

# The impact of non alcoholic fatty liver disease (NAFLD) on carotid artery intima-media thickness as a risk factor for atherosclerosis

Cristina Alina Silaghi<sup>1,2</sup>, Horațiu Silaghi<sup>3</sup>, Anca Elena Crăciun<sup>4,5</sup>, Andrada Oltean<sup>4</sup>, Daniel Tudor Cosma<sup>4</sup>, Nicolae Hâncu<sup>5</sup>, Carmen Emanuela Georgescu<sup>2</sup>

<sup>1</sup>County Clinic Emergency Hospital, Cluj-Napoca, Romania; <sup>2</sup>Endocrinology Department, <sup>3</sup>Surgery V Department, <sup>4</sup>Diabet, Nutrition and Metabolic Diseases Department, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania; <sup>5</sup>Regina Maria Clinic, Cluj-Napoca, Romania.

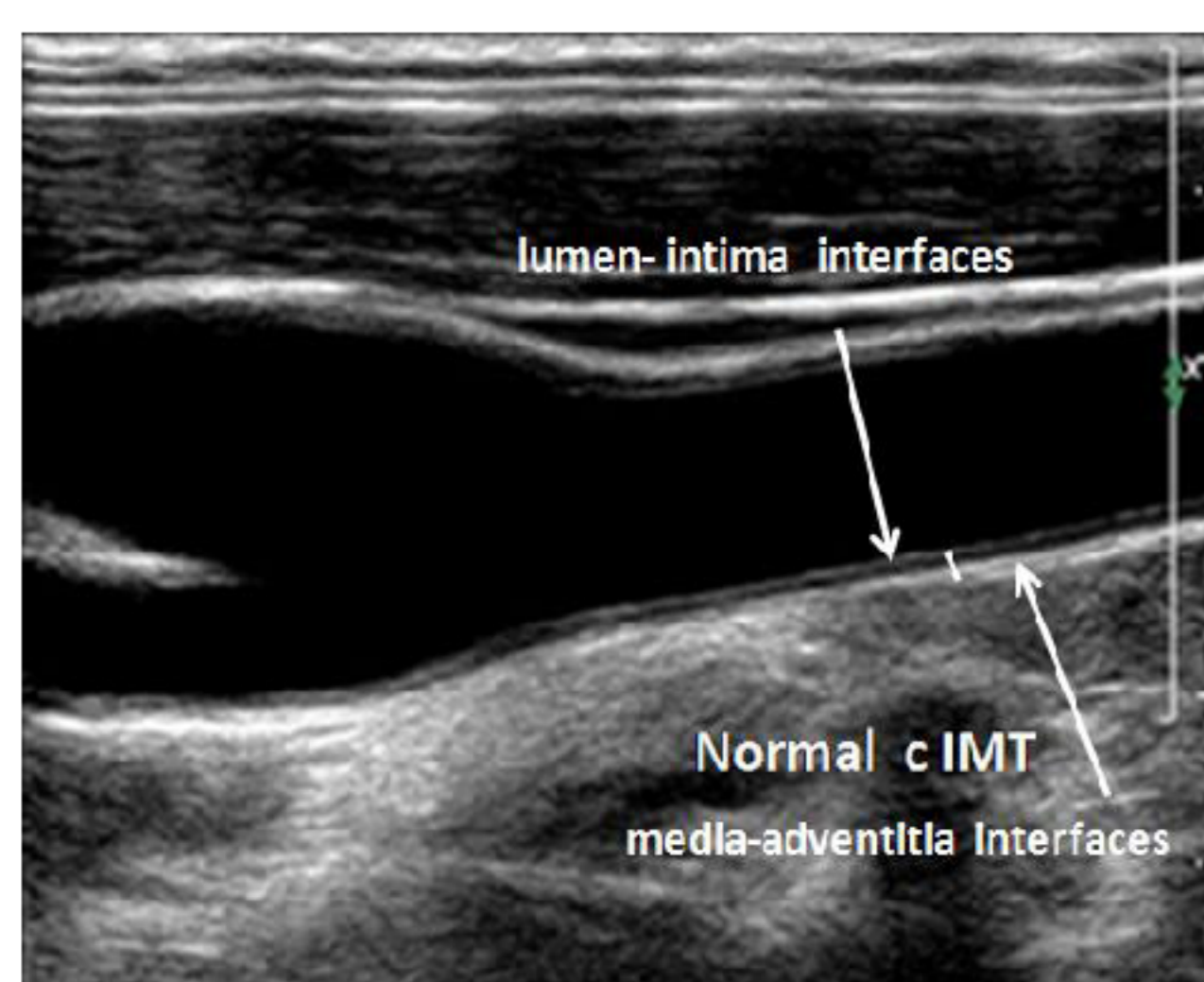
## Introduction

Nonalcoholic fatty liver disease (NAFLD) is a common and underdiagnosed chronic liver disease affecting up to one-third of the global population in Western countries. The prevalence of NAFLD is increased up to 70% to 90% among T2DM persons and makes it an important public health problem. NAFLD is considered a hepatic manifestation of metabolic syndrome and is closely associated with abdominal obesity, atherogenic dyslipidemia, and diabetes exposing subjects with NAFLD to an increased risk of developing cardiovascular disease. Carotid intima-media thickness (cIMT) is a reliable index of subclinical atherosclerosis and a mirror of atherosclerosis progression in NAFLD patients. Carotid IMT is higher for individuals with hepatosteatosis than for those with simple steatosis and the histological severity of NAFLD independently predicts cIMT (1,2).

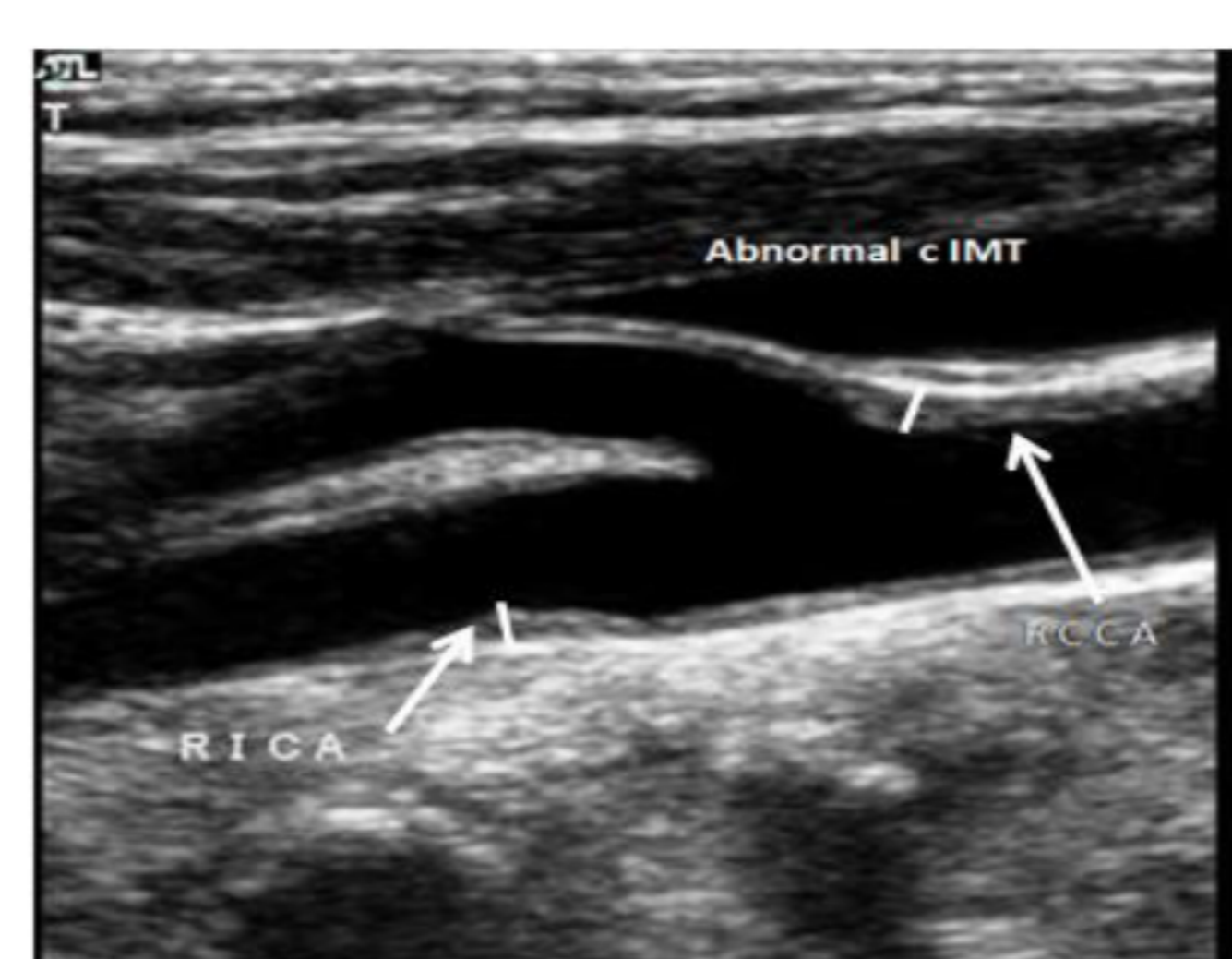
**The aim** of this study was to determine the prevalence of NAFLD in diabetes mellitus (DM) patients, to evaluate the impact of clinical parameters and indices of body composition on the relation between NAFLD and carotid intima-media thickness (cIMT), in a type 2 diabetes mellitus population (T2DM).

## Methods

We retrospectively enrolled 120 T2DM outpatients who regularly attended a Consulting Clinic in Cluj. Clinical, anthropometric and biochemical parameters were measured. NAFLD was diagnosed using fatty liver index (FLI, 3), an algorithm based on body mass index (BMI), waist circumference, triglycerides and gammaglutamyl-transferase (GGT). Hepatic steatosis (HS) and cIMT were evaluated by ultrasonography (US). Body composition was assessed by bioelectric impedance (BIA, InBody 720) in all subjects.



**Figure 1.** Normal cIMT measured as the distance between the lumen-intima and media-adventitia interfaces (indicated by white flashes) of the far wall of common carotid artery (CCA). cIMT thickness is marked by a white short line.



**Figure 2.** Abnormal cIMT - thickening of intima and media of the vascular wall of CCA, the carotid bulb and the first cm of the internal carotid artery (ICA). cIMT thickness is marked by a white short line and the lumen-intima interface is indicated by a white flash.

## Results

HS was correlated with NAFLD – FLI ( $p \leq 0.0001$ ). Patients were divided into three groups: G1: FLI < 30 ( $n = 56$ ); G3: FLI > 60 ( $n = 40$ ), G2: intermediate group ( $n = 28$ ). The prevalence of NAFLD using FLI  $\geq 60$  in DM patients was 40 patients (32%). cIMT increased with FLI (G3 =  $0.54 \pm 0.08$  versus G1 =  $0.40 \pm 0.08$  mm,  $P < 0.0001$ ). FLI was associated with increased low-density lipoprotein cholesterol ( $r = 0.38$ ), alanine aminotransferase ( $r = 0.55$ ), BMI ( $r = 0.34$ ), diastolic blood pressure ( $r = 0.41$ ) and reduced high-density lipoprotein cholesterol ( $r = -0.52$ ) and insulinemia ( $r = -0.30$ , all  $P < 0.0001$ ). The correlations hold also in multivariate analysis after adjusting for age and gender. Behavioral variables (smoking, diet) and fasting plasma glucose, did not significantly differ between subjects with and without FLI.

Table 1 - Clinical and biochemical characteristics of diabetic patients grouped according to NAFLD evaluated by FLI. Data are presented as means  $\pm$  SD or number.  $p \leq 0.05$  were considered significant.

Variable	With NAFLD-FLI mean $\pm$ SD (median)	Without NAFLD-FLI mean $\pm$ SD (median)	P (Mann Withney test)
Age (years)	55.7 $\pm$ 8.9 (56)	58.7 $\pm$ 8.5 (58)	$p = 0.005$
Diabetes duration (years)	5.78 $\pm$ 5.56 (5.0)	6.61 $\pm$ 5.77 (5.0)	$p = 0.22$
SBP (mmHg)	147.42 $\pm$ 23.32 (140)	151.67 $\pm$ 25.23 (150)	$p = 0.75$
DBP (mmHg)	87.41 $\pm$ 12.55 (86)	87.0 $\pm$ 9.73 (86)	$p = 0.3$
TC (mmol/l)	5.21 $\pm$ 1.7 (5.1)	4.67 $\pm$ 1.25 (4.68)	$p = 0.006$
HDLc (mmol/l)	1.06 $\pm$ 0.43 (1.06)	1.16 $\pm$ 0.46 (1.13)	$p = 0.008$
LDLc (mmol/l)	2.79 $\pm$ 1.62 (2.99)	2.80 $\pm$ 1.18 (2.94)	$p = 0.82$
TGL/HDLc	7.57 $\pm$ 20.07 (4.03)	3.12 $\pm$ 3.3 (1.95)	$p \leq 0.0001$
FPG (mmol/l)	169.97 $\pm$ 63.5 (157)	186.72 $\pm$ 95.05 (162.5)	$p = 0.4$
HOMA-IR	8.94 $\pm$ 15.23 (5.42)	4.38 $\pm$ 5.16 (2.73)	$p \leq 0.0001$
HbA1C	10.53 $\pm$ 40.8 (7.9)	8.2 $\pm$ 1.87 (7.9)	$p = 0.99$
ASAT (units/l)	29.43 $\pm$ 18.8 (24.5)	21.43 $\pm$ 9.23 (20)	$p \leq 0.0001$
ALAT (units/l)	39.79 $\pm$ 24.4 (33)	27.93 $\pm$ 17.34 (24.6)	$p \leq 0.0001$
VFA (cm <sup>2</sup> )	175.47 $\pm$ 43.18 (170.8)	135.1 $\pm$ 46.35 (133.45)	$p \leq 0.0001$
BFM (cm <sup>2</sup> )	36.36 $\pm$ 14.07 (34.2)	25.35 $\pm$ 12.78 (23.1)	$p \leq 0.0001$
PFB (%)	35.74 $\pm$ 8.66 (35.3)	31.76 $\pm$ 9.29 (30.6)	$p = 0.001$

BMI = body mass index, SBP = systolic blood pressure, DBP = diastolic blood pressure, TC = total cholesterol, HDLc = high density lipoprotein, LDLc = low density lipoprotein, TGL = triglycerides, FPG = fasting plasma glucose, HbA1C = glycated hemoglobin, HOMA-IR = homeostasis model assessment -insulin resistance, ALAT = alanine aminotransferase, ASAT = aspartate aminotransferase, BFM = body fat mass, VFA = visceral fat area, PFB (%) = percent body fat.

Table 2. Multiple regression analysis. Model 1,2: age, sex, VFA, and ALAT are independently correlated with NAFLD-FLI

Model	Independent variable	Unstandardized Coefficients		Standardized Coefficients Beta	P
		B	Std Error		
Model 1 $r = 0.387$ $P \leq 0.0001$	Age (years)	-0.007	0.002	-0.161	0.001
	VFA(cm <sup>2</sup> )	0.003	0.0001	0.362	$\leq 0.0001$
Model 2 $r = 0.409$ $P \leq 0.0001$	Age (years)	-0.006	0.002	-0.138	0.004
	VFA(cm <sup>2</sup> )	0.003	0.0001	0.341	$\leq 0.0001$
	Sex (male/female)	0.117	0.041	0.137	0.005
Model 3 $r = 0.426$ $P \leq 0.0001$	Age (years)	-0.005	0.002	-0.119	0.013
	Sex (male/female)	0.098	0.041	0.115	0.018
	VFA(cm <sup>2</sup> )	0.003	0.0001	0.336	0.0001
	ALAT (U/l)	0.003	0.001	0.128	0.008

Table 3. Multiple regression analysis. Model 1 and 2: age, HbA1C, HOMA-IR and VFA are independently correlated with cIMT

Model	Independent variable	Unstandardized Coefficients		Standardized Coefficients Beta	P
		B	Standard Error		
Model 1 $r = 0.39$ $P = 0.002$	Age (years)	0.009	0.004	0.22	0.023
	HbA1C (%)	-0.001	0.0001	-0.286	0.003
	HOMA-IR	0.014	0.006	0.22	0.026
Model 2 $r = 0.45$ $P \leq 0.0001$	Age (years)	0.006	0.002	0.27	0.001
	HbA1C (%)	0.033	0.011	0.24	0.004
	VFA (cm <sup>2</sup> )	0.001	0.0001	0.27	0.001
	SBP (mmHg)	0.001	0.001	0.15	0.074

**Conclusions:** The results of our study are suggestive for the fact that, in T2DM patients, fatty liver is not a direct mediator of early carotid atherosclerosis. Our data indicate that visceral fat accumulation and glycated hemoglobin are determinant factors of cIMT suggesting that controlling abdominal obesity and hyperglycemia might reduce atherosclerotic disease risk in NAFLD-T2DM subjects. These findings support the hypothesis that the identification of NAFLD abdominal obese T2DM patients may help in CVD risk prediction, with important management implications.

## Bibliography

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