Comparison of point-shear wave elastography (ElastPQ) and FibroScan for liver fibrosis staging in patients with NAFLD

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Ethical Approval Statement

According to the law and the national ethical guidelines of our country, we did not require an ethical approval as this was a retrospective study and categorized as an audit.

Authorship Statement

- **Davide Roccarina** is the author who is acting as the submission's guarantor.
- **Davide Roccarina** designed the study, collected the data, performed the analysis and wrote the manuscript.
  Laura Iogna Prat, **Giada Pallini**, **Anna Mantovani** and **Francesco Marcello Arico'** collected the data and reviewed the manuscript.
  Marta Guerrero Misas contributed to the design of the study and reviewed the manuscript.
  Matteo Rosselli reviewed the manuscript and improved the English.
  Atul Goyale and **Evangelia Koutli** contributed to the collection of the data and reviewed the manuscript.
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- All authors approved the final version of the manuscript.

Conflict of Interest Statement

All authors disclose any potential sources of conflict of interest.

Data Sharing and Data Accessibility Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ABSTRACT

Background and aims:

ElastPQ is a point shear wave elastography (pSWE) technique used to non-invasively assess liver fibrosis. We compared liver stiffness measurements (LSM) by ElastPQ and Fibroscan Transient Elastography (F-TE) in a cohort of patients with non-alcoholic fatty liver disease (NAFLD). We further evaluated the performance of ElastPQ in a subgroup of patients with available liver histology.

Materials and Methods:

We included patients with NAFLD who presented in a dedicated multidisciplinary clinic. Anthropometric parameters, blood tests and elastography measurements were obtained using F-TE and ElastPQ as part of routine clinical care.

Results:

We enrolled 671 patients with NAFLD, mean age 55.8±13 years, BMI 31.5±5.7 kg/m^2, 56.6% males, 41% diabetes, 53.7% hypertension, 68% dyslipidaemia. ElastPQ showed an excellent correlation with F-TE (Spearman's r=0.80, p<0.001), which was better for mild/moderate stages of fibrosis. Independent predictors of a >2kPa discrepancy between the two techniques were a larger waist circumference and F-TE ≥10 kPa. In the subgroup of 159 patients with available histology, ElastPQ showed similar diagnostic accuracy with F-TE in staging liver fibrosis (ElastPQ AUCs 0.83, 0.84, 0.88 and 0.96, for F≥1, F≥2, F≥3 and F=4, respectively). Optimal cut-off values of ElastPQ for individual fibrosis stages were lower than those of F-TE.

Conclusions:

ElastPQ shows an excellent correlation with F-TE in patients with NAFLD, which was better for lower LSM. The optimal cut-off values of ElastPQ are lower than those of F-TE

for individual stages of fibrosis. ElastPQ has similar diagnostic accuracy to F-TE for all stages of fibrosis.

LAY SUMMARY: ElastPQ is a point shear wave elastography (pSWE) technique used to non-invasively assess liver fibrosis. We evaluated the diagnostic accuracy of ElastPQ for detecting liver fibrosis compared to F-TE (Fibroscan Transient Elastography) in a cohort of patients affected by non-alcoholic fatty liver disease (NAFLD). Our results showed that ElastPQ has an excellent correlation with F-TE and a similar diagnostic accuracy for all stages of fibrosis.

ABBREVIATIONS:

- NAFLD, Non-alcoholic fatty liver disease;
- NAFL, Non-alcoholic fatty liver;
- NASH, Non-alcoholic steatohepatitis;
- HCC, Hepatocellular carcinoma;
- SWE, Shear-wave elastography;
- TE, Transient elastography;
- ARFI, Acoustic radiation force impulse;
- 2D, 2-dimensional;
- 3D, 3-dimensional;
- F-TE, Fibroscan Transient Elastography;
- LSM, Liver stiffness measurement;
- IQR, Interquartile range;
- ALT, Alanine aminotransferase;
- ULN, Upper limit of normal;
- SD, Standard deviation;
- CCC, Concordance correlation coefficient;
- ROC, Receiver operating characteristic;
- AUROC, Area under ROC;
- BMI, Body Mass Index;

- OR, Odd ratio;
- CI, Confidence interval;
- WC, Waist circumference;
- KPa, kilopascal;
- AST, Aspartate aminotransferase;
- ALP, Alkaline phosphatase;
- GGT, Gamma-glutamil transpeptidase;
- AUC, Area under the curve
- LS, Liver stiffness;
- cACLD, compensated advanced chronic liver disease.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is characterised by excessive accumulation of fat in the liver, usually associated with insulin resistance, and defined by the presence of liver fat content in ≥5% of hepatocytes (1). It is often associated with presence of the metabolic syndrome and its components, which also increase the risk of more severe and advanced disease. NAFLD encompasses a spectrum of liver disease that ranges from the relatively benign non-alcoholic fatty liver (NAFL) to non-alcoholic steatohepatitis (NASH) that can lead to fibrosis, cirrhosis and hepatocellular carcinoma (HCC) (2).

Liver fibrosis staging represents one of the most significant prognostic factors for the occurrence of liver-related complications (3). Liver biopsy remains the reference standard for the assessment of fibrosis, despite its limitations which include cost, invasiveness, sampling variability and potential of serious adverse events (4). All these limitations have steered research to develop non-invasive tests based on serum markers or imaging methods (5, 6). Imaging methods are based on elastography principles and assess the tissue reaction to an acoustic or mechanical deformation. There are different techniques depending on the applied force, how the tissue reaction is shown (displayed or measured) and the type of assessment (qualitative and/or quantitative).

Shear wave elastography (SWE) techniques are based on shear waves generated by a stress which can be externally applied by pushing the skin with the tip of the FibroScan probe (transient elastography, TE) or made directly into the liver by the push pulse of the ultrasound beam (acoustic radiation force impulse, ARFI) either in a small and fixed region of interest (point SWE, pSWE) or along several ARFI lines providing a colour

velocity/elasticity map of the analysed tissue (2-dimensional and 3-dimensional SWE, 2D-SWE and 3D-SWE, respectively) (7).

TE with FibroScan (F-TE) was the first available technique and subsequently the best validated in multicentre trials and meta-analyses. However, current guidelines mention that all SWE techniques (TE and ARFI-based) can be used as first line tools for the assessment for liver fibrosis (8).

ElastPQ is an ARFI-based pSWE technique with preliminary data suggesting a good diagnostic accuracy in staging fibrosis (9, 10)(11).

Our first aim was to compare liver stiffness values measured by both ElastPQ and F-TE in a cohort of patients with NAFLD. Our second aim was to assess the diagnostic accuracy of ElastPQ for staging fibrosis in a subgroup of patients with available liver histology.

PATIENTS AND METHODS

In this retrospective cross-sectional study, we included patients who attended the NAFLD clinic of the Royal Free Hospital (London, UK) from November 2014 to January 2020 and had liver stiffness measurement (LSM) as part of their routine clinical care. All included patients underwent LSM using ElastPQ performed with the Affiniti70G® US system (Philips, The Netherlands) and F-TE with FibroScan® 502 Touch (Echosens, France).

The inclusion criteria were: NAFLD diagnosis according to the EASL guidelines (2), a valid F-TE (10 valid measurements with an interquartile range (IQR)/median≤30%) and a valid ElastPQ (10 valid measurements with an IQR/median≤30%), both performed on

the same day. Patients with a daily alcohol consumption ≥30 gr in males and 20 gr in female, alanine-aminotransferase (ALT) >5 Upper Limit of Normal (ULN), heart failure or with co-existing aetiologies of liver disease were excluded.

Patients were scanned after fasting for at least 4 hours and in a supine position, after 10 minutes of rest. ElastPQ measurements were performed by a single expert operator (DR), following the recommended procedure for ARFI-based techniques (8). A median value of 10 measurements was recorded for each patient. LSMs with F-TE were performed after ElastPQ measurements by the same single operator (DR), under ultrasound guidance and following the methodology reported in the literature (12). Examinations were carried out with either the M or the XL probe, according to the automated machine recommendation. Patients had their routine blood tests on the same day of the liver stiffness assessment.

In the subgroup of patients with available histology, we considered liver biopsies performed within 12 months of the non-invasive assessment. Fibrosis was staged according to the Brunt classification system by a single expert liver pathologist (TVL) (13).

Statistical analysis

Test of normality was used to assess the distribution of quantitative variables. When quantitative variables were normally distributed, results were expressed as mean values and standard deviation (SD), otherwise the median and IQR were reported. Qualitative variables were expressed as counts and percentages. The correlation between quantitative variables was assessed by Spearman's and Pearson's tests and Lin's

concordance correlation coefficient (CCC), which can be expressed as the product of Pearson's r (the measure of precision) and the bias-correction factor (Cb, as measure of accuracy). CCC ranges in values from 0 to +1. Agreement was classified as poor (0.00–0.20), fair (0.21–0.40), moderate (0.41–0.60), good (0.61–0.80) or excellent (0.81–1.00). The agreement between two quantitative variables was also evaluated by the Bland–Altman plot analysis, with 95% limits of agreement defined as the mean difference ± 1.96 SD of differences.

The correlation between quantitative and qualitative variables was assessed using parametric tests (Student's or ANOVA) or non-parametric tests (Mann-Whitney or Kruskal-Wallis) if the quantitative variable was normally or not normally distributed, respectively.

Predictors were assessed with a multivariate analysis using the binary logistic regression model and the factors retained in the final multivariate model were chosen based on univariate analysis and clinical knowledge. Potential multicollinearity between variables was checked by Spearman's rank correlation coefficient.

The diagnostic performance of ElastPQ for staging liver fibrosis was assessed by receiver operating characteristic (ROC) curves and the area under the ROC (AUROC) curve analysis. The optimal ElastPQ cut-off values were chosen maximising the sum of sensitivity and specificity.

$P<0.05$ was considered statistically significant. All tests were two-sided. The data analysis was performed with SPSS (version 24, IBM, New York, NY, USA) and MedCalc (Software for Windows, Version 14.8.1, Ostend, Belgium).

RESULTS

Baseline characteristics

Overall, 671 patients (380 males; mean age 55.8±13.1 years) were included. The baseline characteristics of the cohort are presented in Table 1. LSMs with ElastPQ were available in all patients and successful in 96% (645), while LSMs with F-TE were available in 653 patients and successful in 99% (647) (p=0.618). Measurements performed with both ElastPQ and F-TE were available in 621 patients. Significant predictors of ElastPQ LSM failure were higher body mass index (BMI) (odd ratio (OR) 1.14, 95% confidence interval (CI) 1.04-1.26, p=0.005) and larger waist circumference (WC) (OR 1.05, 95% CI 1.02-1.08, p<0.001). No significant predictors were found for F-TE LSM failure. The F-TE XL probe was used in 271 patients (41.6%). One hundred fifty-nine (24%) patients had a liver biopsy performed within 12 months of the LSM assessment.

Correlation of LSM using ElastPQ and F-TE

The median values of liver stiffness of the whole population measured by ElastPQ and F-TE were statistically different (5.6 kiloPascal (kPa) vs. 6.3 kPa, respectively, p=0.001). The correlation between ElastPQ and F-TE was excellent (Spearman's r=0.804, p<0.001; Lin's CCC 0.878, 95% CI 0.859-0.895, Pearson precision 0.881, bias correction 0.996) (Figure 1). This was further confirmed by the Bland-Altman plot analysis, which showed that 98% of the differences in LSM between ElastPQ and F-TE were inside the 95% agreement limits. Those outside of these limits were mainly represented by patients with high liver stiffness values (Figure 2).

One hundred forty-eight patients (23.8%), of whom 73 (49%) had a F-TE of >10 kPa, had a difference of LSM between F-TE and ElastPQ ≥2 kPa. On multivariate analysis, independent predictors of such a difference were larger WC (OR 1.018, 95% CI 1.00-1.04, p=0.024) and F-TE ≥10 kPa (OR 7.30, 95% CI 4.43-12.02, p<0.001) (Table 2).

Diagnostic accuracy of ElastPQ for staging fibrosis

In the subpopulation of 159 patients with available liver histology, the distribution of the fibrosis stages was as follow: F0=16 (10.1%), F1=51 (32.1%), F2=31 (19.5%), F3=37 (23.2%), F4=24 (15.1%).

In the whole subpopulation, the median values of liver stiffness measured by ElastPQ and F-TE were statistically different (8.3 kPa vs. 9.5 kPa, respectively, p=0.021).

On univariate analysis, LSM with ElastPQ showed a significant correlation with fibrosis stage (p<0.001), lobular inflammation (p<0.001), ALT (Spearman's 0.226, p<0.001), AST (Spearman's 0.389, p<0.001), ALP (Spearman's 0.092, p=0.023), GGT (Spearman's 0.339, p<0.001) and platelet count (Spearman's -0.199, p<0.001). On multivariate analysis with a linear regression model, LSM with ElastPQ was independently associated only with fibrosis stages (B 4.234, 95%CI 3.192-5.175, p<0.001) (Supplementary Material Figure 1). Steatosis was not significantly associated with LSM measured by ElastPQ in both univariate (p=0.898) and multivariate analysis (B 0.42, 95%CI -1.50-2.32, p=0.669).

A similar absence of association was observed between steatosis and LSM measured by F-TE as well as lobular inflammation and its grade were associated with LSM measured by F-TE only in univariate analysis (results not shown).

The optimal cut-off values of ElastPQ for staging mild (F≥1), moderate (F≥2), advanced (F≥3) fibrosis and cirrhosis (F=4) were lower than those of F-TE across all stages of liver fibrosis and were: 6.0, 8.0, 9.0 and 11.9 kPa vs. 6.6, 8.5, 10.6 and 12.5 kPa, for ElastPQ and F-TE, respectively. There was no statistically significant difference between the ROC curves of F-TE and ElastPQ across all stages of liver fibrosis, even though the AUROC curves values of ElastPQ for F≥1 and F=4 were higher than those of F-TE. The diagnostic accuracy of F-TE was better for detecting liver cirrhosis (AUC 0.76, 95%CI 0.60-0.91; AUC 0.84, 95%CI 0.78-0.91; AUC 0.85, 95%CI 0.79-0.91 and AUC 0.90, 95%CI 0.83-0.96, for F≥1, F≥2, F≥3 and F=4, respectively) (Figure 3). As for F-TE, the diagnostic accuracy of ElastPQ was better for detecting liver cirrhosis (AUC 0.83, 95%CI 0.72-0.93; AUC 0.84, 95%CI 0.78-0.90; AUC 0.88, 95%CI 0.82-0.93 and AUC 0.96, 95%CI 0.92-0.99, for F≥1, F≥2, F≥3 and F=4, respectively) (Figure 3). Cut-offs achieving 90% sensitivity and 90% specificity for each fibrosis stage are shown in the supplementary index (Supplementary Material Table 2 and Supplementary Material Figure 2).

The performance and the misclassification of ElastPQ compared to F-TE in staging liver fibrosis, (Table 3 and Supplementary Material Table 1, respectively), showed that ElastPQ, as well as F-TE, is more accurate in diagnosing severe fibrosis and cirrhosis compared to lesser fibrosis stages.

DISCUSSION

In this study, we compared ElastPQ and F-TE for staging liver fibrosis in a large cohort of patients with NAFLD. Our results showed that liver stiffness (LS) values measured with ElastPQ and F-TE have excellent correlation. However, the agreement was not equally good, since the higher the LS, the larger the reading values discrepancy between the two techniques. We found that larger waist circumference and a liver stiffness >10 kPa were independently associated with a difference of >2 kPa between F-TE and ElastPQ. In the subpopulation of patients with an available liver biopsy, ElastPQ showed the same diagnostic accuracy as F-TE in staging fibrosis across all stages. Similar to F-TE, ElastPQ was more accurate in diagnosing severe fibrosis and cirrhosis compared to lesser fibrosis stages.

Our study is unique in the sense that it comprehensively assessed a new shear wave modality in the prevalent aetiology of chronic liver disease and compared this to F-TE, which is the most commonly used elastography technique.

Other studies have already pointed out differences in liver stiffness readings between ARFI techniques and F-TE, which become more pronounced when WC or stiffness values increase significantly (9, 14). The fact that WC and high stiffness values can influence these measurements might be explained by the physical principles on which ARFI techniques are based upon. Larger WC and higher liver stiffness generate lower reading values mainly by increasing the attenuation of ultrasound waves. Patients with large WC have an increased subcutaneous fat thickness. In order to maintain a distance of 1.5-2 cm from the liver capsule to avoid reverberation artefacts, the region of interest (ROI) is placed farer from the skin. ElastPQ is an ARFI imaging where acoustic push

pulses, travelling along the main US beam, induce shear stresses within tissues, with modalities and intensities depending on tissue attenuation (mainly due to absorption, which is greater in a very stiff liver), acoustic frequency, and intensity of the acoustic beam. It has been largely demonstrated that the speed of propagation of the shear waves decreases at greater source-to-target distances, paralleling the progressive attenuation of the pulses generating the shear waves as they travel within the tissues and this is generally due to decreased signal-to-noise ratios. Interestingly, significantly lower shear wave velocity values were obtained in the deep compared to the superficial portion of the right lobe of the liver in healthy volunteers (15, 16), and in the deeper parts of homogeneous phantoms in experimental studies (15, 17).

In the subpopulation of patients with available histology, after adjusting the analysis for confounding variables, ElastPQ stiffness values were directly and linearly correlated with the stages of fibrosis. Moreover, in our cohort liver stiffness did not correlate with liver steatosis neither on univariate nor on multivariate analysis; thus, steatosis was not a confounding factor. This result is consistent to what observed in other studies using ARFI techniques, and appears to indicate that the obtained value is a true estimate of the liver stiffness (18-22). Lobular inflammation and its grade did not show a significant correlation with liver stiffness measured by ElastPQ on multivariate analysis, confirming that the necro-inflammatory activity has no influence on the LSM in the absence of significant elevation of the transaminases. Furthermore, liver stiffness measured by F-TE was not associated with steatosis while lobular inflammation and its grade did not correlate with liver stiffness values on multivariate analysis.

Data in the literature regarding the influence of necro-inflammation on liver stiffness are controversial; some studies showed an influence (18, 21, 23, 24) and others did not (12, 19, 20, 25).

We have also shown that ElastPQ has the same diagnostic accuracy as F-TE in staging liver fibrosis. However, in the clinical practice the detection of compensated advanced chronic liver disease (cACLD) is very important and the new guidelines are made based on the probability of cACLD for given stiffness values. Alike F-TE, ElastPQ showed a good diagnostic accuracy to detect cACLD, since it performs better in ruling out significant fibrosis and detecting cirrhosis. In this regard, the cut-offs obtained in our series are in agreement with the recommendation for liver elastography of the updated consensus of the Society of Radiologists in Ultrasound, which proposes a simple and more clinically relevant vendor-neutral "rule of four" method for the interpretation of stiffness values obtained with the ARFI techniques (26).

The cut-off values of ElastPQ for staging liver fibrosis were lower than those of F-TE across all stages of liver fibrosis, in line with previously published data (14, 27). In 2017, Lee et al. showed that ElastPQ had the same diagnostic accuracy of F-TE, in a population of 106 patients mainly affected by HCV and HBV with an available liver biopsy. They also found a good correlation between ElastPQ and F-TE, although this was assessed in a subgroup of only 51 patients (28). In another study comparing ElastPQ and F-TE in a cohort of 134 patients with available liver histology (9), the diagnostic performance of the two techniques was similar, which is consistent with our results. However, 97% of this population was, again, composed of patients with viral hepatitis. In another study, Cassinotto et al. showed that two different elastography techniques, a 2D-SWE technique

(Supersonic Imaging, SSI) and a pSWE technique (VTQ®), had the same accuracy of F-TE in staging liver fibrosis in a population of 291 NAFLD patients with available histology. Although our results are in agreement with their conclusion, they used a different pSWE product, integrated in a Siemens Medical Ultrasound Device (29). In all these studies, the cut-off values of ElastPQ were lower than those of F-TE across all stages of liver fibrosis. This is likely due to the different physical principles that these techniques are based upon. There are other studies assessing the diagnostic accuracy of ElastPQ, but they consist of patients with chronic liver disease of various aetiologies, in which the proportion of NAFLD patients is very low.

Our results on the diagnostic accuracy of ElastPQ are also similar to those reported by studies using a different point shear wave elastography method, which did not report any improvement in accuracy compared to F-TE (18, 30, 31). In 2011, Rizzo et al. (19) found that ARFI was more accurate than TE for staging significant and severe liver fibrosis. However, those results were not confirmed by a recent meta-analysis that compared ARFI with F-TE and found comparable diagnostic accuracy for the diagnosis of severe fibrosis and a slightly but significantly higher diagnostic accuracy of F-TE for the diagnosis of significant fibrosis and cirrhosis (32).

The cut-off values we found were different from those of other ARFI techniques. This is also in agreement with a previous study (33) where the mean LSM obtained using ElastPQ and VTQ® exhibited a statistically significant difference. For this reason, another study, which correlated liver stiffness values measured using ElastPQ and VTQ®, suggested that the two techniques cannot be used interchangeably, despite the excellent correlation of liver stiffness values (34). This might be due to the fact that the

liver stiffness values are affected by differences in the direction of the push pulses and the frequency range which might differ among different ultrasound systems. Even though the results are very similar, it is important to highlight that all these studies did not use liver histology as reference standard and the patients included were mainly affected by viral chronic liver disease.

There is a single study on the diagnostic performance of ElastPQ in a large population of patients affected by NAFLD (35). This showed that F-TE is more accurate than ElastPQ in staging F≥2 and F≥3 liver fibrosis, which is in disagreement with our findings. However, in the above-mentioned study only three measurements for each set of ElastPQ examination were taken. A recent study about reliability quality criteria of ElastPQ (11), aiming to assess the accuracy of ten, five and three measurements, concluded that three measurements did not suffice to reliably stage liver fibrosis. Moreover, in the study by Leong et al., ElastPQ was performed by operators who had never performed pSWE previously and had received training to perform pSWE specifically for the purpose of the study (35).

In our study, the rate of failure did not differ significantly between the two techniques. Predictors of ElastPQ LSM failure were high BMI and large WC. Patients with a high BMI and WC usually have a very thick subcutaneous fat and severe liver steatosis, with or without capsule reverberation artefacts. These conditions increase physical phenomena as absorption, reflection, refraction and scattering, which limit the efficacy of ultrasound- based techniques. It is also important to highlight that, in our study, all F-TEs were performed under ultrasound-guidance and this might have influenced the

diagnostic accuracy and failure rate of a technique which is usually performed in a blind manner.

Strengths of our study include a single liver disease aetiology cohort, inclusion of patients at all disease severity stages, central pathology reading for liver histology and the performance of all elastography measurements by a single experienced operator. The availability of liver biopsy in just 25% of the included population represents the main limitation. Another limitation is the interval between the non-invasive assessment and the liver biopsy, which was up to 12 months. However, anthropometric data at the time of ElastPQ/F-TE were not significantly different compared to the time of the liver biopsy.

In conclusion, our study demonstrated that ElastPQ has an excellent correlation and good agreement with F-TE, for liver stiffness measurement, and similar diagnostic accuracy in staging liver fibrosis. Similar to F-TE, ElastPQ is more accurate in ruling out significant liver fibrosis and detecting liver cirrhosis. However, compared to F-TE, routine ultrasound systems with an elastography software, such as ElastPQ, are advantageous since they also allow the evaluation of other parameters that are complementary to stiffness, are highly accurate for the diagnosis of cirrhosis and features of decompensation and can be used, in a one-stop shop setting, for the screen for focal liver lesions.

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Table 1. Patient's baseline characteristics

Total Population, n		671
Age, years		55.8±13.1
BMI, kg/m^2		31.5±5.7
WC, cm		107±14.5
Male, n (%)		380 (56.6)
Diabetes, n (%)		274 (41)
Arterial hypertension, n (%)		359 (53.7)
Dyslipidaemia, n (%)		455 (68)
Available ElastPQ		671 (100)
ElastPQ Liver Stiffness, kPa		5.6 (3.9)
ElastPQ successful, n (%)		645 (96)
Available F-TE, n (%)		653 (97)
F-TE Liver Stiffness		6.2 (4.1)
F-TE XL probe, n (%)		271 (41.6)
F-TE successful, n (%)		647 (99)
CAP, dB/m		308.7±55.8
Biopsies, n (%)		159 (23.7)
Histological parameters		
Steatosis, n (%)	Absent	3 (1.9)
	Mild	66 (41.5)
	Moderate	72 (45.3)
	Severe	18 (11.3)
Grade of lobular inflammation, n (%)	Absent	20 (12.6)
	Mild	100 (62.9)
	Moderate	35 (22)
	Severe	4 (2.5)
Fibrosis, n (%)	F0	16 (10.1)
	F1	51 (32.1)
	F2	31 (19.5)

	F3	37 (23.2)
	F4	24 (15.1)
Ballooning, n (%)		131 (82.4)
NASH, n (%)		131 (82.4)
Biochemistry/haematology		
Triglycerides, mmol/L		1.6 (1.1)
Total Cholesterol, mmol/L		4.7 (1.6)
HDL Cholesterol, mmol/L		1.2±0.5
LDL Cholesterol mmol/L		2.6±1.6
Hb1Ac, %		41 (13.4)
ALT, U/l		48 (41)
AST, U/l		33 (20)
ALP, U/l		79 (33)
GGT, U/l		52 (73)
Platelets x10^9/L		244±67

BMI, body mass index; WC, waist circumference; F-TE, FibroScan transient elastography; CAP, controlled attenuated parameter; NASH, non-alcoholic steatohepatitis; HDL, high density lipoprotein; LDL, low density lipoprotein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transpeptidase; NAFLD, non-alcoholic liver disease. Quantitative variables are expressed as mean±standard deviation if the distribution is normal, otherwise as median (IQR).

Table 2. Univariate and multivariate analysis of a difference of liver stiffness values between F-TE and ElastPQ of ≥ 2 kPa

UNIVARIATE ANALYSIS				**MULTIVARIATE ANALYSIS**		
VARIABLE	Delta <2 kPa	Delta ≥2 kPa	**p value**	**OR**	**95% CI**	**p value**
Age, y	56	57	0.308			
Male, %	56	62	0.183			
***BMI, Kg/m²**	30.8	32.4	0.001	1.040	1.002-1.079	0.041
***Waist circumference, cm**	105.3	110	0.006	1.019	1.002-1.035	0.023
Diabetes, %	37	55	<0.001	0.710	0.437-1.154	0.167
Arterial hypertension, %	51	62	0.023	1.120	0.68-1.824	0.649
Dyslipidaemia, %	68	72	0.310			
ALT, IU/L	47	60	0.001	1.002	0.997-1.006	0.415
CAP, dB/m	305	316	0.606			
TE LS >10kPa, %	*11*	*49*	*<0.001*	*7.306*	*4.435-12.034*	*<0.001*

BMI, body mass index; ALT, alanine aminotransferase; CAP, controlled attenuated parameter; TE LS, Transient Elastography Liver Stiffness.

*Inserted in the analysis separately because of collinearity between them.

Table 3. Diagnostic performance of ElastPQ and F-TE for staging liver fibrosis inpatients with available histology.

	Fibrosis stage	Cut-off value (kPa)	Se (%) (95%CI)	Sp (%) (95%CI)	NPV (%) (95%CI)	PPV (%) (95%CI)	LR+ (95%CI)	LR- (95%CI)	FN	FP
ElastPQ	F≥1	6	79 (72-86)	81 (62-100)	30 (16-44)	97 (94-100)	4.21 (1.51-11.72)	0.26 (0.17-0.38)	30/143 (21%)	3/16 (19%)
	F≥2	8	78 (70-86)	81 (71-90)	73 (63-83)	85 (78-92)	4.03 (2.45-6.65)	0.27 (0.18-0.40)	20/92 (22%)	13/67 (19%)
	F≥3	9	79 (69-89)	78 (70-86)	85 (77-93)	70 (59-81)	3.59 (2.38-5.27)	0.27 (0.16-0.44)	13/62 (21%)	21/94 (22%)
	F=4	11.9	92 (82-102)	85 (79-91)	98 (96-100)	54 (40-68)	6.13 (4.05-9.39)	0.09 (0.02-0.36)	2/25 (8%)	20/134 (15%)
F-TE	F≥1	6.6	85 (79-91)	69 (47-91)	33 (17-49)	96 (93-99)	2.74 (1.30-5.62)	0.22 (0.13-0.37)	22/143 (15%)	5/16 (31%)
	F≥2	8.5	83 (76-90)	70 (59-81)	75 (65-85)	79 (71-87)	2.77 (1.89-4.04)	0.24 (0.15-0.40)	16/92 (17%)	20/67 (30%)
	F≥3	10.6	76 (65-87)	81 (73-89)	84 (77-91)	72 (61-83)	4 (2.63-6.34)	0.30 (0.19-0.47)	15/62 (24%)	18/97 (19%)
	F=4	12.5	88 (76-100)	83 (77-89)	97 (94-100)	49 (34-64)	5.17 (3.44-7.64)	0.14 (0.05-0.42)	3/25 (12%)	23/134 (17%)

F-TE, Fibroscan Transient Elastography; Se, sensitivity; Sp, specificity; FN, false negative; FP, false positive; NPV, negative predictive value; PPV, positive predictive value; LR+, positive likelihood ratio; LR-, negative likelihood ratio

Figure 1. Correlation between ElastPQ and F-TE

Figure 2. Bland-Altman plot analysis. Agreement between F-TE and ElastPQ

Figure 3. ROC curves of median values of ElastPQ and F-TE for different stages of liver fibrosis.