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Evaluation of liver fibrosis in HCV-infected patients using two-dimensional shear-wave elastography (2D-SWE) before and after antiviral treatment

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Abstract

Aim: Chronic hepatitis C virus infections can lead to liver fibrosis. Appropriate treatment of chronic hepatitis C may result in significant fibrosis reversal. The best method to assess liver fibrosis is an invasive hepatic biopsy. Among non-invasive options, one of the most recent methods is two-dimensional shear-wave elastography, which allows real-time visualization of liver stiffness. The purpose of this study was to analyze changes in liver fibrosis among patients with hepatitis C virus receiving direct-acting antiviral therapy. **Material and methods:** Five different elastographic measurements in kilopascals were performed in a group of 50 patients before direct-acting antiviral treatment, at the end of treatment, and 24 weeks after the end of treatment, using an Aixplorer® (Supersonic Imagine, France) ultrasound device. The results were correlated with biochemical serum tests, specifically the Fibrosis-4 and AspAT-to-platelet ratio indices. **Results:** Time-dependent alterations of all of the parameters were observed, including a significant decrease in liver stiffness in comparison to baseline values (before treatment). A moderate correlation between liver stiffness measurement values and both Fibrosis-4 and AspAT-to-platelet ratio indices was observed. Interestingly, only liver stiffness and blood platelet count changed over time, regardless of the sex and age of the patient. **Conclusions:** Two-dimensional shear-wave elastography combined with non-invasive serologic tests like Fibrosis-4 and AspAT-to-platelet ratio indices is a sufficient tool for evaluating liver fibrosis regression during and after direct-acting antiviral therapy.

Introduction

Approximately 80% of hepatitis C virus (HCV) infections progress to chronic infection⁽¹⁾, which gives approximately 56.8 million chronic cases globally⁽²⁾. HCV can lead to increased accumulation of extracellular matrix (ECM) proteins resulting in liver fibrosis regarded as a repair process of chronic liver injury⁽³⁾. Further substitution of hepatic lobules by regenerating hepatocyte nodules causes hepatocellular cirrhosis, which is a risk factor for pathologies including hepatic insufficiency, portal hypertension, and hepatocellular carcinoma (HCC)⁽⁴⁾. Appropriate treatment of chronic hepatitis C (CHC) may result in the elimination of HCV and, consequently, reverse significant fibrosis⁽⁵⁾. Therefore,

monitoring the stage of fibrosis may potentially serve as a good prognostic factor of CHC progression. Moreover, it may help avoid further complications in patients suffering from CHC⁽⁶⁾. The best known and the most frequently applied method for assessing liver fibrosis is histopathological examination of hepatic biopsy⁽⁷⁾. However, there are some contraindications to this invasive technique including ascites, coagulation disorders, biliary obstruction, and anatomical abnormalities. Furthermore, post-biopsy complications, such as hemorrhage, pneumothorax, and pain, are relatively common and contribute significantly to patient complaints and anxiety⁽⁸⁾. Therefore, non-invasive methods can be used as an alternative for assessing liver disease severity⁽⁹⁾.

Dynamic elastography methods are most suitable for the assessment of liver fibrosis. However, they also measure tissue stiffness which is influenced by hepatic inflammation and/or hepatic hypertension. These techniques rely on the evaluation of the velocity of shear waves as they travel through tissue⁽¹⁰⁾. The stiffer the examined tissue, the faster the wave velocity. Shear waves can be generated mechanically or electromechanically. Mechanically-generated waves are used in transient elastography (TE). TE was the first elastographic method designed to assess liver fibrosis⁽¹¹⁾. In 2001, Echosens commercialized this technique, creating FibroScan devices⁽¹²⁾. Nevertheless, TE has some limitations, such as patient obesity, ascites, or limited operator experience. Referring to the available studies, over 18% of the examinations may yield non-diagnostic results⁽¹³⁾. Two-dimensional shear-wave elastography (2D-SWE) is the most recent elastographic method. Unlike other techniques, 2D-SWE allows the investigator to visualize liver stiffness in real time, as 2D-SWE devices combine B-mode ultrasound images with acoustic radiation pressure.

The aim of this study was to analyze the extent of liver fibrosis among patients with HCV on direct antiviral therapy (DAA) over multiple hospital visits over time, with the use of elastography. These results were compared with the values of two of the most common serum tests for evaluating fibrosis: FIB-4 and APRI. Additionally, the study included a set of other parameters commonly used in monitoring HCV and liver fibrosis – to gain more insights into changes in the clinical status of patients with every subsequent measurement.

Materials and methods

The study group

Ethical approval was obtained from the Wrocław Medical University Bioethics Committee under reference number 355/2021. Written informed consent was acquired from every patient according to the principles outlined by the World Medical Association in the Declaration of Helsinki.

The prospective study was conducted in the Department of General and Pediatric Radiology in cooperation with the Hepatology Clinic at Wrocław Medical University in 2021–2022. The study was carried out among recently diagnosed patients suffering from chronic liver inflammation. The study group was selected based on appropriate inclusion criteria such as the age of majority, no coexisting diseases, and no previous antiviral therapies. All patients received DAA treatment within a maximum of two months after the diagnosis. Minors, patients with other coexisting chronic liver diseases, and ascites were excluded from the study.

Parameters measured in this study

Liver stiffness measurement (LSM) was conducted with use of Aixplorer® (Supersonic Imagine, France) ultrasound device. Patients were positioned in the dorsal decubitus position, with both arms in maximal abduction to increase the intercostal acoustic window. The region of interest (ROI) was placed at least 1.5 cm from the hepatic capsule, carefully avoiding areas without large liver vessels,

bile ducts, and rib shadows. During the acquisition, the patients were asked to hold their breath. Five different valid elastographic measurements in kilopascals (kPa) were obtained, with median values recorded in all subjects before DAA treatment, at the end of treatment (EOT), and 24 weeks after the EOT.

Data analysis

Data analysis was conducted using STATISTICA v.13.3 under the Wrocław Medical University license. Alpha-value of 0.05 was used for statistical inference. Assumptions of normality of distribution and equality of variances was checked with the Shapiro-Wilk and Levene tests. Sphericity was assessed with use of Mauchly's *W* statistic. If necessary for fulfilling the normality of distribution assumption, variables were log-transformed.

Due to the bimodal distribution of age in the population sample (Fig. 1) and the limited suitability of repeated measures analysis of covariance for this study (it was not possible to check some of the assumptions of this method), age was discretized as an 'Age group' variable. The cut-off age value used for the classification into two age groups was set at 50 years.

Pairwise comparisons were performed using the Mann-Whitney *U* test (quantitative variables) or the Chi-square test (qualitative variables).

Variability between time points was analyzed with the use of multi-way repeated measures analysis of variance (RM-ANOVA) with sigma-restricted parametrization. 'Time' and two additional factors, 'Sex' and 'Age group' (a discretized age variable), were used in the model. The Greenhouse-Geisser correction for degrees of freedom was used if the sphericity assumption was violated. In case of no significance of any interactions, Tukey's Honestly Significant Difference (HSD) post-hoc test was used. In the presence of a statistically-significant interaction, linear contrast analysis was conducted to provide more insights into the data. Monotonic correlations were analyzed based on Spearman's ρ index. Non-transformed (raw) values for each parameter (variable) were used in the analysis.

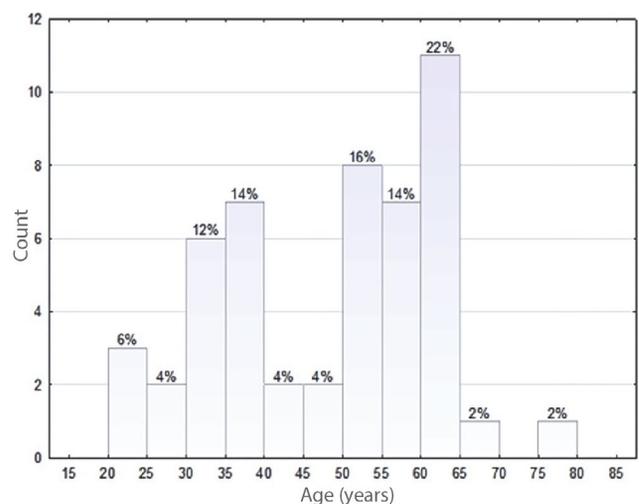


Fig. 1. Age distribution in the studied population sample

Tab. 1. Baseline characteristics of the study group

Variable (quantitative)	Sex: Female (n = 24)					Sex: Male (n = 26)					P
	Median value	Min	Max	1st quartile	2nd quartile	Median value	Min	Max	1st quartile	2nd quartile	
Age [1]	55.50	25.00	78.00	43.50	62.00	43.00	23.00	63.00	34.00	57.00	0.028
LSM [1]	12.38	6.00	40.00	9.92	15.11	11.39	6.12	25.00	8.48	16.80	0.795
AST [1]	68.00	31.00	300.00	39.50	133.00	57.00	22.00	212.00	42.00	88.00	0.494
ALT [1]	86.00	17.00	271.00	54.50	154.50	75.50	22.00	324.00	57.00	146.00	0.946
PLT [1]	164.00	45.00	277.00	115.00	220.00	145.00	35.00	220.00	98.00	187.00	0.293
FIB-4 [1]	2.70	0.60	13.09	1.64	4.60	2.07	0.59	9.12	1.38	3.91	0.275
APRI [1]	1.25	0.34	7.16	0.58	2.81	1.25	0.32	4.64	0.56	2.59	0.722
Variable (qualitative)	n (%)					n (%)					p
F category: F0	1 (4.17%)					0 (0.00%)					
F category: F1	3 (12.50%)					4 (15.38%)					
F category: F2	1 (4.17%)					4 (15.38%)					
F category: F3	7 (29.17%)					6 (23.08%)					
F category: F4	12 (50.00%)					12 (46.15%)					

Results

Out of a total of 88 patients in total, 12 did not consent to participate in the study, 14 met the exclusion criteria, 10 did not complete all the necessary measurements, and two patients did not achieve viral response. Consequently, 50 remaining patients who attained sustained viral response (SVR) are described in this study (Tab. 1).

Changes in values of selected clinical parameters over time

All analyzed parameters showed significant time-dependent changes (Tab. 2, Tab. 3), although only two of them, LSM (Fig. 2) and blood platelet count (Fig. 3), were independent of the sex and age of the individuals ('Time' factor $p < 0.0001$ and 0.0066 , respectively). All of the parameters, except for the blood platelet count (increasing trend), demonstrated a decreasing trend over time. Interestingly, unlike the other parameters, which markedly decreased in the before-to-after treatment period, the blood platelet count increased mostly during the post-treatment period. Post-hoc analysis revealed that the differences in values obtained from elastography were significant between each set of time points (approximately $p = 0.0001$ for each pair). Conversely, the differences in blood platelet count were significant only between two pairs of time points: before the treatment vs. during the control ($p = 0.0020$) and after the treatment vs. during the control ($p = 0.0282$). No significant differences in blood platelet count were observed during the before-to-after treatment period ($p = 0.6345$).

The changes in the values of all analyzed parameters (except for blood platelet count and liver stiffness) were dependent on both sex and age ('Time*Sex*Age group $p: 0.0017, 0.0135, 0.0432, 0.0061$ for AST, ALT, and indices FIB-4 and APRI, respectively). Results from the linear contrast analysis are presented in Tab. 4.

Significant differences in the analyzed changes in AST over time were found among females between the two age groups ($p = 0.0045$)

Tab. 2. Changes in values of evaluated parameters over time in the studied population sample (n = 50)

Variable	Mean	SE	F	p
LSM [1]	12.06	1.06	161.62	<0.001
LSM [2]	7.77	1.05		
LSM [3]	6.69	1.04		
AST [1]	63.43	1.08	91.05	<0.001
AST [2]	29.08	1.06		
AST [3]	24.29	1.04		
ALT [1]	80.64	1.09	131.67	<0.001
ALT [2]	25.28	1.08		
ALT [3]	22.42	1.07		
PLT [1]	153.08	8.85	6.03	0.007
PLT [2]	157.49	8.95		
PLT [3]	169.90	8.25		
FIB-4 [1]	2.29	1.11	21.23	<0.001
FIB-4 [2]	1.73	1.08		
FIB-4 [3]	1.49	1.07		
APRI [1]	1.13	1.13	83.46	<0.001
APRI [2]	0.50	1.09		
APRI [3]	0.38	1.07		

Brackets in the names of variables indicate time: [1], before treatment; [2], after treatment; [3], control after treatment. The data are shown as estimated marginal means ('Mean') and standard error ('SE'). Degrees of freedom ('df') for repeated measures ANOVA of non-spheric data (sph. $p < 0.05$) have been adjusted for with use of the Greenhouse-Geisser ('GG') correction. Significant differences are marked in bold.

and among older adults between the two sexes ($p = 0.0014$). As shown in Fig. 4, females in the 'older adults' group exhibited a greater post-treatment decrease in AST activity, compared to females in the 'younger adults' group ($p = 0.0395$). Moreover, among individuals

Tab. 3. Repeated measures ANOVA models for variables studied in the population sample (n = 50)

Variable	LSM		AST		ALT		PLT		FIB-4		APRI	
	F	p	F	p	F	p	F	p	F	p	F	p
Time	161.62	0.000	91.05	0.000	131.67	<0.001	6.03	0.007	21.23	0.000	83.46	<0.001
Time*Sex	1.70	0.198	0.51	0.553	0.67	0.515	0.62	0.509	0.19	0.779	0.34	0.657
Time*Age group	0.57	0.501	0.45	0.584	0.01	0.994	0.08	0.888	0.58	0.526	0.35	0.649
Time*Sex*Age group	2.13	0.143	8.25	0.002	4.51	0.014	0.06	0.910	3.54	0.043	6.26	0.006

Information on sphericity and Greenhouse-Geisser correction of degrees of freedom (if applied) is shown in Tab. 1

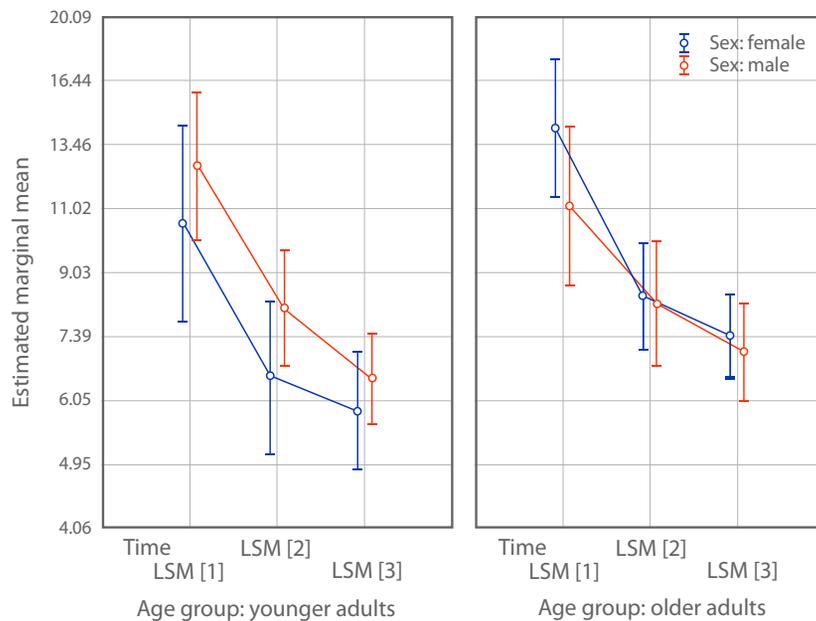


Fig. 2. Values [kPa] obtained with elastography in the population sample over time. Values are given as estimated marginal means and 95% confidence intervals

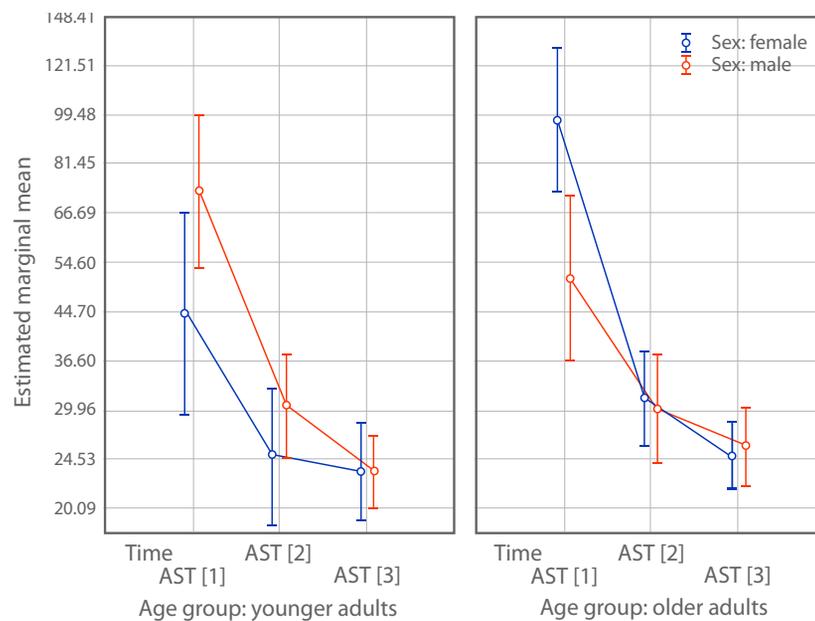


Fig. 3. Blood platelet count (PLT) observed in the population sample over time. Values given as estimated marginal means and 95% confidence intervals

Tab. 4. Analysis of pre-defined linear contrasts associated with changes in the values of selected parameters in the context of two factors: sex and age group, in the selected population sample ($n = 50$)

Variable: AST					
Group 1	Group 2	F	Univariate <i>p</i>	[1] vs. [2]; <i>p</i>	[2] vs. [3]; <i>p</i>
Sex: female Age group: younger adults	Sex: female Age group: older adults	5.73	0.005	0.039	0.290
Sex: male Age group: younger adults	Sex: male Age group: older adults	2.68	0.074	-	-
Sex: female Age group: younger adults	Sex: male Age group: younger adults	2.39	0.097	-	-
Sex: female Age group: older adults	Sex: male Age group: older adults	7.06	0.001	0.013	0.576
Variable: ALT					
Group 1	Group 2	F	Univariate <i>p</i>	[1] vs. [2]; <i>p</i>	[2] vs. [3]; <i>p</i>
Sex: female Age group: younger adults	Sex: female Age group: older adults	2.21	0.116	-	-
Sex: male Age group: younger adults	Sex: male Age group: older adults	2.32	0.104	-	-
Sex: female Age group: younger adults	Sex: male Age group: younger adults	0.96	0.386	-	-
Sex: female Age group: older adults	Sex: male Age group: older adults	4.79	0.011	0.035	0.592
Variable: FIB-4					
Group 1	Group 2	F	Univariate <i>p</i>	[1] vs. [2]; <i>p</i>	[2] vs. [3]; <i>p</i>
Sex: female Age group: younger adults	Sex: female Age group: older adults	3.03	0.053	-	-
Sex: male Age group: younger adults	Sex: male Age group: older adults	0.89	0.415	-	-
Sex: female Age group: younger adults	Sex: male Age group: younger adults	1.74	0.181	-	-
Sex: female Age group: older adults	Sex: male Age group: older adults	2.04	0.136	-	-
Variable: APRI					
Group 1	Group 2	F	Univariate <i>p</i>	[1] vs. [2]; <i>p</i>	[2] vs. [3]; <i>p</i>
Sex: female Age group: younger adults	Sex: female Age group: older adults	4.20	0.018	0.0580	0.4443
Sex: male Age group: younger adults	Sex: male Age group: older adults	2.23	0.114	-	-
Sex: female Age group: younger adults	Sex: male Age group: younger adults	2.26	0.110	-	-
Sex: female Age group: older adults	Sex: male Age group: older adults	4.71	0.011	0.0330	0.6615

To facilitate reading the information in this table, the common factor between both compared groups is marked in bold. Contrasts were not analyzed if the univariate *p*-value was greater than 0.05. The numbers in brackets in columns referring to linear contrasts (two last columns) indicate different time points of measurements, as described before in this study.

in the ‘older adults’ group, women showed a greater post-treatment decrease in AST activity compared to men ($p = 0.0132$). In both of these comparisons, there were no differences between post-treatment and control values ($p = 0.2902$ and $p = 0.5756$, respectively).

Regarding changes in ALT over time, significant differences (Fig. 5) were found among older adults between males and females ($p = 0.0105$). Females in the ‘older adults’ group showed a greater decrease in ALT activity during the before-to-after treatment period ($p = 0.0345$), but not during the post-treatment-to-control time ($p = 0.5921$).

Based on the analyzed sets of contrasts, no significance was observed for time-related FIB-4 alterations. Within this stratum, a more

prominent decrease in FIB-4 index values could be observed in the ‘older adults’ age group, compared to ‘younger adults’ (Fig. 6). This hypothesis, however, needs further evidence to be considered true. Based on the same figure, it could be also hypothesized that FIB-4 index values were higher in the ‘older adults’ at each time point, compared to the ‘younger adults’ group. According to a two-way ANOVA model with interactions, where both sex and age group were treated as factors, this hypothesis is likely to be true (Tab. 5, Fig. 7).

Significant differences in the time-related linear APRI trend were found among females between the two age groups ($p = 0.0179$) and among older adults between both sexes ($p = 0.0113$). Among

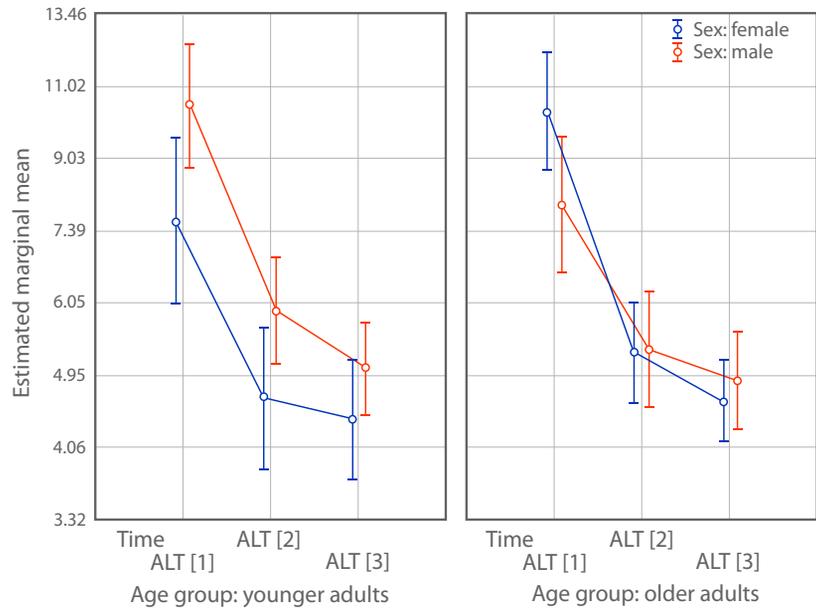


Fig. 4. Logarithmic values of serum aspartate aminotransferase (AST) activity observed in the population sample over time. Values given as estimated marginal means and 95% confidence intervals

Tab. 5. Between-group differences (according to sex and/or age) in values of the FIB-4 index at each analyzed time point

Factor	FIB-4 [1]			FIB-4 [2]			FIB-4 [3]		
	SS	F	p	SS	F	p	SS	F	p
Sex	0.05	0.11	0.741	0.00	0.01	0.929	0.11	0.43	0.516
Age group	5.65	13.04	0.001	3.63	10.96	0.002	4.07	15.79	0.000
Sex*Age group	1.08	2.48	0.122	0.03	0.10	0.749	0.02	0.07	0.786
Error	19.93	-	-	15.24	-	-	11.86	-	-

SS – type VI sum of squares; MS – mean square. Numbers in brackets indicate the time point: [1] before treatment, [2] after treatment, [3] control – after treatment.

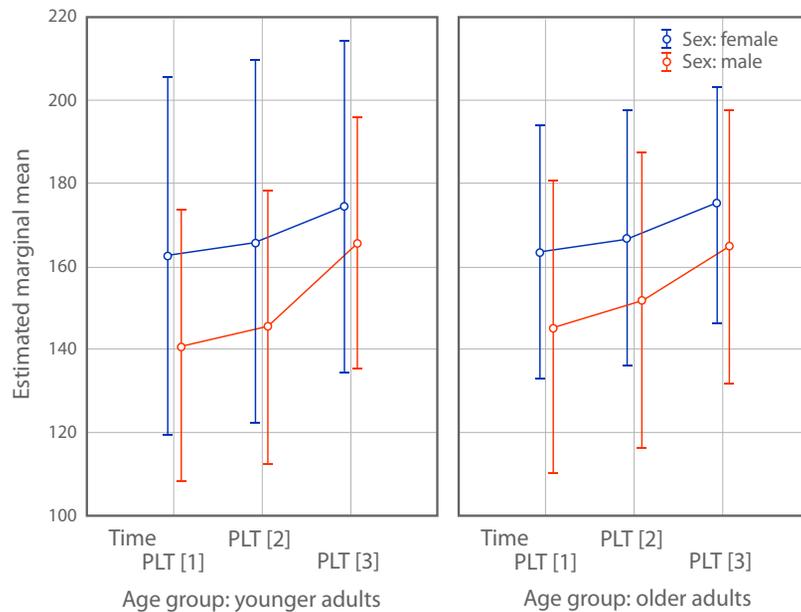


Fig. 5. Logarithmic values of serum alanine aminotransferase (ALT) activity observed in the population sample over time. Values given as estimated marginal means and 95% confidence intervals

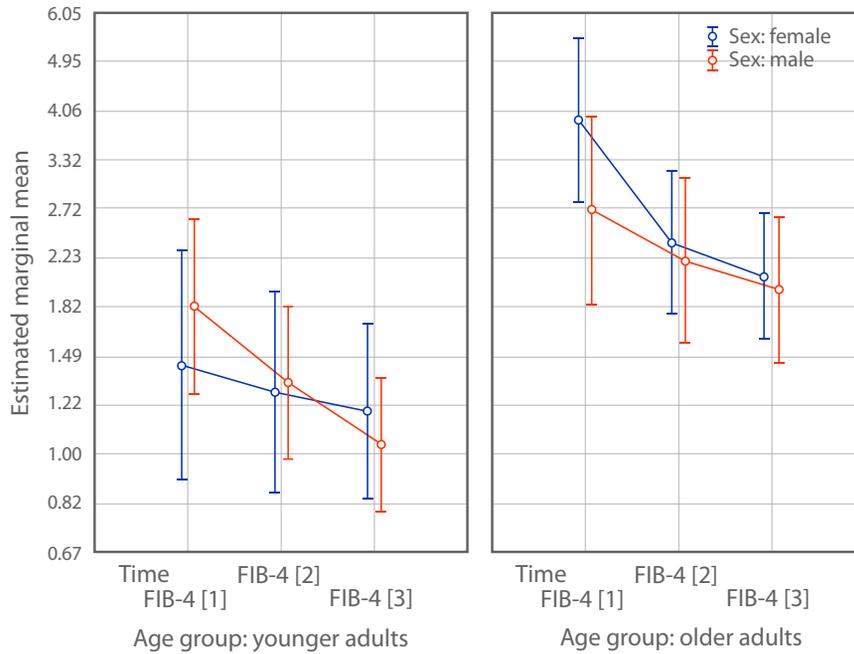


Fig. 6. Logarithmic values of the Fibrosis-4 index (FIB-4) calculated for the individuals in the population sample over time. Values given as estimated marginal means and 95% confidence intervals

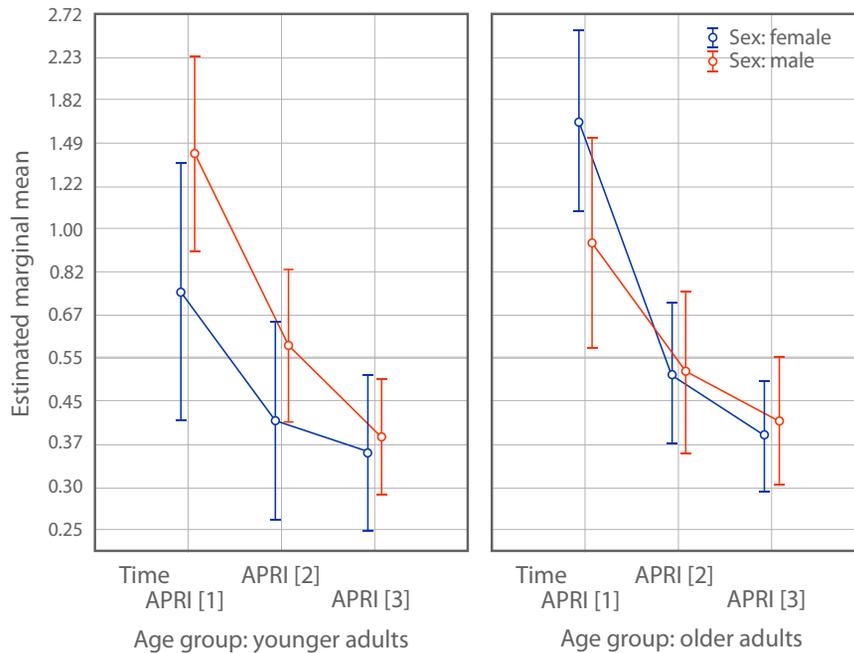


Fig. 7. Values of the FIB-4 index at each time point depending on the age group in the population sample. Values given as estimated marginal means and 95% confidence intervals

‘older adults’, females showed a greater decrease in the mentioned time period compared to males ($p = 0.0330$). Although females in the ‘older adults’ age group showed a greater decrease in the APRI index during the before-to-after treatment period compared to the ‘younger adults’ (Fig. 8), an ambiguous p -value ($p = 0.0580$) does not allow confirming this hypothesis based solely on this study.

Correlation analysis

Regardless of whether the values of each parameter were analyzed as raw values at the first time point (before treatment) or as the difference during the before-to-after treatment period (first two time points), values obtained from LSM were positively correlated with AST and ALT activity, and negatively – with PLT. Values of the FIB-4 and APRI

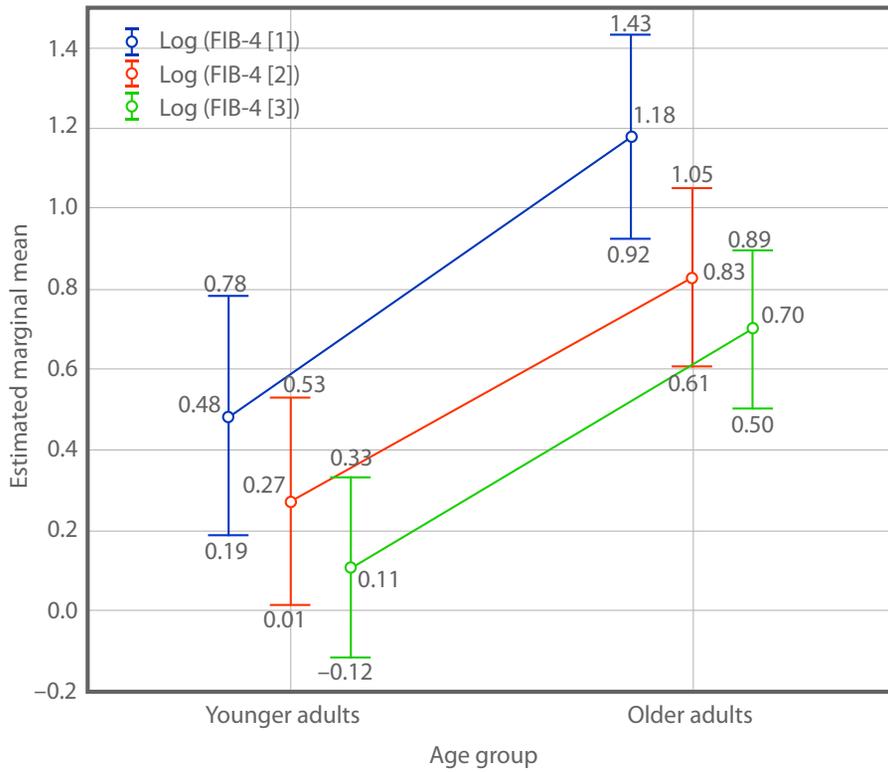


Fig. 8. Logarithmic values of the AST-to-platelet ratio index (APRI) calculated for the individuals in the population sample over time. Values given as estimated marginal means and 95% confidence intervals

Tab. 6. Monotonic correlations matrices between the selected parameters

Variable	LSM [1]	AST [1]	PLT [1]	ALT [1]	FIB-4 [1]	APRI [1]
Age [1]	0.077	0.107	0.0062	-0.075	0.503	0.081
LSM [1]	1.000	0.511	-0.600	0.379	0.582	0.652
AST [1]	0.511	1.000	-0.349	0.882	0.671	0.878
PLT [1]	-0.600	-0.349	1.000	-0.272	-0.670	-0.708
ALT [1]	0.379	0.882	-0.272	1.000	0.446	0.761
FIB-4 [1]	0.582	0.671	-0.670	0.446	1.000	0.841
APRI [1]	0.652	0.878	-0.708	0.761	0.841	1.000

Variable	LSM [2-1]	AST [2-1]	PLT [2-1]	ALT [2-1]	FIB-4 [2-1]	APRI [2-1]
Age [1]	0.007	-0.037	0.093	0.026	-0.318	-0.065
LSM [2-1]	1.000	0.410	-0.325	0.334	0.359	0.462
AST [2-1]	0.410	1.000	0.017	0.895	0.650	0.855
PLT [2-1]	-0.325	0.017	1.000	0.027	-0.516	-0.303
ALT [2-1]	0.334	0.895	0.027	1.000	0.460	0.781
FIB-4 [2-1]	0.359	0.650	-0.516	0.460	1.000	0.801
APRI [2-1]	0.462	0.855	-0.303	0.781	0.801	1.000

Numbers in brackets in the names of variables indicate time points or time intervals: [1] before treatment; [2-1] before-to-after treatment time interval difference. Values of Spearman's ρ are shown in each matrix. Only correlations of $p < 0.05$ are colored - red (negative correlation) or green (positive correlation). Color saturation reflects each p value.

indices were characterized by stronger correlations with elastographic measurement values, likely due to the fact that these indices are dependent on AST, ALT, and PLT. Other observed correlations, along with their respective rho values, are presented in Tab. 6.

Discussion

The introduction of DAA has significantly facilitated the treatment process in chronic HCV infections. A very high percentage of patients receiving DAA treatment achieve SVR⁽¹⁴⁾. However, patients with SVR remain vulnerable to liver-related morbidity caused primarily by the development of HCC. The risk of liver-related morbidity is substantially higher in cirrhotic patients⁽¹⁵⁾. Therefore, the assessment of liver parenchyma is a crucial element of the health monitoring process among HCV patients after the EOT. Among imaging techniques, the most common are elastography-based methods, including TE, point shear-wave elastography (pSWE) using acoustic radiation force impulse (ARFI), and 2D SWE. Both TE and pSWE have their own limitations. In TE, measurements are made without imaging the examined tissue. Consequently, many false positive results are present in patients with obesity, ascites, or narrow intercostal spaces⁽¹⁶⁾. In pSWE using ARFI, the main limitation is the small ROI gate, which cannot be enlarged⁽¹⁷⁾. In contrast to pSWE, 2D-SWE allows the investigator to measure a larger area of the organ after freezing the image. Furthermore, 2D-SWE creates a two-dimensional color map of tissue elasticity.

In our study of patients with SVR, a significant decrease in liver stiffness was observed with 2D SWE examination in comparison to baseline values before DAA treatment. Most of the literature focused on LSM only at the EOT⁽¹⁸⁾ or at the EOT and three months after the EOT^(19,20), according to treatment efficiency assessment guidelines. Only Kohla *et al.*⁽²¹⁾ measured liver stiffness among the Egyptian population six months after the EOT. In our study, liver stiffness measurements among Polish patients were additionally compared six months after the EOT to further explore the post-treatment use of elastography for monitoring purposes. Interestingly, in contrast to the North African study⁽²¹⁾, our patients with liver cirrhosis (F4 on the METAVIR scale) showed a significant decrease in liver stiffness. This observation seems to challenge the hypothesis that the reversibility of liver fibrosis after exceeding a certain tissue stiffness threshold is very unlikely. Yaras *et al.* conducted a similar study (on a Turkish patient group)⁽²⁰⁾ in which, unlike in the aforementioned Egyptian research, the last LSM was performed 12 weeks after the EOT. In this study, a significant regression of liver stiffness was observed in patients with cirrhosis as well. It is important to note that the above-mentioned Turkish group (Yaras *et al.*) was mostly female, while in our study the sex distribution was approximately equal (54% : 46% male – female ratio). Both these studies focused on the efficacy of DAA in the treatment of HCV-infected patients, and the associated fibrosis regression as measured by 2D SWE. The aim of our research, as stated in the Introduction, was the evaluation of the regression of liver fibrosis in patients with SVR using elastography (2D-SWE). Another important aim of this study was to explore the relationship between the results from 2D-SWE and two commonly used serum laboratory test indices – APRI and FIB-4.

In our study, a moderate correlation between the values obtained with LSM (during admission) and the values of both APRI and FIB-4 was observed. The fact that these correlations were not strong may stem from the different nature of these methods. LSM, unlike FIB-4 or

APRI, does not utilize laboratory parameters which may be affected by a series of factors such as sex or coexisting conditions other than HCV (such as dehydration or overhydration). Therefore, its precision in the assessment of liver fibrosis may be higher (which is yet to be tested in future studies).

The entire population sample in our study was stratified by sex and age (under and over fifty years old). There was no significant association between the decrease in liver stiffness and the sex or age of the patient. Surprisingly, a greater decrease in the APRI score was observed in the group of older females compared to older males, mainly in the before-to-after treatment period. This gradient of values may potentially prove to be an interesting predictor for the regression of liver fibrosis; however, developing clinical applications of this information will require at least a few comprehensive studies reinforced by artificial intelligence (such as machine learning).

The most recent study conducted by Argalia *et al.*⁽²²⁾ evaluated liver stiffness in HCV patients 48 weeks post-therapy, comparing two elastographic methods other than 2D SWE – TE and pSWE using ARFI. In this study, no significant differences in liver stiffness were found between 24 and 48 weeks after the EOT.

Two-dimensional shear-wave elastography, combined with other non-invasive methods like the APRI or FIB-4 score, may serve as a very promising alternative to hepatic biopsy or FibroScan – in the assessment of liver fibrosis, regardless of the sex and age of the patient. Further studies should be performed using the above-mentioned methods on an extended population sample, considering a greater number of potential factors for investigation. Also, age-related difference in females should be explored in future studies, as this comparison was on the brink of statistical significance in regard to this study ($p = 0.053$).

Conclusions

Liver injury is a major issue in chronic HCV-infected patients. DAA have revolutionized HCV therapy, with the majority of patients achieving a SVR. However, the assessment of liver parenchyma remains a crucial element of post-treatment evaluation. In recent years, numerous non-invasive methods have been developed, including serum biomarkers and elastography techniques. 2D SWE is the newest elastography method, relying on the assessment of the velocity of shear waves travelling through the tissue. Combined with serologic tests, 2D SWE is a sufficient tool for evaluating liver fibrosis regression during and after DAA therapy.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

Author contributions

Original concept of study: MI, UZD. Writing of manuscript: PP, PM. Analysis and interpretation of data: LL, MB. Final acceptance of manuscript: PP, UZD. Collection, recording and/or compilation of data: MI, PP, KFS. Critical review of manuscript: PM, KFS, MB.

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