Utility of ElastPQ point-shear wave elastography in the work-up of patients with primary sclerosing cholangitis

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LSM ElastPQ was significantly correlated with MELD (Spearman's rho 0.46, p<0.001), PSC Mayo risk score (Spearman's rho 0.65, p=0.003) and Oxford-Amsterdam score (Spearman's rho 0.57, p<0.001). The highest correlation coefficient for Mayo risk score was significantly better than the correlation coefficient for MELD (p=0.014). No statistically significant difference was found between the correlation coefficients of PSC Mayo risk and Oxford-Amsterdam scores (p=0.29). A positive and significant correlation was found between LSM ElastPQ and serum bilirubin (Spearman's rho 0.61, p<0.001), alkaline phosphatase (ALP) (Spearman's rho 0.47, p<0.001), ALT (Spearman's rho 0.47, p<0.001) and AST (Spearman's rho 0.64, p<0.001) levels.

There was no statistically significant difference between the correlations of ElastPQ and those of F-TE with the prognostic scores and serum markers of inflammation and cholestasis (Table S1).

Table S1. Correlation between liver elastography, prognostic scores and serum markers of inflammation and cholestasis (Spearman's rank correlation coefficient used; p≤0.05 represents the significance level).

		MELD	**PSC Mayo RS**	**Oxford-Amsterdam score**	**ALT**	**AST**	**Bilirubin**	**ALP**
F-TE	*rho*	0.392	0.649	0.568	0.494	0.655	0.587	0.476
	P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
ElastPQ LSM (median)	*rho*	0.455	0.651	0.574	0.470	0.643	0.608	0.468
	P	<0.001	0.003	<0.001	<0.001	<0.001	<0.001	<0.001
ElastPQ SSM (median)	*rho*	0.295	0.364	0.451	0.193	0.328	0.237	0.228
	P	0.002	<0.001	<0.001	0.044	<0.001	0.013	0.017

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; MELD, model of end-stage liver disease; PSC, primary sclerosing cholangitis; RS, risk score; F-TE, liver transient elastography performed with FibroScan; LSM, liver stiffness measurement; SSM, spleen stiffness measurement.

A difference of LSM ≥2 kPa between F-TE and ElastPQ was found in 33 patient (22%). On the univariate analysis, variables significantly associated with a LSM difference ≥2 kPa were the Mayo risk score, total bilirubin, ALT, AST, ALP, platelet count and the presence of cirrhosis. On the binary logistic regression analysis, the diagnosis of liver cirrhosis (as defined by F-TE values) was the only independent predictor (OR 9.87, 95%CI 3.35-29.10, P<0.001) (Table S2). The results did not change with a LSM difference ≥5 and ≥10 kPa.

Table S2. Factors associated with a difference of ≥ 2 kPa between liver stiffness measured by F-TE and ElastPQ (Student's, Mann-Withney and Chi-square tests used; p≤0.05 represents the significance level).

	Univariate			**Multivariate**		
	F-TE - ElastPQ liver < 2 kPa (119)	**F-TE - ElastPQ liver ≥2 kPa (33)**	**P value**	**OR**	**95% CI**	**P value**
PSC Mayo RS	-0.46 (1.22)	0.34 (1.49)	<0.001	1.28	0.73-2.27	0.392
MELD score	7 (3)	7 (4)	0.611			
Small duct PSC, n/n (%)	17/119 (14.3)	2/33 (6.1)	0.251			
Age, years	46 ± 16	49 ± 16	0.501			
Gender, female n/n (%)	46/119 (39)	13/33 (39)	0.546			
Bilirubin (mg/dL)	0.58 (1.0)	0.94 (0.8)	0.009	0.94	0.75-1.17	0.570
ALT (IU/L)	45 (73)	78 (68)	<0.001	1	0.99-1.01	0.507
AST (IU/L)	37 (55)	67 (60)	<0.001	1	0.99-1.01	0.507
ALP (IU/L)	145 (256)	222 (193)	0.147			
Platelets/mmc	255 (129)	200 (142)	0.023	0.99	0.98-1.01	0.625
Cirrhosis (F-TE = F4), n/n (%)	22/119 (18)	25/33 (76)	<0.001	9.87	3.38-28.88	<0.001

Numerical variables are expressed as median (IQR) or mean ± SD according to distribution, dichotomous variables are expressed as n (%).

F-TE, liver transient elastography performed with FibroScan; kPa, kilopascal; OR, odd ratio; CI, confidence interval; PSC, primary sclerosing cholangitis; RS, risk score; MELD, model of end-stage liver disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; IQR, interquartile range; SD, standard deviation.

The factors potentially associated with the presence of OVs were investigated in the subgroup of 35 patients who underwent an UGIE within 12 months from the date of the elastographic assessment. Eighteen patients had OVs, with only two patients having varices at high-risk of bleeding (HRVs). The differences in clinical, biochemical and elastographic parameters between the groups of patients with and without OVs are shown in Table S3. In particular, median values of F-TE, ElastPQ LSM, ElastPQ SSM and LSPS were significantly higher in patients with OVs compared to those without ($p<0.001$).

Table S3. Comparison between patients with and patients without oesophageal varices (Mann-Withney and Chi-square tests used; $p\leq0.05$ represents the significance level).

	No OVs	**OVs**	**P value**
PSC Mayo RS	-0.27 (1.43)	1.06 (1.5)	<0.001
Child-Pugh score	5.0 (0)	7 (3)	<0.001
MELD score	7.01 (3)	12.46 (7)	<0.001
Spleen area, cm2	55 (56)	87 (55)	0.040
Spleen LD, cm	12 (4.4)	16 (4.3)	0.007
Bilirubin mg/dL	0.9 (1.2)	3.0 (5.5)	<0.001
AST (IU/L)	70 (60)	81 (71)	0.045
ALP (IU/L)	256 (292)	210 (243)	0.566

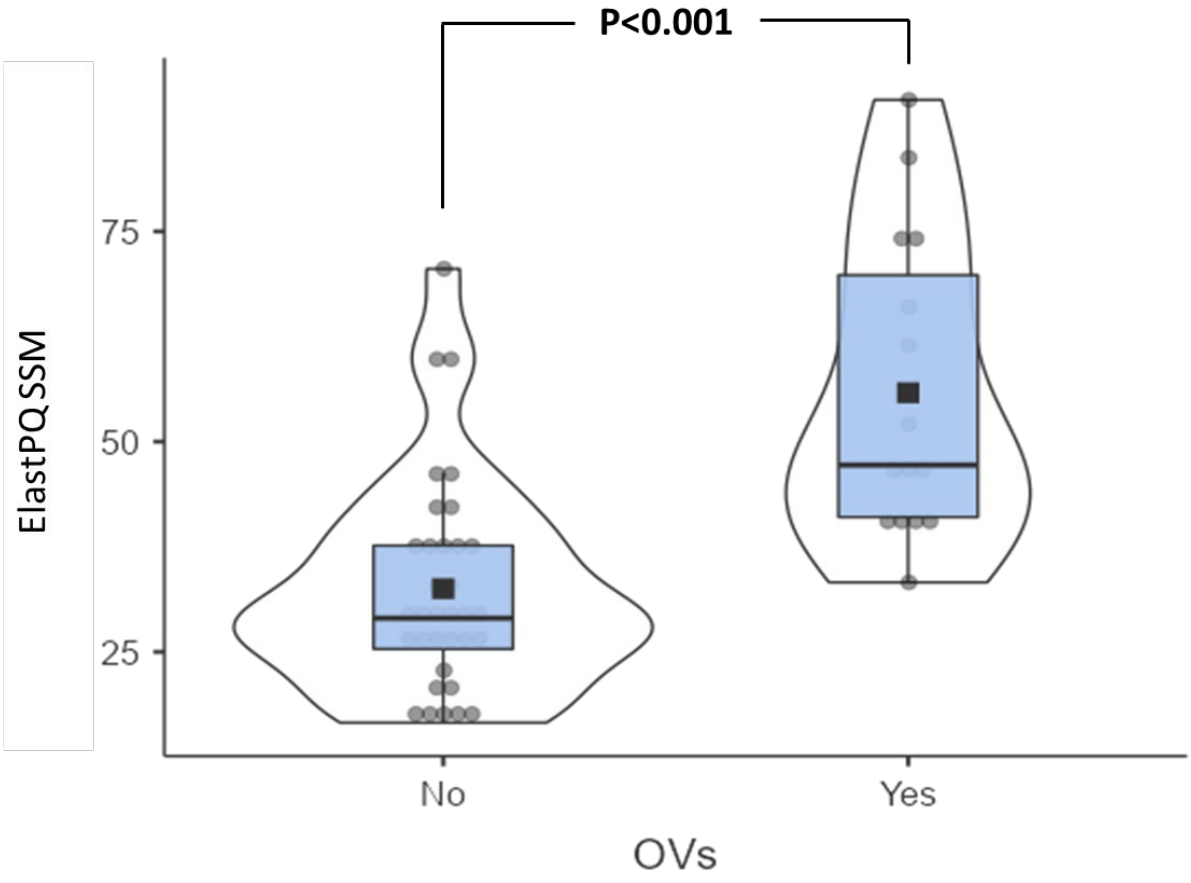
Platelets/mmc	254 (483)	102 (138)	0.001
Albumin g/dL	4.3 (0.6)	3.4 (0.9)	0.001
INR	1 (0.1)	1.2 (0.8)	<0.001
F-TE LSM, kPa	12 (22.2)	46.5 (44.5)	<0.001
ElastPQ LSM, kPa	12 (14.1)	39.8 (28)	<0.001
ElastPQ SSM, kPa	31.6 (14.1)	51.8 (26.5)	<0.001
LSPS	0.61 (2.1)	6.3 (12.6)	<0.001

Values are expressed as median (IQR) or mean ± SD, according to distribution.

OVs, oesophageal varices; PSC, primary sclerosing cholangitis; RS, risk score; MELD, model of end-stage liver disease; LD, longitudinal diameter; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; INR, international normalized ratio; F-TE, liver transient elastography performed with FibroScan; kPa, kilopascal; LSM, liver stiffness measurement; SSM, spleen stiffness measurement.; LSPS, liver stiffness x platelet count to spleen length ratio.

ElastPQ SSM was the only independent predictor of the presence of OVs on multivariate analysis (OR 1.14; CI 1.02-1.27; p=0.021), regardless of whether the Mayo risk score, MELD or Child-Pugh score was included in the model as indicator of liver disease severity (Figure S1).

Figure S1. Violin Plots. Difference in the median values of ElastPQ spleen stiffness between patients with and without oesophageal varices. Black squares represent the mean value; black bars represent the median value; the upper and lower edges of the boxes represent the interquartile range. The gray dots represent the members of the population. The thin gray lines represent the rest of the distribution, except for points that are determined to be outliers. On each side of the gray line is a kernel density estimation to show the distribution shape of the data. Wider sections of the violin plot represent a higher probability that members of the population will take on the given value; the skinnier sections represent a lower probability (Mann-Withney test used; p-value ≤0.05 represents the significance level).



SSM, spleen stiffness measurement; OVs, oesophageal varices