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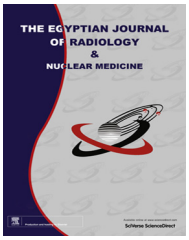

ORIGINAL ARTICLE

Diffusion weighted MRI and transient elastography assessment of liver fibrosis in hepatitis C patients: Validity of non invasive imaging techniques

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KEYWORDS

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Abstract *Objective:* Treatment for hepatitis C infection and monitoring of progression were based on degree of fibrosis, which were traditionally diagnosed by liver biopsy but it has many limitations. We aim to evaluate noninvasive imaging methods, so-called diffusion-weighted MRI (DW MRI) and transient elastography [(TE), fibroscan] in diagnosing liver fibrosis in hepatitis C (HCV) patients.

Patients: The Study included 102 hepatitis C patients (62 male) with mean age of 38 ± 5. For all patients liver biopsy was done followed by DW MRI and TE. METAVIR classification system was used for staging liver fibrosis. Data obtained were collected and results of DW MRI and TE were compared with those of histopathology. The diagnostic performance of ADC and TE was determined using areas under receiver operating characteristic (AUROC) curves for significant fibrosis ⩾F3.

Results: Measuring ADC at different *b*-values had a significant negative correlation with stage of fibrosis $P = 0.001$, the best negative correlation at *b*-value of 700 mm^2/s. TE had a significant positive correlation with stage of fibrosis $P = 0.005$. Both examination showed a significant difference between fibrosis stage <F3 and stages ⩾F3 with $P < 0.00$ for ADC measure at each *b*-value and TE respectively.

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Conclusion: This study suggests that DW MRI and TE had favorable comparable results with liver biopsy for the diagnosis of significant liver fibrosis.

1. Introduction

Patients with hepatitis B and hepatitis C virus infections are at high risk for development of hepatic fibrosis that proceeds to cirrhosis, once cirrhosis occurs the risk of complication as portal hypertension and hepatocellular carcinoma increases (1), liver fibrosis in chronic liver disease results from excessive accumulation of an extracellular matrix in response to chronic inflammation. Viral hepatitis C infection represents the most common cause of hepatic fibrosis in Egypt (2).

The assessment of liver fibrosis in patients with viral hepatitis is essential not only to determine prognosis but also to select patients who are in need for antiviral therapy (3,4). Liver biopsy was the standard reference method for evaluation of liver fibrosis (3), but it has several limitations such as hemorrhage, pain, interobserver variability, sampling errors and also it lacks the patient acceptance (5).

This made the need for a noninvasive, fast, safe and reliable method that allows evaluation of liver fibrosis, and repetitive measurements for monitoring disease progression and treatment response (5).

These non invasive methods include routine biochemical and hematological liver function tests, serum markers of connective tissue, and scoring systems using a combination of clinical and/or laboratory tests. Unfortunately, these methods had a failure rate reaching about 50% of the patients to quantify liver fibrosis (6).

Recently, a wide variety of non invasive promising imaging-based methods had been used for assessing hepatic fibrosis, including ultrasound, CT and MRI (7). The measurement of liver stiffness with ultrasound transient elastography (fibroscan) was proven to be accurate in the detection of significant fibrosis in patients with hepatitis C. However, transient elastography (TE) cannot be used in obese patients or patients with ascites or narrow intercostal spaces (6,8,9).

Magnetic resonance imaging (MRI) based techniques, such as diffusion weighted magnetic resonance imaging (DW-MRI) and measuring apparent diffusion coefficient (ADC) value have become an important noninvasive diagnostic tool in the evaluation of liver fibrosis. DW MRI allows whole liver examination with an insight into distribution of liver fibrosis permitting detection of the most affected liver segments (5).

The aim of this study is to evaluate the diagnostic performance of non invasive technique used in measuring the liver stiffness as measuring ADC value in diffusion weighted magnetic resonance imaging DW MRI and fibroscan (FS) in diagnosis of liver fibrosis in patients with hepatitis C virus (HCV) infection.

2. Patients and methods

2.1. Study population

This prospective study was conducted at Radiology and Internal Medicine Departments, Zagazig University Hospitals, Egypt, between June 2011 and May 2013, and included all patients having hepatitis C of any severity, aged $\geqslant$18 years old and referred to our department for ultrasound guided liver biopsy.

Chronic hepatitis C was proven by using standard diagnostic techniques (detection of hepatitis C antibodies and positive serum HCV-RNA by polymerase chain reaction for six months). Exclusion criteria were: (1) patients with other chronic liver diseases as hepatitis B, metabolic disease, fatty liver or focal mass in the liver either benign or malignant; (2) patients classified as fibrosis stage 0 (F0) according to METAVIR scoring system (10); (3) contraindications to biopsy (e.g. pregnancy, ascites); (4) patients with body mass index (BMI) > 28 kg/m^2; (5) contraindication to MRI examination; (6) previous liver transplant; (7) known malignancy or other terminal disease and (8) patients refused to undergo biopsy or to participate in the study.

The study protocol was approved by the local ethics committee. And an informed consent was obtained from all patients before participating in the study.

From 132 referred patients, only 102 met the inclusion criteria and completed the study, there were 62 males and 40 females. Their age ranged from 19 to 52 years with mean age of 38 ± 5.

All patients subjected to full clinical and laboratory evaluation, liver biopsy followed by transient elastography and MRI evaluation.

Liver fibrosis stages were evaluated according to the METAVIR scoring system (16). Fibrosis (F) was staged on a five-point scale as follows: F0 = no fibrosis; F1 = portal fibrosis without septa; F2 = portal fibrosis and few septa; F3 = numerous septa without cirrhosis; F4 = cirrhosis (16).

2.2. Clinical and laboratory evaluation

Clinical parameters were determined for all patients including age, weight, height, duration of the disease, past history of ascites or bleeding varices. Laboratory evaluation included liver function test, platelet count, and prothrombin time.

2.3. Liver biopsy

Percutaneous liver biopsy was done before MRI and TE with mean time of delay 10 ± 6 days; (range, 9–30 days). Liver biopsy was taken by an experienced radiologist with ultrasound guidance using a 16–18 gauge needle. Liver biopsy samples were fixed in formalin, embedded in paraffin, and stained with hematoxylin–eosin and Masson trichrome. The mean size of liver biopsy specimens was 18 mm (range: 15–21 mm). All samples were analyzed by a pathologist, blinded to clinical results.

2.4. Radiological evaluation

All patients were subjected to both TE and MRI, either of the technique was done first according to the availability or both done at same sitting, with an interval time ranging from the

same day to seven days (mean interval time of three days). Both TE and MRI evaluated by different radiologists, who were unaware of the results of the other exam.

2.4.1. Transient elastography

Transient elastography was performed using FibroScan (Philips – iU22 xMATRIX). The idea of TE in measuring liver stiffness is based on eliciting elastic shear wave propagating through the liver tissue, followed by pulse-echo ultrasound acquisitions. Their velocity is measured and is directly related to the degree of liver stiffness. The examination was done by applying the probe over the right lobe of the liver through the intercostal spaces, while patients lay supine with the right arm abducted over the head and breathing normally (11). TE measure liver stiffness in a volume of nearly a cylinder 1 cm wide and 4 cm long at 25 and 65 mm below the skin surface, the area must be devoid of any large vascular structures.

2.4.1.1. Interpretation of results. Ten successful measurements were performed, and the median value of these measurements was considered as a value for liver stiffness, expressed in kilopascal (kPa). The machine software determines if the measurement is successful or not (unsuccessful measuring gives no reading). Liver stiffness values range from 2.5 to 75 kPa. The result is immediately available, and it is operator-independent. Only examinations with 10 valid measurements and a success rate of at least 60% were considered reliable.

2.4.2. b-DW MRI examination

DWI of the liver was performed on a 1.5 Tesla MR scanner (Philips Medical Systems, Achieva). A transverse single-shot echo-planar imaging sequence was performed using a quadrature phased-array coil with respiratory and finger pulse triggering.

We used multiple diffusion sensitivities of *b*-values (200, 500, 700 and 1000 s/mm^2), with the following acquisition parameters: average TR of 1300–1600 ms; ET of 60–86 ms; matrix size of 256 × 256; field of view of 32–40 cm; bandwidth of 1736 Hz/pixel; number of excitation = 2; slice thickness = 6 mm; gap = 1 mm number of slices = 30, average (respiratory cycle dependent) acquisition time = 2 min.

DW MRI was performed without intravenous contrast injection.

ADC maps were formed automatically by MRI software regions of interest (ROIs) approximately 1–1.5 cm in diameter was placed in four locations within the liver for each *b* value and the combination of all *b* values. ADCs were measured in the lateral and medial segments of the left lobe and the anterior and posterior segments of the right lobe, considering avoiding the site of GB and liver vasculature. The final ADC was the average of the four ROIs. A routine MRI examination of the liver was performed after the DWI sequence only if clinically indicated.

2.5. Data interpretation

Data for each patient were collected, and the results of TE and MRI were compared with those of the histopathology.

2.6. Statistical analyses

All data were reported as mean, slandered deviation and proportions. Patients ADC value of liver stiffness at different *b* values was compared using the repeated measures of ANOVA test, and for values of TE we used one-way analysis of variance (F or ANOVA) test and the values followed the least significant difference (LSD). The impact of specific predictors of discordance on ADC and TE performance was determined using areas under receiver operating characteristic (AUROC) curves for significant fibrosis ⩾F3. AUROCs were compared using the method of DeLong et al. (12). All analyses were performed using (Spss 16). *P*-values < 0.05 and 0.001 were considered statistically significant and highly significant respectively.

3. Results

This study included 102 patients with hepatitis C virus, they were 62 males and 40 females. Their age ranged from 19 to 52 years with mean age of 38 ± 5. The mean duration of the disease was 2 ± 7/years, the BMI (kg/m^2) ranged from 17.8 to 28 with mean BMI of 22 ± 8.3, all patients undergone liver biopsy and staged according to METAVIR scoring system; including 35 patients in F1; 22 patients in F2; 25 patients in F3 and 20 patients in F4. The demographic data of the patients and the results of liver biopsy are illustrated in Table 1.

3.1. Mean ADC values and fibrosis stages

The mean ADC values for each stages of liver fibrosis using different *b* values (200, 500, 700, 1000) was shown in Table 2. There is evident negative correlation between the ADC value and degree of fibrosis at each *b*-values, the *r* value was 0.935, 0.927, 0.965 and 0.898 with *b* value of 200, 500, 700 and 1000 respectively, 1 *P* value 0.001 which is highly significant, the best negative correlation was achieved at a *b* value of 700.

Comparing mean hepatic ADC between patients with fibrosis stages < F3 versus fibrosis stage ⩾F3 (Table 3), there was a highly significant difference at the mean hepatic ADC at each *b*-values between the two groups (*P*-value = 0.000).

Table 1 Demographic data of the patient and fibrosis stages by liver biopsy.

Patient characteristics	Value
M/F patients (%) *	62(60.8%)/40(39.2%)
Patient age (y)	38 ± 5
Duration of the disease (year)	2 ± 7
Body mass index (kg/m^2)	24 ± 8.3
AST level (UI/I)	51 ± 23
ALT level (UI/I)	73 ± 45
GGT level (UI/I)	120 ± 65
Total bilirubin level (mg/dL)	10.5 ± 18
Platelet count (103/mm^3)	198 ± 76
Fibrosis stages (liver biopsy results)	
F1	35(34.3%)*
F2	22(21.6%)*
F3	25(24.5%)*
F4	20(19.6%)*

* Data are given as mean ± SD or *n* (%).

3.2. Transient elastography and fibrosis stages

The value of liver stiffness by FS ranged from 4.2 to 72.5 kPa with a mean value of 5.7 ± 0.81.

The values of liver stiffness measurement by transient elastography increased with an increase the stage of fibrosis from F1 to F4 with a significant positive correlation ($r = 0.879$; $P < 0.001$), it is lower for patients with stages F1 and F2 than stages F3 and F4. Table 4 shows the mean values of LSM stratified by stage of fibrosis (see Figs. 1–4).

3.3. Mean hepatic ADC values and transient elastography performance in liver fibrosis

Receiver operating characteristics (ROC) curve analysis was used to evaluate the ability of hepatic ADC (at different *b*-values 200, 500, 700 and 1000 mm^2/s) and transient elastography to predict liver fibrosis stages $<$F3 versus $\geqslant$F3, the best cut off value of mean hepatic ADC was 2.17×10^{-3}, 1.66×10^{-3} mm^2/s, 1.62×10^{-3} mm^2/s and 1.59×10^{-3} mm^2/s at *b*-value of 200,500,700 and 1000 respectively, while the cut off value of transient elastography was 12.95 kPa (above this value patient belongs to fibrosis stage $<$F3 and below this value the patient belongs to stage $\geqslant$F3), the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) as well as degree of significance for mean ADC at each *b*-value and TE is shown in Table 5.

4. Discussion

Liver fibrosis (LF) in chronic hepatitis C progresses as the period of infection prolongs, and may reach liver cirrhosis with the increase in the risk of development of hepatocellular carcinoma (13), the accurate assessment of LF is very important in order to predict the prognosis and start the appropriate prophylactic therapy to prevent disease progression (11).

In patients with chronic viral hepatitis, the liver biopsies are used to assess prognosis, guide antiviral therapy, and predict treatment efficacy (1,14), liver biopsy still the gold standard method for evaluation of liver fibrosis in hepatitis C patients, but there are many drawbacks for liver biopsy as: it is invasive methods, the liver specimen obtained from a single area out of the whole liver mass (these lead to high sample inaccuracy owing to the patchy distribution of liver fibrosis) (15), sample size may affect the results obtained, liver biopsy is contraindicated in patients with ascites or abnormal coagulation profile which is frequently encountered in patients with advanced fibrosis or cirrhosis due to chronic hepatitis C, moreover there are 10–20% of inter- and intraobserver disagreement in rating the degree of fibrosis was reported (15–17). From other point of view liver biopsy has poor patient acceptance and the risk of complication is still present such as, bleeding, pain, infections, anxiety, pneumo or hemothorax, injury to biliary tree leading to hemobilia or bile peritonitis, puncture of adjacent organ as the kidney and the intestine, and even death with a mortality rate of 1:1,000–1:10,000 (1,16,18–20)

These limitations increased the need for a fast, safe and reliable technique to assess liver fibrosis and to follow up progression or regression of the disease during treatment (7). Recently developed non invasive methods, such as the sonographic based technique as transient elastography (FibroScan, Echosens) (8,21,22), and MRI based techniques as measuring ADC value in diffusion weighted-MRI, perfusion-weighted MRI and MR elastography represent major advances in the prediction of fibrosis and cirrhosis (1,21,23).

The use of DW MRI in the assessment of liver fibrosis is based on altered diffusion of water protons in fibrotic tissue (24). Many previous studies had advised the use of multiple *b*-values to obtain accurate quantitative analysis of DW images and consequently reliable ADC map as well as the ADC measurement. They proposed that at low *b*-values the ADC measurement was not reliable for accurately assessed diffusion of the tissue due to the mixed effect of perfusion and diffusion that could not be separated at this level (1,5,25–27).

In our study, we used multiple *b* values of 200, 500, 700, 1000 mm^2/s, also to eliminate the effect of perfusion, we did not use small *b*-value in order to obtain accurate ADC measurement in accordance with Kovac et al. (5), and HR Ibrahim et al. (25). While in a study of Taouli et al. (1), Zhu et al. (26)and Girometti et al. (27), they used *b* value of 0 mm^2/s.

Previous studies reported that ADC values were significantly lower values in cirrhotic liver compared with normal liver (9,28–32), these may be due to the presence of a larger amount of connective tissue deposited within the liver, narrowed sinusoids, and altered blood flow (33).

In our study, we found a negative correlation between ADC values and stages of liver fibrosis according to METAVIR scoring system which is significant at all *b* values ($r = 0.935$, 0.927, 0.965, 0.898 for *b*-value of 200, 500, 700 and 1000 mm^2/s respectively). The best negative correlation was achieved by *b*-value of 700 and the least negative correlation seen at *b*-value = 1000.

This negative correlation was matched with many published studies (1,5,25–27,34), but unlike our study the best negative correlation was achieved at *b*-value of 500 in study of zhu et al (26) this difference may be owed to the use of different *b*-values.

Owing to current treatment strategy, the diagnosis of stage 2 or greater fibrosis is clinically important because, due to cost,

Table 2 The mean ADC values of different stages of liver fibrosis (value $\times 10^{-3}$ mm^2/s).

Fibrosis stage	*N*	*b*-Values (mm^2/s)				*P* value
		b = 200	*b* = 500	*b* = 700	*b* = 1000	
F1	35	2.26 ± 0.3	1.85 ± 0.03	1.71 ± 0.01	1.53 ± 0.01	0.001
F2	22	1.88 ± 0.11	1.64 ± 0.04	1.52 ± 0.05	1.36 ± 0.03	0.001
F3	25	1.75 ± 0.06	1.61 ± 0.05	1.45 ± 0.05	1.30 ± 0.04	0.001
F4	20	1.44 ± 0.01	1.37 ± 0.03	1.29 ± 0.01	1.04 ± 0.01	0.001

Table 3 Comparison of mean hepatic ADC at each value between stages $<$F3 and stages $\geqslant$F3.

b-values (mm^2/s)	Mean ADC		P value
	Stage $<$F3 (n = 57)	Stage $\geqslant$F3 (N = 45)	
b = 200	2.21 ± 0.09	1.71 ± 0.23	0.000
b = 500	2.21 ± 0.09	1.71 ± 0.23	0.000
b = 700	1.71 ± 0.02	1.45 ± 0.10	0.000
b = 1000	1.49 ± 0.0	1.26 ± 0	0.000

Table 4 The mean LSM stratified by stage of fibrosis.

Fibrosis stage	N	Mean Liver stiffness, kPa (range)	P value
F1	35	6.06 ± 0.71	0.001
F2	22	10.88 ± 3.79	0.001
F3	25	14.58 ± 4.86	0.001
F4	20	35.96 ± 10.83	0.001

KPa value was expressed as mean ± SD.

risk of toxicity, and limited efficacy, only patients with stage 2 or greater fibrosis should receive antiviral treatment (14).

ADC measures in our study can perform well in differentiating the patients into two groups $<$F3 and $\geqslant$F3 fibrosis, there is a significant difference in mean hepatic ADC measurement at all examined b-values between patients at different stages of liver fibrosis (P values was 0.001). Furthermore, there was highly significant difference in mean hepatic ADC when comparing patients with fibrosis stage $<$F3 and those with stage $\geqslant$F3 (P value = 0.000), these were in agreement with (1,5,25).

ROC analysis of prior DW MRI studies, reported AUC values of 0.783–0.790 for the detection of liver fibrosis stage $\geqslant$2 and 0.717–0.92 for the detection of fibrosis stage $\geqslant$3 (5,15,22,35), in consistent with these studies our results showed AUC values ranging from 0.937 to 0.898 for differentiating stages $<$ and $\geqslant$F3.

ADC cut off values of advanced fibrosis, and cirrhosis varied in previous literature, a value of 1.41×10^{-3} mm^2/s described by (1), 0.88×10^{-3} mm^2/s by (14), 1.11×10^{-3} mm^2/s by (27), and more recently 1.63×10^{-3} mm^2/s by (5), these

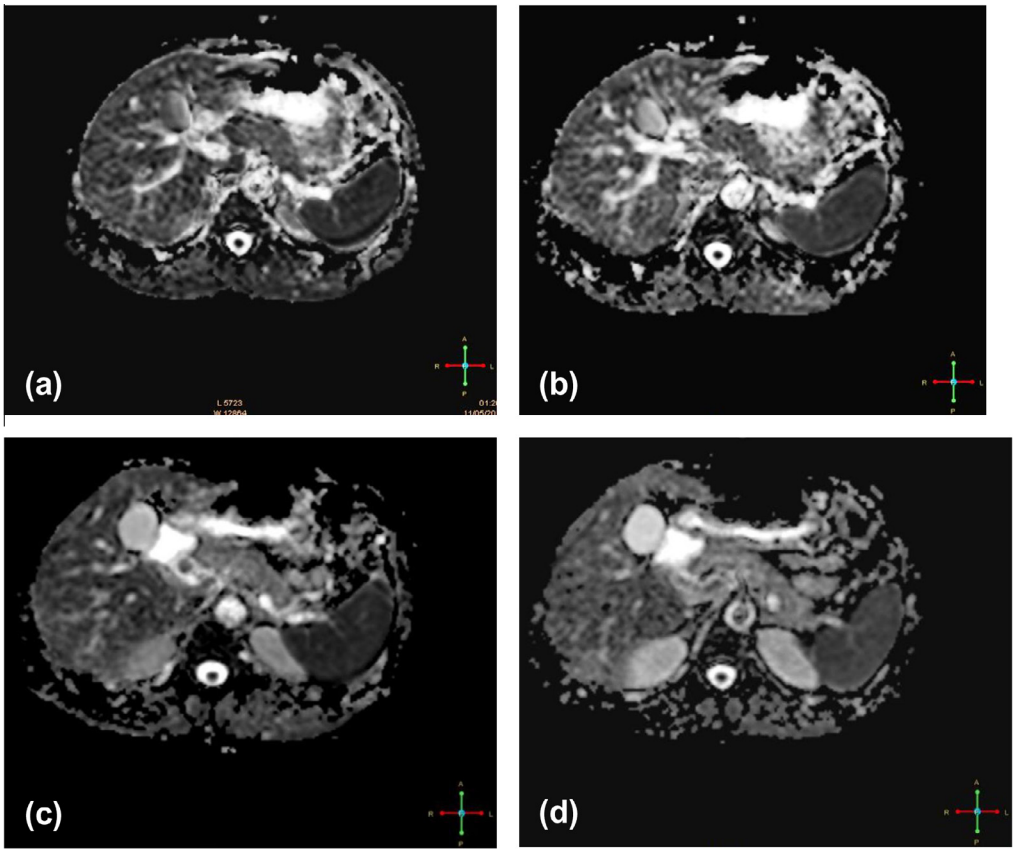

Fig. 1 31 year-old male patient with chronic hepatitis C virus (fibrosis stage 1 on liver biopsy). ADC mapping of breath-hold axial single-shot echo-planar diffusion-weighted images obtained at different b-values, b = 200 s/mm^2 (a), 500 s/mm^2 (b), 700 s/mm^2 (c), 1000 s/mm^2 (d). The calculated mean ADC value was 2.29×10^{-3} mm^2/s, 1.85×10^{-3} mm^2/s, 1.73×10^{-3} mm^2/s, and 1.53×10^{-3} mm^2/s respectively for each b-value.

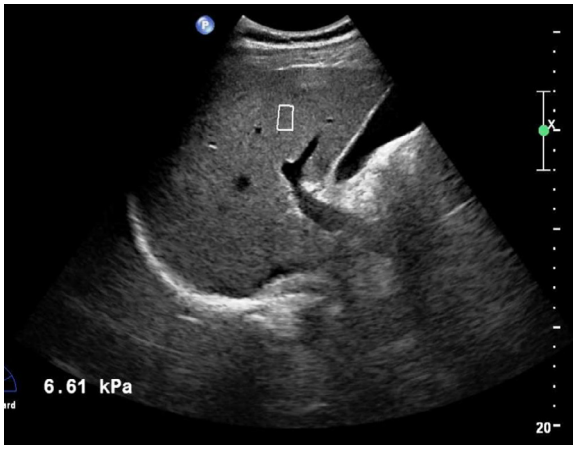

Fig. 2 Fibroscan (transient elastography) ultrasound of same patient in Fig. 1, liver stiffness measurement equal to 6.61 kPa.

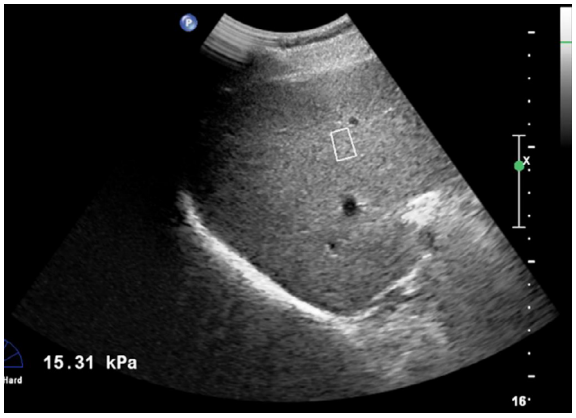

Fig. 4 Fibroscan (transient elastography) ultrasound of same patient in Fig. 3, liver stiffness measurement equal to 15.31 kPa.

variations are attributed to the use of multiple *b*-values for ADC measuring. We found a cut off value of 2.17×10^{-3}, 1.66×10^{-3} mm^2/s, 1.62×10^{-3} mm^2/s and 1.59×10^{-3} mm^2/s at *b*-value of 200, 500, 700 and 1000 mm^2/s respectively in the current study for differentiating stages $<$ and $\geqslant$F3.

By using ROC curve we obtain, a sensitivity of 86.7%, 80%, 93.3% and 86.7%, and with specificity of 66.7%, 93.3%, 93.3% and 46.7% for *b*-values 200, 500, 700 and 1000 mm^2/s respectively, but the best predictive value was achieved with *b*-value 700 mm^2/s with high sensitivity of 93.3%, specificity of 93.3%, the PPV of 93.3% and NPV of 93.3%, and the least predictive value was at *b*-value of 1000 mm^2/s, these may be attributed to the risk of noise contamination at high *b*-value.

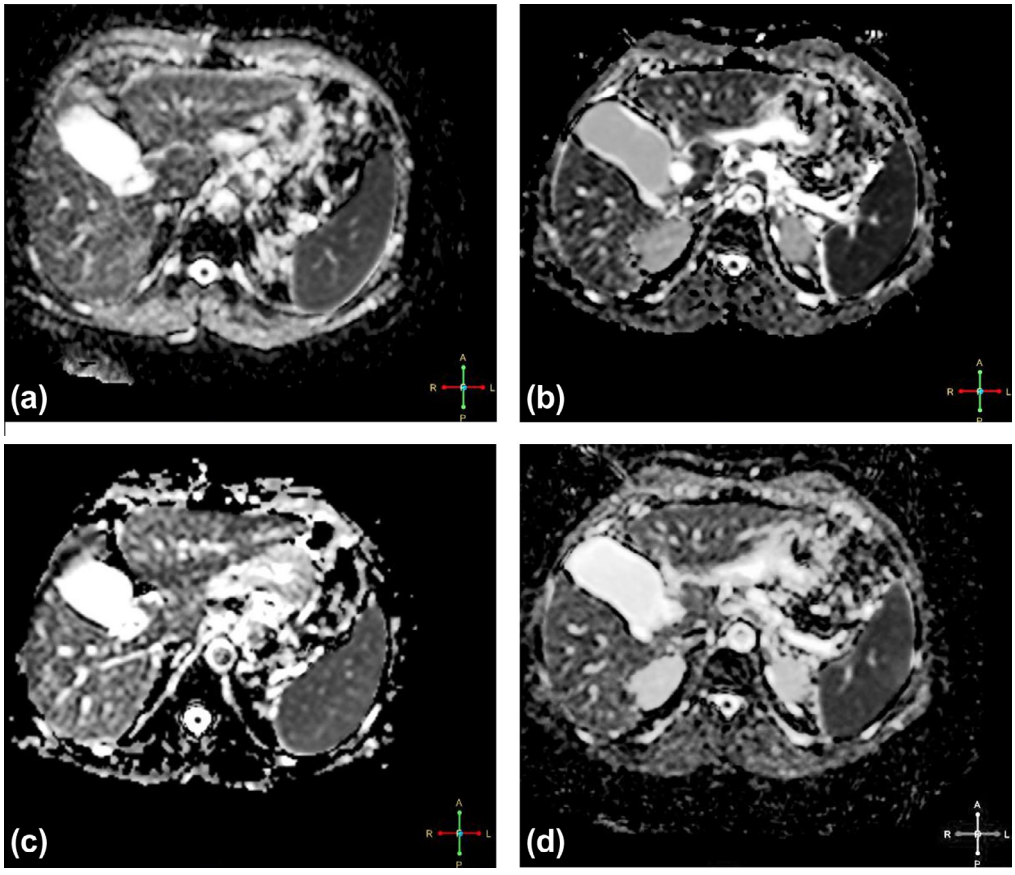

Fig. 3 49 year-old male patient with chronic hepatitis C virus (fibrosis stage 3 on liver biopsy). ADC mapping of breath-hold axial single-shot echo-planar diffusion-weighted images obtained at different *b*-values, $b = 200$ s/mm^2 (a), 500 s/mm^2 (b), 700 s/mm^2 (c), 1000 s/mm^2 (d). The calculated mean ADC value was 1.75×10^{-3} mm^2/s, 1.63×10^{-3} mm^2/s, 1.45×10^{-3} mm^2/s, and 1.29×10^{-3} mm^2/s respectively for each *b*-value.

Table 5 Receiver Operating Characteristics Curve (ROC) for ADC (200–1000) and FS for quantification of liver fibrosis stage $F < 3$ versus fibrosis stage $\geqslant$F3.

	AUC (95% CI)	Cut off value	Sensitivity	Specificity	PPV	NPV	Kappa value	*P*
ADC 200 mm^2/s	0.937 (0.835–1.023)	2.17×10^{-3} mm^2/s	86.7%	66.7%	72.2%	83.3%	0.533	0.000
ADC 500 mm^2/s	0.971 (0.918–1.029)	1.66×10^{-3} mm^2/s	80%	93.3%	92.3%	82.4%	0.733	0.000
ADC 700 mm^2/s	0.991 (0.981–1.010)	1.62×10^{-3} mm^2/s	86.7%	83.7%	81.9%	77.8%	0.633	0.000
ADC 1000 mm^2/s	0.898 (0.784–1.016)	1.59×10^{-3} mm^2/s	93.3%	93.3%	93.3%	93.3%	0.867	0.000
TE	0.935 (0.89–0.98)	12.95 kPa	91.1%	78.9%	77.9%	91.8%	0.688	0.005

By these results, we share with previous studies done in the promising utility for using DW-MRI and ADC measurement in quantification of liver fibrosis with reported sensitivity, and specificity ranged from 84% to 92.3% and 76% to 92.1%, respectively (1,5,36).

But in a study of Sandrasegaran et al. (34), they described a significant difference of ADC values of F0 (non fibrosis) and F4 (cirrhosis) $P = 0.008$ but we differ in our study as there were better differentiation between individual stages of liver fibrosis. Also Zhu et al. (26), described a best predictive value at 500 mm^2/s with sensitivity of 84% and specificity of 80% and the least value at 200 mm^2/s, these may be owed to the difference at the used *b*-value.

There was also difference between our study and Taouli et al. (1), as they evoked that ADC cannot perform well in differentiating individual stages of fibrosis, this could be due to limited number of patients and intermediate stages of fibrosis in Taouli et al. (1) study. However we agree with Taouli et al. (1) who reported that ADC was a significant predictor of stage $\geqslant$F3 versus $\leqslant$F2, but they had best correlation at *b*-value of 1000 with sensitivity of 80% and specificity of 90%.

A higher specificity of 100% had been reported by Girometti et al. (27)., but in their study they included healthy individuals and cirrhotic patients only.

TE has become an important tool for the noninvasive assessment of fibrosis (7,37). Some recent extensive studies, have demonstrated that measurement of liver stiffness with fibroscan is a good alternative for liver biopsy (38).

Our results show that liver stiffness measurement with transient elastography had a significant positive correlation with fibrosis stage from F1 to F4 with *P*-value of 0.005, with mean kPa value ranged from 6.06 ± 0.71, 10.88 ± 3.79, 14.58 ± 4.86, 35.96 ± 10.83 at stage F1, F2, F3 and F4 respectively with *P* value of 0.005.

Many previous studies reported that transient elastography correlated positively with the histological score of liver fibrosis D (5,8,16,22,39,40).

We also detected a significant difference in liver stiffness measurement using TE between patients with liver fibrosis of stages f3 with *P* value 0.000, these were in agreement with. (5,39).

In previous published studies, the cut off value reported for diagnosis of fibrosis of stages >F3 ranged from 9.5 to 9.6 kPa (8,11,22,38,40,41) In the present study, we recorded a similar cut off value of 9.8 kPa. However, foucher et al. (16) described a higher cut off value of 12.5 kPa, and they attributed this difference due to the study population that included patients with chronic liver disease of various etiologies.

Using ROC analysis, we recorded the cutoff point of TE at 8.9 to be a significant predictor for differentiation between fibrosis stage <F3 and those >F3 with AUC 0.935 (confidence interval (CI) 95%: 0.88–0.98), and sensitivity 91.1%, specificity 78.9%, PPV 77.4%, NPV 91.8%, and *P*-value of 0.000.

In other published studies in accordance with our result, AUROC (95% confidence interval) was 0.80 (0.75–0.84) for patients with significant fibrosis ($F > 2$), 0.90 (0.86–0.93) for patients with severe fibrosis (F3) and 0.96 (0.94–0.98) for patients with cirrhosis (F4) (38,42–44).

Adebajo et al. (44) performed a systematic review and diagnostic accuracy meta-analysis of studies comparing ultrasound-based TE to liver biopsy for the detection of hepatic fibrosis they found six fully published studies (42,45–49) were identified for analysis, and they concluded that in the five studies that evaluated significant fibrosis were identified. Among these studies, the pooled estimates were 83% for sensitivity [95% confidence interval (CI) 77–88%], 83% for specificity (95% CI 77–-88%), 4.95 for the positive likelihood ratio (95% CI 3.4–7.2), 0.17 for the negative likelihood ratio (95% CI 0.09–0.35), and 30.5 for the diagnostic odds' ratio (95% CI 12.8–72.4). The other five studies that assessed cirrhosis; the pooled estimates were 98% for sensitivity (95% CI 90–100%), 84% for specificity (95% CI 80–88%), 7 for the positive likelihood ratio (95% CI 2.8–17.3), 0.06 for the negative likelihood ratio (95% CI 0.02–0.19), and 130 for the diagnostic odds' ratio (95% CI 36.5–462.1). Our result was nearly falling in the range described in these studies.

We recorded a PPV and NPV of 77.4% and 91.8% respectively similar to that reported in many previous studies that described positive and negative predictive values ranging from 70% to 95% and 77% to 95%, respectively (7,8,16,48).

Our results show that the diagnostic performance of the non invasive technique we used (DW MRI and TE) was reliable and accurate with good sensitivity, specificity, PPV and NPV in assessing liver fibrosis, and the result of both tests was comparable to each other. Measuring degree of liver stiffness by applying ADC value and TE can give significant results in assessing the stage of liver fibrosis according to METAVIR staging, also a significant difference was obtained by both techniques in differentiating patients with fibrosis stage F3.

The advantage over biopsy is that both techniques are non invasive, well accepted by the patients, painless, easy and safe with no risk of complication.

Ultrasound has more advantage as it is of low cost, widespread, rapid, can be done at bed side or outpatient clinics. There are some technical limitations of TE, as obesity (particularly the fatness of the chest wall), narrow intercostal space and ascites. Moreover, Fraquelli et al. (50) found that TE reproducibility is significantly reduced in patients with steatosis.

While the advantage of DW MRI and ADC measurement would be in its ability to give a diagnosis about liver fibrosis distribution, with ADC measurements in each liver segment. Moreover, it could be done in obese patients and patients with ascites without affection of accuracy of the results.

Furthermore, DW MRI has slight higher sensitivity and specificity over TE. Limitations related to: the availability of the high-performance scanner; the presence of experienced personnel; the examination takes long time, especially if conventional MRI is added. (7).

We had limitations in this study, first we did not evaluate the effect of iron overload, and edema on stiffness and measurement by TE and ADC, second the use of multiple *b*-value in ADC measurement gives a wide range of variability in measurement.

On the other hand, the strength of our study was that we include only hepatitis C patients, exclusion of patients with high BMI >28 or steatosis to decrease the error of measurement by TE, and lastly we did not use small *b*-value in ADC measurement to eliminate the effect of perfusion.

In conclusion, TE and DW MRI were promising techniques, and they can replace liver biopsy as they can accurately diagnose staging liver fibrosis, mainly the advanced stages, the choice between both techniques depends on the clinician and the general condition of the patients or the presence of contraindications for either techniques, furthermore, the advantage of MRI in measuring ADC value in different liver segments thus gives information about the exact distribution of liver fibrosis adding to its accuracy. More important advantage about the use of non invasive techniques in measuring liver stiffness is that it can be used for monitoring response to treatment and evaluation of progression or regression of the disease.

Conflict of interest

None.

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