patients for endoscopic screening. The difference between threshold values of elasticity between different studies could be explained in part by the difference in the etiologies of cirrhosis, by the preference of authors for more specific rather than sensitive values as well as by a probable peculiarity of Moroccan patients. Further studies with more patients should be conducted to support these results.

The authors disclose no conflict of interest.

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