

Research Article

Early Vascular Remodeling and Hemorheological Alterations in Biopsy-Proven MASLD

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Abstract

Objectives: Metabolic dysfunction-associated steatotic liver disease (MASLD) is increasingly associated with cardiovascular complications and early vascular injury. This study evaluated carotid intima-media thickness (CIMT) and its association with hemorheological parameters in patients with biopsy-proven MASLD.

Methods: This cross-sectional study included 25 patients with histologically confirmed metabolic dysfunction-associated steatohepatitis (MASH) and 28 age- and sex-matched healthy controls. CIMT was assessed using high-resolution ultrasonography. Whole blood viscosity and plasma viscosity were measured using a rotational viscometer at shear rates of 45 s⁻¹ and 225 s⁻¹. Multivariable regression analyses were performed to determine independent predictors of CIMT.

Results: Patients with MASLD had significantly higher CIMT values than controls (0.92±0.16 mm vs. 0.76±0.13 mm, p=0.002). Whole blood viscosity at both shear rates was significantly increased in the MASLD group, whereas plasma viscosity did not differ significantly. In multivariable analyses, systolic blood pressure and waist circumference independently predicted CIMT, while hemorheological parameters were not independently associated with CIMT.

Conclusion: Biopsy-proven MASLD is associated with increased CIMT and altered hemorheological profiles, supporting the presence of early vascular remodeling and increased cardiovascular risk.

Keywords: Blood viscosity, cardiovascular risk, carotid intima-media thickness, MASLD, subclinical atherosclerosis

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Metabolic dysfunction-associated steatotic liver disease (MASLD) is currently the most prevalent chronic liver disorder and is closely linked to obesity, insulin resistance, and metabolic syndrome.^[1] In recent years, MASLD has been increasingly recognized as a multisystem disease

extending beyond hepatic involvement.^[2] Cardiovascular complications are considered the leading cause of mortality in affected individuals.^[2,3]

Early vascular alterations may occur before clinically overt cardiovascular disease develops in MASLD. Carotid intima-

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ma-media thickness (CIMT) is widely used as a noninvasive marker reflecting subclinical arterial remodeling and atherosclerotic burden.^[4–8] Increased CIMT values have previously been demonstrated in patients with metabolic liver disease; however, the underlying biological mechanisms remain incompletely understood.^[2,9,10]

Abnormal blood rheology may contribute to vascular dysfunction in MASLD. Increased blood viscosity can impair endothelial function, alter shear stress, and reduce microvascular perfusion.^[9–11] Nevertheless, evidence regarding the association between hemorheological disturbances and vascular structural changes in biopsy-confirmed MASLD remains scarce.^[11]

The aim of the present study was to investigate carotid intima-media thickness and evaluate its relationship with hemorheological parameters in patients with histologically confirmed MASLD.

Methods

Study design and participants

Twenty-five individuals with biopsy-confirmed metabolic dysfunction-associated steatohepatitis (MASH) and 28 healthy control subjects were included in this cross-sectional study. Histopathological evaluation was performed according to the Brunt classification system.

Individuals with chronic inflammatory disorders, secondary liver disease, significant alcohol intake, active infection, malignancy, hematologic disease, or clinically evident cardiovascular disease were excluded from the study population.

Ethics committee approval was obtained from the Erciyes University Ethics Committee (Approval No. 373; Date: February 12, 2014). The study protocol complied with the ethical principles outlined in the Declaration of Helsinki.

Clinical and biochemical evaluation

Anthropometric assessment included body mass index and waist circumference measurements. Blood pressure was measured after an adequate resting period under standardized conditions.

Fasting venous blood samples were analyzed for glucose, insulin, lipid parameters, liver enzyme levels, ferritin concentrations, and hematologic indices. Insulin resistance was calculated using the homeostasis model assessment formula.

Assessment of Carotid Intima-Media Thickness

CIMT measurements were performed by an experienced radiologist who was blinded to the participants' characteristics. High-resolution B-mode ultrasonography was used for vascular imaging. Bilateral measurements were obtained

from the distal segment of the common carotid artery proximal to the bifurcation, and mean values were recorded.

Hemorheological Analysis

Whole blood and plasma viscosity measurements were obtained using a rotational viscometer at shear rates of 45 s^{-1} and 225 s^{-1} . Lower shear rates were considered representative of microcirculatory conditions.^[11]

Statistical Analysis

All statistical analyses were conducted using SPSS software, version 25.0. Continuous variables were expressed according to their distribution characteristics. Between-group comparisons were performed using appropriate parametric or nonparametric statistical tests. Independent predictors of CIMT were evaluated using multivariable linear regression analysis. Statistical significance was defined as $p < 0.05$.

The overall study design and analytical workflow are summarized in Figure 1.

Results

Compared with controls, patients with MASLD exhibited significantly greater waist circumference, systolic blood

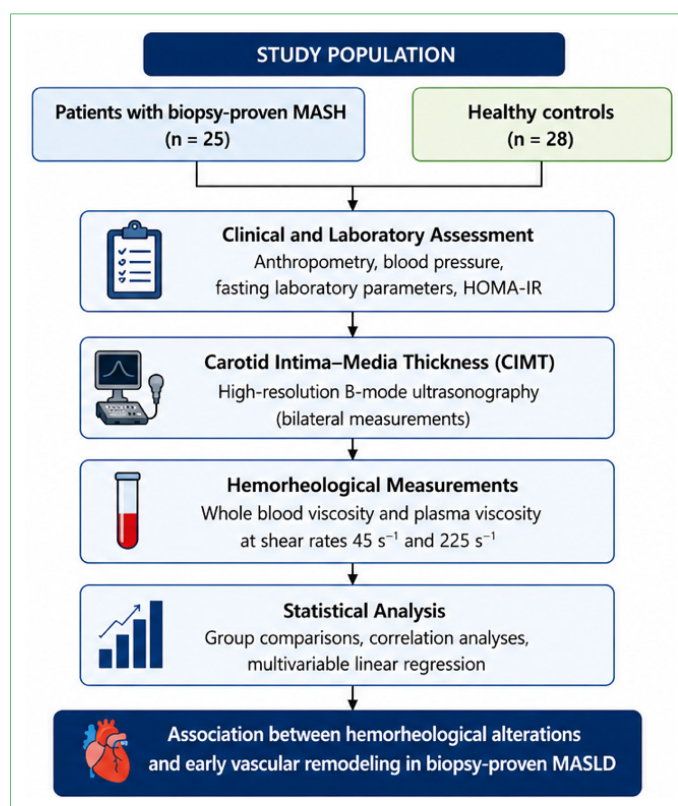


Figure 1. Study design and analytical workflow.

MASH: Metabolic dysfunction-associated steatohepatitis; MASLD: Metabolic dysfunction-associated steatotic liver disease; HOMA-IR: Homeostasis model assessment of insulin resistance

Table 1. Liver histology distribution according to Brunt classification

Histological feature	n (%)
Steatosis 5–33%	13 (52%)
Steatosis 33–66%	10 (40%)
Steatosis >66%	2 (8%)
Fibrosis F0	9 (36%)
Fibrosis F1	11 (44%)
Fibrosis F2	3 (12%)
Fibrosis F3	2 (8%)
Fibrosis F4	0

pressure, insulin resistance indices, liver enzyme levels, and ferritin concentrations (Table 2).

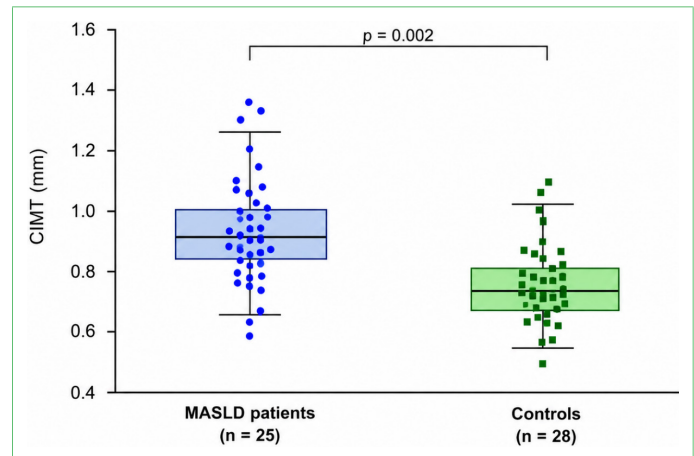
CIMT measurements were significantly higher in the MASLD group, suggesting the presence of early arterial wall remodeling (Fig. 2).

Whole blood viscosity values obtained at both shear rates were elevated in patients with MASLD, whereas plasma viscosity values were similar between the study groups (Table 3). Multivariable regression analysis demonstrated that systolic blood pressure and waist circumference independently predicted CIMT values (Table 4). Hematocrit was identified as an independent determinant of whole blood viscosity (Table 5).

Table 2. Baseline clinical and laboratory characteristics of patients with biopsy-proven MASH and controls

Variable	MASH (n=25)	Controls (n=28)	p
Age (years)	44.12±9.57	39.14±12.32	0.110
Male sex, n (%)	16 (64)	13 (46)	0.200
BMI (kg/m ²)	29.70±5.00	26.32±4.93	0.170
Waist circumference (cm)	103.80±11.53	89.68±20.53	0.003
Systolic BP (mmHg)	132.40±15.68	116.61±19.10	<0.001
Diastolic BP (mmHg)	81.00±12.74	80.00±17.37	0.204
Hematocrit (%)	46.00±3.60	43.21±4.16	0.013
LDL cholesterol (mg/dL)	122.52±29.57	100.82±34.00	0.017
Insulin (μU/mL)	19.00±9.78	8.80±3.97	<0.001
HOMA-IR	4.61±2.16	1.93±0.91	<0.001
ALT (U/L)	57.92±38.93	18.25±7.65	<0.001
AST (U/L)	35.24±15.13	18.79±4.69	<0.001
Ferritin (ng/mL)	141.40±109.55	87.78±87.12	0.026

Values are presented as mean±SD or n (%). Statistically significant values are shown in bold (p<0.05). BMI: Body mass index; BP: Blood pressure; LDL: Low-density lipoprotein; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; HOMA-IR: Homeostasis model assessment of insulin resistance.

**Figure 2.** Comparison of carotid intima-media thickness between groups.

CIMT: Carotid intima-media thickness; MASLD: Metabolic dysfunction-associated steatotic liver disease

Discussion

The present study demonstrated increased carotid intima-media thickness and elevated whole blood viscosity values in patients with biopsy-confirmed MASLD. These findings indicate that vascular and hemorheological alterations may accompany metabolic liver disease even before overt cardiovascular events become clinically apparent.

Growing evidence suggests that MASLD contributes to accelerated vascular aging and subclinical atherosclerosis.^[4–8] Consistent with previous reports, our study identified significantly

Table 3. Comparison of vascular and hemorheological parameters between groups

Parameter	MASH	Controls	p
CIMT (mm)	0.92±0.16	0.76±0.13	0.002
Whole blood viscosity – 45 s ⁻¹ (cP)	6.84±0.98	6.14±0.76	0.010
Whole blood viscosity – 225 s ⁻¹ (cP)	5.10±0.81	4.66±0.66	0.040
Plasma viscosity – 45 s ⁻¹ (cP)	1.79±0.23	1.73±0.23	0.631

Values are presented as mean±SD. CIMT: Carotid intima-media thickness; cP: Centipoise.

Table 4. Multivariable regression analysis identifying independent predictors of carotid intima-media thickness

Variable	β	Standardized β	p
Systolic BP	0.003	0.41	0.006
Waist circumference	0.002	0.35	0.018
Whole blood viscosity	NS	–	>0.05

Model R²=0.42; Adjusted R²=0.38; Model p<0.001; BP: blood pressure; β: Regression coefficient; R²: Coefficient of determination

Table 5. Multivariable regression analysis identifying determinants of whole blood viscosity			
Variable	β	Standardized β	p
Hematocrit	0.082	0.67	<0.001
Model R ² =0.58; Adjusted R ² =0.54; β : Regression coefficient; R ² : Coefficient of determination.			

higher CIMT measurements in the MASLD group. Chronic inflammation, oxidative stress, endothelial dysfunction, insulin resistance, and metabolic imbalance may collectively contribute to vascular remodeling in these patients.^[2,3,9,10]

A major strength of the present study is the histopathological confirmation of the disease. Many previous investigations relied primarily on imaging modalities or surrogate biochemical markers for diagnosis. Liver biopsy increases diagnostic precision and strengthens the reliability of the present findings.^[8,12]

Whole blood viscosity was also significantly elevated in patients with MASLD. Increased viscosity may adversely affect endothelial physiology and microvascular blood flow.^[9–11] However, viscosity-related variables did not remain independently associated with CIMT after adjustment for cardiometabolic risk factors. This finding suggests that hemorheological abnormalities may reflect systemic metabolic dysregulation rather than act as direct determinants of vascular structural change.

Several limitations should be considered when interpreting these findings. The cross-sectional design prevents causal interpretation, and the relatively modest sample size may have limited statistical power. In addition, residual confounding factors associated with metabolic risk cannot be fully excluded.

Conclusion

Patients with biopsy-confirmed MASLD demonstrated increased carotid intima–media thickness together with altered hemorheological characteristics. These findings support the concept that MASLD is associated with early vascular remodeling and increased cardiovascular risk.

Disclosure

Ethics Committee Approval: Ethics committee approval was obtained from Erciyes University Ethics Committee (Approval No: 373, Date: 12 February 2014).

Informed Consent: Written informed consent was obtained from all participants prior to enrollment.

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