ORIGINAL RESEARCH ARTICLE

Clinical value of acoustic radiation force impulse elastography in the prediction of hepatocellular carcinoma in chronic hepatitis C patients

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Abstract

Background and purpose of the study Acoustic radiation force impulse elastography (ARFI) represents an innovative non-invasive tool for the evaluation of liver fibrosis, cirrhosis, and early identification of neoplastic nodules during the follow-up of cirrhotic patients; however, its diagnostic accuracy in the prediction of hepatocellular carcinoma (HCC) is still controversial.

Purpose of the study To assess the potential role of ARFI elastography as a non-invasive tool for the prediction of HCC development among chronic hepatitis C (CHC) patients with advanced hepatic fibrosis and liver cirrhosis.

Methods The present study recruited 440 patients: 349 CHC patients with advanced hepatic fibrosis and cirrhosis and 91 patients with HCC-related hepatitis C virus (HCV). ARFI-imaging of the liver and transient elastography (TE) was carried out in all patients. ARFI imaging indices include the mean shear wave velocity of HCC, peritumoral parenchyma, and hepatic parenchyma in non-HCC patients. The area under the receiver operating characteristic curve (AUROC) and optimal cutoff values were obtained using a receiver operating characteristic curve analysis to assess the diagnostic performance of ARFI elastography in the predication of HCC.

Results The mean hepatic shear wave velocities by ARFI elastography of peri-tumoral cirrhotic hepatic parenchyma were significantly higher than in hepatic parenchyma in non-HCC patients (3.09 vs. 2.26 m/s, p <0.001). The AUROC for the identification of HCC was 0.8, 0.76, 0.76, 0.66, 0.72, and 0.7 for hepatic ARFI elastography, TE, fibrosis-4 score (FIB-4), AST to Platelet Ratio Index (APRI), AST/ALT ratio (AAR), and Age platelets index (API), respectively. Moreover, univariate regression analysis revealed that hepatic ARFI has the highest odd ratio in the prediction of HCC.

Conclusion ARFI elastography had a superior diagnostic performance in the prediction of HCC compared to TE and non-invasive markers in CHC patients with advanced fibrosis and cirrhosis, thus putting such patients on the top of the HCC screening list.

Keywords Acoustic radiation force impulse elastography, Chronic hepatitis C, Fibrosis scores, Hepatocellular carcinoma, Transient elastography

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Introduction

Hepatitis C virus (HCV) infection is one of the leading contributors of chronic liver disorders worldwide [1]. It represents one of the main etiologies of progressive liver fibrosis which leads to cirrhosis, hepatic decompensation, and hepatocellular carcinoma (HCC) [2]. The annual

incidence of HCC, hepatic failure, and death is estimated to be 3.2%, 2.9%, and 2.7%, respectively, if chronic HCV-infected patients with advanced hepatic fibrosis were not treated [3].

Liver fibrosis staging is critical for the management of chronic HCV patients, including the prognosis of chronic liver diseases and making therapeutic decisions [4]. Moreover, the severity of liver fibrosis and advanced liver disease necessitates need for further evaluations for HCV-related complications such as hepatic decompensation, HCC surveillance, and esophageal varices screening.

Liver biopsy (LB) is the reference method for the staging of liver fibrosis [5]; however, it is limited by its invasiveness, sampling error, and unavoidable complications such as bleeding [6].

Several non-invasive approaches have been proposed to stage hepatic fibrosis [7] and gradually replaced LB. These methods consist of serum markers and imaging modalities. The liver fibrosis marker panel consists of direct and indirect serologic tests while imaging modalities commonly consist of ultrasound-based elastography and magnetic resonance elastography (MRE). Transient elastography (TE) and elastographic modalities based on shear waves generated via an acoustic beam, i.e., elastography point quantification (ElastPQ; Philips) and acoustic radiation force impulse elastography (ARFI) or virtual touch tissue quantification (VTTQ; Siemens) and supersonic shear imaging (SSI) [8–10].

ARFI elastography is an ultrasound-based, non-invasive imaging technique that is integrated into conventional ultrasound machine for assessing liver stiffness (LS) and predicting the complications of patients with chronic liver disease (CLD) in chronic viral hepatitis such as hepatitis B virus (HBV) or hepatitis C virus (HCV) and non-alcoholic fatty liver disease (NAFLD) [10, 11].

The current study aimed at comparing the parenchymal stiffness of the hepatic tissue adjacent to HCC to hepatic parenchymal stiffness in HCV patients with advanced fibrosis (≥F3) and cirrhosis (F4) using the ARFI 2D images in order to set a cutoff value of hepatic parenchymal stiffness that could predict the development of HCC in HCV patient with advanced hepatic fibrosis and cirrhosis, thus putting such patients on the top of the HCC screening list.

Methods
Patient population
The present retrospective case-control study was carried out at Cairo University Center for Hepatic Fibrosis (CUC-HF), Endemic Medicine Department, Faculty of Medicine, Cairo University, during the period from January 2015 to July 2016.

Over the study period, 94 patients with post-hepatitis C HCC diagnosed according to the European Association for the Study of the Liver (EASL) guidelines [12], as well as 349 patients with HCV-related advanced hepatic fibrosis (≥F3) and cirrhosis (F4) as measured by TE were enrolled consecutively.

Inclusion criteria
For CHC patients, chronic HCV infection was established with the positivity of anti-HCV antibody and HCV ribonucleic acid (RNA) polymerase chain reaction (PCR) for more than 6 months, the presence of advanced hepatic fibrosis (≥9.5 kPa; ≥F3) and cirrhosis (≥12.5 kPa; F4) as detected by TE while for HCC patients that they had the history of HCV infection and were diagnosed according to the latest EASL guidelines [12].

Exclusion criteria
The HCC patients had a history of any previous local therapy, i.e., radiofrequency ablation (RFA), percutaneous ethanol injection (PEI), patients with hepatic focal lesions other than HCC (i.e., metastasis, hemangioma), and patients with ARFI failure.

Collected data
Demographic characteristics and laboratory findings were obtained for each patient at the time of TE measurements and ARFI imaging. The presence of HCC was assessed. Furthermore, the assessment of the degree of liver dysfunction and the presence of hepatic decompensation were recorded.

Imaging technique
Abdominal ultrasonography and TE were done for all patients. TE examination was performed using Fibro-Scan® 502 Touch according to the manufacturer's recommendations taking into consideration the reliability criteria of at least ten successful attempts with a success rate >60% and an interquartile range (IQR) <30% [13].

After a B-mode US image, the ARFI 2D images were carried out by Virtual Touch TM tissue imaging button which was operated by 2 expert hepatologists who were blind to patients' data. The part of hepatic parenchyma to be examined for elastic properties is described utilizing a Region of Interest (ROI), defined by a box with a fixed dimension of 1 cm × 0.5 cm and a maximum depth of 5.5 cm. The ROI did not include any vessels or biliary structures, and any potential presence of fibrotic scar was excluded from the ROI. The target hepatic parenchyma is mechanically "pushed" by short-duration forces (less than 1 m/s) that produce localized displacements. The shear waves generated propagate perpendicular to the acoustic pulse away from the target ROI. The shear

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wave velocity (SWV) was expressed in meters per second (m/s). To reduce cardiac- and respiration-related tissue motion in the ROI, all measurements were done in the right hepatic lobe by the intercostal approach during a brief breath hold (neither full inspiration nor full expiration). Successful ARFI liver elastography was only considered if 10 attempts could be obtained with a success rate of ≥60% and the interquartile range (IQR) was <30% of the mean value. Non-valid measurements due to the inability to hold breath as required or an inappropriate ROI positioning (i.e., vessels or biliary structures within the ROI), expressed by the system as "N/A" (not-available) or "XXXX" or "0", were ruled out. In the absence of validated quality criteria, ARFI failure was established as the acquisition of fewer than 10 valid measurements [14]. The hepatic shear wave velocity (SWV) by ARFI was calculated for HCC, hepatic parenchyma adjacent to HCC, and compared to the ARFI values in patients with advanced fibrosis and cirrhosis in the non-HCC group.

Calculated scores

The following scores were used in predicting HCC.

- AST to Platelet Ratio Index (APRI) score = (AST/upper limit of normal)/platelet count (expressed as platelets $\times 10^9$/L) $\times 100$ [15].
- Fibrosis-4 score (FIB-4) = Age (y) $\times$ AST (IU/l)/platelet count ($\times 10^9$/liter) $\times \sqrt{\text{ALT (IU/l)}}$ [16].
- Age platelets index (API) = Age (year)/PLT ($\times 10^9$/L) [17]
- AST/ALT ratio (AAR) = AST (IU/l)/ALT (IU/l) [18]

Statistical analyses

STATA 14 software was used to validate and analyze the data. Patients' demographic and routine laboratory values were expressed as number (percent) for categorical variables and as mean ($\pm$ SD) or median (inter quartile range) for continuous variables. All quantitative parametric and non-parametric variables were analyzed using either Students' *t* test or Mann-Whitney test for comparison of the HCC group and non-HCC group whenever appropriate. The non-HCC group of patients was further stratified according to hepatic stiffness measured by TE into patients with fibrosis stage 3 (F3, stiffness 9.5–14.4 kPa) and patients with fibrosis stage 4 (F4, stiffness ≥14.5 kPa). A comparison of 3 groups was done using Kruskal-Wallis for non-parametric or ANOVA (analysis of variance) test for parametric variables whenever appropriate. Chi-square test was used for comparison of categorical data. A univariate logistic regression model was constructed to identify significant predictors for HCC in our cohort. The diagnostic performance of hepatic parenchymal stiffness measured by ARFI in the prediction of HCC occurrence among patients with post hepatitis C significant hepatic fibrosis was evaluated using receiver operator characteristic (ROC) curves. The area under the ROC curves (AUROC) and the 95% confidence interval (95%CI) were used as indexes of accuracy. All statistical analyses were based on two-sided hypothesis tests with a significance level of $p < 0.05$.

Results

From January 2015 to July 2016, a total of 443 CHC patients were recruited. Of these, three patients were ruled out because of ARFI measurement failure due to the inability to hold their breath as required or poor compliance of patients. Finally, 440 CHC patients with ten valid ARFI measurements obtained from the right lobe of the liver were enrolled and they were further classified as 349 CHC patients with advanced hepatic fibrosis (≥F3) and cirrhosis (F4) and 91 patients with HCV-related HCC.

Demographic and laboratory parameters in both groups were shown in Table 1. Patients with HCC were significantly older with male predominance (76.9%) than non-HCC patients (p=<0.001).

Regarding fibrosis scores, they were significantly higher in HCC patients than in non-HCC patients as shown in Table 2.

Liver stiffness measurement (LSM) by TE displayed a highly significant difference (p<0.001) between the non-HCC (22.2 $\pm$ 12.8 kPa) and the HCC group (38.1 $\pm$ 21.4 kPa). The mean hepatic SWV by ARFI of peri-tumoral cirrhotic hepatic parenchyma was significantly higher than in hepatic parenchyma in non-HCC patients (3.09 vs. 2.26 m/s, p <0.001) as shown in Fig. 1A and Table 2. Moreover, a significant difference was found between the mean of hepatic SWV within HCC nodules and peri-tumoral cirrhotic hepatic parenchyma and hepatic parenchyma in non-HCC patients (2.09 vs. 3.09 vs. 2.26 m/s, p <0.001) as shown in Fig. 1B.

AUROC for predicting HCC was 0.8 and 0.76 for hepatic ARFI and TE, respectively, with a cutoff value of 2.28 m/s for hepatic SWV by ARFI and 28.8 kPa by TE. Hepatic ARFI displayed 95.6% sensitivity and 54.2% specificity while TE displayed 65% sensitivity and 80.2% specificity as shown in Table 3 and Fig. 2.

The AUROC for FIB-4, APRI, AST/ALT ratio, and API were 0.76, 0.66, 0.72, and 0.7, respectively, for predicting HCC with a p value =< 0.01 for all methods. The best cutoff levels for FIB-4, APRI, AST/ALT ratio, and API were 3.2, 1, 1.4, and 8, respectively, with a sensitivity of 63.7%, 67.03%, 56.04%, and 70.3%, respectively, and a specificity of 73.7%, 61.7%, 81.1%, and 68%, respectively, as shown in Table 3.

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Table 1 Demographic and laboratory data of the studied patients (*n*= 440)

Variables	Non-HCC group (HCV ≥ F3and F4) (*n*=349)	HCV-HCC group (*n*=91)	*P* value
Demographic data			
Age, years	52.89 ± 8.95	60.37 ± 6.99	**<0.001**
Gender, *n* (%)			
Male	209 (59.89%)	70 (76.92%)	
Female	140 (40.11%)	21 (23.08%)	**0.003**
Laboratory data			
White blood cell (10^3/mm^3)	5.95 ± 2.2	5.9 ± 2.8	0.88
Hemoglobin (gr/dl)	13.3 ± 1.91	11.3 ± 2.03	**<0.001**
Platelet (10^3/mm^3)	163.1 ± 69.5	134.7 ± 77.8	**0.0001**
Serum albumin (g/dL)	3.8 ± 0.6	3.02 ± 0.6	**<0.001**
Total bilirubin (mg/dl)	1.1 ± 1.2	1.98 ± 1.9	**<0.001**
AST (U/L) (40U/L)	58.4 ± 43.99	75.02 ± 60.4	**0.0034**
ALT (U/L) (40U/L)	59.8 ± 47.1	56.9 ± 56.5	0.6244
INR	1.14 ± 0.2	1.43 ± 1.1	**<0.001**
AFP (ng/dl)	7.7 (9.8)	95 (287)	**<0.001**
Characteristics of HCC			
1. No. of focal lesion, *n* (%)	-	-	**-**
Single	-	57 (62.6%)	**-**
Multiple	-	34 (37.4%)	**-**
2. Site of focal lesion, *n* (%)	-		**-**
Right lobe	-	69 (75.8%)	**-**
Left lobe	-		**-**
Bi-lobar	-	22 (24.2%)	**-**
3. Size of focal lesion, *n* (%)	-		**-**
< 5cm	-	71 (78%)	**-**
>5cm	-	20 (22%)	**-**
4. Maximum diameter of focal lesion	-	3.7 ± 1.74 cm	**-**

Data expressed as mean ± SD, number (%), or median (IQR)

ALT Alanine aminotransferase, *AST* Aspartate aminotransferase, *HCC* Hepatocellular carcinoma, *INR* International normalized ratio

Table 2 Liver stiffness measurements and fibrosis scores in the studied patients (*n*=440)

Variables	Non-HCC group (HCV≥ F3 and F4) (*n*=349)	HCC group (*n*=91)	*P* value
Liver stiffness measurement			
TE (kPa)	22.21 ± 12.84	38.1 ± 21.4	**<0.001**
ARFI (m/s)	2.26 ± 0.79	3.09 ± 0.6	**<0.001**
Fibrosis scores			
FIB-4	3.03 ± 2.24	6.2 ± 4.9	**<0.001**
APRI	0.77(0.97)	1.35 (1.52)	**<0.001**
Age platelets index	5.9 ± 2.2	7.39 ± 1.9	**<0.001**
AST/ALT ratio	1.09 ± 0.461	1.6 ± 0.88	**<0.001**

Data expressed as mean±SD or median (IQR)

ARFI Elastography, acoustic radiation force impulse elastography, *ALT* Alanine aminotransferase, *AST* Aspartate aminotransferase, *APRI* Aspartate aminotransferase-to-platelet ratio index, *FIB-4* Fibrosis-4 score, *TE* Transient elastography

Univariate regression analysis revealed that ARFI elatography and TE as well as fibrosis scores (FIB-4, API, and AST/ALT ratio) were significantly dependent variables in the prediction of HCC; however, hepatic ARFI has the highest odd ratio in the prediction of HCC as shown in Table 4.

Discussion

HCC is a common malignancy worldwide [19] with more than 700,000 new cases annually and ranking third as a cause of cancer-related death [20]. HCV is the leading cause of advanced liver fibrosis and cirrhosis, with an increased risk of developing HCC [21]. The early diagnosis and prediction of HCC are highly essential to implement curable management to reduce HCC-related deaths. Egypt has the highest burden of HCV infection in the world [22]. HCV is a major contributor to liver cirrhosis and cancer in Egypt [23].
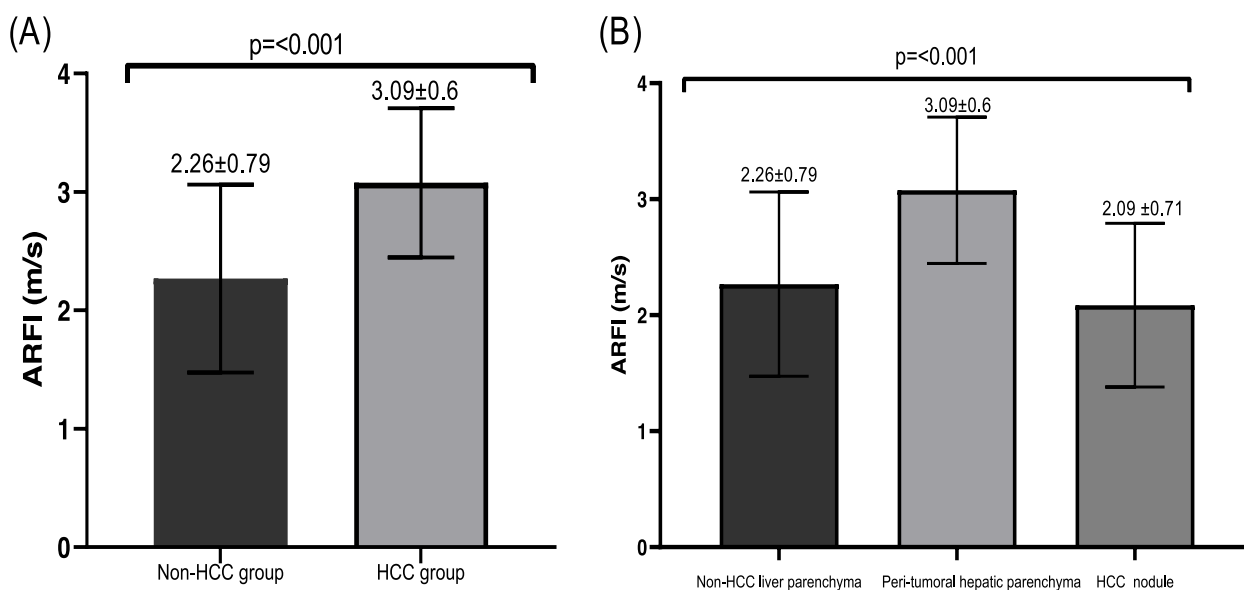
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Fig. 1 **A** Acoustic radiation force impulse (AFRI) values in non-hepatocellular carcinoma (HCC) group and HCC group. **B** AFRI values in HCC nodule vs. liver parenchyma beside HCC nodule vs. non-HCC liver parenchyma

Table 3 Diagnostic performance, optimal cutoffs, and validity of hepatic ARFI, TE, and fibrosis scores for the prediction of HCC among patients with advanced hepatic fibrosis (≥F3) and cirrhosis (F4)

	P value	AUROC (95% CI)	Optimal cutoff	Sensitivity	Specificity	PPV	NPV
Liver stiffness measurement							
SWV of hepatic ARFI (m/s)	<0.001	0.80 (2.81–5.76)	2.28	95.6	54.2	35.5	97.4
Hepatic parenchyma stiffness by TE (kPa)	<0.001	0.76 (1.03–1.07)	28.8	65	80.2	26.1	94.6
Fibrosis scores							
FIB-4	<0.001	0.76 (1.05–1.18)	3.2	63.7	73.7	35.9	88.2
APRI	<0.001	0.66 (0.98–1.16)	1	67.03	61.7	31.4	87.2
AST/ALT ratio	<0.001	0.72 (2.46–6.03)	1.4	56.04	81.1	43.96	87.4
Age platelets index	<0.001	0.70 (1.26–1.65)	8	70.3	68	34.8	86.6

ARFI Elastography, acoustic radiation force impulse elastography, *ALT* Alanine aminotransferase, *AST* Aspartate aminotransferase, *APRI* Aspartate aminotransferase-to-platelet ratio index, *AUC* Area under the receiver operating characteristics curve, *FIB-4* Fibrosis-4 score, *TE* Transient elastography, *SWV* Shear wave velocity

The risk factors for HCC in chronic HCV patients have been widely studied and the degree of liver fibrosis is known to be the strongest one [24].

In this study, we investigated the clinical use of hepatic SWV measured with ARFI imaging in a large cohort of CHC patients with advanced hepatic fibrosis (≥ F3) and cirrhosis (F4) to set cutoff value for predicting HCC and early therapeutic decisions are made.

It was well known that serum albumin, bilirubin, and international normalized ratio (INR) reflecting the synthetic function of hepatocytes while AST and ALT correlated with both necroinflammation and hepatic fibrosis stage as well as platelets count reflect the severity of hepatic fibrosis. In addition, high AST and low platelets count were related to a higher stage of hepatic fibrosis and portal hypertension denoting severe hepatic fibrosis which favors progression to HCC [25].

These parameters were used to calculate non-invasive markers such as FIB-4, APRI, AAR ratio, and AP index which were previously studied and evaluated in predicting the risk of developing HCC [26–31].

Among these non-invasive markers, FIB-4 has been validated with regard to its longitudinal perspective to predict the development of HCC and other prognostic outcomes in viral hepatitis [26–28]. Our study was able to predict the development of HCC at a cutoff value of 3.2 in agreement with Ito et al. (2015) and Tamaki et al. (2014) who concluded that FIB-4 index >2.0 and ≤4.0, as
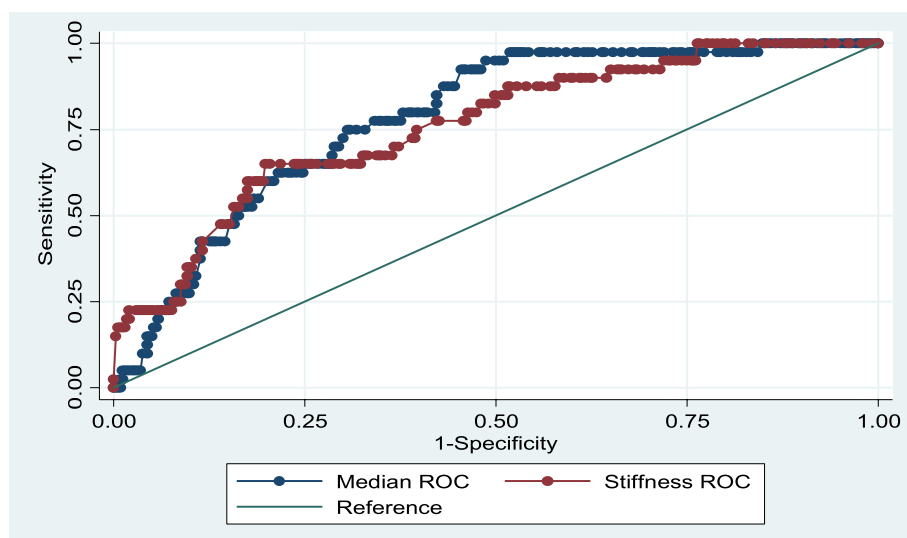
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Fig. 2 Receiver–operator curve (ROC) curve of ARFI elastography and TE for diagnostic performance in the prediction of HCC occurrence in patients with advanced hepatic fibrosis (≥ F3) and cirrhosis (F4)

Table 4 Univariate logistic regression model with non-invasive methods in the prediction of HCC among patients with advanced hepatic fibrosis (≥ F3) and cirrhosis (F4)

	OR (95% CI)	*P* value
Hepatic ARFI, m/s	4 (2.8–5.8)	**<0.001**
Hepatic stiffness by TE, kPa	1.1 (1.0–1.1)	**<0.001**
FIB-4	1.3 (1.2–1.5)	**0.001**
Age platelets index	1.5 (1.3–1.7)	**<0.001**
AST/ALT ratio	3.9 (2.5–6.0)	**<0.001**

ARFI Elastography, acoustic radiation force impulse elastography, *ALT* Alanine aminotransferase *AST* Aspartate aminotransferase *APRI* Aspartate aminotransferase-to-platelet ratio index *FIB-4* Fibrosis-4 score, *TE* Transient elastography

well as FIB-4 index >3.25, could predict HCC development, respectively [29, 30]. Moreover, the present study showed APRI, AAR ratio, and AP index could predict HCC at a cutoff of 1, 1.4, and 8, respectively, and this was in agreement with Tseng et al. (2013) who showed APRI, AAR, and AP index at cutoff >1.4, ≥1, and ≥8, respectively, could predict the highest risk for HCC development in HCV patients [31].

In addition, LSM by TE was significantly higher among HCC patients in comparison to patients with advanced hepatic fibrosis (≥F3) and cirrhosis (F4) (non-HCC patients) and this was in accordance with previous studies which stated LS is significantly higher in patients with HCC than in patients without HCC [32, 33].

Furthermore, TE and fibrosis scores predict not only the hepatic fibrosis stage in CHC patients but they also

seem to be a non-invasive alternative in predicting complications of cirrhosis including large esophageal varices, variceal bleeding, and HCC [34–37]. However, the presence of ascites in cirrhotic patients limits TE performance because of its inability to generate valid measurements [13].

Our study showed also that the AUROC curve of TE for prediction of HCC was 0.76 with a cutoff value of 28.8 kPa (sensitivity 65%, specificity 80.23%). This cutoff value is very similar to those reported by Masuzaki et al. [35] and Yosry et al. [38].

Several studies have confirmed that ARFI elatography is a more reliable method than TE in analyzing the progression of CLD toward cirrhosis [39] and demonstrated its usefulness in the evaluation of hepatic focal lesions because ARFI allows the dynamic visualization of the liver parenchyma and the placement of the ROI directly on the liver tissue; thus, ARFI elastography showed a satisfactory specificity for discriminating malignant lesions from benign lesions [40, 41].

Based on this fact, our study showed that the mean hepatic SWV measured with ARFI within HCC were significantly lower than hepatic parenchyma adjunct to HCC in HCC patients. This could be explained by the fact that HCC had a lower amount of collagen deposition, resulting in much softer than the surrounding hepatic parenchyma with very low elastometric values as was stated in previous studies [40–43], and another important finding was that ARFI values of HCC seemed to be similar to hepatic parenchyma in non-HCC in patients with advanced hepatic fibrosis ≥F3.

Similar to TE and fibrosis scores, ARFI was also studied for predicting complications of liver cirrhosis, especially portal hypertension and HCC [44, 45].

The present study reported that the AUROC curve of hepatic ARFI for predicting HCC was 0.79 with a cutoff of 2.28 m/s (sensitivity 95.6% and specificity 54.23%). This AUROC curve differed from the one obtained by Vermehren et al. [45] being higher this might be attributed to the patient numbers were consistently low in the study.

The limitations of the study are as follows: First, the diagnosis of HCC was based on imaging modalities [triphasic computed tomography (CT) or magnetic resonance imaging (MRI)], not on histological examination. Second, the size of the ROI did not cover the entire HCC; therefore, it might not reflect the heterogeneity of the entire HCC and stiffness measurement in the HCC ROI may not be representative of the full extent of stiffness variation within a tumor. Third, the number of HCC patients was relatively small. Therefore, further studies with larger numbers of HCC patients are warranted to determine the usefulness of ARFI elastography in this special patient population.

Conclusion

In conclusion, ARFI elastography can reflect changes in the stiffness of malignant focal liver lesions accurately and can be used in the prediction of HCC among patients with advanced hepatic fibrosis and cirrhosis in contrast to TE which cannot asses the focal lesion elasticity itself and also cannot be performed in decompensated cirrhotic patients (i.e., ascites).

Abbreviations

AAR	AST/ALT ratio
ALT	Alanine transaminase
API	Age platelets index
APRI	AST to Platelet Ratio Index
ARFI	Acoustic radiation force impulse elastography
AST	Aspartate transaminase
AUROC	Receiver operating characteristic curve
CHC	Chronic hepatitis C
CI	Confidence interval
CLD	Chronic liver disease
EASL	European Association for the Study of the Liver
ElastPQ	Elastography point quantification
FIB-4	Fibrosis-4 score
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
INR	International normalized ratio
IQR	Interquartile range
kPa	Kilopascal
LB	Liver biopsy
LS	Liver stiffness
LSM	Liver stiffness measurement LSM
MRE	Magnetic resonance elastography
NAFLD	Non-alcoholic fatty liver disease
PCR	Polymerase chain reaction
PEI	Percutaneous ethanol injection
RFA	Radiofrequency ablation
RNA	Ribonucleic acid
ROI	Region of Interest
SSI	Supersonic shear imaging
SWV	Shear wave velocity
TE	Transient elastography
VTTQ	Virtual touch tissue quantification

Availability of data and materials
The data supporting the results are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
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 (approval code; N-53-2014), Cairo University. Written informed consent was obtained from each patient prior to the TE and ARFI examinations.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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