Liver Stiffness Measurement Predicts Severe Portal Hypertension in Patients with HCV-Related Cirrhosis

Francesco Vizzutti,[1] Umberto Arena,[1] Roberto G. Romanelli,[1] Luigi Rega,[2] Marco Foschi,[1] Stefano Colagrande,[2] Antonio Petrarca,[1] Stefania Moscarella,[1] Giacomo Belli,[3] Anna Linda Zignego,[1] Fabio Marra,[1] Giacomo Laffi,[1] and Massimo Pinzani[1]

Measurement of hepatic venous pressure gradient (HVPG) is a standard method for the assessment of portal pressure and correlates with the occurrence of its complications. Liver stiffness measurement (LSM) has been proposed as a noninvasive technique for the prediction of the complications of cirrhosis. In this study, we evaluated the ability of LSM to predict severe portal hypertension compared with that of HVPG in 61 consecutive patients with HCV-related chronic liver disease. A strong relationship between LSM and HVPG measurements was found in the overall population ($r = 0.81$, $P < 0.0001$). However, although the correlation was excellent for HVPG values less than 10 or 12 mm Hg ($r = 0.81$, $P = 0.0003$ and $r = 0.91$, $P < 0.0001$, respectively), linear regression analysis was not optimal for HVPG values ≥10 mm Hg ($r^2 = 0.35$, $P < 0.0001$) or ≥12 mm Hg ($r^2 = 0.17$, $P = 0.02$). The AUROC for the prediction of HVPG ≥10 and ≥12 mm Hg were 0.99 and 0.92, respectively and at LSM cutoff values of 13.6 kPa and 17.6 kPa, sensitivity was 97% and 94%, respectively. In patients with cirrhosis, LSM positively correlated with the presence of esophageal varices ($P = 0.002$), although no correlation between LSM and esophageal varices size was detected. The area under the ROC for the prediction of EV was 0.76 and at a LSM cutoff value of 17.6 kPa sensitivity was 90%. *Conclusion:* LSM represents a non-invasive tool for the identification of chronic liver disease patients with clinically significant or severe portal hypertension and could be employed for screening patients to be subjected to standard investigations including upper GI endoscopy and hemodynamic studies. (HEPATOLOGY 2007;45:1290-1297.)

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Measurement of the hepatic venous pressure gradient (HVPG), currently employed for the evaluation of portal hypertension, has been suggested as a reliable end-point to assess the therapeutic benefit of antiviral therapy in patients with advanced hepatic fibrosis due to chronic HCV infection.[1] This suggestion is based on two assumptions: (1) portal hypertension is a direct consequence of the fibrotic transformation of liver tissue, therefore HVPG provides a dynamic assessment of disease progression, and (2) HVPG reflects the status of a significant portion of the liver and it is not prone to sampling error as in the case of liver biopsy. In addiction, considering the relative contraindications of percutaneous liver biopsy in patients with advanced fibrosis or cirrhosis, measurement of HVPG could represent a valuable method to evaluate disease progression in this group of patients. Conversely, HVPG measurements is invasive, relatively expensive, and available only in major centers, indicating the need to develop reliable, non-invasive, and widely available methods.

Transient elastography has been introduced as a rapid and non-invasive technique that measures liver tissue stiffness.[2] Cohort studies have investigated its potential use for the prediction of hepatic fibrosis stage in patients with HCV-related chronic hepatitis.[3,4] A recent study has

Abbreviations: HVPG, hepatic venous pressure gradient; LSM, liver stiffness measurement; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating characteristic; LR, likelihood ratio.

From the [1]Dipartimento di Medicina Interna, Center for Research, Higher Education and Transfer DENOThe; the [2]Dipiartimento di Fisiopatologia Clinica Sezione di Radiodiagnostica; and [4]S.O.D. Fisica Sanitaria Università degli Studi di Firenze/Azienda Ospedaliero Universitaria Careggi, Firenze, Italy.

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Address reprint requests to: Prof. Massimo Pinzani, M.D., Ph.D., Dipartimento di Medicina Interna, Viale G.B. Morgagni, 85, 50134 Firenze, Italy. E-mail: m.pinzani@dmi.unifi.it; fax: (39) 055-417123.

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proposed the use of transient elastography for the detection of cirrhosis and prediction of related complications including the presence of esophageal varices and variceal bleeding.[5] In addition, another recent study has proposed that liver stiffness measurement (LSM) is able to predict the presence of large esophageal varices and could be useful for selecting patients for endoscopic evaluation.[6] The possibility that transient elastography could serve as a non-invasive alternative to HVPG is also suggested by the study by Carrion and co-workers performed in patients with HCV recurrence after liver transplantation.[7] However, to what extent this assumption is valid for patients with advanced fibrosis or cirrhosis who did not undergo liver transplantation is unknown.

The aim of the current study was to evaluate the diagnostic accuracy of transient elastography compared with that of HVPG measurement, used as a gold standard for the assessment of portal hypertension, in a group of patients with HCV-related chronic liver disease with advanced fibrotic evolution.

Patients and Methods

Patients. Sixty-one consecutive patients (39 men and 22 women, mean age 55.6 ± 11.7; age range 32-75 years) with chronic HCV infection underwent HVPG measurement between March 1, 2005 and July 1, 2006 upon referral to the Hemodynamic Laboratory of our Institution. All patients had previous histopathological evidence of cirrhosis (METAVIR F4)[8] or a diagnosis of cirrhosis suspected on the basis of standard clinical, ultrasonographic, and biochemical parameters. These patients were subjected to the hemodynamic study to obtain a basal assessment of portal pressure before starting a prophylactic treatment with beta-blockers (primary prophylaxis, n = 31) or to confirm the diagnosis of cirrhosis (n = 30). In this latter group of patients, a transjugular liver biopsy was performed. All specimens were characterized by a length > 2.5 cm and included more that 11 portal tracts. Histopathological analysis confirmed the diagnosis of cirrhosis in 16 patients (METAVIR F4) and revealed the presence of advanced fibrosis in 14 patients (METAVIR F3). Exclusion criteria were a body mass index ≥35, the presence of ascites at clinical or ultrasound examinations, the presence of other overt complications of cirrhosis including cardiopulmonary and renal involvement, hepatocellular carcinoma, transaminases >10 upper limit of normal, ongoing antiviral therapy, co-infection with HBV and/or human immunodeficiency virus, active infectious diseases other than HCV, any alcohol intake within the 6 months preceding the study, previous derivative treatments for portal hypertension, concomitant pre-sinusoidal and extrahepatic causes of portal hypertension, use of vasoactive drugs including beta-blockers, diuretics, and anti-inflammatory drugs, age younger than 18 or older than 75 years, and pregnancy. In each patient, all experimental procedures were performed on the same study day. In all patients but one, an upper GI endoscopy was performed on the following day. Laboratory tests, including serum bilirubin, albumin, ammonia, creatinine, blood urea nitrogen, aminotransferase (AST, ALT) levels, platelet count, and international normalized ratio, were performed in all patients within 1 week from the study beginning. The study protocol was approved by the Investigation and Ethics Committee of the Azienda Ospedaliero Universitaria Careggi, Firenze. The nature of the study was explained to the patients, each of whom provided written informed consent before the beginning of the study, in accordance with the principles of the Declaration of Helsinki (revision of Edinburgh, 2000).

Transient Elastography. After an overnight fasting, patients underwent a complete upper abdomen ultrasound examination. Immediately after, transient elastography was performed using the FibroScan® apparatus (Echosens, Paris, France), which consists of a 5-MHz ultrasound transducer probe mounted on the axis of a vibrator. Mild amplitude and low-frequency vibrations (50 Hz) are transmitted to the liver tissue, inducing an elastic shear wave that propagates through the underlying liver tissue. The velocity of the wave is directly related to tissue stiffness. The tip of the transducer was covered with a drop of gel and placed perpendicularly in the intercostal space with the patient lying in dorsal decubitus position with the right arm in the maximal abduction. Under control TM and A-mode, the operator choose a liver portion within the right liver lobe at least 6 cm thick, free of large vascular structures and gallbladder.[3,4] Stiffness was measured on a cylinder of hepatic tissue of 1 cm of diameter and 2 to 4 cm of length. The operator was a staff physician (U.A.) who had previously performed at least 100 determinations in patients with chronic liver disease. The median value of 10 successful acquisitions, expressed in kilopascal (kPa), was kept as representative of the LSM. As previously described in the literature[4,7] and as suggested by the provider of the instrumentation, we considered representative measurements 10 successful acquisitions with a success rate of at least 60%, and with an interquartile range lower than 20.

Measurements of HVPG and Transjugular Liver Biopsy. Immediately after undergoing LSM, the patients were transferred to the Hepatic Hemodynamic Laboratory. With the patient under local anesthesia, a venous introducer was placed in the right internal jugular vein by the Seldinger technique. A 7 French balloon-tipped cath-

Table 1. Clinical and Laboratory Findings in the Study Population

Variable		All Patients (n = 61)	F4 (n = 47)	F3 (n = 14)	F4 Versus F3
Age, y		55.6 ± 11.7	57.8 ± 10.9	48 ± 11.4	$P = 0.002$
Male gender, n (%)		39 (64%)	30 (63.8%)	9 (64.2%)	P = NS
BMI, kg/m^2		23 ± 3	22 ± 3.6	24 ± 3.1	P = NS
Ex-drinker, n		5	5	0	-
Creatinine, mg/dl		0.94 ± 0.28	0.96 ± 0.31	0.86 ± 0.11	P = NS
Bilirubin, mg/dl		1.34 ± 0.83	1.47 ± 0.89	0.92 ± 0.37	$P = 0.01$
Albumin, g/dl		3.58 ± 0.76	3.33 ± 0.67	4.43 ± 0.33	$P < 0.0001$
Platelet count, 10^9/l		127 ± 64	107 ± 48	193 ± 66	$P < 0.0001$
INR		1.22 ± 0.47	1.32 ± 1.08	1.20 ± 0.18	P = NS
AST, U/l		61 ± 23.51	65.64 ± 20.87	52.17 ± 15.39	$P = 0.04$
ALT, U/l		72 ± 17.87	71 ± 20.56	75 ± 15.75	P = NS
Child-Pugh	A		28 (59.57%)		
	B		14 (29.79%)		
	C		5 (10.64%)		
Esophageal varices	Absent		16 (34.1%)		
	Small		12 (25.5%)		
	Large		18 (38.2%)		
	ND		1 (2.2%)		
GOV and IGV			5 (10.64%)		
PHG			26 (55.3%)		
	Moderate		18 (38.3%)		
	Severe		8 (17%)		
Variceal bleeding history		0			

NOTE. Results are expressed as mean ± SD.

Abbreviations: BMI, body mass index; MAP, mean arterial pressure; CRP, C-reactive protein; INR, international normalized ratio; AST, aspartate aminotransferases; ALT, alanine aminotransferases; GOV, gastric esophageal varices; IGV, isolated gastric varices; PHG, portal hypertensive gastropathy; ND, not done; NS, not significant.

eter (Medi-Tech Boston Scientific Cork, Cork, Ireland) was guided into the right hepatic vein for measurement of wedged and free hepatic venous pressures. Adequacy of occlusion was checked by injection of a small amount of radiological contrast medium. The portal pressure gradient was measured as the HVPG, in other words, the difference between wedged and free hepatic venous pressures.[9] All measurements were performed at least in triplicate, and permanent tracings were obtained on a multi-channel recorder (PowerLab; ADI Instruments, Milford, MA).[10] Hemodynamic studies, evaluation, and assessment of pressure tracing were performed by an experienced operator (F.V.) unaware of the results of transient elastography. Clinically significant portal hypertension was defined as an HVPG ≥10 mm Hg according a consensus definition.[11] For transjugular liver biopsy, a 16G needle (Cook, Bjaverskov, Denmark) connected to a 20-mL syringe was introduced 2 to 4 cm within the liver tissue while aspirating. This procedure was repeated up to 5 times until an optimal tissue sample was obtained. Tissue samples, processed and stained with hematoxylin-eosin and Masson's trichromic, were scored by an expert pathologist unaware of the condition of the patient and of the study protocol. Necroinflammatory activity and fibrosis stage were scored according to the METAVIR scoring system.[8]

Statistical Analysis. Statistical analysis was carried out using the STATA Statistical Software Release 9.0 for Windows (STATA Corp., College Station, TX). All results are expressed as mean ± standard deviation (SD). The unpaired Student *t* test was applied for comparisons of normally distributed variables. The statistical significance of inter-group differences, for non-normal distributed data, were evaluated by means of Kruskall-Wallis or Wilcoxon rank-sum (Mann-Whitney) tests. Spearman rank correlation coefficient was used when appropriate. Linear regression analyses were calculated according to the least squared methods. *P* values less than 0.05 were considered statistically significant. The relationship between sensitivity and specificity of LSM at different cutoff points, as predictor of patients with HVPG ≥10 mm Hg or patients with HVPG ≥12 mm Hg, and finally of patients with esophageal varices, was evaluated by receiver operating characteristic (ROC) curves.[12] Optimal liver stiffness cutoff values were selected on the basis of sensitivity, specificity, positive and negative predictive values (NPV and PPV, respectively), positive and negative likelihood ratios (+LR and −LR, respectively).

Results

Characteristics of Patients. The major clinical and biochemical parameters of the patients included in the study are listed in Table 1. Among the 47 patients with

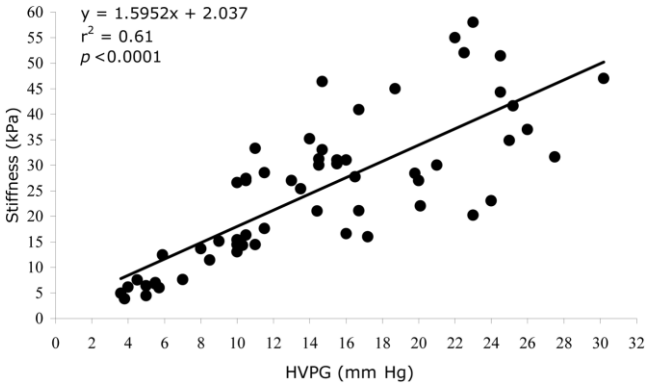

Fig. 1. Linear regression analysis between HVPG and LSM in whole patient population. Abbreviations: HVPG, hepatic vein pressure gradient; kPa, kilopascal.

previous or confirmed diagnosis of cirrhosis, 28 (59.57%) were classified as Child-Pugh class A, 14 (29.79%) as Child-Pugh class B, and 5 (10.64%) as Child-Pugh class C. Considering the whole population, six patients (9.83%) had no portal hypertension (i.e., HVPG ≤5 mm Hg), 8 patients (13.11%) had a pre-clinical portal hypertension (i.e., HVPG more than 5 but less than 10 mm Hg), 47 patients (77.05%) had a clinically significant portal hypertension (i.e., HVPG ≥10 mm Hg), of whom 35 (57.38%) had severe portal hypertension (i.e., HVPG ≥12 mm Hg).[13-17] Twelve patients were listed in the HVPG range ≥10 <12 mm Hg (19.67%). Esophageal varices were present in 30 of 47 patients with cirrhosis, gastroesophageal varices in 4, isolated gastric varices in 1, and moderate to severe portal hypertensive gastropathy in 26. At the time of the study no patient with cirrhosis showed clinical features of clinical decompensation (encephalopathy, recent gastrointestinal bleeding, ascites, or peripheral edema), or ultrasonographic evidence of HCC and portal vein thrombosis. Patients with cirrhosis showed significantly higher HVPG and liver stiffness when compared with patients with advanced liver fibrosis ($P < 0.0001$ and $P < 0.0001$, respectively). The success rate of liver stiffness measurements was 90.22% ± 14.72%, and the mean interquartile range 3.45 ± 3.

Relationship Between HVPG and LSM. Considering the whole patient population, a statistically significant, positive correlation between HVPG and LSM was found ($r = 0.81$, $P < 0.0001$). Figure 1 illustrates linear regression analysis between HVPG and LSM performed in the complete study population ($r^2 = 0.61$, $P < 0.0001$). In patients with HVPG <10 mm Hg or <12 mm Hg there was a statistically significant correlation with LSM ($r = 0.81$, $P = 0.0003$ and $r = 0.91$, $P < 0.0001$, respectively). Liver stiffness was significantly higher in patients with an HVPG ≥10 and ≥12 mm Hg than in patients with an HVPG <10 ($P < 0.0001$) and <12 mm Hg ($P < 0.0001$), respectively. Moreover, a positive correlation also existed in patients with HVPG ≥10 mm Hg and, although less relevant, in patients with HVPG ≥12 mm Hg ($r = 0.59$, $P < 0.0001$ and $r = 0.37$, $P = 0.03$, respectively). Figure 2 illustrates linear regression analysis in the different subgroups of HVPG. Noteworthy, when patients with an HVPG value ≥12 mm Hg were considered, the correlation with LSM hardly reached statistical significance, with very poor r values.

Non-invasive Prediction of Clinically Significant Portal Hypertension (i.e., HVPG ≥10 mm Hg) and Severe Portal Hypertension (i.e., HVPG ≥12 mm Hg). Figure 3 shows the ROC curve of LSM for the prediction of clinically significant portal hypertension

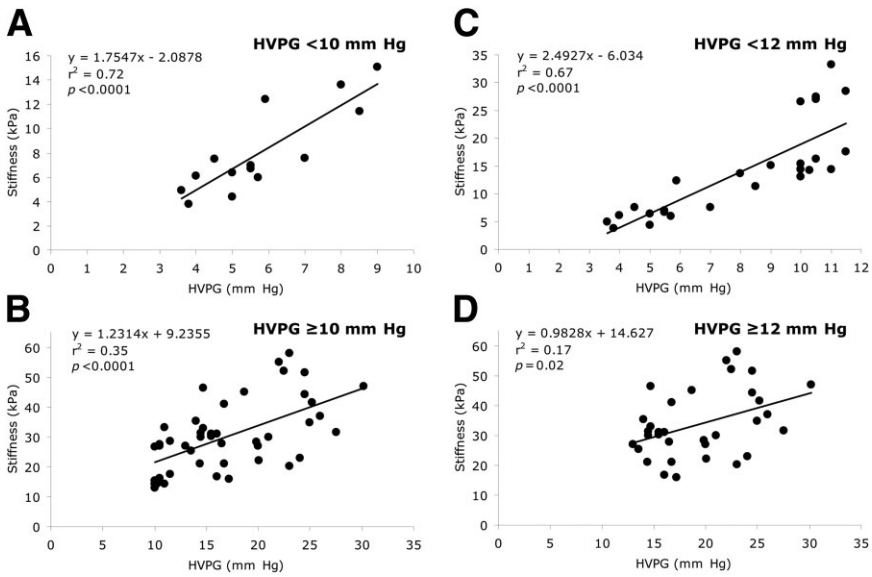

Fig. 2. Linear regression analysis between LSM (kPa) and different degrees of HVPG (mm Hg). (A) Regression values for HVPG <10 mm Hg and panel B for HVPG ≥10 mm Hg ($r^2 = 0.72$, $P < 0.0001$ and $r^2 = 0.35$, $P < 0.0001$, respectively). (C) Regression analysis for HVPG <12 mm Hg and (D) for HVPG ≥12 mm Hg ($r^2 = 0.67$, $P < 0.0001$ and $r^2 = 0.17$, $P = 0.02$, respectively). Between 10 and 12 mm Hg some scattering of values from the theoretical regression line (C) was observed. This became clearly evident for HVPG values ≥12 mm Hg (panel D). Abbreviations: HVPG, hepatic vein pressure gradient; kPa, kilopascal.

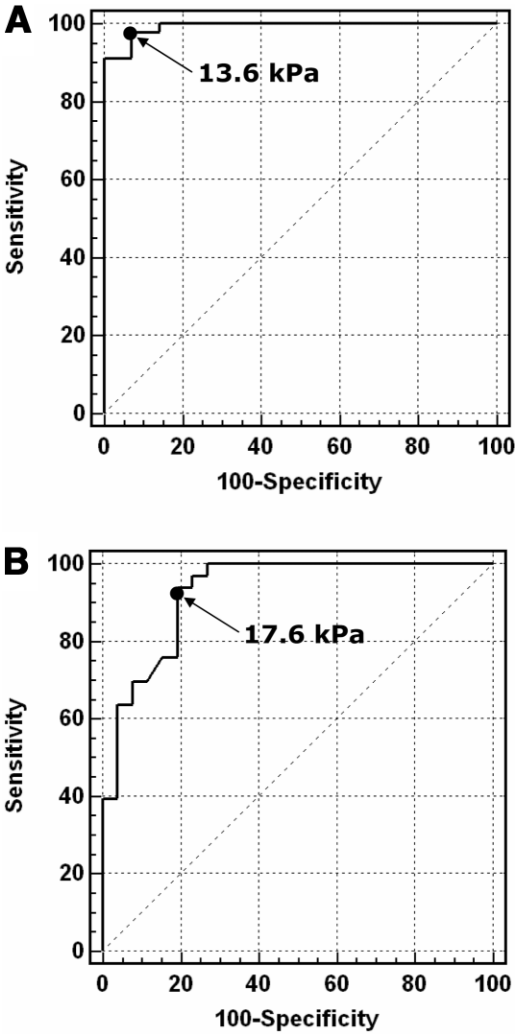

Fig. 3. Receiver operating characteristic curve showing the prediction of clinical significant portal hypertension (*i.e.*, HVPG ≥10 mm Hg; A) and severe portal hypertension (*i.e.*, HVPG ≥12 mm Hg; B) with transient elastography in the whole patient population. The ideal area under the curve is 1.00. The straight line represents that based on chance alone (area under the curve 0.50). The area under the ROC curves were 0.99 (0.01 standard error; 95% confidence index 0.92-0.99) and 0.92 (0.03 standard error; 95% confidence index 0.82-0.97), respectively.

and severe portal hypertension. The areas under ROC curves were 0.99 ± 0.01 and 0.92 ± 0.03, respectively. Based on ROC curves, different cutoff values for LSM were determined. A LSM ≥13.6 kPa had a NPV of 92% with a sensitivity of 97% for the prediction of patients with HVPG ≥10 mm Hg. A LSM ≥17.6 kPa had an NPV of 91% with a sensitivity of 94% for the prediction of patients with HVPG ≥12 mm Hg. Table 2 summarizes the best results for PPV, NPV, +LR, and −LR at different LSM cutoff values.

Only 1 (7.69%) of 13 patients with LSM below 13.6 kPa, had clinically significant portal hypertension (i.e., HVPG ≥10 mm Hg) and had no varices at endoscopy; 2 (9.09%) of 22 patients with LSM below 17.6 kPa had

Table 2. Diagnostic Accuracy of Transient Elastography

	S	Sp	PPV	NPV	+LR	-LR
HVPG ≥10 mmHg						
≥13.6 kPa *	97%	92%	97%	92%	13.69	0.02
≥14.3 kPa	95%	93%	97%	76%	13.38	0.05
HVPG ≥12 mmHg						
≥17.6 kPa *	94%	81%	86%	91%	4.88	0.08
≥16.3 kPa	97%	77%	84%	95%	4.20	0.04
EV						
≥17.6 kPa *	90%	43%	77%	66%	1.58	0.23
≥27.4 kPa	70%	78%	90%	55%	3.27	0.28

NOTE. Diagnostic accuracy of transient elastography to predict HVPG ≥ 10 mmHg, HVPG ≥ 12 mmHg, and esophageal varices. Performance of different LSM cutoff values for diagnosis of clinically significant, severe portal hypertension and esophageal varices.

Abbreviations: S, sensitivity; Sp, specificity; PPV, positive predictive value; NPV, negative predictive value; HVPG, hepatic vein pressure gradient; +LR, positive likelihood ratio; -LR, negative likelihood ratio; HVPG, hepatic venous pressure gradient; EV, esophageal varices.

*Best LSM cutoff values chosen.

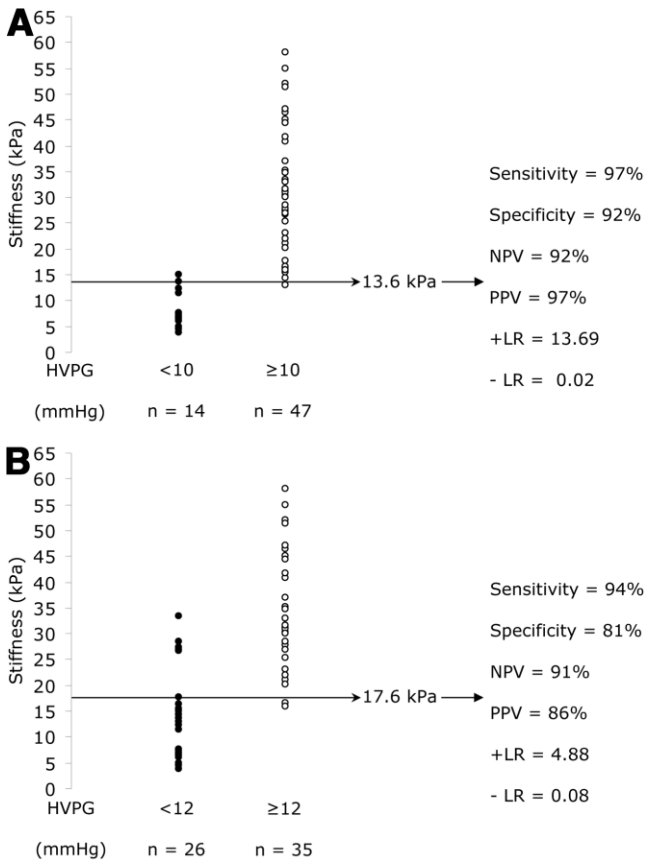

Fig. 4. Relationship between HVPG (≥10 mm Hg, A; ≥12 mm Hg, B) and LSM. HVPG is shown in the X-axis in mm Hg (number of patients in parenthesis) and liver stiffness in Y-axis in kPa. Optimal LSM cutoff values are indicated with a line. Abbreviations: HVPG, hepatic vein pressure gradient; kPa, kilopascal; NPV, negative predictive value; PPV, positive predictive value; +LR, positive likelihood ratio; −LR, negative likelihood ratio.

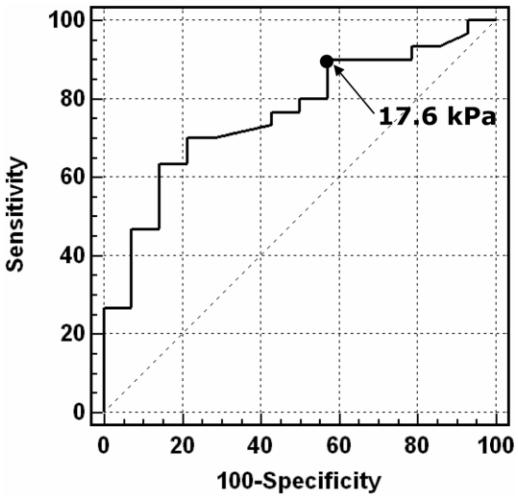

Fig. 5. Receiver operating characteristic curve showing the prediction of esophageal varices with transient elastography in patients with cirrhosis. The ideal area under the curve is 1.00. The straight line represents that based on chance alone (area under the curve, 0.50). The air under the ROC curves was 0.76 (0.07 standard error; 95% confidence index 0.60-0.87).

severe portal hypertension (HVPG ≥12 mm Hg), and only 1 of them had small esophageal varices. Importantly, none of the few false-negative cases had large esophageal varices. Figure 4 illustrates the distribution of LSM values according to the presence or absence of clinical significant/severe portal hypertension.

Relationship Between LSM and Endoscopic Signs of Portal Hypertension. Liver stiffness positively correlated with the presence of esophageal varices by Wilcoxon rank-sum test ($P = 0.002$). No correlation between LSM and the size of esophageal varices (small, F1, or large, F2-F3) was found by Kruskall-Wallis test (chi-squared = NS). No esophageal varices, gastroesophageal varices, and isolated gastric varices were observed in patients with a LSM value below 14.4 kPa.

Non-invasive Prediction of Esophageal Varices. Figure 5 shows the ROC curve of LSM for the prediction of esophageal varices in patients with cirrhosis. The area under the ROC curve was 0.76 ± 0.07. Based on the ROC curve, different cutoff values for LSM were determined. A LSM ≥ 17.6 kPa, identical to the cutoff predicting the presence of severe portal hypertension, had a NPV of 66% with a sensitivity of 90% for the prediction of varices in patients with cirrhosis. Table 2 summarizes the best results for PPV, NPV, and +LR, −LR, at different LSM cutoff values. Importantly, only 3 of 8 patients (37.5%) with LSM below 17.6 kPa had esophageal varices, classified as small at upper GI endoscopy. The 95% confidence interval for +LR ranged from 0.98 to 2.52, indicating the absence of a statistically significant capability of identifying the presence of varices.

Complications Related to the Procedures. Two patients experienced a self-limiting supraventricular arrhythmia during the hemodynamic study. No complications were associated with the execution of transient elastography.

Discussion

The measure of disease progression represents a key challenge in any of the different stages of chronic liver disease. Indeed, a correct and reliable measure of the stage of the disease has relevant implications for assessing the effectiveness of the current therapeutic regimens and predicting the occurrence of complications. Accordingly, a current major effort is directed at evaluating minimally invasive procedures to be employed to substitute or integrate the standard invasive methods, that is, liver biopsy or the measurement of HVPG.

The cirrhotic transformation of the liver is associated with structural and biological changes responsible for an increase in portal pressure.[18,19] These include major angio-architectural modifications involving neo-angiogenesis and the presence of cell types undergoing active contraction in response to an intra-hepatic predominance of vasoconstrictor stimuli.[20,21] As a result, the progressive rise in portal pressure represents a reliable indicator of the tissue changes and, to a certain extent, of the biological microenvironment typical of fibrotic and cirrhotic liver. These remarkable changes are also characterized by a progressive increase in liver tissue stiffness attributable to the accumulation of fibrillar extracellular matrix. It is therefore conceivable that this latter parameter may also reflect these changes, although with much less biological accuracy.

In agreement with this hypothesis, the results of the current study show that a highly significant relationship exists between LSM, measured by transient elastography, and portal pressure in a population of patients chronically infected by HCV at stages of fibrotic evolution ranging from F3 to F4.

The threshold value of the HVPG for the formation of varices is 10 mm Hg, whereas 12 mm Hg is the threshold for the appearance of other complications, such as variceal bleeding and ascites.[13-17] In addition, as recently reported in patients with compensated cirrhosis, an HVPG level ≥10 mm Hg represents a reliable predictor of clinical decompensation in a median follow-up of 4 years.[22] Interestingly, an HVPG value of 10 to 12 mm Hg appears to be a key determinant in the relationship between HVPG and LSM. Indeed, the correlation between the two parameters seems optimal for HVPG values ≤10 and ≤12 mm Hg, whereas it hardly reaches statistical significance for values ≥12 mm Hg. This important observation sug-

gests that beyond a certain degree of portal pressure, *i.e.*, ≥10 to 12 mm Hg, the development of portal hypertension becomes at least partially independent from the simple accumulation of fibrillar extracellular matrix responsible for the increase in liver tissue stiffness. Indeed, in advanced cirrhosis several extrahepatic factors such as the hyperdynamic circulation, the splanchnic vasodilatation, and the resistance opposed to portal blood flow by the portosystemic collaterals contribute to the rise in portal pressure.[9,19] It is also likely that, beyond a certain degree of cirrhotic transformation of liver tissue, the measure of liver stiffness does not reflect the changes in liver angio-architecture and the active contraction of scar tissue secondary to the predominance of vasoconstrictors. All together, these factors constitute important mechanistic variables that can independently affect portal pressure with a different impact in different patients.

With a cutoff of LSM ≥13.6 kPa, NPV and PPV for the diagnosis of clinically significant portal hypertension (*i.e.,* HVPG ≥10 mm Hg) were 92% and 97%, respectively. This observation is in agreement with previous reports indicating cutoff values of 12.5 kPa and 14.5 kPa for the diagnosis of liver cirrhosis.[3,4,7] Moreover, the presence of severe portal hypertension (*i.e.,* HVPG ≥12 mm Hg) could be suspected when a cutoff value ≥17.6 kPa is reached, with NPV and PPV of 91% and 86%, respectively. This cutoff value for the presence of HVPG ≥12 mm Hg is in agreement with that preliminarily reported by Lemoine and co-workers (17 kPa) in a mixed population of HCV and alcoholic patients with cirrhosis.[23] These results suggest that transient elastography could represent a methodology for identifying patients with HVPG values compatible with the development of portal hypertension–related complications to be subjected to further investigations including upper GI endoscopy and hemodynamic studies. However, these results need to be validated in larger populations, especially in those patients with body mass index > 30 kg/m^2, in which LSM reproducibility could not be optimal.

An additional important finding is the relation between LSM and the presence of esophageal varices. Although LSM positively correlated with the presence of esophageal varices, using a cutoff value of stiffness ≥17.6 kPa, NPV and PPV for the detection of varices were 66% and 77%, respectively, which are far from being satisfactory. Moreover, this study failed to demonstrate a correlation between LSM and variceal size, in disagreement with the recent study performed by Kazemi and co-workers in a larger series of patients with cirrhosis.[9] However, the cutoff value for the presence of large varices reported by these authors (19 kPa) is characterized by low specificity of the prediction that makes it difficult to be reliably employed in clinical practice.[24] Considering these observations and the importance of assessing the endoscopic features of varices for predicting bleeding risk,[25] it is not advisable, at this time, to suggest transient elastography as a surrogate of upper GI endoscopy.

A collateral observation of this study is the excellent correlation between LSM and HVPG values <10 mm Hg. Although this correlation needs to be further substantiated in a large cohort of patients, it may have implications for the clinical assessment of patients at stages of evolution of chronic liver disease preceding the development of clinically significant portal hypertension. This is in agreement with the study of Carrion and co-workers, performed in patients with HCV recurrence after liver transplantation.[7] Indeed, no reliable non-invasive surrogate methods are available for the follow-up of patients with advanced fibrosis before the occurrence of clinically significant portal hypertension. In this context, transient elastography could be useful in differentiating stages of the progressive cirrhotic evolution of liver tissue once the histological stage of cirrhosis has been reached. To address this point, the results of the current study need to be further confirmed in larger populations and in specifically designed studies.

In summary, we suggest that measurement of liver stiffness by transient elastography may represent a reliable non-invasive methodology for the prediction of clinically significant and severe portal hypertension, although not good enough to replace endoscopy for the detection of varices.

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