



ORIGINAL RESEARCH ARTICLE

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# Evaluation of long-term changes of aspartate—platelet ratio index, FIB4, and liver stiffness in chronic hepatitis C patients successfully treated by direct-acting antivirals

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## Abstract

**Background:** A large number of chronic hepatitis C patients had been successfully treated by directly acting antivirals; therefore, strategies for the long-term follow-up of these patients have to be planned based on the post-treatment fibrosis stage—the main determinant of prognosis. In this study, we aim to evaluate changes in aspartate-platelet ratio index, FIB4, and liver stiffness in chronic hepatitis C patients who achieved SVR and ended treatment more than 1 year by DAAs.

**Results:** One hundred chronic hepatitis C patients who achieved SVR were enrolled at a median of 16 months after the end of treatment by DAAs. According to the baseline liver stiffness, 63 and 37 patients belonged to early (F0, F1, and F2) and advanced (F3 and F4) fibrosis stages, respectively. Both groups showed a decline of the degree of liver stiffness at follow-up compared to the baseline that was statistically significant in the early fibrosis group ( $5.9 \pm 1.5$  vs  $5.4 \pm 2.2$  Kpcal,  $p=0.04$ ), while measurements in the advanced group were ( $18 \pm 8.8$  vs  $15.9 \pm 7.8$  Kpcal,  $p=0.07$ ). Also, serum biomarkers of fibrosis improved in both groups, where the recorded APRI and FIB4 before and after treatment were  $0.42 \pm 0.3$  vs  $0.24 \pm 0.1$ ,  $p < 0.01$  and  $1 \pm 0.6$  vs  $0.93 \pm 0.5$ ,  $p=0.1$  in the early group and  $0.85 \pm 0.5$  vs  $0.4 \pm 0.2$ ,  $p < 0.001$  and  $2.9 \pm 2.3$  vs  $1.8 \pm 1.4$ ,  $p < 0.02$ ) in the advanced group, respectively. Changes in APRI and FIB4 correlated with changes in AST and ALT, but liver stiffness changes were not affected by changes in liver enzymes.

**Conclusion:** Although long-term improvement of APRI, FIB4, and liver stiffness scores could be achieved in chronic HCV patients after SVR by DAAs. High measurements of liver stiffness before treatment likely persist. We recommend transient elastography as a reliable tool for fibrosis assessment post-treatment.

**Keywords:** Liver stiffness, APRI, FIB4, Chronic HCV, DAAs, SVR, Long-term

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## Background

Hepatitis C virus (HCV) chronic infection is an important etiology of chronic liver disease that is prevalent worldwide; therefore, discovering an effective antiviral therapy was a major target for research [1]. Additionally, chronic HCV is considered the main risk factor for cirrhosis and development of hepatocellular carcinoma [2].

The introduction of direct-acting antiviral drugs (DAAs) was a revolution in HCV management with great safety and efficacy profile. Also, successful treatment of HCV decreases cirrhosis-related complications [3]. Many studies discussed the possibility of fibrosis regression following sustained virological response (SVR) achievement by DAAs which is debatable [4].

Chronic HCV infection and the resultant hepatocyte injury induce an inflammatory response that produces cytokines leading to stimulation of hepatic stellate cells (HSC) and fibrogenesis initiation, and elimination of the injurious agent would halt this inflammatory process. At later stages, fibrosis regression would depend on apoptosis of activated HSC and degradation of the extracellular matrix which is affected by the duration and components of the scar tissue [5].

CHCV patients with advanced liver fibrosis are at risk of developing hepatocellular carcinoma (HCC), despite HCV eradication [6]. So the determination of the liver fibrosis stage after treatment is essential to detect the patients' need for continuous surveillance [7].

Liver biopsy is the gold standard for the evaluation of the degree of tissue damage and hepatic fibrosis. Due to its limitations and procedure-related complications, the use of non-invasive methods for fibrosis assessment has become an alternative. Among the most widely used and validated are serum biomarkers and transient elastography. Aspartate to platelet ratio index (APRI) and fibrosis-4-index (FIB4) are serum biomarkers that have high applicability and reproducibility being calculated by using routine laboratory indices. While transient elastography (TE) physically assessed liver fibrosis by measuring liver stiffness with the advantages of being reliable, safe, and easy to perform [8].

In Egypt, the National Committee for Control of Viral Hepatitis (NCCVH) implemented a national strategy aiming to eradicate HCV, and this target became feasible by the availability of DAAs since 2014. Initially, patients with advanced fibrosis stages were only included in the treatment program, but later in 2015, all fibrosis stages (F0–F4) received antiviral therapy without discrimination [9]. By 2018, 40% of the total HCV-infected population (2 million patients) were treated by DAAs with SVR above 90% [10]. So, a strategy for the follow-up of this large number of cured patients has to be planned to put into consideration patients with utmost priority. In the current study, we aim to share our center experience

in the follow-up of successfully treated CHCV patients as regards the changes in scores of non-invasive tests of fibrosis APRI, FIB4, and TE.

## Methods

This is a single-center retrospective and prospective cohort study, which was conducted at the Viral Hepatitis Treatment Unit, Ain Shams University Hospitals, during the time period from October 2017 to December 2018. Chronic HCV patients who ended treatment with DAAs and attended at our outpatient clinic for follow-up were included if fulfilling the following criteria:

1. Chronic HCV patients who were treated with a complete course of all oral DAAs regimens, achieved SVR and at least 1 year has passed since the end of treatment.
2. Patients who had baseline transient elastography (TE) done before DAAs initiation.
3. Complete data available in files.

## Exclusion criteria

Patients who developed ascites and/or HCC at the time of follow-up.

The following workup was done for re-evaluation of included patients:

1. Clinical assessment for symptoms or signs of liver cell failure and laboratory investigations as CBC, AST, ALT, total and direct bilirubin, and albumin and INR.
2. Liver stiffness measurement (LSM) using TE: The device used is FibroScan® (Echosens, Paris, France). The operator placed the transducer in the intercostal space at the mid-axillary line in the right hypochondrium and took at least 10 measurements. An interquartile range of  $\leq 30\%$  and a success rate of  $>80\%$  were required for a valid interpretation [8].

TE results were correlated to different stages of liver fibrosis according to the histological staging system of METAVIR (Table 1) [11].

## Non-invasive serum fibrosis biomarkers

Aspartate aminotransferase-to-platelet ratio index (APRI) and fibrosis-4 index (FIB-4) were calculated at baseline and at follow-up by using the following equations:

1. **APRI score** by Wai's formula [12]:  $(\text{AST}/\text{upper limit of normal})/\text{platelet count (expressed as platelets} \times 10^9 /\text{L)} \times 100$

**Table 1** Histological staging system of METAVIR

Stage	Metavir Scoring System	Fibroscan cut-off values (Kpcal)
F0	No fibrosis	0–5.4
F1	Portal fibrosis without septa	5.5–6.9
F2	Portal fibrosis with few septa	7–9.4
F3	Numerous septa without cirrhosis	9.5–12.4
F4	Cirrhosis	12.5

2. **FIB-4 score** by Sterling's formula [13] : Age (years) × AST (IU/L)/platelet count (×10<sup>9</sup>/L) × √ALT (IU/L).

### Statistical analysis

The collected data was revised, coded, tabulated, and introduced to a computer using Statistical package for Social Science (SPSS 20). Parametric numerical data was presented as mean, standard deviation (± SD), and range while non-parametric numeric data were presented as the median and interquartile range (IQR). Non-numeric data were presented as the frequency and percentage.

We used Student *T* test to compare two paired study group means. Pearson correlation (*r*) was used for measuring a linear dependence between two variables. The McNemar test is used to analyze pretest-posttest fibrosis study groups. Regression analysis was used for [estimating](#) the relationships between baseline factors and changes in LSM. Repeated-measures ANOVA was used to compare the changes of LSM across time between the early and advanced fibrosis group.

### Results

During the time period from October 2017 to December 2018, 120 chronic HCV patients attended our clinic for follow-up after the end of treatment with DAAs, only 100 patients fulfilled the inclusion criteria and were enrolled in this study while 20 patients were excluded, as 2 were relapsers, 7 developed HCC and/or ascites while 11 patients refused to participate.

Among the included patients, 63 belonged to early fibrosis stages (F0, F1, and F2), while 37 patients belonged to advanced stages (F3 and F4) classified according to baseline TE readings retrieved from patients' files.

The median duration since the end of treatment in included patients was 16 months (minimum and maximum—12 and 33 months, respectively), where most of the patients (75th percentile) were re-examined at 21 months after the end of treatment.

### Baseline patient characteristics

The mean age of included patients was 48±15 years: 52 males and 48 females. Diabetes and hypertension were reported in 14 and 12 patients, respectively (Table 2).

The mean LSM of patients in the early fibrosis stage was 5.9±1.5 Kpcal while that of the advanced stage was 18±8.8 Kpcal (Table 3).

Before treatment initiation, the median of HCV RNA quantitative was 2066.45 (IQR=4000), SVR was confirmed by undetectable HCV PCR at week 12 post-treatment in all included patients. Treatment regimens used were Sofosbuvir/Daclatasvir for 12 weeks in 58 patients; most of them (*n*=51) were at early fibrosis stages, while 32 patients including 18 with advanced fibrosis received Sofosbuvir/Daclatasvir/Ribavirin for 12–24 weeks; finally, only 10 patients were treated by PAR/OMB/RBV; and most of them belonged to F0.

**Table 2** Baseline patients' characteristics

Age (years)	48 ±15
BMI	26 ±3.7
Female (%)	48
Male (%)	52
Diabetes (%)	14
Hypertension (%)	12
Other co-morbidities*(%)	11
HCV RNA quantitative*	2066.45±4000
ALT (IU/L)	53.5±40
AST (IU/L)	48±29
AFP (IU/L)	4.3±3.4
Albumin (g/dL)	4.1±0.5
Total bilirubin (mg/dL)	0.75±0.4
Indirect bilirubin (mg/dL)	0.48±0.4
WBC×10 <sup>3</sup> /mm <sup>3</sup>	7.1±2.2
Hb (g/dL)	13.5±1.8
Creatinine (mg/dL)	0.9±0.2
INR	1.1±0.1
Platelets×10 <sup>3</sup> /mm <sup>3</sup>	231.7±72
Fibrosis stage (F) by TE (%)	<b>F0 (23%)</b> <b>F1 (26%)</b> <b>F2 (14%)</b> <b>F3 (9%)</b> <b>F4 (28%)</b>

\*Ischemic heart diseases and bronchial asthma

**Table 3** Laboratory and fibrosis score changes in early and advanced groups

	Early stage			Advanced stage		
	Baseline	Follow-up	P value	Baseline	Follow-up	P value
Stiffness	5.9±1.5	5.4±2.2	0.04	18±8.8	15.9 ±7.8	0.077
APRI score	0.42±0.3	0.24±0.1	<0.01	0.85±0.5	0.4±0.2	<0.001
Fib4	1±0.6	0.93±0.5	0.1	2.9±2.3	1.8±1.4	0.002
ALT (IU/L)	53±42	21±10	<0.01	55±37	26±11	<0.001
AST (IU/L)	42±30	24±10	<0.01	58±26	28±11	<0.001
AFP (IU/L)	3.3±2	3.5±1.8	0.5	6±4.2	5.5±3	0.4
Albumin (g/dL)	4.2±0.35	4.1±0.3	0.35	3.9±0.6	3.9±0.4	0.5
Total bilirubin (mg/dL)	0.6±0.2	0.7±0.2	0.2	0.9±0.5	0.86±0.3	0.4
Indirect bilirubin (mg/dL)	0.4±0.4	0.4±0.2	0.7	0.6±0.3	0.5±0.2	0.5
WBCx10 <sup>3</sup> /mm <sup>3</sup>	7±2.4	6.8±1.7	0.3	7.1±1.8	6.7±2.1	0.2
Hb	13.8± 1.6	12.5±1.2	<0.001	13±1.9	12.4±1.5	0.008
plateletsx10 <sup>3</sup> /mm <sup>3</sup>	251.5 ± 58	265 ± 72	0.05	199±80	215±67	0.08
INR	1±0.09	1 ±0.09	0.3	1.12.	1.16	0.1
Creatinine	0.87±0.2	0.85±0.15	0.6	0.8±0.1	0.9±0.1	0.8

At baseline, AST and ALT of all included patients were elevated  $48 \pm 30$  (IU/L) and  $53 \pm 40$  (IU/L), respectively, while other liver function tests were normal (Table 2).

#### Changes at the time of follow-up

##### Laboratory

In both groups, improvement of ALT ( $53 \pm 42$  vs  $21 \pm 10$ ) and ( $55 \pm 37$  vs  $26 \pm 11$ ) ( $p < 0.01$ ) as well as AST ( $42 \pm 30$  vs  $24 \pm 10$ ) and ( $58 \pm 26$  vs  $28 \pm 11$ ) ( $p < 0.01$ ) were reported for early and advanced fibrosis stages, respectively. No significant changes of LFTs (total bilirubin, albumin, and INR) were found in both groups. The platelet count improved in both groups, but the increase was statistically significant only in the early fibrosis group ( $251.5 \pm 57$  vs  $266 \pm 72$ ,  $p = 0.001$ ) and not the advanced group ( $199 \pm 80$  vs  $215 \pm 67$ ,  $p = 0.08$ ). However, most patients at advanced fibrosis stages (12 out of 16) who had thrombocytopenia at baseline showed an improvement (mean = 124 vs 188) (Table 3).

#### Analysis of changes in FIB4, APRI, and LSM in both groups

##### Non-invasive biomarkers

**Early fibrosis stages** APRI score significantly decreased at follow-up compared to baseline ( $0.42 \pm 0.3$  vs  $0.24 \pm 0.1$ ,  $p < 0.01$ ), while non-significant improvement was reported in Fib4  $1 \pm 0.6$  vs  $0.93 \pm 0.5$ ,  $p = 0.1$ ) (Table 3). The change in APRI is correlated with that of FIB4 ( $p = 0.000$ ) but not with the change in LSM (Table 4).

**Advanced fibrosis stages** APRI and Fib4 score significantly decreased at follow-up compared to baseline ( $0.85 \pm 0.5$  vs  $0.4 \pm 0.2$ ,  $p < 0.001$ ) and ( $2.9 \pm 2.3$  vs  $1.8 \pm 1.4$ ,  $p < 0.02$ ), respectively (Table 3). The change in APRI correlated with that of FIB4 ( $p = 0.000$ ) but not with the change in LSM (Table 4).

In all included patients, the percent of change of APRI is correlated with that of AST and ALT, and the percent of change of Fib4 is correlated with AST (Table 5).

**Table 4** Correlation between change in APRI, FIB4, and LSM

	Early stage						Advanced stage					
	APRI diff		Fib4 diff		Stiffness diff		APRI diff		Fib4 diff		Stiffness diff	
	r	P value	r	P value	r	P value	r	P value	r	P value	r	P value
APRI diff			0.677	0.000	0.105	0.4			0.706	0.000	-0.148	0.4
Fib4 diff	<b>0.677</b>	0.000			0.086	0.5	0.7	0.000			0.001	0.1
Stiffness diff	0.105	0.413	0.086	0.505			-0.148	0.381	0.001	0.993		

**Table 5** Correlation between the percentage of change of liver enzymes and fibrosis scores

	Percent of change									
	STIFFNESS		ALT (IU/L)		AST (IU/L)		APRI score		Fib4 calculation	
	<i>r</i>	<i>P</i> value	<i>r</i>	<i>P</i> value	<i>r</i>	<i>P</i> value	<i>r</i>	<i>P</i> value	<i>r</i>	<i>P</i> value
STIFFNESS			-0.084	0.408	-0.031	0.758	0.037	0.715	0.095	0.347
ALT (IU/L)	-0.084	0.408			0.394	0.000	0.373	0.000	-0.069	0.494
AST (IU/L)	-0.031	0.758	0.394	0.000			0.820	0.000	0.678	0.000
APRI score	0.037	0.715	0.373	0.000	0.820	0.000			0.743	0.000
Fib4 Calculation	0.095	0.347	-0.069	0.494	0.678	0.000	0.743	0.000		

### Transient elastography in early and advanced stages at baseline and follow-up

**Early stages** LSM markedly improved at the time of follow-up ( $5.9 \pm 1.5$  vs  $5.4 \pm 2.2$  Kpcal,  $p=0.04$ ) (Table 3).

Subgroup analysis revealed that LSM significantly decreased in patients classified as F1 at baseline ( $6 \pm 0.4$  vs  $5 \pm 1.2$ ,  $p < 0.001$ ) (Table 6).

**Advanced stages** LSM improved at the time of follow-up, but was statistically insignificant ( $18 \pm 8.8$  vs  $15.9 \pm 7.8$  Kpcal,  $p=0.07$ ) (Table 3); however, subgroup analysis demonstrated a significant decrease of LSM in patients classified as F3 at baseline ( $11.1 \pm 0.8$  vs  $8.5 \pm 2$  Kpcal,  $p=0.02$ ) (Table 6).

In all included patients, the percent of change of LSM was not correlated with either AST nor ALT (Table 5).

### The distribution of fibrosis stages among the studied patients at baseline and follow-up

The percentage of patients stratified as early fibrosis stages significantly increased at follow-up compared to baseline ( $p < 0.001$ ) (Fig. 1).

### Comparison between the two groups regarding the degree of change in stiffness score

Although the amount of change was bigger in advanced than early fibrosis stages, the difference was statistically insignificant ( $p$  value=0.1) (Fig. 2).

### Baseline factors affecting fibrosis scores at a long-term follow-up (Table 7)

Baseline FIB4 and liver stiffness measured by fibroscan are the main determinants of fibrosis at the time of follow-up regardless of age, BMI, and existence of diabetes. For patients with high FIB4 and LS before treatment, their scores will remain high in a long term.

### Discussion

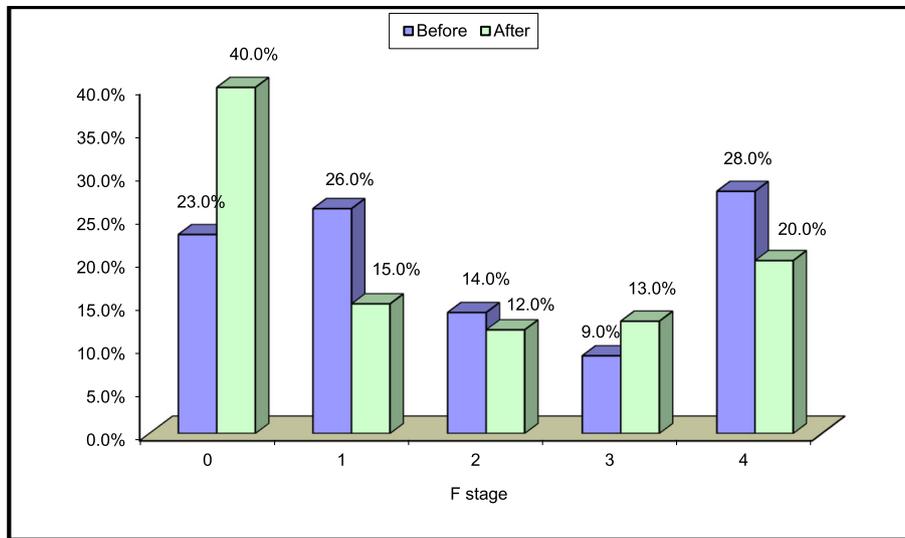
A long-term follow-up of CHCV patients after being successfully treated with DAAS should be directed to selected patients who still have the risk to develop hepatic complications in spite of achieving SVR. As post-treatment prognosis is mainly determined by the fibrosis stage, many studies have been conducted to evaluate whether regression of fibrosis can be achieved after completion of DAAS therapy; however, most of these studies were done at a short duration after the end of treatment (12 and 24 weeks) [14, 15]. Additionally, the selection of the most reliable method to categorize the fibrosis stage in treated patients would help clinicians to identify those needing regular medical care and HCC surveillance.

In our study, patients were recruited at an average of 16 months after the end of DAAs and classified according to TE done before treatment initiation into 2 groups early and advanced fibrosis. LSM decreased in both early and advanced fibrosis groups ( $5.9 \pm 1.5$  vs  $5.4 \pm 2.2$  Kpcal and  $18.8 \pm 8.8$  vs  $15.9 \pm 7.8$  Kpcal, respectively).

Our results agree with those of a study that evaluated the long-term changes of liver elasticity in 143 CHCV patients who achieved SVR by DAAs [16], where LSM

**Table 6** Subgroup analysis of changes in fibrosis scores

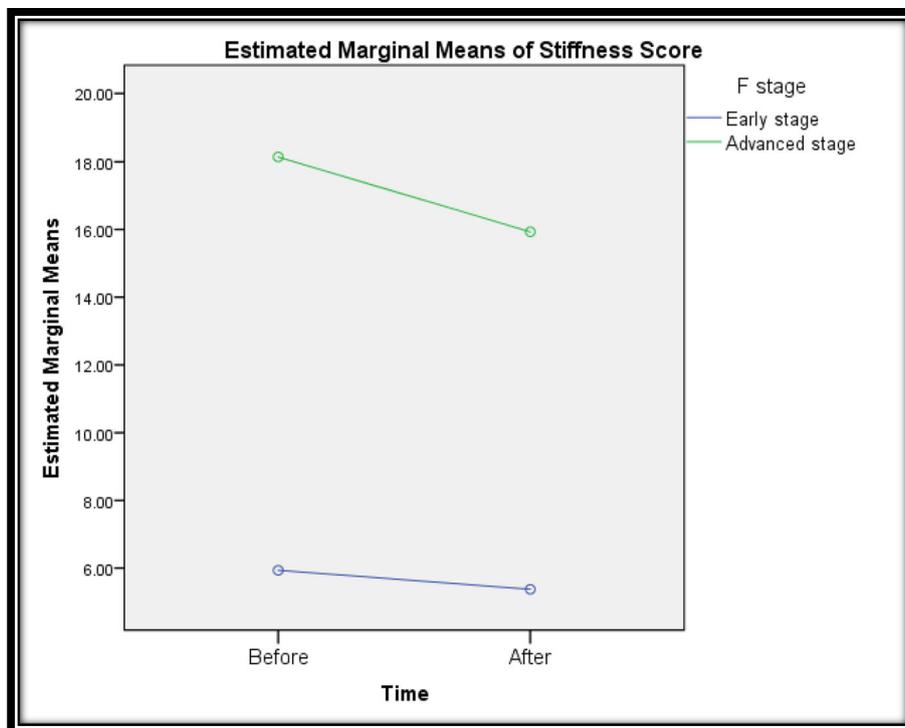
Baseline TE	LSM			APRI			FIB4		
	Baseline	Follow-up	<i>P</i> value	Baseline	Follow-up	<i>P</i> value	Baseline	Follow-up	<i>P</i> value
F0	4.34±0.7	5.05±2.4	0.19	0.46±0.34	0.24±0.13	0.004	1±0.6	0.9±0.6	0.5
F1	6 ± 0.4	5 ± 1.2	<0.001	0.4±0.3	0.26±0.1	0.006	1.1±0.8	0.98±0.5	0.37
F2	8.1±0.8	6.9±3	0.15	0.48±0.2	0.2±0.1	0.001	1.15±0.5	0.95±0.5	0.13
F3	11±0.8	8.5±2	0.02	0.78±0.7	0.3±0.1	0.06	1.47±0.8	0.95±0.4	0.08
F4	21±8.6	18.5±7.5	0.14	0.86±0.5	0.4±0.25	<0.001	3.3±2.5	2±1.5	0.01



**Fig. 1** Comparison of distribution of fibrosis stages among the studied patients at baseline and follow up: difference was statistically significant (<0.001)

improved significantly in cirrhotic and non-cirrhotic patients 25.9 vs 14.5 Kpcal and 7.8 vs 5.4 Kpcal, respectively, at week 96 post-treatment. In the same study, it was reported that patients with early compensated cirrhosis (baseline LSM=20.4pkcal) had significant progressive improvement of LSM at 6 and 24 months ((14.8 Kpcal and 11.2Kpcal), respectively, while patients at

more advanced cirrhosis stage denoted by impaired liver function with baseline LSM=32.6pkcal initially achieved a significant decrease in LSM at week 24 post-treatment that was not significantly sustained at week 96 (24 months) after treatment (22.7 vs 19.1 Kpcal). Finally, the change was significantly greater in the cirrhotic group given that they had higher readings at baseline, and



**Fig. 2** Estimated marginal means of stiffness score in the early and advanced fibrosis groups

**Table 7** Regression analysis for baseline factors affecting stiffness score after treatment

	Unstandardized coefficients		Standardized coefficients	t	Sig.	95% Confidence interval for B	
	B	Std. error				Beta	Lower bound
Age (years)	.044	.036	.092	1.214	.228	-.028	.116
BMI	-.071	.114	-.037	-.624	.534	-.298	.155
Diabetes	-.020	1.265	-.001	-.016	.988	-2.531	2.492
Stiffness score before treatment	.553	.062	.618	8.940	<0.001	.430	.676
APRI Score before treatment	-1.438	1.557	-.088	-.924	.358	-4.531	1.654
Fib4 before treatment	1.304	.489	.313	2.668	.009	.333	2.274

similarly in our study, the amount of change of LSM was bigger in advanced than early fibrosis stages. A meta-analysis attributed the higher decline of liver stiffness in advanced stages after antiviral therapy to a higher inflammatory burden, in which patients with high baseline ALT also showed a higher magnitude of the decline in LSM [17].

In the present study, the subgroup analysis showed that the significant reduction of LSM was reported in patients classified as F1 and F3 ( $6.1 \pm 0.4$  vs  $5 \pm 1.2$ ,  $p = 0.001$  and  $11.1 \pm 0.8$  vs  $8.5 \pm 2$  Kpcal,  $p < 0.02$ ). Subsidence of necro-inflammatory reaction is most likely responsible for the improvement reported in early stages [5]. As regards the advanced group, F3 is characterized histologically by numerous immature septae and bridges that precedes nodular formation characteristic of cirrhosis (F4) [18], after withdrawal of the insulting agent (HCV) immature septae might reverse, while mature cross-linked septae rich in elastin and associated with matrix modification are more likely to persist [19].

Clinically elevated liver enzymes are a marker of necro-inflammatory reaction, and in our study, AST and ALT significantly declined and were normalized at follow-up. Also, the non-invasive fibrosis serum biomarker of APRI significantly decreased in both groups and a marked reduction of Fib4 was recorded in advanced stages. The percent of change of APRI is correlated with that of AST and ALT, and the percent of change of Fib4 is correlated with AST; therefore, this improvement of serum biomarkers might be due to normalization of liver enzymes only and not representing fibrosis regression, especially that our results showed that the percent of change of liver stiffness is not correlated with that of liver enzymes, APRI, or Fib4.

Therefore, we could suggest that TE is the reliable method for evaluation of significant fibrosis in the context of follow-up after HCV treatment because as explained above, it is not affected by changes in liver enzymes and also we found that baseline TE scores is the main determinant of liver stiffness at follow-up which means that high scores before treatment are likely to persist after treatment even if a decline was achieved.

Additionally, patients in the advanced fibrosis group at follow-up recorded APRI score of  $0.4 \pm 0.2$  which is lower than the validated cut-off value for significant fibrosis (0.77 and 0.83) [8], and also, the recorded Fib4 for the same group (1.8) is indeterminate [8] for the fibrosis stage.

In a prospective study designed to identify factors influencing fibrosis regression after DAAs, baseline BMI, steatosis, and hepatic stiffness were documented as independent factors [20]; this partially agrees with our study in which baseline LSM but not BMI affected LSM at follow-up; however, in another meta-analysis, BMI was not found to affect change in stiffness [17].

Importantly, LSM of 15.8 Kpcal that was recorded in our advanced group patients alarms us that they are still at an increased risk to develop HCC. As evidenced by a study done by Pons et al. [21], in which LSM  $< 10$  Kpcal at follow-up is correlated with a lower risk of HCC than the higher score of 10–20 Kpcal. He documented that the higher the LSM at follow-up, the greater the risk of HCC.

## Conclusion

Although the scores of non-invasive methods of fibrosis assessment (TE, APRI, and FIB4) may improve after successful treatment of CHCV by DAAs, liver stiffness persists high in patients with pre-treatment advanced fibrosis stages. We recommend that TE should be done at least once after treatment to evaluate the further plan of follow-up especially if it is not done before treatment.

The limitations of the current study are the small number of patients specifically those included in the advanced stage group.

## Abbreviations

CHCV: Chronic hepatitis C virus; TE: Transient elastography; LS: Liver stiffness; LSM: Liver stiffness measurement; Kpcal: Kilopascal; BMI: Body mass index; LFT: Liver function tests; HCC: Hepatocellular carcinoma

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## Authors' contributions

Dr. NA and Dr. OA created the conception and design of the study; Dr. AM, MS, and DK were responsible for the acquisition of laboratory and clinical

data. Data analysis and/interpretation were done by Dr. A.F. Drafting and revision of the manuscript were done by Dr. A.M, D.K, and A. F. The authors have read and approved the manuscript.

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None was received.

#### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on a reasonable request.

#### Declarations

##### Ethics approval and consent to participate

This study was approved by the research ethical committee at Ain Shams University, Faculty of Medicine, MS 124/2020. Verbal and written consent was taken from all participants before inclusion after approval of the research ethical committee at Ain Shams University.

##### Consent for publication

Not applicable

##### Competing interests

The authors declare that they have no competing interests.

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