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Diagnostic accuracy of acoustic radiation force impulse elastography (ARFI) in comparison to other non-invasive modalities in staging of liver fibrosis in chronic HCV patients: single-center experience

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Abstract

Purpose To evaluate the reliability of ARFI elastography for liver fibrosis staging and compare it to other non-invasive assessment of hepatic fibrosis (FIB-4 and APRI) in chronic HCV (CHC) patients.

Methods A single-center, prospective study included 2103 CHC patients. Liver stiffness (LS) was evaluated by TE and ARFI elastography. FIB-4 and APRI were calculated. The area under the receiver-operating characteristic curve (AUROCs) was used to assess the diagnostic performance of ARFI elastography for staging of liver fibrosis using TE as a reference standard.

Results The best cut off values of ARFI elastography for diagnosis of $\geq F2$, $\geq F3$and $F4$ were 1.36 m/s, 1.45 m/s, and 1.7 m/s with AUROCs of 0.89, 0.94 and 0.95, respectively. ARFI elastography cut offs are lower in patients with normal ALT level compared to those with ALT level (1.1–< 3 ULN) and those with ALT level ≥ 3ULN (1.35 m/s vs 1.39 m/s vs 1.54 for $F \geq 2$, 1.44 m/s vs 1.58 m/s vs 1.6 m/s for $F3$, 1.69 m/s, 1.84 m/s, 1.86 m/s for $F4$). FIB-4 (0.82–0.86) and APRI (0.78–0.82) yielded lower AUC in prediction of significant fibrosis and cirrhosis than ARFI elastography (0.89–0.95).

Conclusion ARFI elastography is a reliable method for non-invasive staging of liver fibrosis in CHC patients when compared to TE with a good diagnostic performance comparable to FIB-4 and APRI scores for the prediction of significant fibrosis and cirrhosis.

Keywords Chronic hepatitis C virus · ARFI elastography · Transient elastography · Fibrosis scores · Liver fibrosis

Introduction

Chronic liver disease with different etiologies is a substantial worldwide problem; its more frequent causes are chronic viral hepatitis (B or C), non-alcoholic steatohepatitis, autoimmune hepatitis, and cholestatic liver disease. Nowadays, non-alcoholic fatty liver disease (NAFLD) is one of the major causes of chronic liver disease worldwide, however, the prevalence of cause of chronic liver diseases in different geographical areas can differ. Egypt is the country that carries the highest prevalence of hepatitis C virus (HCV) infection in the world with higher rates of morbidity and mortality due to complications [1]. A precise estimation of liver fibrosis is still crucial for monitoring of treatment response and also the prediction of clinically relevant complications such as development of varices, hepatic decompensation and hepatocellular carcinoma (HCC) especially after the introduction of highly effective direct-acting antiviral agents (DAAs).

For years, liver biopsy has remained the standard reference for the evaluation of liver fibrosis in patients with chronic liver disease but due to its invasiveness, sampling errors, intra- and inter-observer variability in staging of fibrosis [2–4]. It becomes no longer accepted by patients or doctors. Therefore, non-invasive methods for liver fibrosis assessment have been developed in clinical practice gradually replacing liver biopsy and become more popular including serologic methods and elastographic methods involving ultrasound-based elastography and magnetic resonance elastography (MRE).

Shear wave elastography (SWE) including transient elastography (TE) and acoustic radiation force impulse

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(ARFI)-based techniques is widely used for non-invasive evaluation of liver fibrosis. Transient elastography (TE) (FibroScan®) is the first validated ultrasound-based elastographic method for liver fibrosis evaluation in patients with chronic hepatitis C and subsequently in other etiologies of chronic hepatopathies [5]. The usefulness of TE elastography for non-invasive fibrosis assessment especially for predicting advanced fibrosis and cirrhosis was demonstrated in several studies [5, 6]. Thus, TE is endorsed nowadays by clinical guidelines for the diagnosis of liver fibrosis and management of patients with chronic liver disease [7, 8].

Acoustic Radiation Force Impulse (ARFI) elastography is another promising ultrasound-based elastography method for evaluation of liver fibrosis in chronic liver disease. This dynamic method uses acoustic radiation force to produce an acoustic "push" pulse which generates shear waves and propagate into the tissue allowing the quantification of the liver stiffness at a single location as in point SWE (pSWE) or inside a larger region of interest as in two-dimensional SWE (2DSWE); their speed reflects the underlying tissue stiffness and severity of liver fibrosis. The shear wave speed will be expressed in meter per second which will be calculated using the time-varying displacement data to measure the arrival time of a shear wave at various locations [9, 10]. ARFI elastography has several advantages over TE by displaying a conventional ultrasound image that allows multiple LS measurements on the direct visualization of the anatomical structures and being able to examine ascitic patients [11].

The aim of this study is to evaluate the diagnostic performance of ARFI elastography in staging of liver fibrosis and comparing it with other non-invasive methods such as FIB-4 and APRI scores in a large cohort of chronic HCV patients using transient elastography (TE) as reference method.

Materials and methods

Patient population

This is a single-center, prospective study including 2103 patients with chronic hepatitis C who were recruited from Cairo University Center for Hepatic Fibrosis (CUC-HF), Endemic Medicine Department, Faculty of Medicine, Cairo University between 2015 and 2017. All enrolled chronic HCV patients aged 18–75 years with HCV RNA positive for more than 6 months. Patients who had hepatitis B virus co-infection, human immunodeficiency virus or associated liver pathology e.g. autoimmune hepatitis, decompensated liver cirrhosis, hepatocellular carcinoma or extra—hepatic malignancy were excluded. In addition, none of our patients had any confounding factors that lead to overestimation of liver stiffness due to other reasons than fibrosis as in liver inflammation [elevated transaminases > 5 times upper limit of normal (ULN)], acute hepatitis, obstructive cholestasis and hepatic congestion at ultrasound [12–16].

Detailed history taking, clinical examination and routine laboratory work up were done. For each patient, liver stiffness measurement (LSM) was evaluated after fasting for at least 6 h by ARFI elastography (Siemens AG, Erlangen, Germany) and TE (FibroScan, EchoSens using the M probe for patients with body mass index (BMI) < 30 kg/m^2 and the XL probe for patients with BMI ≥ 30 kg/m^2) in the same session as well as Fibrosis scores (FIB-4 and APRI) were calculated.

The study was conducted according to the principles of the Declaration of Helsinki and was approved by Institutional Review Board (IRB) of Faculty of medicine, Cairo University. Written informed consent was obtained from each patient before TE and ARFI elastography measurements.

Laboratory tests and calculated scores

Laboratory tests were done in the form of complete blood count, liver biochemical profile (serum bilirubin, liver enzymes, serum albumin and INR) and renal function tests (serum urea and creatinine). The upper limit of normal (ULN) for aminotransferase level (ALT and AST) was defined as 40 IU/L.

In addition, FIB-4 and Aspartate aminotransferase-to-platelet ratio index (APRI) scores were calculated using the following formulas:

- FIB-4 score was calculated using Sterling's formula: [17, 18]

$$\text{Age (years)} \times \text{AST (IU/l)} / \text{platelet count } \left(\times 10^9/\text{l}\right) \times \sqrt{\text{ALT (IU/l)}}.$$

- APRI score was calculated using Wai's formula: [19]

$$(\text{AST}/\text{upper limit of normal})/\text{platelet count } \left(\text{expressed as platelets} \times 10^9/\text{l}\right) \times 100.$$

FIB-4 cut off < 1.45 predict non-significant fibrosis ($< F2$), cut off 1.45–< 3.25 predict significant fibrosis ($\geq F2$–$< F4$) and cut off > 3.25 predict cirrhosis ($F4$) [17] while APRI cut off < 0.7 predict non-significant fibrosis ($< F2$), cut off 0.7–< 1 predict significant fibrosis ($\geq F2$–$< F4$) and cut off ≥ 1 predict cirrhosis ($F4$) [20].

Transient elastography (TE)

TE examination was performed to all enrolled patients with a FibroScan® (EchoSens FibroScan 502, Paris, France). Examinations were performed in the right liver lobe with the same technique usually used in previous studies and according to the manufacturer's instructions [21]. A median of 10 valid measurements with success rate > 60%, and interquartile range (IQR) < 30% was considered reliable measurements and included in the analysis. In our study, TE was considered as the reference method for liver fibrosis evaluation to which the performance of ARFI elastography was compared. To discriminate between various fibrosis stages by TE we used the proposed cut offs: < 7.1 kPa for non-significant fibrosis ($F < 2$), ≥ 7.1 kPa for significant fibrosis ($F \geq 2$), ≥ 9.5 kPa for advanced fibrosis ($F \geq 3$) and ≥ 12.5 kPa for liver cirrhosis ($F4$) [5] [22, 23].

ARFI elastography

ARFI elastography using a Siemens ACUSON S3000 Ultrasound System (Siemens AG, Erlangen, Germany) with a 6C1 HD transducer, by using Virtual Touch Tissue Quantification (VTTQ) application was carried out in all patients. The measurement of ARFI elastography was performed in the right lobe of the liver while the patient lying supine position with the right arm in abduction. Patients were asked to hold their breath for a moment at the end of expiration to minimize breathing motion during the examination. ARFI measurements were obtained at a depth of 1–2 cm from the liver capsule, avoiding large vessels and bile ducts. Reliable measurements were defined as median of 10 valid measurements with an interquartile range (IQR) to median value ratio less than 30% and the result is expressed in m/s [24]. The operators who performed ARFI elastography examinations were blinded to all patients' clinical, serological data and TE results. ARFI elastography and TE were done in the same session and performed successfully in all enrolled patients. None of our patients reported failure either for ARFI elastography or TE measurements.

Statistical analysis

Data analysis was done using Statistics/Data Analysis (STATA) version 13.1 software. Mean value and standard deviation were calculated for numerical variables with normal distribution, or in the case of non-normally distributed data as median and interquartile range. The diagnostic performance of ARFI elastography for staging liver fibrosis was evaluated using sensitivity, specificity, positive likehood ratio (LR+), negative likehood ratio (LR-), and receiver operating characteristic (ROC) curve analysis. ROC curves were constructed to determine the best cut offs values for LSM by ARFI elastography, APRI and FIB-4 scores that can discriminate significant fibrosis ($F \geq 2$), advanced fibrosis ($F \geq 3$) and cirrhosis ($F4$). AUC values were interpreted as follows: 0.90–1.0 = excellent; 0.80–0.90 = good; 0.70–0.80 = fair; and less than 0.70 = poor. A P value > 0.05 was considered to indicate statistical significance.

Results

The main characteristics of enrolled patients are presented in Table 1. The median age was 48 years (range 36–56) with male predominance (59.9%). The median body mass index (BMI) was 27.6 kg/m^2. Stages of hepatic fibrosis using TE as the reference method were as follows: $F0$ in 704 (33.5%), $F1$ in 360 (17%), $F2$ in 260 (12%), $F3$ in 188 (8.9%), $F4$ in 601 (28.6%). The median values of ARFI elastography, FIB-4, and APRI were 1.31 m/s (IQR 1.07–1.98), 1.32 (IQR 0.79–2.43), and 0.48 (IQR 0.28–0.94), respectively.

The median values of liver stiffness (LS) measured using ARFI elastography, FIB-4, and APRI scores for different fibrosis stages determined by TE as reference method were shown in Table 2. The median values of ARFI elastography,

Table 1 Demographic and laboratory data of the study population ($n = 2103$)

	(Median (IQR), *n* %)
Demographics	
Age (years)	48 (36–56)
Sex, *n* (%)	
Male	1258 (59.9%)
Female	844 (40.1%)
BMI (Kg/m^2)	27.6 (24.5–31.14)
Laboratory parameters	
Hemoglobin (g/dl)	13.2 (11.9–14.5)
White blood cell (10^3/mm^3)	5.9 (4.6–7.5)
Platelets (10^3/mm^3)	198 (148–254)
Total Bilirubin (mg/dl)	0.72 (0.5–1)
Aspartate aminotransferase (IU/L) (40 IU/L)	33 (23–53.2)
Alanine aminotransferase (U/L) (40 IU/L)	34 (22–55)
Albumin (g/dL)	4 (3.7–4.4)
INR	1.06 (1–1.17)
Non-invasive modalities	
ARFI elastography (m/s)	1.31 (1.07–1.98)
FIB-4	1.32 (0.79–2.43)
APRI	0.48 (0.28–0.94)

Data expressed as median (IQR)

BMI body mass index, *INR* international normalized ratio, *ARFI elastography* acoustic radiation force impulse elastography, *APRI* aspartate aminotransferase-to-platelet ratio index

Table 2 ARFI elastography, FIB-4 and APRI values in relation to fibrosis stage by Transient Elastograhy (TE) (the reference method)

Fibrosis stage by TE	*F*0 (*n* = 704)	*F*1 (*n* = 360)	*F*2 (*n* = 260)	*F*3 (*n* = 188)	*F*4 (*n* = 601)	*P* value
ARFI elastography	1.07 (0.96–1.17)	1.19 (1.05–1.33)	1.3 (1.13–1.55)	1.6 (1.38–1.8)	2.6 (2.04–3.1)	0.0001*
FIB-4	0.84 (0.57–1.23)	1.01 (0.72–1.48)	1.42 (0.92–2.05)	1.56 (0.94–2.37)	3.06 (1.85–5.06)	0.0001**
APRI	0.28 (0.19–0.41)	0.34 (0.24–0.55)	0.45 (0.31–0.74)	0.48 (0.30–0.74)	0.99 (0.57–1.68)	0.0001***

Data expressed as median (IQR)

ARFI elastography acoustic radiation force impulse elastography, *TE* transient elastography, *APRI* aspartate aminotransferase-to-platelet ratio index

*Post hoc Mann–Whitney: $P < 0.0001$ for *F*0 versus *F*1, $P < 0.0001$ for *F*1 versus *F*2, $P < 0.0001$ for *F*2 versus *F*3, $P < 0.0001$ for *F*3 versus *F*4

**Post hoc Mann–Whitney: $P < 0.0001$ for *F*0 versus *F*1, $P < 0.0001$ for *F*1 versus *F*2, $P = 0.005$ for *F*2 versus *F*3, $P < 0.0001$ for *F*3 versus *F*4

***Post hoc Mann–Whitney: $P < 0.0001$ for *F*0 versus *F*1, $P < 0.0001$ for *F*1 versus *F*2, $P = 0.02$ for *F*2 versus *F*3, $P < 0.0001$ for *F*3 versus *F*4

FIB-4, and APRI scores were significantly increased with increase in fibrosis stage (all $P = 0.0001$).

ROC curves were constructed to determine the best cut off values for LS measurement by ARFI elastography, APRI and FIB-4 scores that can discriminate significant fibrosis ($F \geq 2$), advanced fibrosis ($F \geq 3$) and cirrhosis (*F*4). ARFI elastography showed good diagnostic accuracy in identifying $\geq F2$, $\geq F3$ and *F*4, with an AUC of 0.89, 0.94 and 0.95, respectively, optimal cut off values to predict significant fibrosis ($F \geq 2$), advanced fibrosis ($F \geq 3$) and cirrhosis (*F*4) were 1.36 m/s, 1.45 m/s, and 1.7 m/s, respectively, as shown in Table 3.

Comparing the diagnostic performances of ARFI elastography, FIB-4, and APRI for the prediction of different fibrosis stages revealed that ARFI elastography, FIB-4 and APRI yielded AUCs of 0.89, 0.82, and 0.78, respectively,

Table 3 Diagnostic performance of ARFI elastography, FIB-4, and APRI in predicting significant fibrosis, advanced fibrosis and cirrhosis

	Significant fibrosis ($\geq F2$)	Advanced fibrosis ($F \geq 3$)	Cirrhosis (*F*4)
ARFI			
AUC (95% CI)	0.89 (0.88–0.91)	0.94 (0.92–0.95)	0.95 (0.94–0.96)
Cut off	1.36	1.45	1.7
Specificity	87.5%	87.5%	90.3%
Sensitivity	80.6%	90.3%	90.9%
LR+	6.46	7.22	9.34
LR−	0.22	0.11	0.10
Accuracy	84.1%	88.5%	90.4%
FIB-4			
AUC (95% CI)	0.82 (0.79–0.82)	0.83 (0.81–0.84)	0.86 (0.83–0.86)
Cut off	1.17	1.42	1.62
Specificity	64.4%	70.4%	73.6%
Sensitivity	80%	80.1%	80.03%
LR+	2.24	2.71	3.03
LR−	0.31	0.28	0.27
Accuracy	72.7%	74.3%	75.5%
APRI			
AUC (95% CI)	0.78 (0.76–0.80)	0.79 (0.78–0.81)	0.82 (0.80–0.84)
Cut off	0.35	0.43	0.48
Specificity	57.4%	65.4%	66.2%
Sensitivity	80.2%	80.1%	80.1%
LR+	1.88	2.31	2.37%
LR−	0.34	0.3	0.3%
Accuracy	69.6%	71.2%	70.3%

ARFI elastography acoustic radiation force impulse elastography, *APRI* aspartate aminotransferase-to-platelet ratio index; *AUC* the area under the receiver operating characteristics curve, *LR+* positive likehood ratio, *LR−* negative likehood ratio

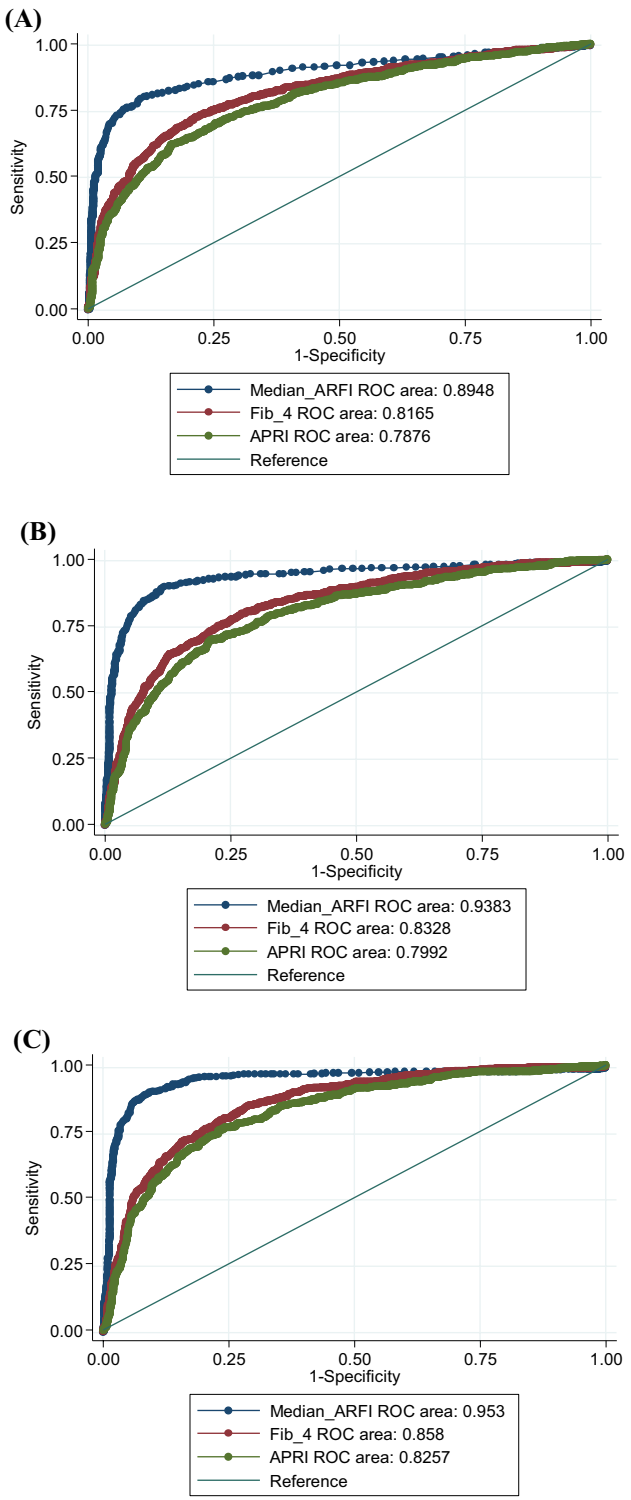

Fig. 1 Receiver-operating characteristic curves for different fibrosis stages. The performance of ARFI elastography, FIB-4 and APRI considering transient elastography (TE) as the reference method. The AUROC of ARFI elastography, FIB-4 and APRI for predicting **a** significant fibrosis ($F \geq 2$), **b** advanced fibrosis ($F \geq 3$) and **c** cirrhosis ($F = 4$)

for significant fibrosis while AUCs for liver cirrhosis was 0.95, 0.86, and 0.82 for ARFI elastography, FIB-4 and APRI, respectively. For prediction of significant fibrosis and liver cirrhosis; ARFI elastography performed better than FIB-4 and APRI as shown in Table 3 and Fig. 1 as the Chi squared test yielded a significance probability of less than 0.0001 between the three curves.

Since the mean BMI was towards the overweight side (27.6 kg/m^2) so we analyzed the predictability of LS values assessed by ARFI elastography adjusting for BMI. It revealed non-significant influence of BMI on LS values assessed by ARFI elastography ((95% CI: 0.18, *P-value* = 0.2). However, there was significant correlation between ALT level and ARFI elastography values ($r = 0.3$, $P = 0.0001$). For this analysis, we stratified our study population into three groups according to ALT levels (normal level, elevated level from 1.1 to < 3 times ULN, elevated ≥ 3timesULN). Cut off values for LSM by ARFI elastography were lower in patients with normal ALT level than in those with ALT level between 1.1 and < 3times ULN and those with ALT level ≥ 3 times ULN among different stage of fibrosis (1.35 m/s vs 1.39 m/s vs 1.54 for $F \geq 2$, 1.44 m/s vs 1.58 m/s vs 1.6 m/s for $F3$, 1.69 m/s, 1.84 m/s, 1.86 m/s for $F4$, respectively) as shown in Table 4.

Discussion

Liver fibrosis is one of the most important sequels of chronic HCV infection. Cirrhosis represents the severest form of fibrosis with the worst clinical outcomes [25]. Thus, the assessment of liver fibrosis is highly needed in the prediction of liver-related complications.

Nowadays, international guidelines accepted that shear wave elastography, mainly TE, is a reliable method substitute for non-invasive assessment of liver fibrosis and is currently used as a reference method in clinical practice replacing liver biopsy [10, 23, 26].

The current study aimed to assess the performance of ARFI elastography for liver fibrosis staging and to compare the diagnostic accuracy of ARFI elastography with FIB-4 and APRI scores in a large cohort of chronic HCV patients using transient elastography (TE) as the reference method.

The overall results suggested that ARFI elastography has high accuracy in diagnosing $F \geq 3$ (sensitivity 90.3%, specificity 87.5%) and cirrhosis ($F4$) (sensitivity 90.9%, specificity 90.3%) in comparison to $\geq F2$ with sensitivity 80.6% and specificity was 87.5%, while AUROCs curve values of 0.89, 0.94, and 0.95 for $F \geq 2$, $F \geq 3$ and $F4$, respectively. This confirms the ability of ARFI elastography to differentiate advanced fibrosis and cirrhosis ($F3$ and $F4$) from significant fibrosis ($\geq F2$). These results were in good agreement with

Table 4 ARFI elastography cut offs in relation to ALT level in different fibrosis stages

	Best cut off (m/s)	Sensitivity (%)	Specificity (%)	AUROC (95% Conf. interval)
Significant fibrosis ($F \geq 7.1$ kPa)				
ALT < ULN	1.35	80.1	87.5	0.89 (0.87–0.91)
ALT = 1.1–< 3 ULN	1.39	84.7	86.7	0.92 (0.89–0.95)
ALT ≥ 3ULN	1.54	84.8	87.5	0.89 (0.80–0.97)
Advanced fibrosis ($F \geq 9.5$ kPa)				
ALT < ULN	1.44	90.03	90.4	0.93 (0.92–0.96)
ALT = 1.1–< 3 ULN	1.58	88.9	90.7	0.94 (0.92–0.97)
ALT ≥ 3ULN	1.6	94.6	80	0.91 (0.83–0.99)
Cirrhosis ($F \geq 12.5$ kPa)				
ALT < ULN	1.69	90.2	92.1	0.95 (0.93–0.97)
ALT = 1.1–< 3 ULN	1.84	88.5	91.7	0.96 (0.94–0.98)
ALT ≥ 3ULN	1.86	81.3	86.7	0.91 (0.82–0.99)

those of meta-analyses that have been studied extensively in CHC patients and concluded that ARFI elastography was highly accurate in the diagnosis of $F \geq 2$, $F \geq 3$ and $F4$ with AUROCs of 0.85–0.89, 0.91–0.95, and 0.89–0.93, respectively [27–29].

Another important point for any elastography technique is to establish the cut off values that could be used in the prediction of different fibrosis stages. The results of our study showed that the optimal cut off values for ARFI elastography were 1.36 m/s, 1.45 m/s, and 1.7 m/s for diagnosing significant fibrosis, advanced fibrosis and cirrhosis, respectively, which were similar to the optimal cut off values of 1.34 m/s, 1.55 m/s, and 1.8 m/s that obtained in several meta-analyses for diagnosing significant fibrosis, advanced fibrosis and cirrhosis, respectively [11, 23, 27–29]. Its important to differentiate between mild fibrosis and advanced fibrosis/cirrhosis as the later need regular follow-up for the possibility of HCC development, hepatic decompensation, and liver failure.

Similar to previous studies on TE, necroinflammation of the liver as reflected by a high alanine aminotransferase (ALT) level which characterized by extensive inflammatory infiltration, hepatocyte swelling, and tissue edema is accepted as the most important confounder that lead to overestimation of LSM values which result in diminishing the accuracy of LSM values obtained by TE [12, 14]. Additionally, a study conducted by Chan et al. observed that CHB patients with elevated serum ALT levels had higher LSM values despite having the same degree of liver fibrosis. To avoid false positive results, they have proposed using modified TE cut offs based on ALT levels in CHB patients [30]. For this purpose, we sub-divided the patients according to ALT levels and evaluated the performance and optimum cut off values for ARFI elastography in this situation. We observed that the cut off LSM values using ARFI elastography were higher for patients with high ALT than for those with normal ALT at the same fibrosis stage probably due to the overestimating effect of high ALT. Sporea et al. and Bota et al. reported that among HCV patients with the same fibrosis stage, those with elevated ALT levels tended to have higher ARFI elastography values than those with normal ALT levels, consistent with our results [31, 32]. Thus, the interpretation of LSM values using ARFI elastography should take into account the concurrently measured biochemical profile of the patient.

In addition to imaging techniques, Aspartate aminotransferase (AST)-to-platelet ratio (APRI) and FIB-4 which are based on routine laboratory parameters and are readily available in clinical practice performed well in fibrosis staging in chronic HCV patients [33, 34]. Our results reported that ARFI elastography exhibited higher diagnostic accuracy than FIB-4 and APRI scores for the diagnosis of significant fibrosis, advanced fibrosis and cirrhosis (AUROC: 0.89 vs 0.82 and 0.78, 0.94 vs 0.83 and 0.79, 0.95 vs 0.86 and 0.82, respectively) and our finding was consistent with Silva Junior et al. who concluded that ARFI elastography yielded a higher diagnostic accuracy than FIB-4 and APRI scores for liver fibrosis staging (AUROC: 0.9 vs 0.86 and 0.82 for significant fibrosis while 0.98 vs 0.94 and 0.82 for cirrhosis) [35].

Finally, the current study adds on previous reports demonstrating that ARFI Elastography can efficiently assess liver stiffness (LS) in a large cohort of patients with chronic HCV infection using TE as reference method. In the evolving landscape of HCV therapy which leads to high cure rate, identifying and monitoring patients who remain at a high risk of complications after achieving sustained virological response (SVR) continues to be an issue of major concern. ARFI elastography is one of non-invasive methods for assessment of liver fibrosis that can be used to monitor fibrosis regression in responders to HCV treatment. As opposed to TE, ARFI elastography integrated into ultrasound machines which can perform

a standard ultrasound examination, Doppler examination, or Contrast Enhanced Ultrasound examinations, besides elastographic measurements for early detection of liver-related complications after sustained virological response (SVR) such as HCC, and hepatic decompensation. Thus, ARFI elastography is a valuable, cost-effective and a reliable method that can be widely used in daily practice with good accuracy in assessing liver stiffness for therapeutic decision-making, and assessment of virological response to therapy that may have a great impact on the treatment outcome in Egypt and other resource-limited countries.

A limitation of our study is that TE and not liver biopsy was used as a reference method. As said before, TE is the only elastographic technique included in international guidelines for evaluation of hepatic fibrosis in chronic hepatitis rather than liver biopsy. Second, patients with ascites were not included since TE cannot be performed in this category of patients.

In conclusion, considering TE as the reference method for liver fibrosis evaluation, ARFI elastography is a feasible technique for the non-invasive assessment of liver fibrosis with a good diagnostic performance comparable to FIB-4 and APRI scores for predicting the presence of significant, advanced fibrosis and cirrhosis in chronic HCV-infected patients.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest

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