



## ORIGINAL RESEARCH

## Utility of Splenic Elastography as a Predictor of Increased Portal Pressure in Patients with Liver Cirrhosis

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### Summary

**Objective:** Determine the use of splenic elastography in patients with cirrhosis and to correlate tissue hardness values with the increase in the portosystemic pressure gradient.

**Materials and methods:** A comparative cross-sectional study was carried out in which (n = 12) adult patients over 18-years of old with a confirmed diagnosis of liver cirrhosis who had a portosystemic pressure gradient measurement recently performed by the Interventional Radiology area of our institution, regardless of the sex or age group, a comparative analysis was carried out with a similar group similar in number of non-cirrhotic patients (n = 10). The data collected were analyzed using the statistical program IBM SPSS Statistics 23.0®.

**Results:** The mean of the elastography results in cirrhotic patients was  $12.2 \pm 7.7$  (3.9-25.11) kPa, while in the controls the mean was  $8.4 \pm 2.4$  (6.2-13.11) kPa with a p value  $\leq 0.001$ , we obtain that the best cut-off point for elastography is the 50<sup>th</sup> percentile, corresponds to 7.3 kPa.

**Conclusions:** Splenic elastography is a rapid, accessible, cheap and safe method that provides good diagnostic performance to identify patients with an increase in the portosystemic pressure.

### Introduction

Elastography is a relatively new diagnostic method used to evaluate the stiffness of soft tissues. Its use is based on the conclusion that tissue with pathological changes tends to be harder and less elastic than the tissue that surrounds them [1]. It is currently considered

a promising tool in the last decade for the evaluation of patients with chronic liver disease [2]. Liver elastography is a widely used and accepted method to predict the severity and prognosis of the disease [3].

Liver elastography measures fibrosis and has been correlated with the portosystemic pressure gradient, which is also related to intrahepatic vascular resistance [3].

Splenic elastography is currently being studied as a predictor of increased portal pressure even without clear clinical or ultrasound data of portal hypertension. The hardness of the spleen measured in kiloPascals (kPa) in healthy patients is  $17.3 \pm 2.6$  kPa, greater than the liver hardness 4.4 kPa, and the increase in splenic hardness can help predict the risk of esophageal varices as well as the risk of bleeding from the same, establishing a correlation with the results of patients with proven and confirmed portal hypertension with the portosystemic pressure gradient [4].

Portal hypertension is a common clinical syndrome and is defined as a pathological increase in portal venous pressure. This increase causes that the pressure between the inferior vena cava and the portal vein (known as portal perfusion pressure of the liver or portal pressure gradient) increases above the normal value (1-5 mmHg) [5].

The portosystemic pressure gradient through hepatic vein catheterization is currently considered the

“gold standard” for determining portal pressure [6]. It is calculated as the difference between the hepatic vein wedge pressure and the free pressure of the hepatic veins. The wedge pressure is calculated by occluding a main hepatic vein; stopping the flow creates a static column of blood that transmits the pressure present in the preceding vascular territory (in this case the hepatic sinusoid) which reflects the portal pressure. The hepatic vein is occluded by placing the catheter in a small branch of the hepatic vein or by inflating a balloon at the tip of the catheter (this one is the most commonly used method). Wedge pressure measurement has been shown to provide a very accurate estimate of portal pressure in alcoholic and viral cirrhosis [5].

Free hepatic pressure is the measure of the pressure in an unoccluded hepatic vein. Since the portosystemic pressure gradient reflects portal pressure, changes in said gradient reflect the factors that determine portal pressure, hepatic vascular resistance, collateral and portal resistance to flow [6].

It has been shown that values of 10 mmHg of the portosystemic pressure gradient or greater are necessary for the formation of esophageal varices, therefore it is considered clinically significant portal hypertension. It has also been associated with a higher incidence of decompensation in cirrhotic patients with compensated disease, without varicose veins [7]. With values above

12 mmHg there is a greater risk of variceal bleeding and values greater than 20 mmHg have been used to predict failure in response to medical and endoscopic treatment to treat variceal haemorrhage [6].

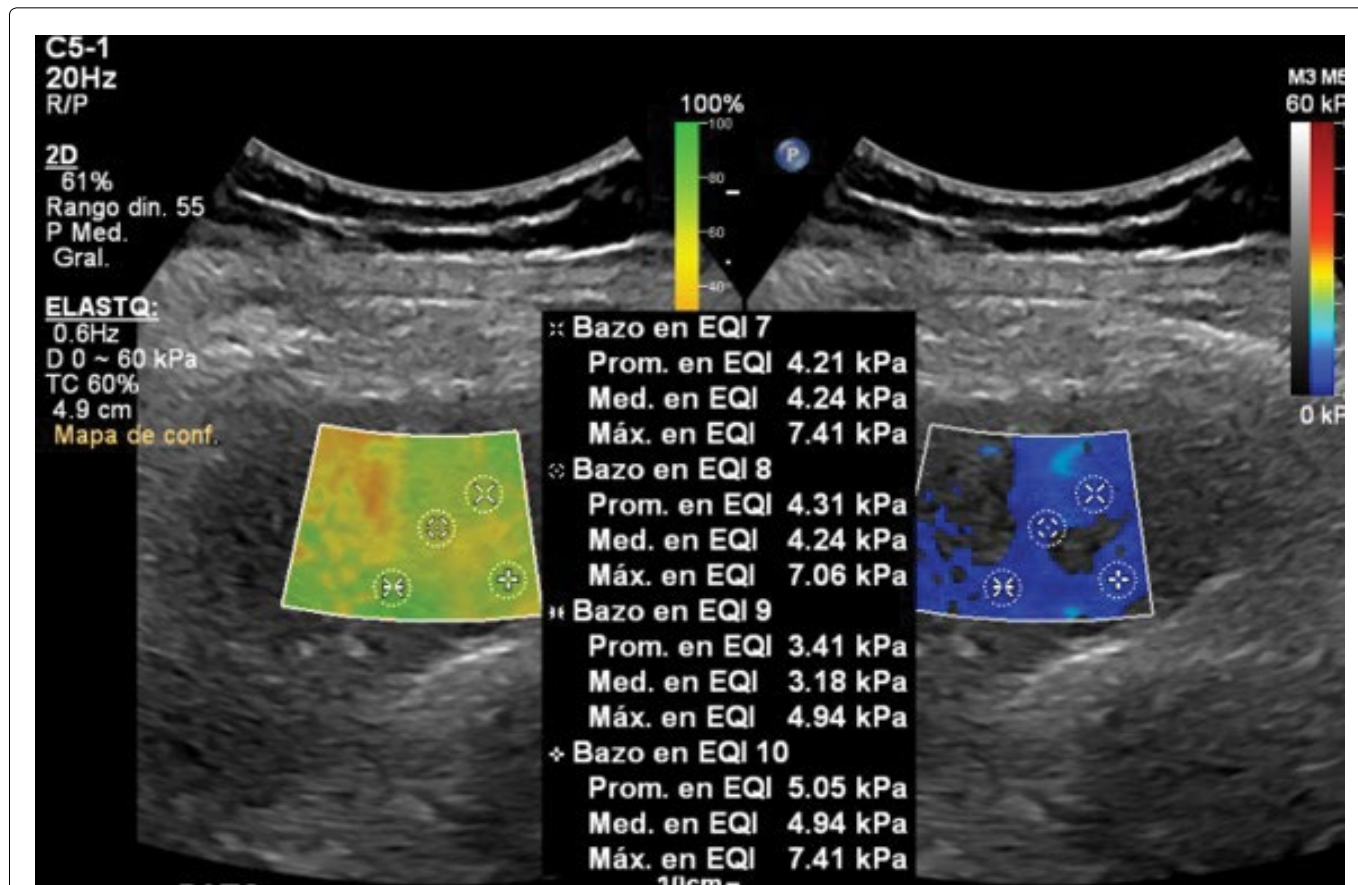
The objective of this study is to determine the use of splenic elastography in patients with cirrhosis and to correlate tissue hardness values with the increase in the portosystemic pressure gradient.

## Materials and Methods

A comparative cross-sectional study was carried out in which (n = 12) adult patients over 18-years of old with a confirmed diagnosis of liver cirrhosis due to any etiology who, at the time of evaluation by elastography, had a portosystemic pressure gradient measurement recently performed by the Interventional Radiology area of our institution, regardless of the sex or age group, a comparative analysis was carried out with a group similar in number of non-cirrhotic patients (n = 10).

Ethical approval for this study was granted by the Medical Research Ethics Committee of our institution, and informed consent was obtained from all the patients.

All ultrasound examination were performed on a Philips Epiq 7G ultrasound with a 2D shear wave elastography (2DSWE) using a curved probe of 5 to 7



**Figure 1:** Elastography in a control patient (healthy), the image on the left shows in green the stability of the image which should be as close as possible to 100%, the image on the right measures the stiffness (which is represented on a scale of colors, being blue not hard and scarlet red very hard), observing the scanned sample in blue.

MHz (Megahertz), measurements were made using the EFSUMB 2017 guidelines for the clinical use of elastography [8-10], through an intercostal space in supine position with left arm extended for splenic evaluation, holding the breath and preventing deep inspiration with a minimum of 10 measurements and each made at least 10 mm under the capsule, with an IQR less than 30%, with a minimum of 2 hours of fasting prior to the exam (Figure 1 and Figure 2).

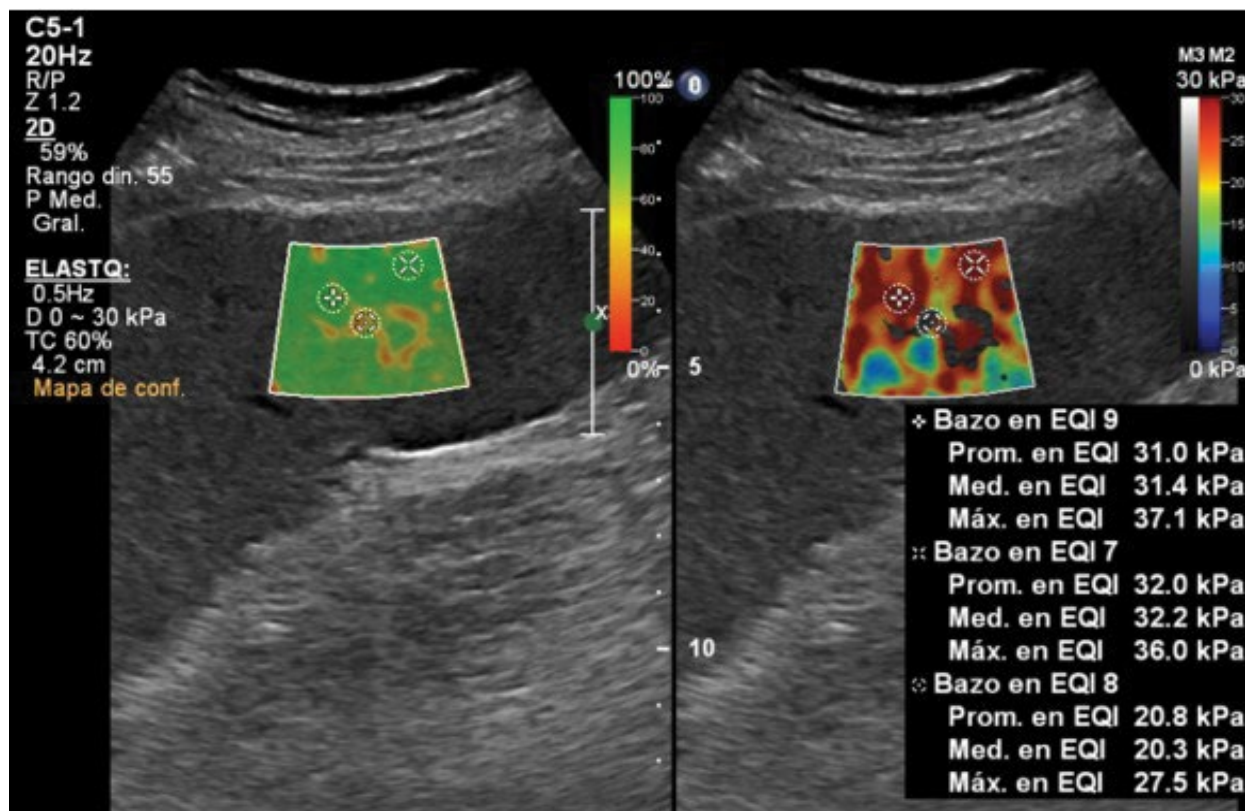
The data collected were analyzed using the statistical program IBM SPSS Statistics 23.0<sup>®</sup>. Descriptive statistics were obtained, to compare the mean between the elastography values between controls and patients, the T-student test was used. The value as a diagnostic test of elastography with respect to the portosystemic pressure gradient was calculated using sensitivity, specificity, positive predictive value, negative predictive value, ROC curves and diagnostic precision indexes (accuracy index and Youden index) with a 95% confidence intervals, different cut-off points were tested by using the percentiles of the controls as a reference. The calculation of the Pearson correlation between the patient's elastography results and the portosystemic pressure gradient was also performed.

## Results

The mean of the elastography results in cirrhotic

patients was  $12.2 \pm 7.7$  (3.9-25.11) kPa, while in the controls the mean was  $8.4 \pm 2.4$  (6.2-13.11) kPa. The other variable studied was the portal-systemic pressure gradient, which had a mean of  $10 \pm 3.8$  (5-15) mmHg. With these variables, a student T test was performed between the elastography values in controls vs. patients, finding a statistically significant difference ( $p$  value < 0.001) as can be seen in Figure 3, so we can say that the values in kPa of the patients are significantly higher than those in the controls. A correlation was sought between elastography in kPa and the pressure gradient in mmHg without finding statistical significance.

Using the data from the controls, the percentiles of the elastography results were determined and then tested as alternative cut-off points to determine the diagnostic test values, the ROC curves, the accuracy index and the Youden index, with which we obtain that the best cut-off point for elastography is the 50<sup>th</sup> percentile, which corresponds to 7.3 kPa, so above this it was considered positive and below it as negative, while the porto-systemic pressure gradient was considered as the cut-off point. above 5 mmHg; With these values, the sensitivity was 88.9%, a specificity of 50%, a positive predictive value of 88.9%, a negative predictive value of 50%, an LR+ of 1.77, an LR- of 0.22, an accuracy index of 0.75 and Youden index 0 (Figure 4).



**Figure 2:** Elastography image in a patient with cirrhosis, the image on the left shows in green the stability of the image which should be as close as possible to 100%, the image on the right measures the stiffness (which is represented on a scale of colors, blue being not hard and scarlet red being very hard), showing in red the highest stiffness on which the ROI (Region of Interest) is placed.

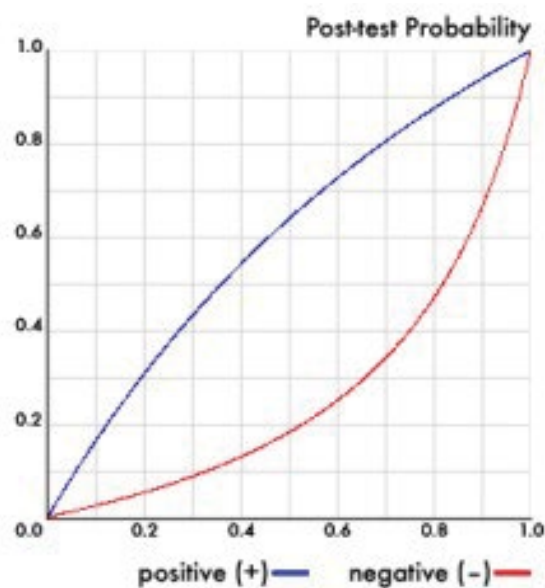


	N	Media	Standard Deviation
ELASTOGRAPHY (Kpa) IN PATIENTS	12	12.2088	7.74406
ELASTOGRAPHY (Kpa) IN CONTROLS	10	8.4491	2.41477

	t	Ig	Sig. (bilateral)	Mena Difference	95% confidence interval of difference	
					Inferior	Superior
ELASTOGRAPHY (Kpa) IN PATIENTS	5.461	11	.000	12.20883	7.2885	17.1292
ELASTOGRAPHY (Kpa) IN CONTROLS	11.065	9	.000	8.44910	6.7217	10.1765

**Figure 3:** Student T test between patients vs. controls with the mean in Kpa of the elastography results. \*p value < 0.05.

	Estimate	95% CI
<b>Sensitivity</b>	0.889	[0.565 to 0.98]
<b>Specificity</b>	0.5	[0.095 to 0.905]
<b>PPV</b>	0.889	[0.565 to 0.98]
<b>NPV</b>	0.5	[0.095 to 0.905]
<b>LR+</b>	1.778	[0.436 to 7.246]
<b>LR-</b>	0.222	[0.022 to 2.238]



**Figure 4:** Diagnostic test results using the 50<sup>th</sup> percentile of elastography in kPa as a cut-off point and a cut-off point of > 5 mmHg of the portosystemic pressure gradient. Accuracy index of 0.75, Youden index 0.3 and diagnostic Odds ratio of 32.

## Discussion

Splenic elastography is a technique that has recently been evaluated to identify the risk of bleeding from esophageal varices, portal hypertension, or splenic fibrosis. In the case of patients with liver cirrhosis, measuring the portosystemic pressure gradient in mmHg is the most specific method for diagnosis, but its measurement requires invasive methods, so elastography is therefore a non-invasive method that can be used. Use as an alternative. We found that there

is no significant correlation between the elastography values and those of the portosystemic pressure gradient, but we find that the elastography values in kilopascals are significantly higher in patients compared to controls, which had already been demonstrated in other studies even with other methods such as Fibrosan, and by doing an evaluation we determined that if we use a cut-off point of 7.3 kPa we can differentiate with acceptable sensitivity patients with a high portosystemic pressure gradient but with little

specificity. In other studies to determine the risk of variceal bleeding and portal hypertension, higher cut-off points were determined between 25 and 36 kPa, so we suggest that this parameter may depend on the type of population studied. We also suggest using splenic elastography as a first approach that helps us determine which patients require a more in-depth evaluation with an invasive method.

Regarding the cut-off point, this was determined using two parameters, the Youden index, which was not acceptable since it was not less than 0.5. This index allows us to measure the effectiveness of the test since it adds those misclassified by the test as a measure. Overall performance but it is not recommended to use it isolated, so we also calculate the accuracy index that gives us an idea in what proportion of cases the diagnostic test is not wrong, found to be 75% (which is quite acceptable).

Splenic elastography is a rapid, accessible, cheap and safe method that provides good diagnostic performance to identify patients with an increase in the portosystemic pressure. More studies need to be carried out with a larger sample of patients, as well as in other populations including patients who have already presented variceal bleeding to continue adjusting these parameters.

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### Conflict of Interest

The authors declare that they have no conflict of interest.

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