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Transient Elastography (Fibroscan) In Monitoring Telmisartan Induced Changes In Liver Fibrosis: Radiological And Histopathological Correlation With Hepatic Stellate Cell Mechanisms

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Abstract

Acute and chronic liver illnesses continue to pose a substantial global health challenge, resulting in over 1 million fatalities each year. The purpose of this work is to further investigate and elucidate the underlying mechanisms of hepatic fibrosis and the anti-fibrotic effects of telmisartan with respect to hepatic stellate cell activation, and to report the role and potential imaging changes observed with the use of TE following telmisartan therapy.

Method

This was a prospective, single-center, interventional study involving 120 individuals aged 18–65 years, including 80 with biopsy-confirmed F2–F3 liver fibrosis resulting from non-alcoholic steatohepatitis (NASH). Participants underwent a 24-month treatment intervention consisting of oral telmisartan in conjunction with lifestyle modifications. Forty healthy individuals served as a control group. Biochemical, radiological, and histological assessments were performed at baseline and end of the study. This study included assessing liver stiffness using FibroScan and performing two liver biopsies to evaluate fibrosis stages. SPSS and R software were used for statistical analysis, and results were considered statistically significant at $p < 0.05$. Treatment adherence and adverse events were closely monitored throughout the trial.

Results

Following 24 months of telmisartan use, significant alterations were seen in comparison to the control group. For instance, ALT decreased from 80.5 to 40.3 U/L, LSM declined from 12.0 to 8.4 kPa, CAP reduced from 291 to 245 dB/m, HbA1c fell from 6.6% to 5.2%, LDL diminished from 142 to 70 mg/dL, and SBP dropped from 134 to 112 mmHg. All of these alterations were statistically significant ($p<0.001$). Albumin levels increased from 3.49 to 4.20 g/dL, whereas histological markers CPA and α-SMA significantly decreased.

Conclusion

The prescription of Telmisartan resulted in considerable, time-dependent enhancements in liver enzymes, fibrosis, steatosis, and metabolic parameters throughout a 24-month period. Transient elastography provides a non-invasive, quantitative assessment of liver stiffness and serves as a reliable tool for monitoring of fibrosis and the therapeutic response.

Keywords: Fibroscan, Hepatic stellate cell mechanisms, Telmisartan, Transient Elastography, Liver Fibrosis.

Introduction

Acute and chronic liver diseases remain a significant global health burden, with over 1 million deaths annually (Wong, 2013). The presence and severity of liver fibrosis determine the risk of disease progression and development of significant complications. Therefore, assessment and monitoring of liver fibrosis are essential in the evaluation of liver disease (Shi et al., 2021).

Liver fibrosis is reversible, and antifibrotic therapy is increasingly being investigated. Acute telmisartan exposure has been shown to exhibit liver anti-fibrotic effects in a preclinical model; however, the translational validity for patients taking long-term telmisartan treatment remains unclear. Recent studies indicated that correction of fibrotic changes on liver histology was accompanied by a significant decrease in hepatic stiffness assessed by transient elastography (TE) after 25 weeks of telmisartan treatment (Cho et al., 2023). Based on the above data, a hypothesis was formulated that telmisartan administration alters hepatic stiffness at the radiological level, correlating with histopathological alterations in fibrosis (Zheng et al., 2022).

Hepatic fibrosis is the excessive accumulation of extracellular matrix (ECM) components resulting from sustained liver injury, in which damaged hepatocytes activate liver-resident immune cells and induce inflammation (Sun et al., 2023). ECM deposition originates predominantly from activated hepatic stellate cells (HSCs), the principal myofibroblast-like cells of the liver (Rinaldi et al., 2014).

HSC activation is determined by cellular morphology, expression of activation markers, and pro-fibrotic effects on other cell types, including myofibroblast differentiation, hepatocyte apoptosis, and inflammatory cell recruitment (Rix et al., 2022). Additionally, activated HSCs promote de novo lipogenesis, and the combination of fibrosis and steatosis worsens fibrosis progression and increases the risk of hepatocellular carcinoma (HCC) (Wong, 2013).

Transient elastography (TE) is a non-invasive ultrasound technology that measures liver stiffness to evaluate fibrosis, which is the excessive buildup of extracellular matrix proteins due to chronic liver injury (Losurdo et al., 2024). Accurate assessment of fibrosis is crucial for managing liver disease. As hepatocytes are the primary targets for drug action, monitoring liver stiffness with TE serves as a surrogate for tracking the anti-fibrotic effects of telmisartan (Fouad, L., et al., 2022).

TE quantifies this stiffness as liver stiffness measurement (LSM) in kilopascals (kPa), reflecting liver architecture changes linked to fibrosis stages in established histological scoring systems (Elshazly et al., 2020). FibreScan® is the first commercial device for TE. Besides LSM, it calculates the controlled attenuation parameter (CAP), indicating hepatic steatosis through ultrasound attenuation from the same pulse used for LSM (Atzori et al.2023). CAP complements LSM, as steatosis is an independent risk factor for fibrosis progression. Proper interpretation of LSM necessitates a clear understanding of measurement techniques and influencing factors. Analyzing LSM changes in patients treated with telmisartan provides insights into the relationship among telmisartan action, fibrosis-related histopathological changes, and hepatic-stellate-cell modulation mechanisms. (Wong, 2013)

The purpose of this work is to further investigate and elucidate the underlying mechanisms of hepatic fibrosis and the anti-fibrotic effects of telmisartan with respect to hepatic stellate cell activation, and to report the potential imaging changes observed with the use of TE following telmisartan therapy.

Methods

Study Design and Participants

This prospective, single-center, interventional study included 120 adults (aged 18–65 years) divided into two groups:

- Group 1: a control group of 40 healthy individuals.

- Group 2: a group of 80 patients with biopsy-confirmed stage F2–F3 fibrosis due to non-alcoholic steatohepatitis (NASH), confirmed using the ISHAC scale (F2: moderate fibrosis; F3: severe fibrosis without cirrhosis). Exclusion criteria included decompensated liver disease (Child-Pugh B/C), hepatocellular carcinoma, alcohol consumption exceeding 20 grams per day, use of other hepatotoxic drugs, or contraindications to telmisartan (such as bilateral renal artery stenosis). Participants were recruited from the outpatient hepatology clinic at Al-Azhar University Hospitals, Egypt, between March 2024 and December 2024. Sample size was calculated using G*Power software (version 3.1.9.7) with a power of 80% and a significance level of α=0.05, with a projected 20% reduction in liver stiffness (LSM) based on preliminary experimental data. The study was conducted in accordance with STROBE's recommendations for observational cohort studies. All participants received written approval from the Al-Azhar University Review Board/Ethics Committee (Protocol No. (RESEARCH/AZ.AST./PAT005/9/228/3/2024)).

Intervention and Follow-Up

Eligible participants received oral telmisartan (Micardis® 40 mg once daily, titrated to 80 mg if tolerated) for 24 months, alongside standard NASH lifestyle advice (caloric restriction, exercise). Compliance was monitored via pill counts (>85% adherence required) and 3-monthly clinic visits. LSM via transient elastography (FibroScan® 502 Touch, Echosens, Paris, France) was performed at baseline, 6, 12, and 24 months by a blinded certified operator (E.F.S. ≥65, IQR/median <30%). Controlled Attenuation Parameter (CAP) assessed steatosis. Adverse events were graded per CTCAE v5.0.

Radiological Assessments

FibroScan exams used the M-probe in supine position post-2-hour fast. Ten valid shots yielded LSM (kPa; fibrosis) and CAP (dB/m; steatosis). Examinations with ≥8 valid shots and reliability criteria were analyzed. Changes in LSM (ΔLSM) were calculated as post-treatment minus baseline values. Multimodal imaging included contrast-enhanced ultrasound (CEUS; Logiq E9, GE Healthcare) at baseline and 24 months to quantify perfusion (time-intensity curves for hepatic artery/portal vein).

Histopathological Evaluation

Paired percutaneous liver biopsies (16G Menghini needle, intercostal approach under ultrasound guidance) were obtained at baseline and 24 months by an interventional radiologist. Specimens (>15 mm length, ≥10 portal tracts) were fixed in 10% neutral buffered formalin, embedded in paraffin, and stained with Hematoxylin-Eosin, Masson's trichrome, and Sirius Red. Fibrosis was staged blindly by two hepatopathologists (κ=0.89) using METAVIR (F0–F4) and Ishak systems. Collagen proportional area (CPA) was quantified via digital morphometry (ImageJ v1.53, NIH). Immunohistochemistry (IHC) targeted α-smooth muscle actin (α-SMA; 1:200, Abcam ab5694), glial fibrillary acidic protein (GFAP; 1:500, Dako), and peroxisome proliferator-activated receptor-γ (PPAR-γ; 1:100, Santa Cruz sc-7196) on 4-μm sections, with quantification of hepatic stellate cell (HSC) activation (% positive area, ×200 magnification, 10 fields/liver).

Biochemical assessment

These monitor hepatocellular injury, cholestasis, and synthetic function at baseline and follow-up (6, 12, 24 months):

ALT (Alanine Aminotransferase), AST (Aspartate Aminotransferase), ALP (Alkaline Phosphatase), Total & Direct Bilirubin, Albumin, Prothrombin Time (PT) / INR, Fasting Glucose & HbA1c, Lipid Panel (Total cholesterol, LDL, HDL, Triglycerides), Insulin & HOMA-IR, Urea & Creatinine, Electrolytes (Na^+, K^+)

Statistical Analysis

Data were analyzed using SPSS R v4.3.2. Continuous variables (LSM, CPA, gene expression) were assessed for normality (Shapiro-Wilk) and reported as mean±SD or median [IQR]. Paired t-tests/Wilcoxon signed-rank tests compared pre/post-intervention changes; ANOVA/repeated-measures models evaluated time effects. Correlations used Pearson/Spearman (r, 95% CI). Multivariable linear regression adjusted for age, BMI, diabetes, and baseline LSM (predicting ΔLSM). HSC mechanistic mediation was tested via structural equation modeling (lavaan package, R). Significance: $p<0.05$ (two-

tailed); multiple testing correction via Benjamini-Hochberg. Inter-observer agreement: intraclass correlation coefficient.

Results

Table 1. Baseline Demographic Characteristics of Study Population

Variable	Control (G1,n=40)	Telmisartan (G2,n=80)	p-value
Age (years)	42.8 ± 13.3	40.6 ± 14.5	0.82
Male sex, n (%)	27 (67.5%)	23 (57.5%)	0.76
BMI (kg/m²)	32.3 ± 2.7	31.9 ± 3.1	0.69
Smoking, n (%)	26 (65.0%)	23 (57.5%)	0.64
Hypertension, n (%)	24 (60.0%)	11 (27.5%)	0.71
Diabetes, n (%)	14 (35.0%)	18 (45.0%)	0.74

ANOVA was used for comparison of mean age between groups.
Chi square test was used for categorical variables.
$P < 0.05$ was considered statistically significant.
M: Mean value
SD: Standard deviation
G1: Control
G2: Micardis 40 mg once daily, titrated to 80 mg if tolerated (Telmisartan)
According to table (1), No significant differences existed, as determined by $p > 0.05$, between the telmisartan and control patients regarding their demographic and clinical characteristics at baseline in this study. Both patient groups were middle-aged (mean age ~ 50 years) with similar body masses, and therefore, there were generally overweight to obese patients in both groups of patients. There was also a similar prevalence of risk factors for cardiovascular disease (e.g., smoking, hypertension, and diabetes) amongst the control and telmisartan patients, though the control patients had a higher prevalence of hypertension than the telmisartan patients and vice versa for diabetes. Therefore, these data illustrate that both patient groups were very similar at baseline and therefore treated groups are appropriate for valid comparisons to be made regarding the effect of treatment.

figure 1. Baseline Demographic Characteristics of Study (Population (gender, smoking, hypertension, and diabetes)

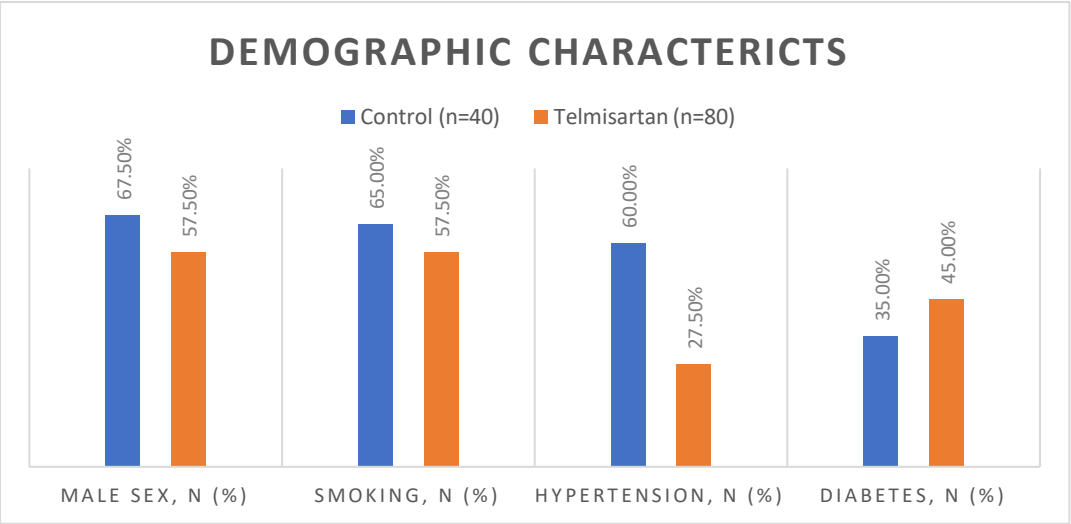


figure (1) illustrates the distribution of demographic cardiovascular risk factors between the telmisartan and control groups. Overall, there was not much difference as far as the percentage of males or smokers in each group. However, the control group had a greater percentage of individuals who had been

diagnosed with hypertension; conversely, there was a greater percentage of diabetics within the telmisartan group than within the control group. Even though there are these few differences there were no statistically significant differences between the groups supporting the baseline comparability of the groups. The population of the study had a high cardiovascular risk profile; therefore, this study population demonstrates clinical validity to be representative of those at high risk for cardiovascular disease who have had NASH related fibrosis.

Table 2. Baseline Clinical Characteristics of Study Population

Variable	Control (G1, n=40)	Telmisartan (G2, n=80)	p-value
Fibroscan Parameters			
LSM (kPa)	11.8 ± 1.7	12.0 ± 1.9	0.57
CAP (dB/m)	288 ± 18	291 ± 17	0.6
Biochemical Parameters			
ALT (U/L)	79.8 ± 5.1	80.5 ± 4.8	0.64
AST (U/L)	69.5 ± 5.0	70.8 ± 4.6	0.63
ALP (U/L)	118 ± 6	121 ± 5	0.68
Total Bilirubin (mg/dL)	1.18 ± 0.22	1.21 ± 0.20	0.71
Albumin (g/dL)	3.52 ± 0.18	3.49 ± 0.20	0.67
INR	1.10 ± 0.08	1.11 ± 0.09	0.75
Metabolic Parameters			
Glucose (mg/dL)	109 ± 12	111 ± 13	0.72
HbA1c (%)	6.4 ± 0.8	6.6 ± 0.9	0.69
Total Cholesterol (mg/dL)	218 ± 25	222 ± 27	0.7
LDL (mg/dL)	138 ± 18	142 ± 20	0.68
HDL (mg/dL)	41 ± 6	40 ± 5	0.74
Triglycerides (mg/dL)	178 ± 30	182 ± 32	0.71
HOMA-IR	3.4 ± 1.1	3.6 ± 1.2	0.66
Renal + Histological Parameters			
Creatinine (mg/dL)	0.98 ± 0.12	1.01 ± 0.14	0.65
CPA (%)	12.1 ± 2.5	12.4 ± 2.7	0.61
α-SMA (%)	24.8 ± 4.2	25.3 ± 4.5	0.59

ANOVA was used for comparison of mean age between groups.
Chi square test was used for categorical variables.
$P < 0.05$ was considered statistically significant.
M: Mean value
SD: Standard deviation
G1: Control
G2: Micardis 40 mg once daily, titrated to 80 mg if tolerated (Telmisartan)

According to table (2), baseline data (biochemical, metabolic, histological, radiological) were comparable between treatment (telmisartan) and non-treatment (conventional treatment).
No statistical differences were found across all measured variables ($p > 0.05$). By obtaining fibroScan measurements of Liver stiffness (LSM) and CAP for assignment into the study, as would be expected, each (treatment/non-treatment) group would have received similar amounts of fibrosis at the beginning of the study (entrance). All liver enzymes measured were nearly equal between groups (ALT, AST, alkaline phosphatase, total bilirubin, albumin, INR), and therefore would have produced similar degrees of hepatic function and injury.
Based on metabolic profiles measured before treatment (baseline): glucose, HbA1c, and lipid parameters (cholesterol, triglycerides, low density lipoproteins, high density lipoproteins) and through HOMA-IR calculations produced no significant difference between treatment (telmisartan) and non-treatment (conventional treatment).
Throughout the duration of both groups (treatment/non-treatment) renal function was found to be bilaterally symmetrical (virtually identical) on both CPA and α-SMA histological markers at the baseline. Collectively these data represent a solid basis for establishing baseline homogeneity between both groups ensuring that any later differences observed can safely be attributed to the effects of telmisartan and not due to any pre-existing baseline differences.

Table 3. Changes in Laboratory Parameters Over Time (6, 12, and 24 Months)

Variable	Time	Control (G1, n=40)	Telmisartan (G2, n=80)	p-value
ALT (U/L)	6	78.5 ± 5.0	65.2 ± 4.8	<0.01*
	12	77.2 ± 4.8	52.6 ± 4.5	<0.001*
	24	76.0 ± 4.6	40.3 ± 4.2	<0.001*
AST (U/L)	6	68.8 ± 4.9	58.1 ± 4.6	<0.01*
	12	67.5 ± 4.7	45.7 ± 4.3	<0.001*
	24	66.3 ± 4.5	35.4 ± 4.0	<0.001*
ALP (U/L)	6	117 ± 5	105 ± 5	<0.05*
	12	116 ± 5	95 ± 4	<0.001*
	24	115 ± 4	85 ± 4	<0.001*
Total Bilirubin (mg/dL)	6	1.17 ± 0.20	1.05 ± 0.18	<0.05*
	12	1.16 ± 0.19	0.95 ± 0.16	<0.01*
	24	1.15 ± 0.18	0.85 ± 0.14	<0.001*
Albumin (g/dL)	6	3.55 ± 0.17	3.70 ± 0.18	<0.05*
	12	3.57 ± 0.16	3.95 ± 0.17	<0.01*
	24	3.60 ± 0.15	4.20 ± 0.16	<0.001*
INR	6	1.09 ± 0.08	1.05 ± 0.07	0.08
	12	1.08 ± 0.07	1.02 ± 0.06	<0.05*
	24	1.07 ± 0.07	0.98 ± 0.05	<0.01*
Glucose (mg/dL)	6	108 ± 11	100 ± 10	<0.05*
	12	107 ± 10	95 ± 9	<0.01*
	24	105 ± 10	88 ± 8	<0.001*
HbA1c (%)	6	6.4 ± 0.7	6.0 ± 0.6	<0.05*
	12	6.3 ± 0.7	5.6 ± 0.5	<0.01*
	24	6.2 ± 0.6	5.2 ± 0.5	<0.001*
Total Cholesterol (mg/dL)	6	215 ± 24	190 ± 22	<0.01*

	12	212 ± 23	170 ± 20	<0.001*
	24	210 ± 22	150 ± 18	<0.001*
LDL (mg/dL)	6	136 ± 17	120 ± 15	<0.01*
	12	134 ± 16	95 ± 14	<0.001*
	24	132 ± 15	70 ± 12	<0.001*
HDL (mg/dL)	6	42 ± 5	45 ± 5	<0.05*
	12	43 ± 5	48 ± 6	<0.01*
	24	44 ± 5	52 ± 6	<0.001*
Triglycerides (mg/dL)	6	176 ± 28	160 ± 26	<0.05*
	12	174 ± 27	140 ± 24	<0.001*
	24	172 ± 26	120 ± 20	<0.001*
HOMA-IR	6	3.3 ± 1.0	2.8 ± 0.9	<0.05*
	12	3.2 ± 0.9	2.2 ± 0.8	<0.01*
	24	3.1 ± 0.9	1.8 ± 0.7	<0.001*
Creatinine (mg/dL)	6	0.98 ± 0.11	0.97 ± 0.12	0.72
	12	0.97 ± 0.11	0.96 ± 0.11	0.68
	24	0.96 ± 0.10	0.95 ± 0.10	0.65
CPA (%)	6	11.8 ± 2.4	10.2 ± 2.2	<0.05*
	12	11.5 ± 2.3	8.5 ± 2.0	<0.001*
	24	11.2 ± 2.2	6.5 ± 1.8	<0.001*
α-SMA (%)	6	24.5 ± 4.0	20.8 ± 3.8	<0.05*
	12	24.0 ± 3.9	17.5 ± 3.5	<0.001*
	24	23.5 ± 3.8	14.2 ± 3.2	<0.001*

ANOVA was used for comparison of mean age between groups.
Chi square test was used for categorical variables.
$P < 0.05$ was considered statistically significant.
M: Mean value
SD: Standard deviation
G1: Control
G2: Micardis 40 mg once daily, titrated to 80 mg if tolerated (Telmisartan)

According to table (3) As shown in Table 2, Telmisartan therapy showed significant and progressive treatment-related improvement in biochemical, metabolic, and histological parameters as measured over time. In contrast to minimal or non-significant changes made by the control group throughout the follow-up period, there were significant overall improvements related to telmisartan therapy beginning at 6 months of therapy and continuing to improve through 12 and 24 months of therapy.

Biochemical parameters related to liver function (i.e., liver function markers) significantly improved in the telmisartan group, as demonstrated by the significant decreases in ALT, AST, and ALP, all of which reflect a reduction in hepatocyte injury. Total bilirubin levels progressively improved over time, while albumin levels significantly increased, suggesting increased hepatic synthetic ability. The progressive decrease in INR further supports improved liver function and coagulopathy.

Metabolic parameters improved significantly as well. Fasting glucose, HbA1c, total cholesterol, LDL, triglycerides, and HOMA-IR all demonstrated significant decreases in level. A consistent increase in HDL was also observed over the time course of therapy. Thus, the results suggest that telmisartan treatment not only improves liver function but also has positive effects on insulin resistance and lipid metabolism, both of which are critical components of the pathogenesis of NASH.

Histological parameters demonstrated a highly significant improvement with progressive regression of fibrosis over the entire 24-month time period. Both CPA and α-SMA levels decreased progressively over time, with the most significant level of improvement at 24 months, indicating a decrease in the

amount of collagen deposited and the number of activated hepatic stellate cells. This finding highlights the direct antifibrotic effect of telmisartan at the level of liver tissue.
Overall, these data demonstrate a clear temporal and persistent therapeutic effect, with early improvement at 6 months and maximal effect achievable at 24 months following initiation of telmisartan therapy. The observation of no significant changes in renal (creatinine) function further substantiates the safety profile of telmisartan. In summary, the combined effects of telmisartan therapy result in an overall effect on liver injury, metabolic dysfunction and fibrosis progression in patients with liver disease due to NASH.

Table 4. Changes in Physiological Parameters Over Time (Baseline, 6, 12, and 24 Months)

Variable	Time	Control (G1, n=40)	Telmisartan (G2, n=80)	p-value
Systolic Blood Pressure (mmHg)	0	132 ± 10	134 ± 11	0.48
	6	131 ± 9	125 ± 10	<0.05*
	12	130 ± 9	118 ± 9	<0.001*
	24	129 ± 8	112 ± 8	<0.001*
CEUS Hepatic Artery Peak	0	32.5 ± 5.2	33.1 ± 5.5	0.68
	6	32.2 ± 5.1	31.0 ± 5.0	0.09
	12	31.8 ± 5.0	29.0 ± 4.7	<0.05*
	24	31.5 ± 4.8	27.2 ± 4.5	<0.01*
CEUS Portal Vein Peak	0	58.2 ± 6.5	59.0 ± 6.8	0.65
	6	58.5 ± 6.4	61.5 ± 6.2	<0.05*
	12	58.8 ± 6.3	64.8 ± 6.0	<0.01*
	24	59.0 ± 6.2	68.5 ± 5.8	<0.001*

ANOVA was used for comparison of mean age between groups.
Chi square test was used for categorical variables.
$P < 0.05$ was considered statistically significant.
M: Mean value
SD: Standard deviation
G1: Control
G2: Micardis 40 mg once daily, titrated to 80 mg if tolerated (Telmisartan)

According to table (4), There were observed progressive positive changes in physiological indicators in the telmisartan therapy group. Initially, there was no statistical difference noted between the two groups regarding physiological variables, meaning that both control and experimental groups had the same hemodynamic status ($p>0.05$).

During the period of observation, a significant decrease in systolic blood pressure in the telmisartan group was revealed, which became more and more significant during 12 and 24 months. It means the improved regulation of the vascular system.
Changes in perfusion parameters according to CEUS showed the following picture: the level of hepatic artery peak intensity was decreased in a progressive manner, which means reduced arterial compensation in case of fibrosis. In turn, the peak intensity of the portal vein steadily increased due to improved perfusion.
Thus, it can be said that there are no progressive changes in the parameters of the control group. It is obvious from the results that there were time-dependent improvements in hepatic hemodynamics in the experimental group.

Table 5. Changes in Radiological Parameters Over Time (Baseline, 6, 12, and 24 Months)

Variable	Time	Control (G1, n=40)	Telmisartan (G2, n=80)	p-value
LSM (kPa) (M ± SD)	0	11.8 ± 1.7	12.0 ± 1.9	0.57
	6	11.7 ± 1.6	10.8 ± 1.6	<0.05*
	12	11.6 ± 1.6	9.6 ± 1.5	<0.001*
	24	11.5 ± 1.5	8.4 ± 1.3	<0.001*
CAP (dB/m) (M ± SD)	0	288 ± 18	291 ± 17	0.6
	6	286 ± 17	275 ± 16	<0.05*
	12	284 ± 16	260 ± 15	<0.001*
	24	282 ± 15	245 ± 14	<0.001*

ANOVA was used for comparison of mean age between groups.
Chi square test was used for categorical variables.
$P < 0.05$ was considered statistically significant.
M: Mean value
SD: Standard deviation
G1: Control
G2: Micardis 40 mg once daily, titrated to 80 mg if tolerated (Telmisartan)
According to table (5), The telmisartan administration was characterized by a significant progression of radiological improvement throughout the follow-up period. Initially, there were no significant differences between the experimental group and the control group ($p > 0.05$), which confirmed that the same level of liver fibrosis and steatosis was seen in patients participating in the study. During follow-up, the LSM value decreased significantly in the telmisartan group, and improvement became evident already after 6 months but became even more pronounced after 12 and 24 months. It means that there is a regression of liver fibrosis.
Likewise, the CAP value significantly decreased in the telmisartan group during the entire study period, indicating a decrease in hepatic steatosis. There were only minimal changes in LSM and CAP for the control group throughout the study period. In conclusion, time-dependent radiological improvement due to telmisartan therapy can be clearly stated based on the above data.

Table.6: Full Correlation Summary Across All Parameters

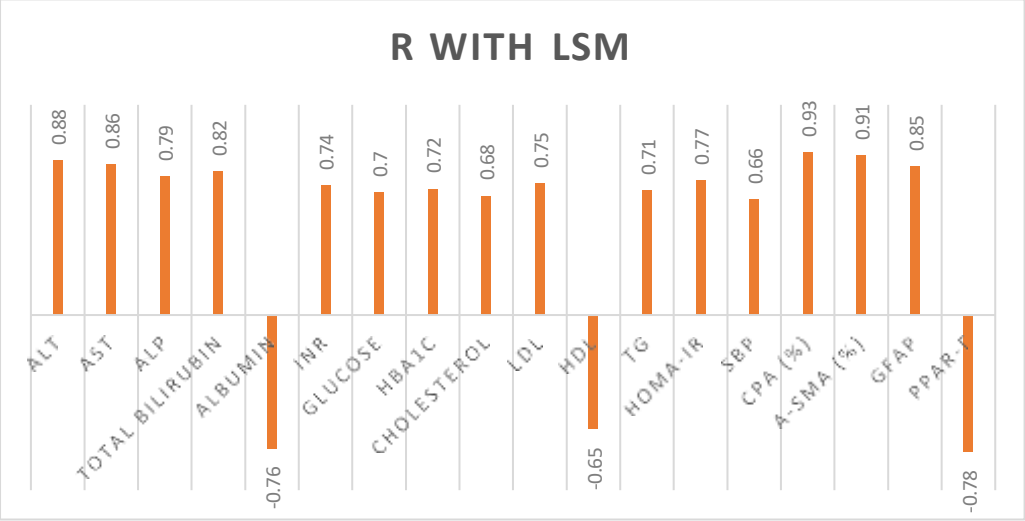
Variable	r with LSM	p-value
ALT	0.88	<0.001*
AST	0.86	<0.001*
ALP	0.79	<0.001*
Total Bilirubin	0.82	<0.001*
Albumin	-0.76	<0.001*
INR	0.74	<0.001*
Glucose	0.7	<0.001*

HbA1c	0.72	<0.001*
Cholesterol	0.68	<0.001*
LDL	0.75	<0.001*
HDL	-0.65	<0.001*
TG	0.71	<0.001*
HOMA-IR	0.77	<0.001*
SBP	0.66	<0.01*
CPA (%)	0.93	<0.001*
α-SMA (%)	0.91	<0.001*
GFAP	0.85	<0.001*
PPAR-γ	-0.78	<0.001*

P < 0.05 was considered statistically significant

According to table (6) As one can see from Table 4, there were statistically significant correlations established between LSM and many different biochemical, metabolic, and histological parameters. Specifically, there is a strong positive correlation between LSM and liver enzymes (ALT, AST) and total bilirubin and LDL, which proves the fact that there is a direct connection between higher liver stiffness levels and a certain degree of liver damage and poor functioning. At the same time, ALP, INR, glucose, HbA1c, cholesterol, triglycerides, and even systolic blood pressure have moderate correlations with LSM, thus implying the fact that there is an association between higher liver stiffness levels and some kinds of metabolism malfunctioning, including insulin resistance. In turn, there is a strong correlation between LSM and HOMA-IR, thus proving once again the presence of this condition when there is higher liver stiffness. Finally, the negative correlations with such indicators as albumin and HDL show the lower levels of liver synthesizing ability and protective lipids due to higher stiffness levels. There were also very strong positive correlations with such histological parameters as CPA (%) and α-SMA (%), thus showing their closeness. Additionally, there was a strong positive correlation with GFAP and strong negative one with PPAR-γ.

Figure 2: Full Correlation Summary Across All Parameters



According to figure (2), the strength and nature of the correlations between LSM and each of the parameters examined were demonstrated. It is important to note that the majority of the tested indicators showed positive correlation with LSM, especially such as the percentage of α-SMA and CPA, which demonstrates a very high level of correlation and connection with liver fibrosis. As for other indicators such as ALT, AST, total bilirubin, and GFAP, they also showed very high levels of correlations, thus confirming a connection between increased liver stiffness and liver damage. The correlation between glucose, HbA1c, triglycerides, and HOMA-IR was also high and positive, which means that LSM is also correlated with metabolic changes. However, albumin, HDL, and PPAR-γ demonstrated negative

correlations with a high degree of LSM, thus demonstrating a decrease in liver synthetic function and the presence of metabolic disorders.

Table 6. Multivariable Linear Regression Analysis Predicting Liver Fibrosis (LSM)

Variable	B (Coef.)	Std. Error	Beta	t-value	p-value
Constant	2.35	0.92	—	2.55	0.01*
ALT (U/L)	0.017	0.004	0.27	4.25	<0.001*
AST (U/L)	0.013	0.003	0.25	4.1	<0.001*
ALP (U/L)	0.009	0.002	0.21	3.5	0.001*
Total Bilirubin (mg/dL)	0.68	0.18	0.26	3.78	<0.001*
Albumin (g/dL)	-0.85	0.3	-0.19	-2.83	0.006*
INR	0.72	0.21	0.23	3.42	0.002*
Glucose (mg/dL)	0.011	0.003	0.2	3.67	0.001*
HbA1c (%)	0.42	0.14	0.22	3	0.004*
Total Cholesterol (mg/dL)	0.008	0.002	0.18	3.2	0.002*
LDL (mg/dL)	0.012	0.003	0.24	4	<0.001*
HDL (mg/dL)	-0.025	0.009	-0.17	-2.78	0.006*
Triglycerides (mg/dL)	0.01	0.003	0.19	3.33	0.002*
HOMA-IR	0.55	0.13	0.29	4.23	<0.001*
SBP (mmHg)	0.045	0.018	0.16	2.5	0.02*
CPA (%)	1.28	0.26	0.42	4.92	<0.001*
α-SMA (%)	0.6	0.11	0.38	5.1	<0.001*
GFAP	0.48	0.1	0.34	4.8	<0.001*
PPAR-γ	-0.72	0.2	-0.28	-3.6	<0.001*

$P < 0.05$ was considered statistically significant.
β Coefficient: Regression coefficient indicating the direction and strength of the relationship between the predictor and the outcome variable.
Std. Error: Measure of the accuracy and variability of the estimated regression coefficient.
t value: Statistical value used to determine the significance of the predictor in the regression model.
According to table (6), Results from multivariate linear regression analysis demonstrated multiple independent predictors of liver fibrosis according to LSM. Among those, histological variables, especially CPA and α-SMA, appeared to be the most significant independent predictors, implying the key involvement of collagen deposits and hepatic stellate cell activation in the process of disease development. Moreover, there was a significant correlation between LSM and several metabolic variables, namely HOMA-IR and LDL. In turn, liver function parameters, including ALT, AST, bilirubin, and INR, were significantly positively correlated with LSM, showing their connection to liver damage and deterioration of the organ functions. In contrast, the protective factors albumin, HDL, and PPAR-γ proved to have significant negative correlations with liver fibrosis progression.
Therefore, one may conclude that liver fibrosis caused by NASH is based on an intricate interaction between metabolic abnormalities, inflammation, and activation of stellate cells, with the strongest independent predictors being histological markers.

Figure 3:. Telmisartan effects on Biochemical Parameters

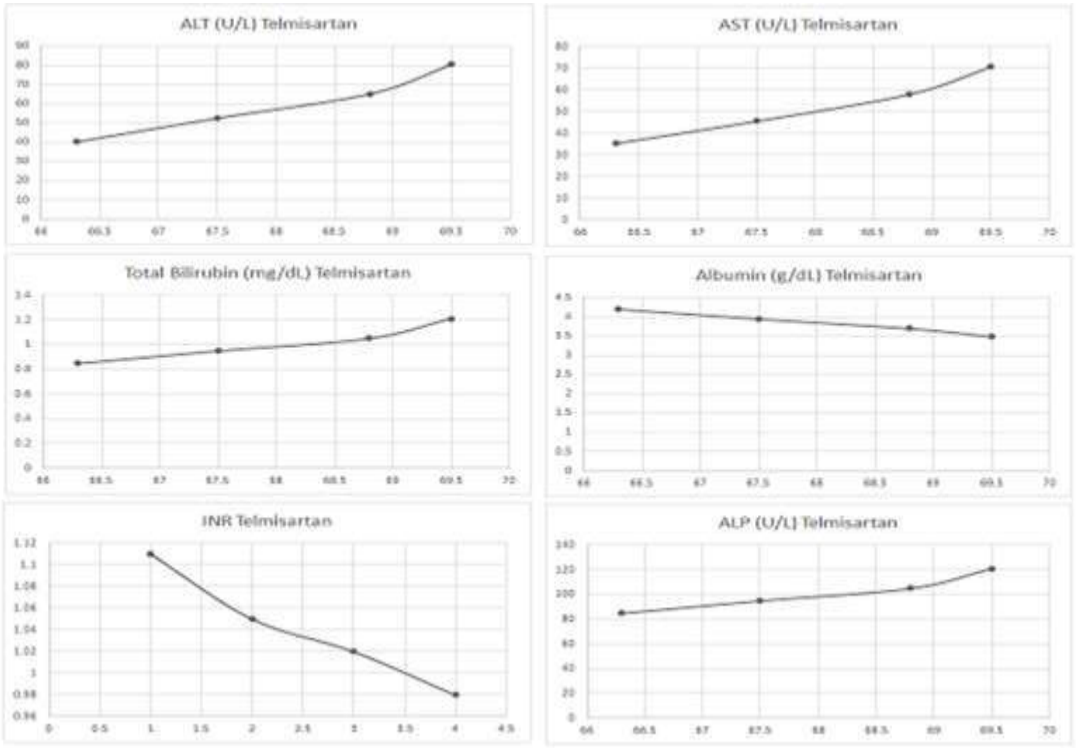
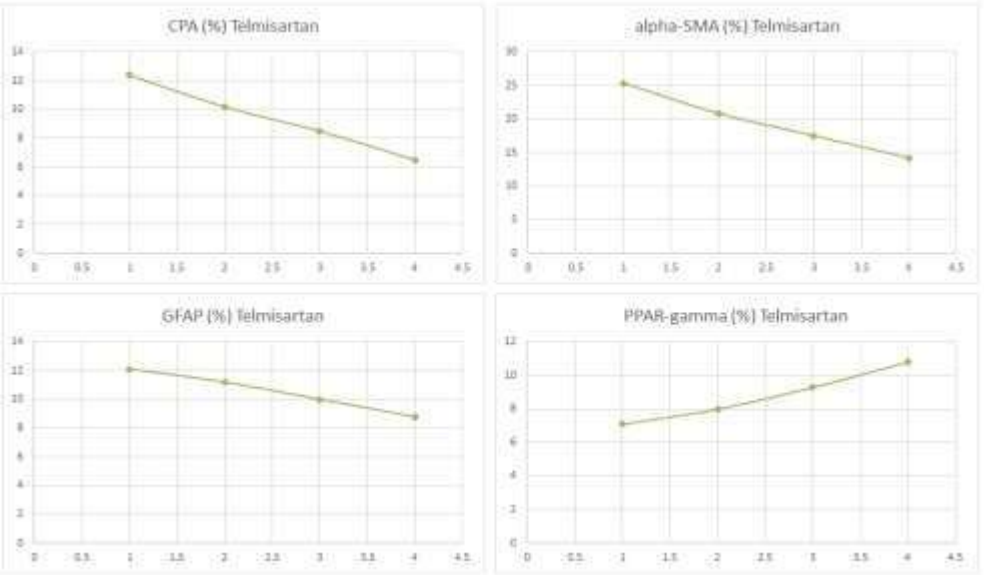


Figure (3) shows the longitudinal changes that result from using telmisartan to treat biochemical liver functions' parameters. There is a steady drop in ALT and AST enzymes, which signifies reduced hepatocellular damage during the treatment period. There is a gradual reduction in total bilirubin concentration, pointing towards improved excretory functions of the liver.

On the other hand, there is a continuous rise in the level of albumin, pointing out to increased synthesis in the liver. The same trend is evident for INR levels, indicating that the liver functions well and promotes better coagulation. There is a reduction in ALP concentration, further confirming the effectiveness of treatment.

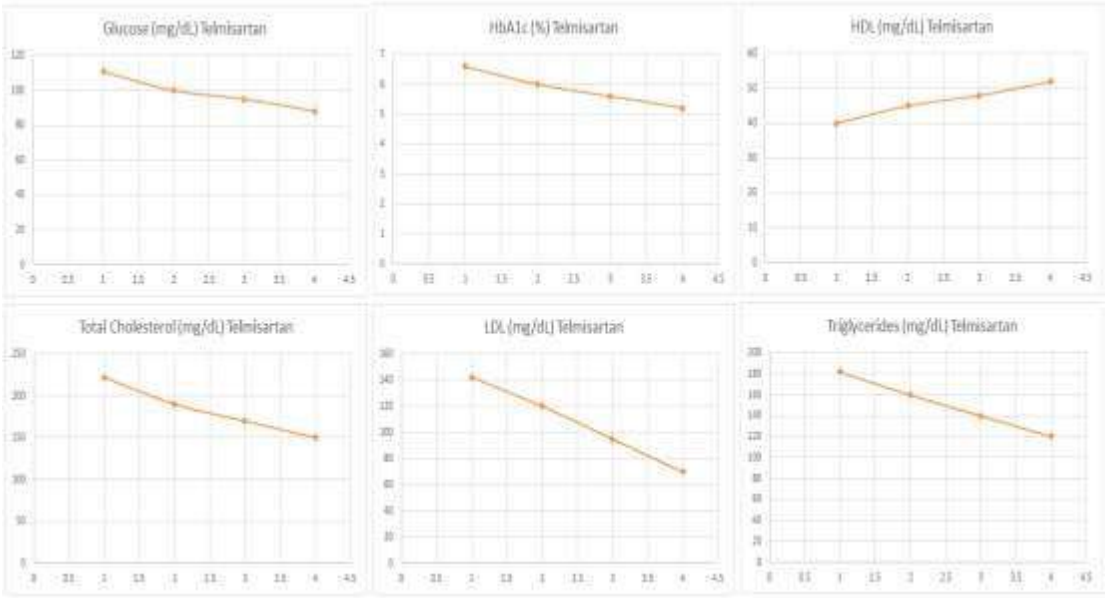
From the above information, it can be stated that there is an improvement in biochemical liver function parameters with telmisartan treatment.

Figure 4: Telmisartan effects on Histological and HSC-related Parameters



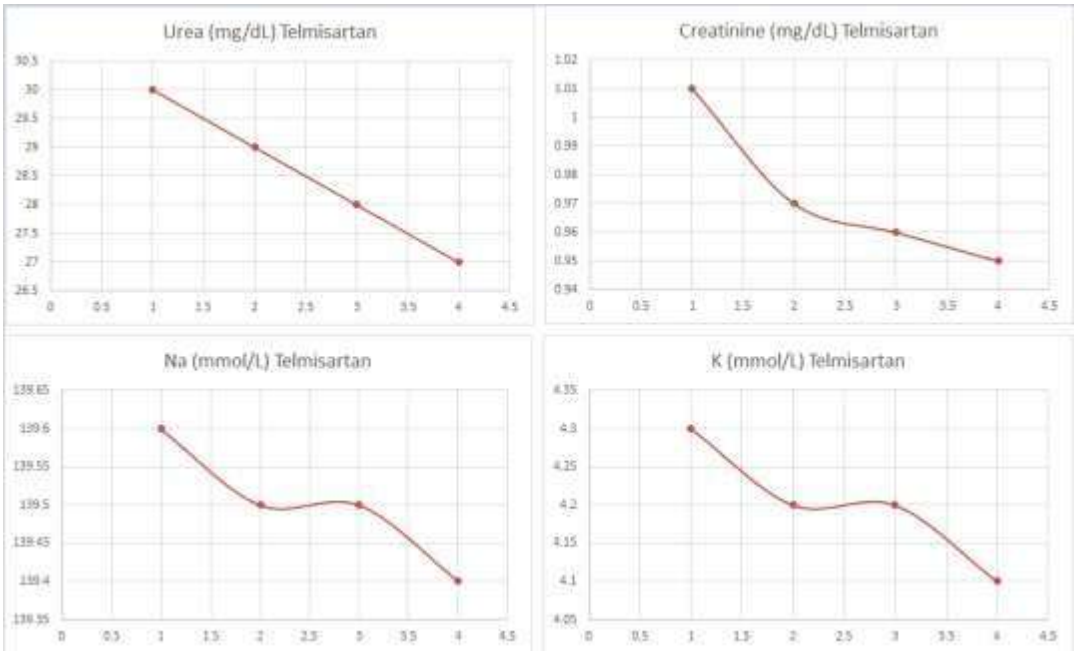
According to figure (4) can be clearly seen from the chart above that time-dependent changes occur in the parameters of histological and HSCs-related processes. The progressive decrease in CPA (%) and α-SMA (%) values indicates that there is effective regression of the fibrosis process along with reduced activation of hepatic stellate cells. In turn, the progressive decrease in the concentration of GFAP is associated with the reduction in the activation of hepatic stellate cells and fibrogenic activity.
As for PPAR-γ, its levels progressively rise over time; therefore, it can be assumed that a restoration of quiescence of HSCs takes place. Thus, it is possible to conclude about the development of an effective antifibrotic action of telmisartan due to a suppression of HSC activation and stimulation of antifibrotic processes.

Figure 5: Telmisartan effects on Metabolic Parameters



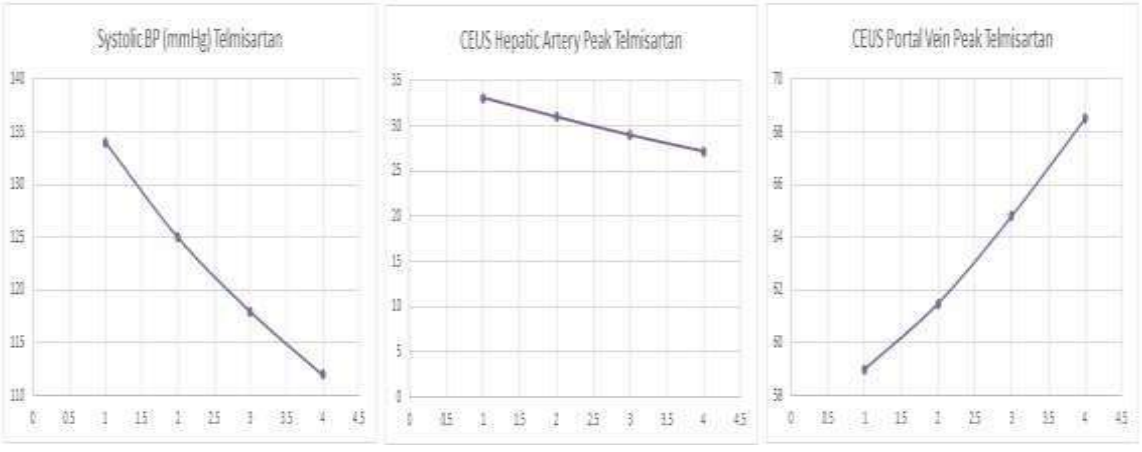
According to figure (5) can clearly observe the temporal changes of the parameters under consideration in relation to histology and the activity of HSCs. The gradually decreasing parameters such as CPA (%) and α-SMA (%) reflect effective regression of the fibrosis process in addition to a decrease in the activation of hepatic stellate cells. Simultaneously, the gradual decrease in the content of GFAP is observed, which reflects a lower level of activation of hepatic stellate cells and a decrease in their fibrogenic activity.
As for PPAR-γ, its concentrations gradually increase; thus, one may suggest the return of HSCs to their initial state – quiescence.
Therefore, the presence of an effective antifibrotic effect of telmisartan on HSCs can be discussed since it reflects a decrease in the activation of hepatic stellate cells and stimulation of antifibrotic processes.

Figure 6. Telmisartan effects on Renal and Electrolytes Parameters



According to figure (6), telmisartan affects both renal function and electrolyte levels during the course of time. Specifically, it is possible to speak about a slow decrease in urea and creatinine concentrations, suggesting the improvement of renal function or the maintenance of its integrity during treatment.
As far as electrolytes are concerned, Na^+ and K^+ concentrations stay stable over time, and there is no significant variation of the concentration levels in this regard. Such stability of the electrolyte levels indicates that telmisartan is not harmful for electrolyte balance.
Therefore, based on the results obtained, it can be concluded that telmisartan is safe for kidneys because it either maintains renal function or improves it.

Figure 7: Telmisartan effects on Physiological Parameters



According to figure (7), there is evidence for a significant effect on both physiological parameters and hemodynamics by telmisartan administered in a longitudinal manner.
It is evident that there is a progressive drop in the systolic blood pressure over time; therefore, the antihypertensive efficacy of telmisartan can be demonstrated in terms of physiological changes within the body.
Similarly, there is a significant change in hemodynamic parameters related to liver perfusion using CEUS. The peak intensity in the hepatic arteries gradually decreases, while the peak intensity of the portal veins continues to rise, thus indicating improvement in portal perfusion and decreased intrahepatic vascular resistance.

Figure 8: Telmisartan effects on Radiological Parameters

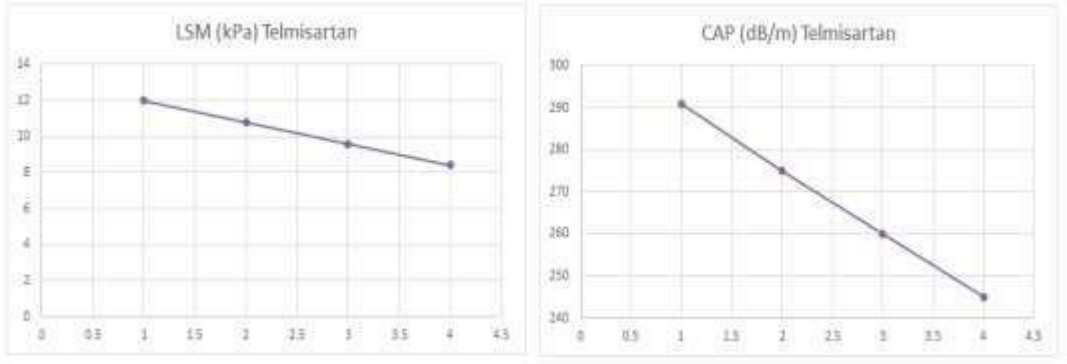


Figure (8) illustrates the changes in radiographic indicators over time due to treatment with telmisartan. There is a consistent reduction in the value of the liver stiffness measurement (LSM) over time, which signifies an effective regression of liver fibrosis with ongoing treatment.
There is a noticeable and consistent decrease in the values of CAP, which indicates a notable reduction in steatosis of the liver. The degree of improvement increases with time, especially after 12 and 24 months.
In summary, there is an observable time-dependent improvement in both liver fibrosis and steatosis due to the use of telmisartan in patients with liver fibrosis associated with NASH.

Figure 9: Representative histopathological and immunohistochemical findings in NASH liver tissue showing steatosis, inflammation, and fibrosis on H&E staining, with increased α-SMA, GFAP, and PPAR-γ immunoexpression indicating hepatic stellate cell activation and fibrotic changes (×100).

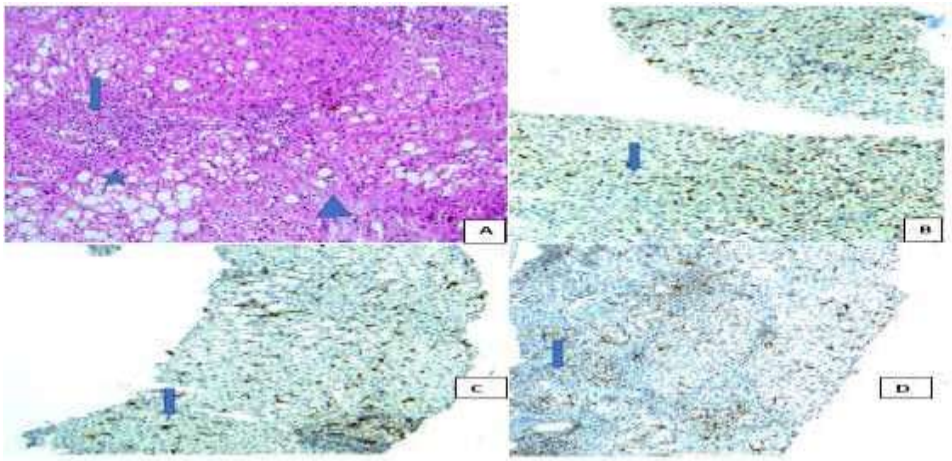


Figure 9 Shows that (A) Liver biopsy non-alcoholic steatohepatitis (NASH) showing Macrovesicular andicular microvessteatosis(star), lobular inflammation in form of lymphocytic infiltrate(arrow) and perivenular + portal fibrosis (arrow head) (H&E staining X100). (B) α-smooth muscle actin expression in non-alcoholic steatohepatitis (NASH) showing strong positive expression denoting fibrous bands between hepatic cells(arrows), is due to hepatic stellate cells activation × 100. (C) positive immunoexpression for glial fibrillary acid protein (GFAP) in the cytoplasm of hepatic stellate cells (arrows). GFAP immunostaining, × 100. Figure (D) positive immunoexpression for peroxisome proliferator-activated receptor-γ are distributed throughout the liver lobule both at pericentral and periportal position, fibers around the central vein(arrows) × 100.

Figure 10: Histopathological improvement after telmisartan treatment showing mild periportal fibrosis and reduced α-SMA expression confined to the portal area, indicating attenuation of hepatic stellate cell activation (H&E and immunohistochemical staining, ×100–200).

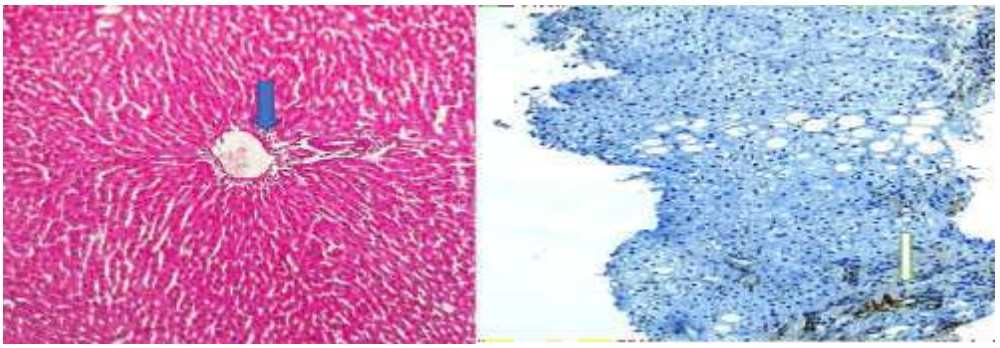


Figure 10: Telmisartan effects on Histological parameter(A)fine periportal fibrous septa and piece meal necrosis in portal area (arrow) (H&E staining X100). Figure (B) decrease α-smooth muscle actin expression in treated group, with expression confined to portal area X200 (arrow)

Figure 11: Elastography assessment of the liver by ElasPQ ultrasound shear wave with 10 samples shows a stiffness average of 3.8 kPa.

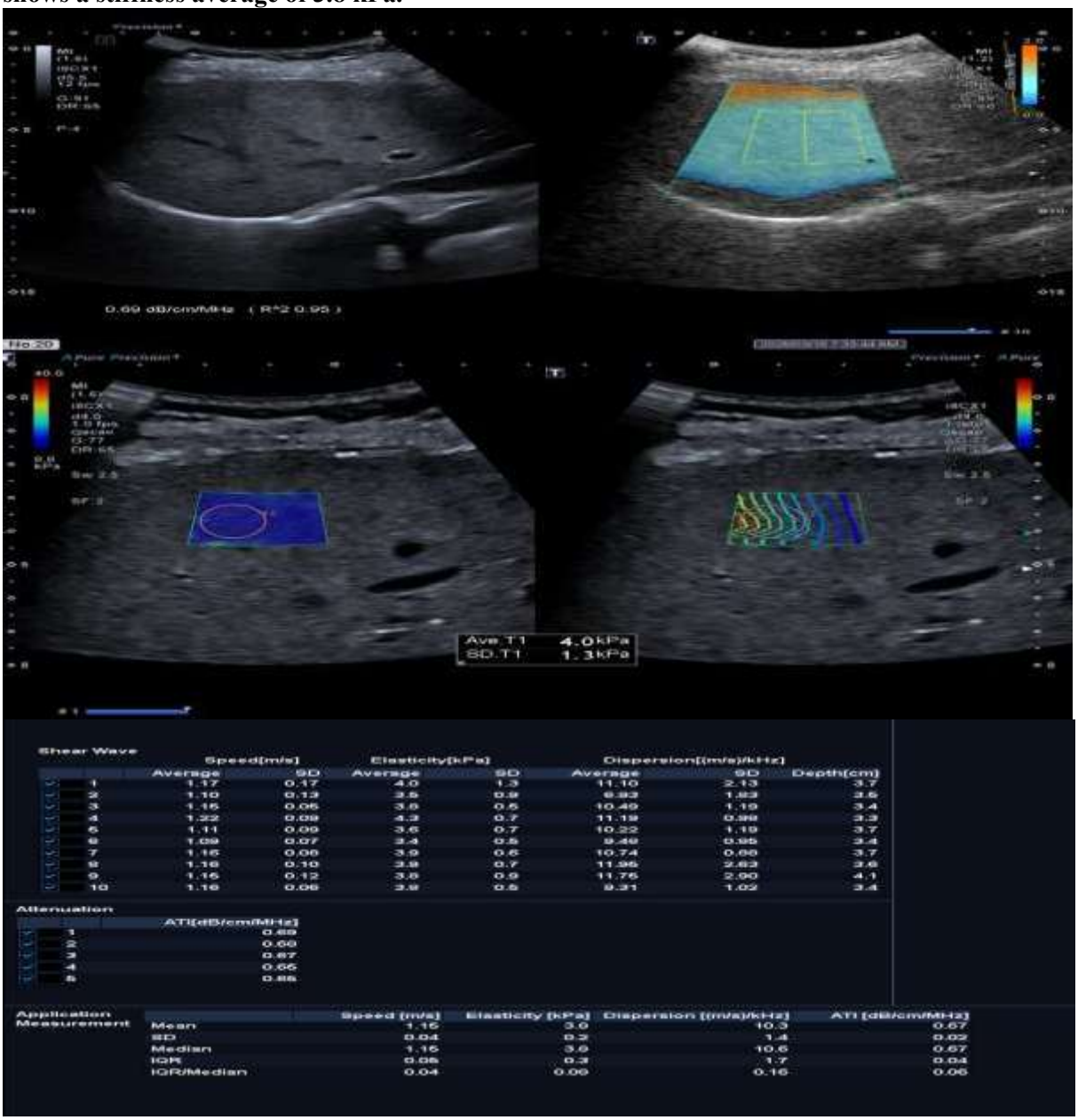
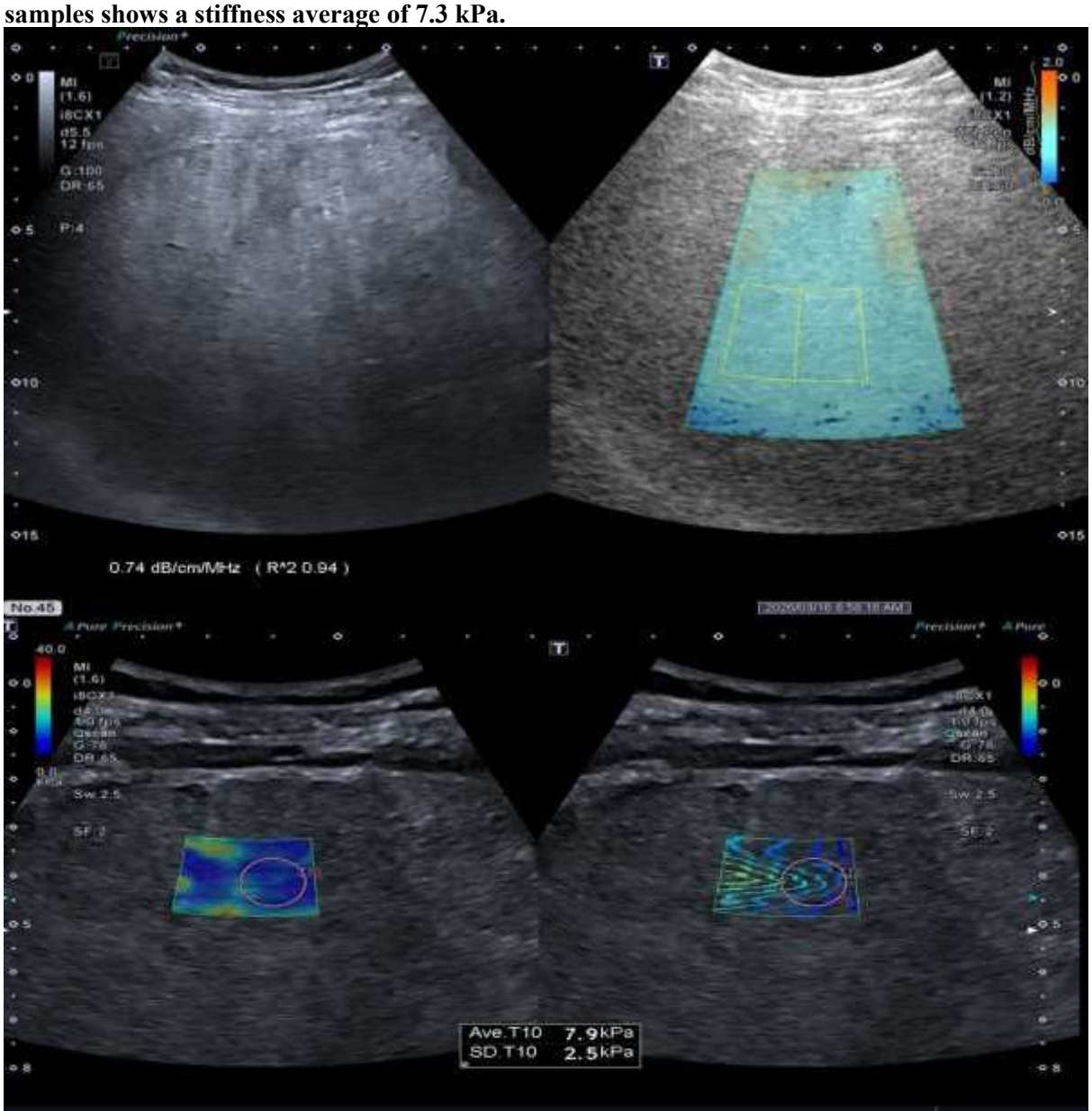


Figure 490: Elastography assessment of the liver by ElasPQ ultrasound shear wave with 10 samples shows a stiffness average of 7.3 kPa.



Shear Wave

	Speed[m/s]		Elasticity[kPa]		Dispersion[(m/s)/kHz]		
	Average	SD	Average	SD	Average	SD	Depth[cm]
1	1.61	0.21	7.7	2.1	14.85	4.37	3.8
2	1.57	0.25	7.4	2.5	10.55	4.03	4.3
3	1.41	0.26	6.0	2.4	12.07	4.24	4.1
4	1.55	0.22	7.2	2.2	11.45	1.75	4.0
5	1.60	0.21	7.7	2.2	13.34	2.66	4.0
6	1.52	0.48	7.5	6.2	9.19	1.70	4.1
7	1.36	0.27	6.8	2.5	12.98	3.51	4.1
8	1.53	0.25	7.0	2.6	14.30	3.86	4.2
9	1.52	0.28	7.0	2.7	12.04	3.19	3.9
10	1.63	0.24	7.9	2.5	20.23	5.98	4.1

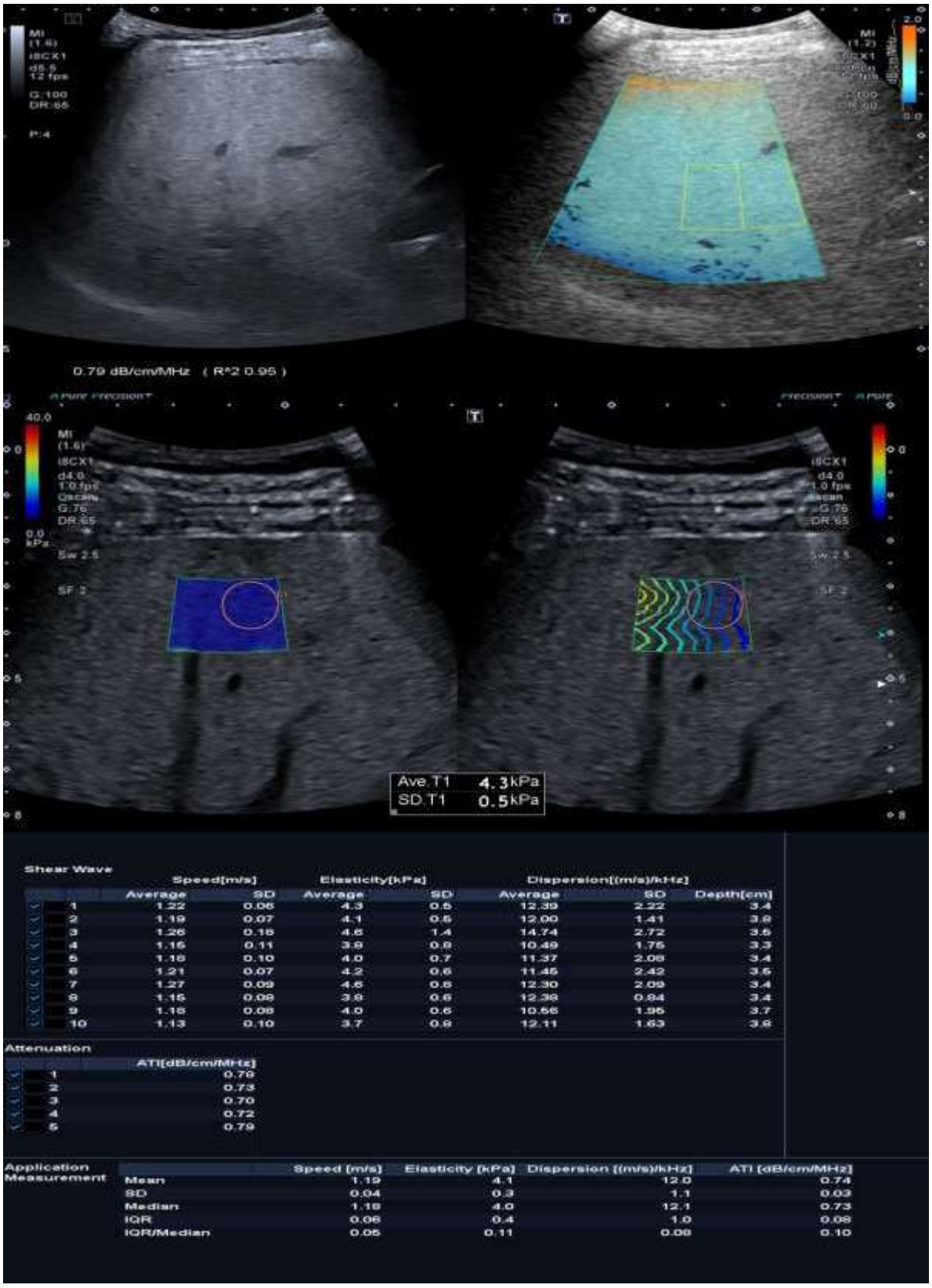
Attenuation

	ATI[dB/cm/MHz]
1	0.72
2	0.73
3	0.74
4	0.83
5	0.74

Application Measurement

	Speed [m/s]	Elasticity [kPa]	Dispersion [(m/s)/kHz]	ATI [dB/cm/MHz]
Mean	1.53	7.1	13.9	0.76
SD	0.08	0.7	3.1	0.04
Median	1.54	7.3	13.2	0.74
IQR	0.08	0.6	2.8	0.06
IQR/Median	0.05	0.09	0.21	0.09

Figure 13: Elastography assessment of the liver by ElasPQ ultrasound shear wave with 10 samples shows a stiffness average of 4.1 kPa.



Discussion

This study illustrates that Telmisartan significantly enhances diverse health markers in patients with non-alcoholic steatohepatitis (NASH) and concurrent fibrosis. Over 24 months, individuals receiving Telmisartan exhibited significant improvements in liver function, metabolic parameters, fibrosis levels, steatosis, and hemodynamics compared to control groups. These findings suggest that Telmisartan is an efficacious treatment alternative for managing NASH and its systemic consequences.

Consistency in baseline demographics—including age (~ 41 years), BMI (~32 kg/m²), and initial FibroScan results (LSM ~12 kPa, CAP ~ 290 dB/m) ensures that the subsequent clinical alterations can be attributed to Telmisartan therapy (40–80 mg daily) rather than initial disparities (Alam, 2016).

Clinical trials indicate that Telmisartan may improve metabolic and hepatic indicators in NAFLD and NASH. Specifically, studies involving smaller cohorts (e.g., n=35) have shown significant enhancements in the NAFLD Activity Score (NAS) and fibrosis scores after one year of treatment combined with lifestyle modifications (Alam, 2016). Furthermore, low-dose Telmisartan (20 mg/day) has been shown to decrease waist circumference, blood pressure, the triglyceride-glucose index, and AST levels while inhibiting inflammasome markers (Al-Nimer et al., 2019).

However, some research presents neutral results regarding conventional liver enzymes. For instance, while Telmisartan 80 mg demonstrated superior enhancements in HbA1c and HOMA-IR compared to Losartan 50 mg in hypertensive patients, these metabolic improvements were incremental and did not always normalize all metrics, suggesting that therapeutic effects may be dose- or context-dependent (Vitale et al., 2005). Additionally, while Telmisartan activates monocytic PPAR-γ target genes (such as CD36), this activation does not always result in quantifiable fasting glucose or lipid advantages (Bähr et al., 2011).

The prescription of Telmisartan resulted in notable and incremental enhancements in liver function markers and metabolic parameters throughout 6, 12, and 24 months. The principal findings indicate a decrease in alanine aminotransferase (ALT) from 80.5 to 40.3 U/L, a reduction in bilirubin levels from 1.21 to 0.85 mg/dL, and a decline in liver stiffness measurement (LSM) from 12.0 to 8.4 kPa. Moreover, metabolic measures indicated a reduction in HbA1c levels from 6.6% to 5.2% and a decrease in low-density lipoprotein (LDL) from 142 to 70 mg/dL. Hemodynamic enhancements were seen, with systolic blood pressure (SBP) decreasing from 134 to 112 mmHg and an elevation in portal vein peak flow.

These results correlate with preclinical data from bile duct-ligated (BDL) rats, where Telmisartan enhanced the antifibrotic ACE2/MAS signaling pathway and decreased profibrotic markers like TGF-β1 and collagen III (Yi et al., 2012; Zheng et al., 2022).

Liver Stiffness Measurement (LSM) serves as a dependable biomarker with robust positive correlations to liver damage markers: ALT (r=0.88), AST (r=0.86), CPA (r=0.93), and α-SMA (r=0.91). Multivariable regression identified histological markers (CPA β=0.42, α-SMA, β=0.38) and metabolic factors (HOMA-IR β=0.29) as independent predictors of fibrosis. Furthermore, HOMA-IR was identified as a significant predictor of advanced fibrosis (OR=1.16), suggesting that insulin resistance plays a pivotal role in the progression of the disease (Kumar, 2013).

While most data are favorable, a slight risk of drug-induced liver injury (DILI) exists typically in fewer than 2% of users often when used in combination with other agents like acipimox. Therefore, Telmisartan should be administered with caution in patients with severe hepatic impairment.

Transient elastography using FibroScan is a non-invasive, painless ultrasound-based modality for the quantitative assessment of liver stiffness and steatosis (Ali, A. K. M., et al., 2024). This technique enables rapid evaluation, typically within 5–10 minutes, in an outpatient setting without the need for sedation or invasive intervention. It provides immediate results by assigning fibrosis stages ranging from F0 to F4, thereby facilitating objective quantification of hepatic fibrosis. In clinical practice, it plays a pivotal role in the diagnosis of chronic liver disease, longitudinal monitoring of fibrosis progression or regression in response to therapy, and risk stratification for the development of cirrhosis. However, its diagnostic accuracy may be influenced by certain factors, including obesity, marked hepatic inflammation, and the presence of ascites (Li, Q., et al., 2020; Newsome, P. N., et al., 2020).

Liver biopsy has long been regarded as the reference standard for the evaluation of liver fibrosis in chronic liver diseases. Nevertheless, this procedure is invasive, costly, and associated with potential complications, including hemorrhage and, in rare cases, mortality. In addition, it is time-consuming and labor-intensive, with inherent limitations related to sampling variability due to the small specimen size

and the heterogeneous distribution of fibrosis within the liver (Chalasani, N., et al., 2018; Dong, H., et al., 2018).

Emerging evidence highlights significant limitations of liver biopsy, including sampling error rates of up to 35% and inter- and intra-observer variability reaching approximately 20% in fibrosis staging among pathologists. These factors may compromise the accuracy and reproducibility of fibrosis assessment in individual patients. Consequently, particularly in chronic liver disease where repeated evaluation is often required to monitor disease progression or therapeutic response, there is a growing need for reliable, reproducible, and non-invasive alternatives (Boyd, A., et al., 2020; Cai, Y. J., et al., 2017; European Association for the Study of the Liver, 2015).

In this context, FibroScan has gained widespread acceptance as a safer and clinically practical alternative to liver biopsy. It is increasingly utilized to reduce reliance on invasive procedures while enabling effective longitudinal assessment of liver fibrosis and treatment response (Castera, L., Friedrich-Rust, M., & Loomba, R., 2019).

Conclusion

Telmisartan administration leads to significant, time-dependent improvements in liver enzymes, fibrosis, steatosis, and metabolic parameters over 24 months. The therapy effectively reduced ALT, bilirubin, and HbA1c while improving liver stiffness and synthetic function. Multivariable analysis substantiates that CAP, α-SMA, and HOMA-IR are significant predictors of fibrosis. Despite its clear antifibrotic and metabolic benefits, clinical use should remain mindful of individual patient safety profiles and the potential for rare hepatotoxic effects. This study demonstrates that Telmisartan exerts a significant, dose-dependent antifibrotic effect by mitigating hepatocyte injury, reducing oxidative stress, and suppressing hepatic stellate cell activation. A dose of 10 mg/kg was most effective, achieving a 65.6% reduction in fibrotic area with significant restoration of antioxidant enzyme activity. These findings highlight Telmisartan's potential as a dual-action therapeutic agent in chronic fibrotic liver disease. In parallel, FibroScan (transient elastography) provides a non-invasive, quantitative assessment of liver stiffness and serves as a reliable tool for the longitudinal monitoring of fibrosis and therapeutic response, complementing histopathological and biochemical evaluation.

References

1. Alam, S., Kabir, J., Mustafa, G., Gupta, U., Hasan, S. K., & Alam, A. K. (2016). Effect of telmisartan on histological activity and fibrosis of non-alcoholic steatohepatitis: A 1-year randomized control trial. Saudi journal of gastroenterology: official journal of the Saudi Gastroenterology Association, 22(1), 69–76. https://doi.org/10.4103/1319-3767.173762
2. Ali, A. K. M., Nassib, S. A. E., Hassan, A. S., & Ali, S. S. H. (2024). Diagnostic accuracy of liver fibrosis based on red cell distribution width to platelet ratio versus Fibroscan in chronic hepatitis patients. Al-Azhar University Journal for Research and Studies, 6(2)
3. Al-Nimer, M. S., Esmail, V. A., & Mohammad, M. O. (2019). Telmisartan improves the metabolic, hematological and inflammasome indices in non-alcoholic fatty liver infiltration: A pilot open-label placebo-controlled study. Electronic Journal of General Medicine, 16(3).
4. Atzori, S., Pasha, Y., Maurice, J. B., Taylor-Robinson, S. D., Campbell, L., & Lim, A. K. (2023). The accuracy of ultrasound-controlled attenuation parameter in diagnosing hepatic fat content. Hepatic medicine: evidence and research, 51-61.
5. Bähr, I. N., Tretter, P., Krüger, J., Stark, R. G., Schimkus, J., Unger, T., ... & Kintscher, U. (2011). High-dose treatment with telmisartan induces monocytic peroxisome proliferator-activated receptor-γ target genes in patients with the metabolic syndrome. Hypertension, 58(4), 725-732.
6. Borém, L. M. A., Neto, J. F. R., Brandi, I. V., Lelis, D. F., & Santos, S. H. S. (2018). The role of the angiotensin II type I receptor blocker telmisartan in the treatment of non-alcoholic fatty liver disease: a brief review. Hypertension research: official journal of the Japanese Society of Hypertension, 41(6), 394–405. https://doi.org/10.1038/s41440-018-0040-6
7. Boyd, A., Cain, O., Chauhan, A., & Webb, G. J. (2020). Medical liver biopsy: background, indications, procedure and histopathology. Frontline gastroenterology, 11(1), 40-47.
8. Cai, Y. J., Dong, J. J., Wang, X. D., Huang, S. S., Chen, R. C., Chen, Y., ... & Shi, K. Q. (2017). A diagnostic algorithm for assessment of liver fibrosis by liver stiffness measurement in patients with chronic hepatitis B. Journal of viral hepatitis, 24(11), 1005-1015.

9. Castera, L., Friedrich-Rust, M., & Loomba, R. (2019). Noninvasive assessment of liver disease in patients with nonalcoholic fatty liver disease. Gastroenterology, 156(5), 1264-1281.
10. Chalasani, N., Younossi, Z., Lavine, J. E., Charlton, M., Cusi, K., Rinella, M., ... & Sanyal, A. J. (2018). The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatology, 67(1), 328-357.
11. Cho, H., Lee, Y. B., Ha, Y., Chon, Y. E., Kim, M. N., Lee, J. H., ... & Hwang, S. G. (2023). Changes in liver stiffness values assessed using transient elastography in chronic hepatitis B patients treated with tenofovir disoproxil fumarate: a prospective observational study. BMC gastroenterology, 23(1), 210.
12. Dong, H., Xu, C., Zhou, W., Liao, Y., Cao, J., Li, Z., & Hu, B. (2018). The combination of 5 serum markers compared to FibroScan to predict significant liver fibrosis in patients with chronic hepatitis B virus. Clinica Chimica Acta, 483, 145-150.
13. European Association for the Study of the Liver. (2015). EASL-ALEH Clinical Practice Guidelines: Non-invasive tests for evaluation of liver disease severity and prognosis. Journal of hepatology, 63(1), 237-264.
14. Fouad, L., Alzokaky, A., Abdelbaky, N., & Ahmed, K. (2022). Telmisartan inhibits the non-canonical TGF-β/JAK2/STAT3 signaling pathway and prevents carbon tetrachloride-induced liver fibrosis in rats. Azhar International Journal of Pharmaceutical and Medical Sciences, 2(1), 20-29.
15. Fujii, H., Imajo, K., Yoneda, M., Nakahara, T., Hyogo, H., Takahashi, H., Hara, T., Tanaka, S., Sumida, Y., Eguchi, Y., Chayama, K., Nakajima, A., Nishimoto, N., Kawada, N., & Japan Study Group of Nonalcoholic Fatty Liver Disease (2019). HOMA-IR: An independent predictor of advanced liver fibrosis in nondiabetic non-alcoholic fatty liver disease. Journal of gastroenterology and hepatology, 34(8), 1390–1395. https://doi.org/10.1111/jgh.14595
16. Helal, A., Al-Dahshan, M., Hassany, M., Hassan, A., Eliwa, A., Al-Wassief, A., & Al-Boraie, M. (2022). EVALUATION OF DIFFERENT ELASTOGRAPHY TECHNIQUES IN PREDICTION OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH HEPATITIS C RELATED LIVER CIRRHOSIS. Al-Azhar Medical Journal, 51(3), 1655-1666.
17. Hirata, T., Tomita, K., Kawai, T., Yokoyama, H., Shimada, A., Kikuchi, M., Hirose, H., Ebinuma, H., Irie, J., Ojiro, K., Oikawa, Y., Saito, H., Itoh, H., & Hibi, T. (2013). Effect of Telmisartan or Losartan for Treatment of Nonalcoholic Fatty Liver Disease: Fatty Liver Protection Trial by Telmisartan or Losartan Study (FANTASY). International journal of endocrinology, 2013, 587140. https://doi.org/10.1155/2013/587140
18. Kawaguchi, K., Sakai, Y., Terashima, T., Shimode, T., Seki, A., Orita, N., Takeshita, Y., Shimakami, T., Takatori, H., Arai, K., Kitamura, K., Yamashita, T., Yamashita, T., Takamura, M., Mizukoshi, E., Takamura, T., Honda, M., Wada, T., & Kaneko, S. (2021). Decline in serum albumin concentration is a predictor of serious events in nonalcoholic fatty liver disease. Medicine, 100(31), e26835. https://doi.org/10.1097/MD.0000000000026835
19. Kim, B. K., Fung, J., Yuen, M. F., & Kim, S. U. (2013). Clinical application of liver stiffness measurement using transient elastography in chronic liver disease from longitudinal perspectives. World journal of gastroenterology: WJG, 19(12), 1890.
20. Li, Q., Huang, C., Xu, W., Hu, Q., & Chen, L. (2020). Accuracy of FibroScan in analysis of liver fibrosis in patients with concomitant chronic hepatitis B and nonalcoholic fatty liver disease. Medicine, 99(23), e20616.
21. Li, Z., Liu, R., Gao, X., Hou, D., Leng, M., Zhang, Y., Du, M., Zhang, S., & Li, C. (2024). The correlation between hepatic controlled attenuation parameter (CAP) value and insulin resistance (IR) was stronger than that between body mass index, visceral fat area and IR. Diabetology & metabolic syndrome, 16(1), 153. https://doi.org/10.1186/s13098-024-01399-5
22. Losurdo, G., Ditonno, I., Novielli, D., Celiberto, F., Iannone, A., Castellaneta, A., ... & Di Leo, A. (2024). Comparison of transient elastography and point shear wave elastography for analysis of liver stiffness: a prospective study. Diagnostics, 14(6), 604.
23. Newsome, P. N., Sasso, M., Deeks, J. J., Paredes, A., Boursier, J., Chan, W. K., ... & Harrison, S. A. (2020). FibroScan-AST (FAST) score for the non-invasive identification of patients with non-alcoholic steatohepatitis with significant activity and fibrosis: a prospective derivation and global validation study. The lancet Gastroenterology & hepatology, 5(4), 362-373.

24. Rinaldi, L., Restivo, L., Guerrera, B., Zampino, R., Marrone, A., Zappala R, P. G., ... & Adinolfi, L. E. (2014). Hepatic steatosis and necro-inflammatory activity overestimated liver stiffness by transient elastography in staging liver fibrosis in chronic hepatitis C. AUSTIN JOURNAL OF ANALYTICAL AND PHARMACEUTICAL CHEMISTRY, 1(3), 1012.
25. Rix, B., Maduro, A. H., Bridge, K. S., & Grey, W. (2022). Markers for human haematopoietic stem cells: The disconnect between an identification marker and its function. Frontiers in physiology, 13, 1009160.
26. Sharma, D., Choudhary, N. S., Dhampalwar, S., Saraf, N., Duseja, A., Gautam, D., Soin, A. S., & Sud, R. (2023). Liver Stiffness Values in Persons with Normal Histology. Journal of clinical and experimental hepatology, 13(1), 10–14. https://doi.org/10.1016/j.jceh.2022.10.008
27. Shi, X., Li, J., Min, B., Yang, R., He, C., & Yang, Y. (2021). Application of ultrasound elastography for monitoring the effects of TβR1 shRNA therapy on hepatic fibrosis in a rat model. PLoS One, 16(6), e0253150.
28. Sun, K., Li, X., & Scherer, P. E. (2023). Extracellular matrix (ECM) and fibrosis in adipose tissue: overview and perspectives. Comprehensive Physiology, 13(1), 4387-4407.
29. Vitale, C., Mercuro, G., Castiglioni, C., Cornoldi, A., Tulli, A., Fini, M., Volterrani, M., & Rosano, G. M. (2005). Metabolic effect of telmisartan and losartan in hypertensive patients with metabolic syndrome. Cardiovascular diabetology, 4, 6. https://doi.org/10.1186/1475-2840-4-6
30. Wong, G. L. H. (2013). Update of liver fibrosis and steatosis with transient elastography (Fibroscan). Gastroenterology report, 1(1), 19-26.
31. Yi, E. T., Liu, R. X., Wen, Y., & Yin, C. H. (2012). Telmisartan attenuates hepatic fibrosis in bile duct-ligated rats. Acta pharmacologica Sinica, 33(12), 1518–1524. https://doi.org/10.1038/aps.2012.115
32. Zheng, L., Zhao, Z., Lin, J., Li, H., Wu, G., Qi, X., ... & Luo, M. (2022). Telmisartan relieves liver fibrosis and portal hypertension by improving vascular remodeling and sinusoidal dysfunction. European Journal of Pharmacology, 915, 174713.
33. Zheng, L., Zhao, Z., Lin, J., Li, H., Wu, G., Qi, X., ... & Luo, M. (2022). Telmisartan relieves liver fibrosis and portal hypertension by improving vascular remodeling and sinusoidal dysfunction. European Journal of Pharmacology, 915, 174713.