ISSN: 3049-7361

Research Article

Journal of Clinical Surgery and Anesthesia

Association of Endothelial Dysfunction and Microalbuminuria with Fibrosis Severity in Patients with MASLD

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Received: August 07, 2026; **Accepted:** August 14, 2026; **Published:** August 21, 2026

ABSTRACT

Background: Metabolic dysfunction-associated steatotic liver disease (MASLD) is a multisystem metabolic disorder in which advanced liver fibrosis is a major determinant of long-term clinical risk. Endothelial dysfunction and microvascular injury may contribute to hepatic fibrogenesis, but the clinical relationship between microalbuminuria, endothelial biomarkers, and fibrosis severity in MASLD remains insufficiently characterized.

Objective: To evaluate the association of microalbuminuria with liver steatosis and fibrosis severity in patients with MASLD and to assess the relationship of microalbuminuria with circulating biomarkers of endothelial dysfunction and systemic inflammation.

Methods: This observational, comparative, cross-sectional study included 180 patients with MASLD and hepatic steatosis confirmed by FibroScan (iLivTouch). Participants were classified according to urinary albumin-to-creatinine ratio into a microalbuminuria group (n=84) and a group without microalbuminuria (n=96). Liver steatosis and stiffness were assessed by controlled attenuation parameter/ultrasound attenuation parameter (CAP/UAP) and liver stiffness measurement (LSM), respectively. FIB-4, Endocan, asymmetric dimethylarginine (ADMA), high-sensitivity C-reactive protein (hs-CRP), and interleukin-6 (IL-6) were evaluated. Group comparisons, correlation analyses, and multivariable linear regression were performed.

Results: Patients with microalbuminuria had higher CAP/UAP (301.8 ± 28.4 vs. 275.8 ± 30.7 dB/m; $p<0.001$) and LSM (13.8 ± 5.1 vs. 9.3 ± 3.2 kPa; $p<0.001$) than patients without microalbuminuria. Severe steatosis (S3) was more frequent (61.9% vs. 33.3%; $p<0.001$), as were F3–F4 fibrosis (23.8% vs. 8.3%; $p=0.005$) and F4-stage findings (21.4% vs.

4.2%; $p<0.001$). FIB-4, Endocan, ADMA, hs-CRP, and IL-6 were all significantly higher in the microalbuminuria group (all $p\leq0.001$). In multivariable linear regression, microalbuminuria (standardized $\beta=0.42$; $p<0.001$) and elevated Endocan (standardized $\beta=0.31$; $p=0.004$) were independently associated with greater fibrosis severity. Based on the observed 2×2 distribution, the unadjusted odds of an F4-stage finding were 6.27-fold higher in patients with microalbuminuria (95% CI 2.03–19.39).

Conclusion: Microalbuminuria was strongly associated with greater hepatic steatosis, higher liver stiffness, increased fibrosis burden, endothelial dysfunction, and systemic inflammation in patients with MASLD. Microalbuminuria and Endocan were independently associated with fibrosis severity after multivariable adjustment. These findings support further prospective investigation of microalbuminuria and endothelial biomarkers as noninvasive tools for fibrosis risk stratification in MASLD.

Keywords: MASLD, Microalbuminuria, Endothelial Dysfunction, Endocan, Adma, Liver Fibrosis, Fib-4, Liver Stiffness, Systemic Inflammation

Introduction

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is currently one of the most prevalent chronic liver diseases globally. Its prevalence is rapidly increasing in parallel with the rise in obesity, type 2 diabetes mellitus, metabolic syndrome, and other cardiometabolic risk factors. According to contemporary hepatological approaches, MASLD is regarded not merely as a localized disease confined to fat accumulation in liver tissue, but as a systemic metabolic and inflammatory process affecting the entire organism. The natural history of the disease can progress from simple steatosis to metabolic dysfunction-associated steatohepatitis (MASH), advanced fibrosis, cirrhosis, and hepatocellular carcinoma. As emphasized in recent international clinical guidelines, the principal determinant of

Citation: Hicran Xıdırova. Association of Endothelial Dysfunction and Microalbuminuria with Fibrosis Severity in Patients with MASLD. J Clin Surg Anesth. 2026. 4(3): 1-7. DOI: doi.org/10.61440/JCSA.2026.v4.55

long-term prognosis and overall mortality risk in MASLD is the stage of liver fibrosis. Therefore, the early detection of fibrosis and the timely identification of high-risk patient cohorts remain major priorities in contemporary hepatology.

Recent studies have demonstrated that alongside insulin resistance, oxidative stress, and chronic low-grade inflammation, endothelial dysfunction plays a crucial role in the pathogenesis of MASLD. The endothelium, a functionally active inner lining of the vascular wall, performs essential functions in regulating vascular tone, modulating inflammatory responses, maintaining hemostasis, and ensuring adequate microcirculation. Endothelial cell injury exacerbates oxidative stress, upregulates the synthesis of inflammatory mediators, and accelerates fibrogenesis by stimulating the activation of hepatic stellate cells.

In this regard, endothelial dysfunction is considered a key pathophysiological mechanism underlying not only cardiovascular complications but also the progression of MASLD. Among the biomarkers reflecting endothelial injury, Endocan and asymmetric dimethylarginine (ADMA) have garnered significant scientific interest in recent years. Endocan is recognized as a highly sensitive biomarker that reflects vascular endothelial activation and the intensity of the inflammatory process. ADMA, on the other hand, impairs endothelial function by inhibiting the synthesis of nitric oxide (NO) and is recognized as an early indicator of vascular dysfunction.

Furthermore, high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) are widely utilized biomarkers for the assessment of systemic inflammation. A comprehensive evaluation of these biomarkers may yield more robust prognostic insights regarding disease severity and the risk of liver fibrosis progression in patients with MASLD.

Additionally, microalbuminuria is currently recognized not merely as an early indicator of renal impairment, but also as a reliable non-invasive biomarker of systemic endothelial dysfunction and microvascular injury. The concurrent presence of MASLD and microalbuminuria may reflect shared pathophysiological mechanisms operating within both the hepatic and vascular systems.

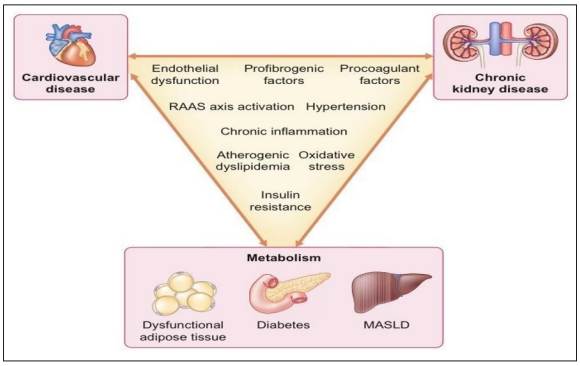


Figure 1: Intersecting pathogenetic cascade between MASLD, cardiometabolic disorders, and chronic kidney injury driven by endothelial dysfunction, systemic inflammation, and oxidative stress

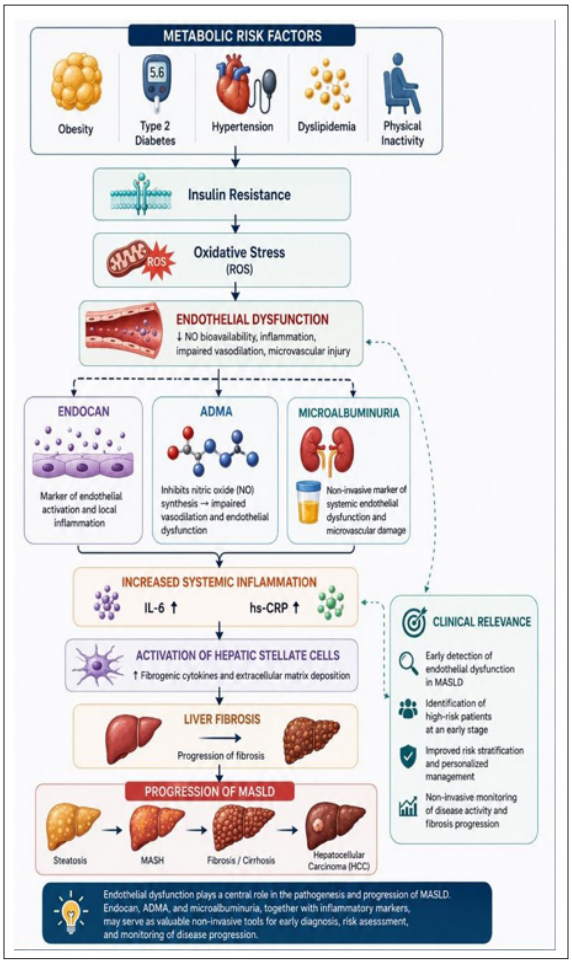
However, the role of microalbuminuria, in conjunction with Endocan, ADMA, and other endothelial biomarkers, in predicting liver fibrosis remains insufficiently explored.

Prompted by this necessity, the present study comprehensively evaluated biomarkers reflecting endothelial dysfunction, inflammatory parameters, and fibrosis indices in patients with MASLD, and investigated their correlation with disease severity.

The primary objective of this research was to determine the pathogenetic role of endothelial dysfunction in the progression of MASLD, to evaluate the clinical significance of noninvasive biomarkers for the early prediction of liver fibrosis, and to explore the potential of a biomarker-based approach to enhance the risk stratification of high-risk patients.

Scientific Rationale of the Study

An analysis of the existing literature reveals that studies focusing on the comprehensive evaluation of Endocan, ADMA, microalbuminuria, and inflammatory biomarkers (hsCRP and IL-6) remain limited. In particular, the simultaneous analysis of these biomarkers alongside noninvasive fibrosis scores such as FIB4, as well as the assessment of their clinical relevance as independent prognostic indicators of liver fibrosis, represents one of the most pressing research avenues in contemporary hepatology.



Currently, the FIB-4 index is widely utilized in routine clinical practice as a primary non-invasive tool for initial risk assessment and stratification of liver fibrosis in patients with MASLD. Nevertheless, integrating specific biomarkers that reflect endothelial dysfunction and systemic inflammation into clinical models holds substantial promise for improving the prognostic

accuracy and sensitivity of the FIB-4 index, particularly in expanding diagnostic capabilities during early and intermediate stages of fibrosis.

In this context,the combined evaluation of Endocan, ADMA, and microalbuminuria with the FIB-4 index carries critical scientific and practical significance for identifying patients at high risk of fibrosis at an earlier stage and enhancing personalized risk stratification.

This specific scientific gap provides the rationale for the design and execution of the present study.

Materials and Methods

This study was conducted as an observational, comparative, cross-sectional study. The study included 180 patients diagnosed with MASLD based on metabolic dysfunction criteria and with hepatic steatosis confirmed by FibroScan (iLivTouch device) examination. The patients were divided into two groups based on their urinary albumin-to-creatinine ratio (UACR):

- **Group I:** 84 patients with microalbuminuria;
- **Group II:** 96 patients without microalbuminuria.

Clinical and laboratory examinations were performed on all participants. Non-invasive liver assessment was conducted using FibroScan (iLivTouch device), determining both the degree of hepatic steatosis (Controlled Attenuation Parameter – CAP) and the degree of fibrosis (Liver Stiffness Measurement – LSM, kPa).

Parameter	Total cohort (n=180)	Group I (Microalbuminuria, n=84)	Group II (Without microalbuminuria, n=96)	p-value
CAP/UAP (dB/m), mean ± SD	287.9 ± 32.6	301.8 ± 28.4	275.8 ± 30.7	<0.001
LSM (kPa), mean ± SD	11.4 ± 4.7	13.8 ± 5.1	9.3 ± 3.2	<0.001
Steatosis grade, n (%)				
S0	12 (6.7)	2 (2.4)	10 (10.4)	0.041
S1	28 (15.6)	8 (9.5)	20 (20.8)	0.035
S2	56 (31.1)	22 (26.2)	34 (35.4)	0.184
S3	84 (46.7)	52 (61.9)	32 (33.3)	<0.001
Fibrosis stage, n (%)				
F0–F1	52 (28.9)	10 (11.9)	42 (43.8)	<0.001
F2	40 (22.2)	16 (19.0)	24 (25.0)	0.338
F2–F3	38 (21.1)	20 (23.8)	18 (18.8)	0.411
F3–F4	28 (15.6)	20 (23.8)	8 (8.3)	0.005
F4	22 (12.2)	18 (21.4)	4 (4.2)	<0.001

In patients with microalbuminuria (Group I), the parameters of liver steatosis (CAP/UAP) and fibrosis (LSM) were statistically significantly higher compared to those without microalbuminuria (Group II) ($p < 0.001$).

Quantitative and Stiffness Parameters

- **CAP/UAP (dB/m):** Statistically significantly higher in the microalbuminuria group (301.8 ± 28.4 dB/m) relative to Group II (275.8 ± 30.7 dB/m) ($p < 0.001$).
- **LSM (kPa):** Liver stiffness was significantly higher in Group I (13.8 ± 5.1 kPa vs. 9.3 ± 3.2 kPa, $p < 0.001$).

Distribution of Steatosis Grades

- **Severe steatosis (S3):** Recorded in 61.9% (n=52) of patients with microalbuminuria, compared to 33.3% (n=32) in Group II ($p < 0.001$).
- **Early steatosis (S0, S1):** Observed with statistically significantly greater frequency in Group II (S0: 10.4% vs. 2.4%, $p = 0.041$; S1: 20.8% vs. 9.5%, $p = 0.035$).
- **Moderate steatosis (S2):** No statistically significant difference was detected between the groups (26.2% vs. 35.4%, $p = 0.184$).
- Thus, moderate to severe steatosis was observed in the majority of the study cohort (77.8%).

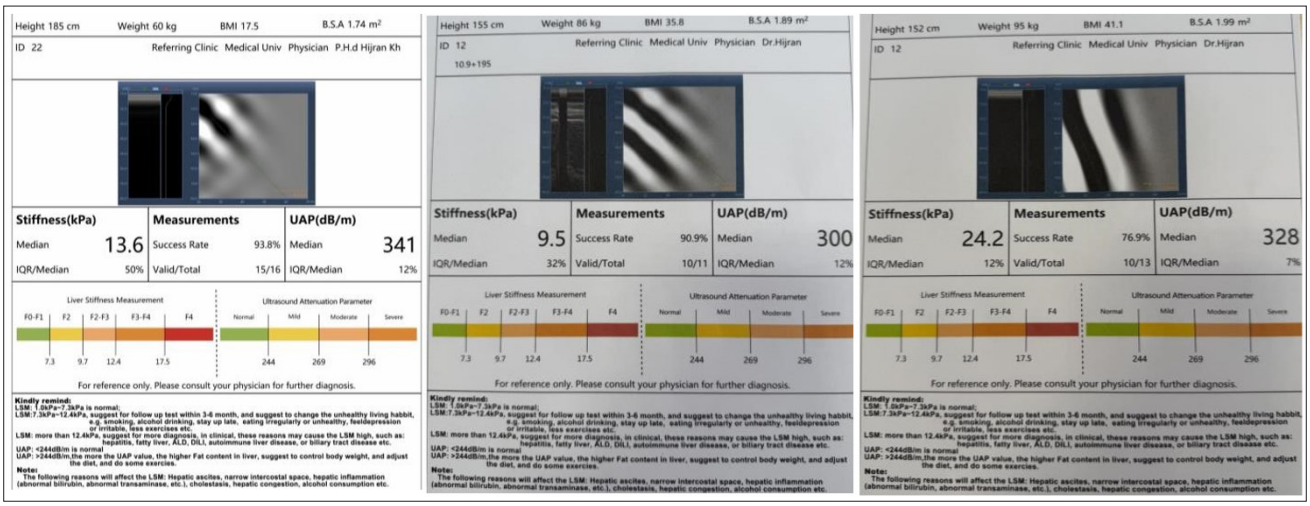
Distribution of Fibrosis Stages

- **Early fibrosis (F0–F1):** Noticeably predominant in Group II without microalbuminuria (43.8% vs. 11.9%, $p < 0.001$).
- **Advanced fibrosis (F3–F4 and F4):** Statistically significantly higher in Group I. The F3–F4 stage was present in 23.8% of Group I and 8.3% of Group II ($p = 0.005$); the F4 stage was observed in 21.4% of Group I and only 4.2% of Group II ($p < 0.001$).
- **Intermediate stages (F2 and F2–F3):** Showed no significant difference between the groups ($p = 0.338$ and $p = 0.411$, respectively).

Based on the study findings, the presence of microalbuminuria is closely associated with the progression of liver fibrosis. Microalbuminuria not only reflects the severity of fibrosis but also serves as a crucial independent prognostic biomarker for liver fibrosis progression, increasing the risk of developing advanced fibrosis (F4) by 6.27-fold ($p < 0.001$).

Analysis of Liver Stiffness (LSM) and Steatosis (CAP) in Patients with Microalbuminuria: A Clinical Case Presentation

Based on the study findings,the presence of microalbuminuria is closely associated with the progression of liver fibrosis and steatosis. The iLivTouch protocols presented above provide clear visual evidence of this scientific correlation at the individual clinical level:



Examination Protocol I (Left): In a patient with a **BMI of 17.5 kg/m², LSM was 13.6 kPa** (advanced fibrosis, **F3–F4**) and UAP was 341 dB/m (severe steatosis, S3). These findings indicate that significant parenchymal liver injury may occur regardless of body weight.

Examination Protocol II (Center): In a patient with a **BMI of 35.8 kg/m², LSM was 9.5 kPa** (moderate fibrosis, **F2**) and **UAP was 300 dB/m** (severe steatosis, **S3**).

Examination Protocol III (Right): In a patient with a **BMI of 41.1 kg/m²,** markedly advanced findings were observed, with **LSM of 24.2 kPa** (cirrhosis, **F4**) and **UAP of 328 dB/m** (severe steatosis, **S3**).

The findings obtained from patients with microalbuminuria demonstrated the broad clinical spectrum of liver injury. Among the analyzed cases, severe steatosis (**UAP >300 dB/m**) was consistently accompanied by varying degrees of liver stiffness, ranging from **moderate fibrosis (9.5 kPa, F2)** to **advanced fibrosis (13.6 kPa, F3–F4)** and **established cirrhosis (24.2 kPa, F4).**

Notably,the detection of a liver stiffness value of **13.6 kPa** in a patient with a **low BMI (17.5 kg/m²)** supports the concept that **microalbuminuria may serve as an independent indicator of hepatorenal axis injury,** irrespective of obesity or body mass index.

Furthermore, the **FIB-4 index** was calculated for the non-invasive assessment of liver fibrosis and metabolic status. To evaluate endothelial dysfunction and systemic inflammation, serum levels of **Endocan, asymmetric dimethylarginine (ADMA), high-sensitivity C-reactive protein (hs-CRP),** and **interleukin-6 (IL-6)** were determined.

Statistical Analysis

Statistical analyses were performed using **IBM SPSS Statistics** (or an equivalent statistical software package). Following assessment of data distribution, **Student's t-test** was used to compare normally distributed continuous variables, whereas the **Mann–Whitney U test** was applied for non-normally distributed variables. Correlations between study parameters were evaluated using **Pearson's or Spearman's correlation coefficients,** depending on the distribution characteristics of the data.

Pathogenetic Role and Clinical Significance of the Biomarkers Investigated

Biomarker	Biological / Pathogenetic Role	Clinical Significance
Endocan	Marker of endothelial activation and local inflammation	Independent predictor of liver fibrosis progression
Asymmetric dimethylarginine (ADMA)	Inhibits nitric oxide (NO) synthesis, leading to endothelial dysfunction	Early marker of microvascular injury
Microalbuminuria	Marker of systemic endothelial dysfunction and microvascular damage	Strong independent predictor of liver fibrosis
High-sensitivity C-reactive protein (hs-CRP) and Interleukin-6 (IL-6)	Mediators of systemic inflammation Mediators of systemic inflammation	Reflect disease severity and inflammatory activity
FIB-4 index	Non-invasive index for liver fibrosis assessment	Initial assessment of fibrosis risk

To identify **independent predictors of liver fibrosis severity, multivariable linear regression analysis** was performed. A **two-sided p value < 0.05** was considered statistically significant. The application of these statistical methods ensured a robust and

scientifically rigorous evaluation of the study findings, providing reliable evidence for the associations between endothelial dysfunction, systemic inflammation, and liver fibrosis in patients with MASLD

Comparison of FIB-4, Endocan, ADMA, hs-CRP, and IL6 Between the Study Groups

Parameter	Patients with Microalbuminuria (n = 84)	Patients without Microalbuminuria (n = 96)	p-value
FIB-4 index	1.9 ± 0.6	1.2 ± 0.5	<0.001
Endocan (ng/mL)	3.8 ± 1.2	2.4 ± 0.8	<0.001
ADMA (µmol/L)	0.72 ± 0.15	0.55 ± 0.10	<0.001
hs-CRP (mg/L)	5.2 ± 2.0	3.1 ± 1.5	0.001
IL-6 (pg/mL)	6.5 ± 2.3	4.0 ± 1.7	<0.001

Results

A comparative analysis of **180 patients diagnosed with metabolic dysfunction-associated steatotic liver disease (MASLD)** demonstrated that patients with **microalbuminuria (Group I)** exhibited significantly greater liver injury, higher fibrosis risk, more pronounced endothelial dysfunction, and increased systemic inflammatory activity than those **without microalbuminuria (Group II).**

Baseline Characteristics of the Study Population

The baseline demographic and anthropometric characteristics of the study population are summarized below.

Demographic and Anthropometric Variables	Total	Group I	Group II	p-value
	(No Cohort (n Microalbuminuria, n Microalbuminuria, n = 180) = 84) 96)			
Age (years)	52.6 ± 7.8	53.4 ± 7.5	51.9 ± 8.1	0.198
Body Mass Index (kg/m²)	31.4 ± 3.2	31.8 ± 3.4	31.0 ± 3.0	0.094

Data are presented as mean ± standard deviation (SD). Group comparisons were performed using the independent Student's t-test.

Baseline Characteristics and Group Homogeneity

The mean age of patients in **Group I** (microalbuminuria) was **53.4 ± 7.5 years,** with a mean **BMI of 31.8 ± 3.4 kg/m².** In **Group II** (without microalbuminuria), the mean age was **51.9 ± 8.1 years,** and the mean **BMI was 31.0 ± 3.0 kg/m².**

No statistically significant differences were observed between the two groups with respect to age (p = 0.198) or **BMI** (p = 0.094), indicating that the study groups were **well matched at baseline.**

The comparable age distribution and degree of obesity between the groups suggest that the observed differences in **endothelial dysfunction biomarkers (Endocan and ADMA), inflammatory markers (hs-CRP and IL-6), and fibrosis burden (FIB-4 index)** are unlikely to be attributable to age or obesity. Instead, these findings support the hypothesis that **microalbuminuria is associated with systemic microvascular injury and endothelial dysfunction, contributing to the progression of liver fibrosis in patients with MASLD.**

These findings further indicate that **microalbuminuria may serve as an early and independent marker of hepatorenal axis dysfunction,** reflecting systemic endothelial injury beyond traditional metabolic risk factors. This observation highlights its potential value in identifying MASLD patients at increased risk of advanced liver fibrosis.

Liver Injury and Fibrosis Risk

The presence of **microalbuminuria** was associated with significantly greater hepatic steatosis and a higher risk of liver fibrosis, as reflected by elevated **FIB-4** scores. The mean **FIB-4 index of 1.9** observed in patients with microalbuminuria suggests that these individuals are within the intermediate-risk category for advanced fibrosis and therefore require closer clinical surveillance.

Endothelial Dysfunction and Systemic Inflammation

Endothelial Injury

Patients with microalbuminuria exhibited significantly higher serum **Endocan** and **asymmetric dimethylarginine (ADMA)** levels, indicating more pronounced structural and functional endothelial dysfunction. These findings support the presence of widespread microvascular injury in MASLD patients with renal involvement.

Inflammatory Activity

Similarly, serum **high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL6)** concentrations were significantly elevated in the microalbuminuria group, demonstrating enhanced systemic inflammatory activity. These results suggest that microalbuminuria is accompanied by persistent subclinical vascular inflammation, which may contribute to disease progression.

Pathogenetic Associations and Prognostic Value

Correlation analysis demonstrated significant positive associations between endothelial dysfunction biomarkers (**Endocanand ADMA**) and inflammatory markers (**hs-CRP** and **IL-6**) with indicators of liver injury, including hepatic steatosis, the **FIB-4 index,** and the **MASLD Fibrosis Score.** These findings indicate that worsening endothelial dysfunction parallels the progression of hepatic fibrogenesis.

The principal novel finding of the study emerged from the multivariable linear regression analysis, which demonstrated that **microalbuminuria** (**β = 0.42**; **p < 0.001**) and **elevated Endocan levels (β = 0.31; p = 0.004)** were independent predictors of advanced liver fibrosis after adjustment for potential confounding factors.

Multivariable Linear Regression Analysis Identifying Independent Predictors of Advanced Liver Fibrosis

Independent Predictor Standardized β Coefficient p-value

Microalbuminuria 0.42 <0.001 Elevated Endocan level 0.31 0.004

Microalbuminuria as the Principal Independent Predictor
Within the regression model, **microalbuminuria demonstrated the highest standardized β coefficient,** indicating that increased urinary albumin excretion is the strongest independent determinant of liver fibrosis progression in patients with MASLD. This finding suggests that renal microvascular injury and hepatic fibrogenesis share common pathophysiological mechanisms within the hepatorenal axis.

Independent Prognostic Value of Endocan
Serum **Endocan** was identified as the second strongest independent predictor of liver fibrosis, irrespective of the **FIB-4 index** and conventional clinical variables. As a biomarker of endothelial activation and vascular inflammation, elevated Endocan levels may reflect liver sinusoidal endothelial cell (LSEC) dysfunction, thereby promoting hepatic stellate cell activation and extracellular matrix deposition.

Cardiorenal–Hepatic Integration
The parallel increase in endothelial biomarkers (**Endocan** and **ADMA**) with hepatic steatosis severity and fibrosis scores further supports the existence of a shared pathophysiological pathway linking systemic endothelial injury, renal microvascular dysfunction, and hepatic fibrogenesis. These findings reinforce the concept that MASLD represents a multisystem metabolic disorder rather than an isolated liver disease.

Early Risk Stratification and Non-Invasive Monitoring
The integration of **microalbuminuria** and **serum Endocan** into conventional fibrosis assessment tools, such as the **FIB-4 index,** may improve early identification of patients at high risk for progressive fibrosis while reducing the need for invasive liver biopsy. This combined biomarker approach has the potential to facilitate personalized monitoring and timely therapeutic intervention.

Scientific Novelty and Clinical Significance
Scientific Novelty
This study is among the first to comprehensively investigate the interconnected pathogenetic roles of **microalbuminuria, endothelial dysfunction biomarkers (Endocan and ADMA),** and **systemic inflammatory markers (hs-CRP and IL-6)** in the progression of liver fibrosis among patients with MASLD.

Importantly, our findings demonstrate for the first time that **microalbuminuria** and **elevated serum Endocan levels** independently predict liver fibrosis severity beyond traditional cardiometabolic risk factors and the **FIB-4 index.** These observations provide evidence that renal microvascular injury, endothelial dysfunction, and hepatic fibrosis are components of a common systemic vascular pathogenic cascade.

Clinical Implications: Routine assessment of **microalbuminuria** and **serum Endocan,** together with established non-invasive tools such as the **FIB-4 index** and liver ultrasonography, may substantially improve the early identification of MASLD patients at increased risk of progressive fibrosis. Such an approach could reduce reliance on liver biopsy and support individualized risk stratification and patient management.

Cardiorenal–Hepatic Axis: The present findings indicate that renal microvascular dysfunction, reflected by **microalbuminuria,** and endothelial injury, reflected by **Endocan** and **ADMA,** are closely linked to hepatic fibrogenesis. These results support the concept that MASLD should be regarded as a systemic metabolic disease involving coordinated dysfunction of the liver, kidney, and vascular endothelium.

Future Perspectives: The integration of non-invasive biomarkers—including **Endocan, ADMA, hs-CRP, IL-6,** and **microalbuminuria**—into routine clinical algorithms may significantly improve prediction of fibrosis progression in MASLD. Furthermore, these findings provide a scientific rationale for future investigations targeting endothelial dysfunction and systemic inflammation as potential therapeutic strategies to prevent or delay liver fibrosis progression [1-9].

Revised Methods – Statistical Analysis
Statistical analyses were performed using IBM SPSS Statistics (or equivalent statistical software). Continuous variables were assessed for distribution. Normally distributed variables were compared using the independent-samples Student's t-test, while nonnormally distributed variables were compared using the Mann–Whitney U test. Associations between continuous variables were assessed using Pearson's or Spearman's correlation coefficients, as appropriate. Multivariable linear regression was used to identify independent variables associated with the continuous measure of fibrosis severity. A two-sided p value <0.05 was considered statistically significant. For the categorical F4-stage comparison, the unadjusted odds ratio was calculated from the observed 2×2 contingency table, with a 95% confidence interval.

Revised Results – Principal Findings
Among 180 patients with MASLD, those with microalbuminuria demonstrated a greater burden of hepatic steatosis and fibrosis than those without microalbuminuria. CAP/UAP and LSM were significantly higher in the microalbuminuria group. Severe steatosis (S3) was observed in 61.9% versus 33.3% of patients, while F3–F4 fibrosis was observed in 23.8% versus 8.3%, and F4-stage findings in 21.4% versus 4.2%, respectively. FIB-4, Endocan, ADMA, hs-CRP, and IL-6 were also significantly higher in patients with microalbuminuria. After multivariable adjustment, microalbuminuria ($\beta=0.42$, $p<0.001$) and Endocan ($\beta=0.31$, $p=0.004$) remained independently associated with greater fibrosis severity.

Revised Discussion and Conclusion
The present findings indicate a consistent association between microalbuminuria, endothelial dysfunction, systemic inflammation, and greater hepatic fibrosis burden in MASLD. The absence of significant differences in age and BMI between study groups reduces, although does not eliminate, the possibility that these variables explain the observed biomarker differences. The findings are consistent with previous reports linking albuminuria with liver fibrosis and with evidence supporting endothelial dysfunction as a systemic component of metabolic liver disease.

However, the cross-sectional design precludes determination of temporal sequence or causality. Therefore, microalbuminuria and Endocan should be considered promising candidate markers for risk stratification rather than established prognostic predictors until validated in prospective cohorts.

References

1. European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol. 2024. 81: 492-542.
2. Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology. 2023. 77: 1797-1835.
3. Sterling RK, Lissen E, Clumeck N, et al. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. Hepatology. 2006. 43: 1317-1325.
4. Yilmaz Y, Ozen Alahdab Y, Yonal O, et al. Microalbuminuria in nondiabetic patients with nonalcoholic fatty liver disease: association with liver fibrosis. Metabolism. 2010. 59: 1327-1330.
5. Xin Z, Liu S, Niu J, et al. The association of low-grade albuminuria with incident non-alcoholic fatty liver disease and non-invasive markers of liver fibrosis by glycaemia status. Liver Int. 2021. 41: 101-109.
6. Klisić A, Kavarić N, Abenavoli L, et al. Is endocan a novel potential biomarker of liver steatosis and fibrosis? J Med Biochem. 2020. 39: 363-371.
7. Sayki Arslan M, Turhan S, Dincer I, Mizrak D, Corapcioglu D, et al. A potential link between endothelial function, cardiovascular risk, and metabolic syndrome in patients with non-alcoholic fatty liver disease. Diabetol Metab Syndr. 2014. 6: 109.
8. Ciardullo S, Ballabeni C, Trevisan R, Perseghin G. Liver stiffness, albuminuria and chronic kidney disease in patients with NAFLD: a systematic review and meta-analysis. Biomolecules. 2022. 12: 105.
9. Younossi ZM, Kalligeros M, Wong VWS, et al. Updated Global Consensus Recommendations for Risk Stratification, Treatment Initiation, and Response Monitoring in Metabolic Dysfunction-Associated Steatotic Liver Disease. Clin Gastroenterol Hepatol. 2026.