Comparison of Elastography Point Quantification with Transient Elastography in Patients with Chronic Viral Hepatitis and Nonalcoholic Fatty Liver Disease: A Pilot Study

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Aims: **The objective of this study was to compare diagnostic accuracy of elastography point quantification (ElastPQ) with transient elastography (TE) and liver histology for measuring liver stiffness in patients with chronic viral hepatitis (CVH) and nonalcoholic fatty liver disease (NAFLD).** ***Methods:*** **Thirty-two patients with chronic liver disease (CVH and NAFLD) were evaluated by ElastPQ and TE within 7 days of liver biopsy. Within the CVH group, subgroup analysis was carried out in patients with end-stage renal disease (ESRD) and without ESRD. Area under the receiver operating characteristic (AUROC) curves were calculated for ElastPQ and TE.** ***Results:*** **There were 15 patients with CVH and 17 patients with NAFLD. In the CVH group, there were 8 patients with ESRD and 7 patients without ESRD. Taking liver histopathology as the gold standard, liver stiffness measurement by ElastPQ ($\rho = 0.826$;$P < 0.0001$) and TE ($\rho = 0.649$; $P < 0.0001$) correlated significantly with the stage of fibrosis. AUROCs of ElastPQ and TE for the diagnosis of any fibrosis ($F \geq 1$), significant fibrosis ($F \geq 2$), and advanced fibrosis ($F \geq 3$) were 0.907, 0.959, 0.926 and 0.870, 0.770, 0.881, respectively, in both CVH and NAFLD groups. However, the accuracy of both these techniques was poor in patients with CVH and ESRD (AUROCs for ElastPQ and TE of 0.667 and 0.167 for the diagnosis of significant fibrosis, respectively, and 0.429 and 0.143 for the diagnosis of advanced fibrosis, respectively). The diagnostic accuracy of both ElastPQ and TE for detecting significant fibrosis was excellent in patients with NAFLD (AUROC of 1.000 and 0.936, respectively). ElastPQ was superior to TE in the diagnosis of significant fibrosis in the combined analysis ($P = 0.0149$) and in the CVH group ($P = 0.0391$), while both modalities were comparable in patients of the NAFLD group ($P = 0.2539$).** ***Conclusion:*** **ElastPQ may be equally accurate as Fibroscan, and large prospective studies are required to validate the same.** **(J Clin Exp Hepatol 2021;11:21–29)**

Liver Fibrosis

Chronic viral hepatitis (CVH) is the commonest cause of chronic liver parenchymal disease worldwide with over more than half the world's population exposed to different hepatotropic viruses.[1–3] Nonalcoholic fatty liver disease (NAFLD) represents a continuum of conditions that are in patients who have not consumed sufficient alcohol in amounts which is considered harmful to the liver and is characterized by presence of macrovesicular hepatic steatosis on histopathology.[4] Prevalence estimates suggest that NAFLD may be the most common cause of chronic liver disease (CLD) across the globe including Asia and India.[5]

Irrespective of the etiology, fibrosis is the final common pathway that subsequently results in morbidity and mortality associated with CLD. Few studies have shown that liver fibrosis can be reversed in its incipient stages, and hence an early diagnosis becomes important.[6] In addition, assessment of fibrosis has an important bearing on monitoring treatment and prognostication of the patients with CLD.[7,8]

Liver biopsy is considered as the gold standard for the evaluation of liver fibrosis.[9] It is, however,invasive and is associated with complications such as bleeding, pain, gall bladder perforation,pneumothorax, and even death.[9–11] In addition, there is a significant sampling error and considerable interobserver and intraobserver variation in assessment of the biopsy specimens.[10,11] Hence, efforts have been focused on developing noninvasive techniques for the assessment of liver fibrosis.[1]

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Abbreviations: ElastPQ: Elastography Point Quantification; TE: Transient Elastography; CVH: Chronic Viral Hepatitis; NAFLD: Nonalcoholic Fatty Liver Disease; ESRD: End-Stage Renal Disease; AUROC: Area Under the Receiver Operating Characteristic; pSWE: Point Shear Wave Elastography; CHB: Chronic Hepatitis B; CHC: Chronic hepatitis C
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Elastography techniques are based on the premise that fibrosis increases tissue stiffness and in turn reduces tissue elasticity.[10] Ultrasound-based elastography methods can be broadly classified into strain and shear wave elastography.[12–14] The various shear wave techniques are transient elastography (TE), 2D shear wave elastography, and point shear wave elastography (pSWE).[12–15]

TE uses an external vibrator to generate elastic shear waves within the liver. This technique has been validated in patients with CVH and NAFLD.[10] However, TE has few limitations. It is associated with failure or unreliable results in up to 10–20% of patients because of various reasons such as obesity, narrow intercostal spaces, and ascites.[16,17]

Elastography point quantification (ElastPQ) is one of the pSWE techniques.[18] There is limited published data related to the utility of ElastPQ in evaluation of liver fibrosis in patients with CVH and NAFLD. However, the results of preliminary studies evaluating the performance of ElastPQ have been encouraging.[15,19,20] We conducted the present study to evaluate the diagnostic accuracy of ElastPQ to detect various stages of hepatic fibrosis in patients with CVH and NAFLD and for comparing the efficacy of ElastPQ with TE and liver histology for liver fibrosis assessment in patients with CVH and NAFLD.

MATERIALS AND METHODS

This was a prospective study on patients with CVH and NAFLD conducted over a period of 18 months and was approved by the ethics committee of the institute. Informed written consent was taken from all the patients enrolled in our study.

Inclusion criteria for patients with CVH were Hepatitis B Virus Surface Antigen (HBsAg)-positive status for >6 months, persistent/intermittent rise in alanine transaminase (ALT) or aspartate transaminase (AST) levels > two times the normal for >6 months, and HBV DNA >2 × 10^3 IU/ml or 2 × 10^4IU/ml in patients having Hepatitis B e-antigen (HBeAg)-negative or HBeAg-positive status, respectively. Patients enrolled as having chronic hepatitis C were Hepatitis C Virus (HCV) RNA positive and anti-HCV positive with normal or elevated ALT/AST levels.

Inclusion criteria of patients with NAFLD were nonalcoholic individuals or total abstainers for at least 6 months or individuals who took <20 g of alcohol/day, or elevated serum transaminase levels (AST/ALT) > 1.5 times the upper most limit of normal value for at least 3 months, hepatic steatosis on ultrasound, negative viral markers, negative autoimmune markers, and normal iron studies.

Patients with NAFLD who were also inactive HBsAg carriers (HBsAg positive, HBeAg negative, and HBV DNA <2 × 10^3 IU/ml) were analyzed as a separate group.

Six patients with clinical, biochemical, endoscopic, or imaging evidence of cirrhosis and those with acute flare of chronic hepatitis B (CHB) were excluded.

Each patient underwent liver elastography using ElastPQ technology (iU22 xMATRIX system, Royal Philips Electronics, the Netherlands) and TE (FibroScan, Echosens, France) within one week of liver biopsy. These two elastography examinations were performed within 24 h of each other by two independent investigators, and each investigator was blinded to the findings of the other technique and also to the liver biopsy findings.

Liver stiffness measurement (LSM) using ElastPQ was performed with the patient in fasting status for 6 h. The footprint of the convex broadband transducer (C5-1) was kept on the skin in the intercostal space overlying the right lobe of the liver. The region of interest (ROI) was set in segments 8, 7, and 5 with a depth of >1 cm and <7 cm below the Glisson's capsule avoiding any blood vessels, any necrotic areas, and the boundary between organs. The patient was instructed to hold breath for less than a second during quantification. Ten validated measurements were acquired, with values less than 1 kilopascal (kPa) being excluded, and the median and average values were taken which were measured in kPa.

LSM by TE was performed in fasting state, in supine position, with the probe kept in the right hypochondrium in the intercostal space overlying the right lobe of the liver. We took ten measurements, with the median value (in kPa) as the final result. Successful measurements were validated using the following criteria:

1. Number of valid shots more than or equal to 10.
2. Ratio of valid shots to the total shots more than or equal to 60% (success rate).
3. Interquartile range (IQR) < 30% of median LSM.

For the purpose of statistical analysis, the categories made based on the histopathological fibrosis stage were as follows: no fibrosis (F0), mild fibrosis (F1), any fibrosis (F ≥ 1), significant fibrosis (F ≥ 2), and advanced fibrosis (F ≥ 3).

Statistical analysis

Categorical variables were presented as absolute values (n) and percentages (%), while the continuous variables were presented as mean ± standard deviation or as median with their IQR intervals. For normally distributed data, comparison of means of 3 groups was performed using one-way Analysis of variance (ANOVA) and post hoc multiple comparisons test. The Kruskal-Wallis test and Mann-Whitney test was applied for the skewed data in the two groups. For normally distributed data, the student's t-test was used to compare the two groups. The Fisher's exact test or Chi square test was used to compare the proportions, depending on their applicability for the 2 groups. To assess the performance of ElastPQ and TE, specifcity,

Table 1 Patient Characteristics in Different Groups.

Variable	CVH	NAFLD	CVH with ESRD	CVH without ESRD	NAFLD with inactive HBsAg carrier	NAFLD without inactive HBsAg carrier	Total
N	15	17	8	7	6	11	32
Age (Y)	38.07 ± 12.74	38.71 ± 9.02	41.25 ± 11.79	34.43 ± 13.70	35.67 ± 12.011	40.36 ± 7.03	38.41 ± 10.74
Sex (M/F)	11/4	12/5	6/2	5/2	6/0	6/5	23/9
ElastPQ (Average) (kPa)	5.52 (4.74–7.48)	5.92 (4.58–6.46)	5.29 (4.78–9.00)	6.21 (5.68–7.28)	4.58 (3.30–5.92)	5.10 (4.78–10.06)	5.29 (4.69–9.40)
ElastPQ (Median) (kPa)	5.54 (4.63–7.20)	5.72 (4.67–6.28)	5.09 (4.62–9.14)	6.16 (5.67–7.03)	4.67 (3.55–5.84)	4.92 (4.52–9.60)	5.12 (4.61–9.18)
TE (Median) (kPa)	9.0 (5.7–11.9)	7.8 (5.7–13.5)	9.2 (5.6–11.2)	12.8 (9.3–15.2)	5.7 (4.7–5.8)	7.3 (5.0–13.3)	9.4 (6.1–11.6)
Fibrosis stage							
F0	4 (26.7%)	6 (35.3%)	0 (0%)	4 (57.1%)	4 (66.7%)	2 (18.2%)	10 (31.3%)
F1	8 (53.3%)	4 (23.5%)	6 (75%)	2 (28.6%)	0 (0%)	4 (36.4%)	12 (37.5%)
F2	2 (13.3%)	3 (17.7%)	1 (12.5%)	1 (14.3%)	1 (16.7%)	2 (18.2%)	5 (15.6%)
F3	1 (6.7%)	1 (5.9%)	1 (12.5%)	0 (0%)	0 (0%)	1 (9.1%)	2 (6.3%)
F4	0 (0%)	3 (17.6%)	0 (0%)	0 (0%)	1 (16.7%)	2 (18.2%)	3 (9.4%)

CVH, chronic viral hepatitis; NAFLD, nonalcoholic fatty liver disease; ESRD, end-stage renal disease; TE, transient elastography.

Table 2 Accuracy of ElastPQ in Total Group.

Stage	AUROC	Cutoff (kPa)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
All patients							
Any fibrosis	0.907	5.37	77.3	100	100	66.7	84.4
Significant fibrosis	0.959	5.96	100	86.4	76.9	100	90.6
Advanced fibrosis	0.926	8.42	80	92.6	66.7	96.2	90.6
CVH							
Any fibrosis	0.955	5.37	90.9	100	100	80	93.3
Significant fibrosis	0.861	5.96	100	75	50	100	80
Advanced fibrosis	0.643	5.96	100	64.3	16.7	100	66.7
CVH with ESRD							
Significant fibrosis	0.667	5.90	100	50	40	100	62.5
Advanced fibrosis	0.429	5.90	100	42.9	20	100	50
CVH without ESRD							
Any fibrosis	0.833	5.57	66.7	100	100	80	85.7
Significant fibrosis	1.000	6.78	100	100	100	100	100
NAFLD							
Any fibrosis	0.902	5.02	81.8	100	100	75	88.2
Significant fibrosis	1.000	5.87	100	100	100	100	100
Advanced fibrosis	0.981	8.04	100	92.3	80	100	94.1
NAFLD with inactive HBsAg carrier state							
Any fibrosis	1.000	5.79	100	100	100	100	100
Significant fibrosis	1.000	5.79	100	100	100	100	100
Advanced fibrosis	1.000	12.57	100	100	100	100	100
NAFLD without inactive HBsAg carrier state							
Any fibrosis	0.944	4.62	88.9	100	100	66.7	90.9
Significant fibrosis	1.000	6.04	100	100	100	100	100
Advanced fibrosis	0.958	8.04	100	87.5	75	100	90.9

CVH, chronic viral hepatitis; NAFLD, nonalcoholic fatty liver disease; ESRD, end-stage renal disease; ElastPQ, elastography point quantification; AUROC; area under the receiver operating characteristic; PPV; positive predictive value; NPV, negative predictive value.

sensitivity, negative predictive value, positive predictive value, diagnostic accuracy, and receiver operating characteristic curves were calculated. The Youden's index was used for determining the optimal cutoff values from the AUROC curve analysis. To compare AUROC curves, the DeLong test was used. To see the relationship between the different variables with ElastPQ and TE, Spearman's correlation coefficient (ρ) was calculated. The reproducibility of ElastPQ was assessed by the intraclass correlation coeffcient (ICC) of reliability analysis. All of the statistical tests were two sided and performed at a significance level of $\alpha = 0.05$. IBM SPSS Statistics (version 22.0) and MedCalc statistical software, version 14.8.1, (MedCalc Software bvba, Ostend, Belgium) were used for performing the statistical analysis.

RESULTS

We enrolled 33 patients in our study. Among these 33 patients, 15 patients with CVH (CHB and chronic hepatitis C [CHC]) and 18 patients with NAFLD presented to the Liver Clinic of our institute and required a liver biopsy as a part of their management protocol. Of the 18 patients with NAFLD, the biopsy was nonrepresentative in 1 patient. Thus, 32 patients (15 patients with CVH and 17 patients with NAFLD) were included in the final analysis.

ElastPQ and TE measurements were successful in all the 32 patients. No poorly reliable LSM or failure of measurement by ElastPQ or TE was encountered. No major complications occurred after liver biopsy. The only minor complication observed in our study was pain at the biopsy site in 5 patients.

Table 3 Comparison of Diagnostic Accuracy of ElastPQ and TE for Detecting Any Fibrosis, Significant Fibrosis, and Advanced Fibrosis in Total Group Fibrosis at Optimal Cutoff (kPa) Values.

Modality	Optimal cutoff (kPa)	AUROC	Std. error	95% CI	Difference between areas	Std. error	95% CI	*P*-value
Any fibrosis (F > 1)								
ElastPQ	5.37	0.907	0.0524	0.751 to 0.980	0.0364	0.0587	−0.0788 to 0.151	0.536
TE	6.0	0.870	0.0648	0.704 to 0.962				
Significant fibrosis (F > 2)								
ElastPQ	5.96	0.959	0.0344	0.823 to 0.998	0.189	0.0775	0.0367 to 0.341	0.015
TE	8.8	0.770	0.0858	0.588 to 0.900				
Advanced fibrosis (F > 3)								
ElastPQ	8.42	0.926	0.0623	0.776 to 0.998	0.0444	0.0425	−0.0388 to 0.128	0.295
TE	11.2	0.881	0.0863	0.718 to 0.968				
CVH								
Any fibrosis (F > 1)								
ElastPQ	5.37	0.955	0.0525	0.710 to 1.000	0.0227	0.0321	−0.0403to 0.0857	0.480
TE	5.8	0.932	0.0719	0.678 to 0.998				
Significant fibrosis (F > 2)								
ElastPQ	5.96	0.861	0.103	0.589 to 0.982	0.333	0.162	0.0167 to 0.650	0.039
TE	5.8	0.528	0.150	0.261 to 0.783				
CVH without ESRD								
Any fibrosis (F > 1)								
ElastPQ	5.57	0.833	0.192	0.397 to 0.993	0.0833	0.118	−0.148to 0.314	0.480
TE	5.8	0.750	0.264	0.321 to 0.975				
NAFLD								
Any fibrosis (F > 1)								
ElastPQ	5.02	0.902	0.0762	0.660 to 0.991	0.0455	0.1020	−0.154to 0.245	0.655
TE	8.8	0.856	0.0958	0.604 to 0.976				
Significant fibrosis (F > 2)								
ElastPQ	5.87	1.00	0.000	0.805 to 1.000	0.0643	0.0563	−0.0461to 0.175	0.254
TE	10.2	0.936	0.0563	0.705 to 0.998				
Advanced fibrosis (F > 3)								
ElastPQ	8.04	0.981	0.0272	0.772 to 1.000	0.0192	0.0272	−0.0341 to 0.0725	0.480
TE	11.2	1.000	0.000	0.805 to 1.000				
NAFLD with inactive HBsAg								
Any fibrosis (F > 1)								
ElastPQ	5.79	1.000	0.000	0.541 to 1.000	0.000	0.000	0.000	1.00
TE	9.0	1.000	0.000	0.541 to 1.000				
Significant fibrosis (F > 2)								
ElastPQ	5.79	1.000	0.000	0.541 to 1.000	0.000	0.000	0.000	1.00
TE	9.0	1.000	0.000	0.541 to 1.000				
NAFLD without inactive HBsAg								
Any fibrosis (F > 1)								
ElastPQ	4.62	0.944	0.0786	0.633 to 1.000	0.167	0.290	−0.402 to 0.735	0.566
TE	4.4	0.778	0.239	0.440 to 0.962				

(*Continued on next page*)

Table 3 (*Continued*)

Modality	Optimal cutoff (kPa)	AUROC	Std. error	95% CI	Difference between areas	Std. error	95% CI	*P*-value
Significant fibrosis (F > 2)								
ElastPQ	6.04	1.000	0.000	0.715 to 1.000	0.100	0.110	−0.115 to 0.315	0.361
TE	10.2	0.900	0.110	0.576 to 0.997				
Advanced fibrosis (F > 3)								
ElastPQ	8.04	0.958	0.0589	0.652 to 1.000	0.0417	0.0589	−0.0738 to 0.157	0.480
TE	11.2	1.000	0.000	0.715 to 1.000				

CVH, chronic viral hepatitis; NAFLD, nonalcoholic fatty liver disease; ESRD, end-stage renal disease; ElastPQ, elastography point quantification; AUROC; area under the receiver operating characteristic; TE, transient elastography.

Of the 15 patients with CVH, 7 had CHB and 8 had CHC. One patient with CHB had end-stage renal disease (ESRD), while 7 patients with CHC had ESRD. Owing to the different characteristics of patients with ESRD and for the purpose of analysis, the CVH group was divided into 2 subgroups, CVH with ESRD (n = 8, 53.3%) and CVH without ESRD (n = 7, 46.7%).

Of the 17 patients with NAFLD, 6 patients (35.3%) were detected to have an associated inactive HBsAg carrier state and were analyzed as a separate subgroup of NAFLD with inactive HBsAg carrier state.

The different characteristics of the all the patients in the different groups are summarized in Table 1.

Patients in all the groups were comparable for gender and age distribution. The mean age in the CVH group was 38.07 years (±12.74), while in NAFLD group, it was 38.71 years (±9.02). There were 11 men and 4 women in the CVH group, while the NAFLD group had 12 men and 5 women.

Histology

Table 1 summarized the patients' distribution in various histological fibrosis stages. The difference in the distribution of patients in various fibrosis stages (F0-4) was not statistically significant between any of the groups.

Diagnostic accuracy of ElastPQ

Accuracy of ElastPQ in total study group is shown in Table 2.

In all 32 patients with CLD, ElastPQ had an AUROC of 0.907, 0.959, and 0.926 at optimal cutoffs of 5.37 kPa, 5.96 kPa, and 8.42 kPa for the detection of any fibrosis, significant, and advanced fibrosis, respectively. At the same cutoffs, ElastPQ also maintained a high sensitivity (77.3%, 100%, and 80%), specificity (100%, 86.4%, and 92.6%), and diagnostic accuracy (84.4%, 90.6%, and 90.6%) for the detection of any fibrosis, significant, and advanced fibrosis, respectively.

When the results in different etiological groups were analyzed separately, ElastPQ maintained high accuracy for detection of any and significant fibrosis in patients with CVH (AUROC values of 0.955 and 0.861 at cutoff values of 5.37 kPa and 5.96 kPa, respectively, and diagnostic accuracies of 93.3% and 80%, respectively), while the accuracy for detecting advanced fibrosis was lower (AUROC value of 0.643 at a cutoff of 5.96 kPa with diagnostic accuracy of 66.7%).

On subgroup analysis, the accuracy of ElastPQ for diagnosing any fibrosis and significant fibrosis was excellent in the CVH without ESRD group (AUROC value of 0.833 at a cutoff of 5.57 kPa with a diagnostic accuracy of 85.7% and AUROC value of 1.000 at a cutoff of 6.78 kPa with diagnostic accuracy of 100% respectively). However, in the CVH with ESRD group, the diagnostic accuracy of ElastPQ for detection of significant fibrosis and advanced fibrosis was lower (AUROC: 0.667 and 0.429, respectively, and diagnostic accuracy of 62.5% and 50%, respectively).

ElastPQ showed high accuracy in diagnosing any fibrosis, significant, and advanced fibrosis in patients with NAFLD having AUROC values of 0.902, 1.000, and 0.981 at cutoffs of 5.02 kPa, 5.87 kPa, and 8.04 kPa, respectively. The presence or absence of inactive HbsAg carrier state had no significant effect on the performance of ElastPQ with AUROCs for diagnosing any, significant, and advanced fibrosis being 1.000, 1.000, and 1.000 and 0.944, 1.000, and 0.958 in the two groups, respectively.

Correlation of ElastPQ with fibrosis stage

A significant positive correlation was found between LSM by ElastPQ and liver fibrosis stage in all patients ($\rho = 0.826$; $P < 0.0001$), in the CVH group ($\rho = 0.737$, $P = 0.002$), in NAFLD group ($\rho = 0.880$; $P < 0.001$), in NAFLD with inactive HBsAg carrier state group ($\rho = 0.845$, $P = 0.034$), and in NAFLD without inactive HBsAg carrier group ($\rho = 0.928$, $P < 0.0001$). In the CVH without ESRD group, there was a positive correlation between liver fibrosis and ElastPQ ($\rho = 0.657$); however, it was statistically insignificant ($P = 0.109$). In the CVH with ESRD group, there was no correlation between histopathological staging and ElastPQ ($\rho = 0.203$, $P = 0.630$).

Reproducibility of ElastPQ measurements

The reliability of ElastPQ measurements was assessed by calculating the intraobserver ICC for 10 measurements performed in all patients. There was excellent intraobserver reproducibility of LSM by ElastPQ with ICC of 0.95 (95% Confidence Interval, CI - 0.92-0.973, $P < 0.0001$).

Correlation of TE with fibrosis stage

A significant positive correlation was seen between the TE and liver fibrosis in all patients ($\rho = 0.649$; $p < 0.0001$), in patients with NAFLD ($\rho = 0.808$; $P < 0.001$), in the NAFLD with inactive HBsAg carrier group ($\rho = 0.845$; $P = 0.034$), and in patients with NAFLD without inactive HBsAg carrier ($\rho = 0.795$, $P = 0.006$). In CVH and CVH without ESRD groups, a positive correlation was seen between liver fibrosis and TE ($\rho = 0.473$ and $\rho = 0.482$); however, it was statistically insignificant ($P = 0.075$ and $P = 0.273$). In the CVH with ESRD group, there was no correlation between histopathological staging and TE ($\rho = -0.514$, $P = 0.192$).

Correlation of ElastPQ and TE

A significant positive correlation was seen between LSM by TE and ElastPQ in all patients ($\rho = 0.704$; $P < 0.0001$), in patients with CVH ($\rho = 0.545$, $P = 0.036$), in patients with NAFLD ($\rho = 0.713$; $P = 0.001$), and in patients with NAFLD without inactive HBsAg carrier ($\rho = 0.733$, $P = 0.01$). A positive correlation was seen between ElastPQ and TE in the CVH without ESRD group ($\rho = 0.631$, $P = 0.129$) and in patients in the NAFLD with inactive HBsAg carrier group ($\rho = 0.486$, $P = 0.329$). In the CVH with ESRD group, no correlation was seen between TE and ElastPQ ($\rho = -0.405$, $P = 0.32$).

Comparison of diagnostic accuracy of ElastPQ and TE for detecting hepatic fibrosis

There was no statistically significant difference in ElastPQ and TE for detecting any fibrosis ($P = 0.536$), as well as advanced fibrosis ($P = 0.295$), while ElastPQ was found to be superior for detecting significant fibrosis ($P = 0.015$) [Table 3].

On subgroup analysis, in the CVH group, there was no statistically significant difference in diagnostic accuracy of ElastPQ and TE for detecting any fibrosis ($P = 0.480$), while ElastPQ was found to be superior to TE in diagnosing significant fibrosis ($P = 0.039$). In the CVH without ESRD group, the diagnostic accuracy of ElastPQ and TE was the same for detection of any fibrosis with no significant difference statistically ($P = 0.480$). In the NAFLD group, no statistically significant difference was found in the diagnostic accuracy of TE and ElastPQ for the diagnosis of any fibrosis ($P = 0.655$), significant fibrosis ($P = 0.254$), and advanced fibrosis ($P = 0.480$). In the NAFLD with inactive HBsAg group, diagnostic performance of ElastPQ and TE for detecting any fibrosis and significant fibrosis was excellent (Area under curve, AUC: 1.000) and similar ($P = 1.00$). In the NAFLD without inactive HBsAg carrier group, the diagnostic performance of ElastPQ and TE for detecting any fibrosis ($P = 0.566$), significant fibrosis ($P = 0.361$), and advanced fibrosis ($P = 0.480$) was similar with no significant difference. Few subgroup comparisons could not be made due to paucity of patients.

DISCUSSION

TE has been extensively used and validated for liver fibrosis assessment. ElastPQ is a pSWE technique with an obvious advantage of being available in the same ultrasound machine with which routine ultrasound scanning is carried out. In addition, the ROI can be placed under visualization, thereby acting as an ideal one-stop shop for evaluating liver fibrosis noninvasively.[19–22]

We found a significant positive correlation of ElastPQ with hepatic fibrosis in all patients with CLD ($\rho = 0.826$, $P < 0.0001$). Good correlation between LSM and hepatic fibrosis was found irrespective of etiology (CVH [$\rho = 0.737$, $P = 0.002$] and NAFLD [$\rho = 0.880$, $P < 0.001$]). Similar results with high correlation between ElastPQ and fibrosis stage in patients with CHC ($r = 0.61$, $P < 0.00001$) have been reported.[22] In their study involving 291 patients with CHB, Ma *et al*[23] found a high correlation between the ElastPQ and the stage of fibrosis ($t = 7.75$, $P < 0.05$).

A statistically significant positive correlation was found between LSM by ElastPQ and TE in all patients ($\rho = 0.704$; $P < 0.0001$), in patients with CVH ($\rho = 0.545$, $P = 0.036$), and in patients with NAFLD ($\rho = 0.713$; $P = 0.001$). Although there is no study at present which has evaluated the correlation of these two modalities, a strong correlation between LSM by ElastPQ and acoustic radiation force impulse (ARFI) elastography ($r = 0.616$, $P < 0.0001$) has been seen.[24] Furthermore, a statistically significant correlation between ARFI elastography and TE has been reported in patients with NAFLD ($r = 0.75$, $P < 0.0001$).[15]

No study has previously compared the diagnostic accuracy of ElastPQ and TE in patients with CLD of different etiologies, although a few studies comparing ElastPQ with ARFI and ARFI with TE have been published in the past. Sporea *et al*[24] compared ElastPQ and ARFI for differentiating patients with CLD from those without CLD. To differentiate between the patients with or without CLD, ARFI elastography has been shown to have an accuracy of 83.1% (AUC = 0.822) with a liver stiffness cutoff value of >1.4 m/s (~5.88 kPa), whereas the best ElastPQ had an accuracy of 83.7% (AUC = 0.851) with a cutoff value of >1.23 m/s (~4.54 kPa). The AUROCs of ElastPQ and ARFI elastography to predict the liver diseases, that is, chronic hepatitis and cirrhosis, have been found to be

comparable (P = 0.48). ARFI has been found to have more accuracy than TE for staging of significant fibrosis in patients with CHC.[25]

On subgroup analysis, in the CVH without ESRD group, the accuracy of ElastPQ and TE was found to be comparable for detecting any fibrosis with no significant difference (AUROC: 0.833 vs. 0.750, P = 0.480). In the CVH with ESRD group, the AUROC values of ElastPQ and TE for diagnosing significant fibrosis were 0.667 and 0.167, while those for advanced fibrosis were 0.429 and 0.143, respectively. Previous studies have reported high accuracy of TE to diagnose significant fibrosis, severe fibrosis, and cirrhosis in patients with HCV and ESRD (AUROC values being 0.96, 0.98, and 0.99, respectively).[26,27] Kellner *et al*[28] evaluated liver stiffness using TE in patients just before and after a dialysis session. The median TE was found be 5.1 kPa (2.8–17 kPa) just before dialysis, whereas the median TE was 7.4 kPa (3.5–12.5 kPa) just after the dialysis.[28] It is said that uremic toxins present in the blood might alter the levels of α-2 macroglobulin and apolipoprotein A1 which may affect the TE results.[26] Taneja *et al*[29] also showed that LSM using TE significantly decreases after HD in patients with ESRD, and therefore, TE should not be performed after hemodialysis (HD) to assess the liver fibrosis accurately. Hence, a number of factors may influence TE and ElastPQ results in patients with ESRD, and further studies need to be carried out to determine the efficacy of these modalities in this subgroup of patients.

In the present study, both ElastPQ and TE had high accuracy for detection of any, significant, and advanced fibrosis in the NAFLD group (AUC: 0.902 vs. 0.856, 1.00 vs. 0.936, and 0.981 vs. 1.00, respectively). No statistically significant difference was found in their diagnostic accuracies (P = 0.655, P = 0.254, and P = 0.480, respectively). Irrespective of the presence or absence of HBsAg carrier state, the diagnostic performance of ElastPQ and TE for detecting any fibrosis and significant fibrosis was excellent and similar.

The present study has few limitations. Firstly, the total number of patients with CLD who were assessed by ElastPQ, TE, and liver histology was small (n = 32). Secondly, various fibrosis stages, advanced fibrosis and cirrhosis in particular, were not distributed uniformly among our patients; and more than two thirds of the patients were in F0–F1 stage. This might have affected the optimal cutoff values which were obtained with the AUROC curves. The nonuniform distribution of stages of fibrosis among the patients was possibly due to exclusion of patients with frank cirrhosis on imaging or exclusion of patients with history of decompensation. Thirdly, a substantial number of patients in the CVH group had ESRD as an important comorbidity. The presence of ESRD could have possibly led to the skewed diagnostic accuracy of these elastography techniques in patients with CVH. This is further substantiated by the fact that our results in the CVH without ESRD group were significantly better than those in the CVH with ESRD group. The assessment of fibrosis in patients with ESRD was performed irrespective of the date of their dialysis. Hence, some patients might have been assessed before dialysis and some patients after dialysis, leading to variability in results. Another limitation of the present study was a lack of precise correlation between the site of liver biopsy and the location of ElastPQ measurements. As the distribution of fibrosis in the liver is not uniform, this could be a possible cause for discordance between stiffness measurement and histopathological fibrosis staging.

To conclude, Elast PQ may be equally accurate as Fibroscan, and large prospective studies are required to validate the same. This noninvasive ultrasound-based elastography technique may allow patients having CLD to be managed without performing liver biopsy routinely. Although presently it may not replace biopsy in all settings, it can help prioritize patients for liver biopsy and be useful for providing the information about liver damage in patients where biopsy probably would not have been considered.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

Savinay Kapur: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing - original draft, Writing - review & editing. **Naveen Kalra:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Visualization, Writing - original draft, Writing - review & editing. **Anmol Bhatia:** Formal analysis, Methodology, Supervision, Writing - original draft, Writing - review & editing. **Ajay Duseja:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Writing - original draft, Writing - review & editing. **Ashim Das:** Investigation, Methodology, Supervision, Validation, Visualization, Writing - review & editing. **Radha K. Dhiman:** Investigation, Methodology, Supervision, Validation, Visualization, Writing - review & editing. **Yogesh Chawla:** Investigation, Methodology, Supervision, Validation, Visualization, Writing - review & editing. **Manavjit S. Sandhu:** Investigation, Methodology, Resources, Supervision, Writing - review & editing.

CONFLICTS OF INTEREST

The authors have none to declare.

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