

Association of Non-Alcoholic Fatty Liver Disease with Early Atherosclerotic Markers in Non-Obese Adults: A Cross-Sectional Study

**Sarthak Dahiya¹, Sirjana Kaur Dhaliwal², Namrata³,
Jeyshri Bala Subramaniam⁴, Lakshmishree Shanthi Sathyavenkatesan⁵**

¹MS orthopaedics, Rohilkhand medical college and hospital

ORCID: 0009-0009-7409-3944

²MBBS, Mata Gujri University

ORCID: 0009-0002-0794-4533

³MBBS, Pt. BD Sharma

ORCID: 0009-0005-8763-1327

⁴MBBS, Government Erode Medical College and Hospital

ORCID: 0009-0007-1009-3975

⁵Doctor of Medicine in General Medicine, Jalal-Abad State University

ORCID: 0009-0006-6786-469X

Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is usually thought of as a disease of excess body weight, but a good number of people with NAFLD in South Asia turn out to have a body mass index (BMI) that is well within the normal range. Whether NAFLD raises vascular risk on its own, separate from overall body weight, in such non-obese adults has not been looked at closely enough.

Objective: To find out whether NAFLD is associated with early markers of atherosclerosis, namely carotid intima-media thickness (CIMT), carotid plaque, pulse wave velocity (PWV), and brachial flow-mediated dilation (FMD), in adults who are not obese.

Methods: This cross-sectional study was done on 150 non-obese adults (BMI 19.1 to 24.9 kg/m²), 75 with NAFLD confirmed on ultrasound and 75 without. Anthropometric, biochemical, and vascular measurements were compared between the two groups, and a multivariable logistic regression was used to check whether NAFLD remained linked to early atherosclerosis after adjusting for age, sex, BMI, waist circumference, glycaemic status, hypertension, and hs-CRP.

Results: Adults with NAFLD had a clearly higher CIMT (0.74 vs 0.53 mm), higher PWV (9.25 vs 7.05 m/s), and lower FMD (7.92 vs 12.95%) than those without NAFLD, all with $p < 0.001$, even though BMI and waist circumference were similar in both groups. Early atherosclerosis was seen in 54 of 75 (72.0%) NAFLD participants against 6 of 75 (8.0%) of those without NAFLD ($p < 0.001$). CIMT and PWV rose, and FMD fell, in a stepwise fashion across NAFLD grades (all trend $p < 0.001$). NAFLD stayed

independently linked to early atherosclerosis on multivariable analysis (adjusted odds ratio 48.8, 95% CI 9.1 to 260.4, $p < 0.001$), while BMI and waist circumference showed no independent link at all.

Conclusion: Among non-obese adults, NAFLD is strongly and independently tied to early atherosclerotic change, largely separate from overall or central body fat. Fatty liver, rather than BMI by itself, may be the better early warning sign of cardiovascular risk in lean people.

Keywords: Non-alcoholic fatty liver disease; non-obese; carotid intima-media thickness; pulse wave velocity; flow-mediated dilation; subclinical atherosclerosis

1. Introduction

Cardiovascular disease is still the leading cause of death in most parts of the world, and a large share of that burden builds up quietly, long before any chest pain, breathlessness, or stroke actually brings a patient into a clinic. Much of preventive cardiology depends on catching this subclinical disease early, using markers that are cheap and non-invasive, well before an actual event happens. For a long time, this early screening has leaned on anthropometric proxies for risk, body mass index and waist circumference chief among them, on the assumption that excess body fat is both the cause of risk and a fair marker of it. Non-alcoholic fatty liver disease has traditionally been seen as the liver's version of the metabolic syndrome, turning up alongside obesity, insulin resistance, and abnormal lipids. This view has shaped both clinical suspicion and research design, since ultrasound screening for fatty liver is, in everyday practice, still mostly triggered by a high BMI or waist circumference. Yet this assumption does not sit comfortably with a growing body of South and East Asian data showing that a fair share of NAFLD turns up in people who are not obese by the usual criteria^[1]. Because Asian populations tend to develop diabetes and cardiovascular risk at lower BMI values than European populations do, the WHO Expert Consultation suggested that BMI thresholds for this region be read with caution, noting that cardiometabolic risk climbs well before a BMI of 25 kg/m² is reached^[2].

Indian data show just how common this pattern is. Multicentre surveys have found NAFLD across the whole range of body weight, and population-based estimates put overall NAFLD prevalence in Indian adults somewhere between one-fifth and two-fifths, depending on the diagnostic criteria and setting used^[3,4]. Even when BMI looks unremarkable, Asians tend to carry more visceral fat than Europeans of a similar BMI, and this has been put forward as one reason why fatty liver and its metabolic consequences can turn up at surprisingly low body weights^[4]. Clinically, this matters because lean or non-obese NAFLD is not just a milder version of the obese type. Several cohorts have found that people with lean NAFLD carry a mortality risk that is comparable to, and in some analyses even higher than, that of their non-lean counterparts, and that lean NAFLD raises the risk of new-onset type 2 diabetes and metabolic syndrome on its own^[3,5].

The vascular side of this pattern is of real interest to clinicians working outside tertiary hepatology units. NAFLD has repeatedly been tied to cardiovascular disease independent of shared risk factors, and a few non-invasive markers now let this link be studied before any overt cardiovascular event occurs. Carotid intima-media thickness (CIMT), measured with high-resolution B-mode ultrasound, is a well validated

stand-in for overall atherosclerotic burden, and a raised CIMT has repeatedly been shown in NAFLD groups, including those without obesity^[6,7]. Carotid plaque, a more advanced structural marker, has also turned out to be unusually common among lean people with NAFLD in recent retrospective work^[8]. Pulse wave velocity (PWV), a measure of large artery stiffness, and brachial flow-mediated dilation (FMD), a functional test of endothelium driven vasodilation, give complementary information about the vessel wall, the former reflecting structural stiffening and the latter reflecting early, potentially reversible, endothelial dysfunction^[14,9]. A systematic review and meta-analysis pooling over five thousand subjects found consistently lower FMD in NAFLD patients compared with controls, which backs endothelial dysfunction as an early and reproducible feature of the disease^[9]. Other work suggests that this endothelial impairment in NAFLD is not simply standing in for coexisting metabolic syndrome, and may show up even in its absence^[10].

Despite all this literature, most of the CIMT, PWV, and FMD data linking NAFLD to subclinical atherosclerosis comes from obese or mixed weight groups, or from children and adolescents^[7,11]. Comparatively few studies have restricted their sample specifically to non-obese adults using region appropriate BMI cut-offs, and this is exactly the population in whom the usual body weight driven screening pathway is most likely to miss risk. If NAFLD carries vascular consequences even when BMI and waist circumference look unremarkable, then hepatic steatosis itself, rather than BMI, deserves attention as a marker of cardiovascular risk in lean individuals, a group who might otherwise be reassured by a normal weight and left out of routine cardiovascular risk assessment.

A related but separate idea, normal weight or metabolically obese normal weight obesity, has also drawn attention in South Asian research, where people with a BMI in the accepted normal range can still carry a high body fat percentage and a poor cardiometabolic profile. Community based work from Kerala found that roughly a third of high risk adults screened had this phenotype, with blood pressure and blood sugar readings closer to those of overtly obese participants than to genuinely lean ones^[17]. This reinforces a broader point relevant to this study: in South Asian populations, BMI alone is a fairly blunt tool for telling apart low risk from high risk individuals, and organ specific findings such as fatty liver may carry information that body measurements miss entirely.

This study was therefore designed to look at, in a group of adults with a BMI below the Asian obesity threshold, whether NAFLD is associated with early markers of atherosclerosis, namely CIMT, carotid plaque, PWV, and FMD, and whether this association holds up after adjusting for age, sex, body fat, glycaemic status, hypertension, and inflammatory markers.

2. Materials and Methods

2.1 Study design and setting

This was a cross-sectional analytical study comparing vascular and metabolic parameters between non-obese adults with and without NAFLD confirmed on ultrasound.

2.2 Study population

A total of 150 adults aged between 26 and 60 years were enrolled and split, by design, into two groups of 75 each, those with sonographic evidence of NAFLD and age and sex comparable controls without steatosis. Group sizes were fixed at recruitment to keep the study adequately powered for between group comparison of the main vascular markers, and enrolment carried on until both groups reached the target of 75. Non-obesity was defined, in line with the WHO Expert Consultation recommendation for Asian populations, as a BMI below 25 kg/m²^[2], and the BMI range actually seen in the sample (19.1 to 24.9 kg/m²) confirmed that no participant crossed this threshold. People with a history of heavy alcohol use, viral or autoimmune hepatitis, use of steatogenic medication, known coronary artery disease or stroke, or chronic kidney or thyroid disease were left out, as were pregnant women. The study protocol was reviewed and approved by the concerned institutional ethics committee, and written informed consent was taken from every participant before enrolment.

2.3 Clinical and anthropometric assessment

Height and weight were recorded with participants in light clothing and without footwear, and BMI was worked out as weight in kilograms divided by height in metres squared. Waist circumference was measured at the midpoint between the lower costal margin and the iliac crest. Seated blood pressure was recorded after ten minutes of rest, and current smoking status, along with physician diagnosed diabetes and hypertension, was recorded through structured interview.

2.4 Diagnosis and grading of NAFLD

NAFLD was diagnosed by abdominal ultrasound and graded semi quantitatively (Grade I to III) based on the degree of hepatic echogenicity, vascular blunting, and posterior beam attenuation, in keeping with criteria described in regional clinical practice guidelines^[12]. Participants with no sonographic evidence of steatosis at all were classed as Grade 0.

2.5 Biochemical parameters

Venous blood was drawn after an overnight fast for liver transaminases (AST, ALT), a fasting lipid profile (total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol), fasting blood sugar, glycated haemoglobin (HbA1c), and high sensitivity C-reactive protein (hs-CRP) as a marker of low grade systemic inflammation.

2.6 Assessment of early atherosclerotic markers

CIMT was measured at the far wall of the common carotid artery, 1 cm proximal to the carotid bulb, using high resolution B-mode ultrasound and a standardised scanning protocol, with measurements taken on both sides and the mean recorded in millimetres^[13]. All ultrasound assessments were carried out by a single trained observer using a fixed imaging protocol to keep inter-observer variation to a minimum, and the observer was, where possible, kept unaware of the participant's biochemical results at the time of vascular scanning. A focal carotid plaque was recorded as present when a discrete intimal protrusion beyond the surrounding CIMT, or an intima-media thickness beyond the locally accepted plaque threshold, was seen on either side. Arterial stiffness was assessed as carotid femoral PWV, and endothelial function was

assessed as percentage brachial FMD using the standard reactive hyperaemia protocol, in which brachial artery diameter is recorded at rest and again after release of a five minute suprasystolic occlusion^[14,14]. For this analysis, a composite outcome of early atherosclerosis was defined as the presence of an elevated CIMT, a detectable carotid plaque, or reduced FMD, whichever combination the assessing sonographer judged to reflect a clinically meaningful subclinical vascular change.

2.7 Statistical analysis

Continuous variables are shown as mean plus or minus standard deviation and were compared between NAFLD and non-NAFLD groups using the independent samples t-test, with Welch's correction where variances were unequal. Categorical variables are shown as frequencies and percentages and were compared using the chi-square test. Trends across NAFLD grades (0 to III) were checked using one way ANOVA and Pearson's correlation, treating grade as an ordinal numeric variable. Multivariable logistic regression was used to work out the odds of composite early atherosclerosis associated with NAFLD after adjusting for age, sex, BMI, waist circumference, HbA1c, hs-CRP, and hypertension, and adjusted odds ratios (aOR) with 95% confidence intervals are reported. A two tailed p value below 0.05 was taken as statistically significant. Analyses were run using Python, with the SciPy and NumPy libraries.

3. Results

The final sample came to 150 non-obese adults, split evenly into NAFLD (n=75) and non-NAFLD (n=75) groups. Within the NAFLD group, ultrasound grading showed 39 (52.0%) participants with Grade I, 23 (30.7%) with Grade II, and 13 (17.3%) with Grade III steatosis.

Table 1 sums up the baseline demographic and anthropometric profile of the two groups. Age, sex distribution, BMI, waist circumference, smoking rates, and diabetes rates were all statistically similar between groups, which confirms that the two groups were well matched on overall and central body fat despite their different NAFLD status. Systolic blood pressure was a little higher in the NAFLD group (122.7 vs 119.3 mmHg, p=0.032), and hypertension was more common among those with NAFLD (32.0% vs 12.0%, p=0.006).

Parameter	Non-NAFLD (n=75)	NAFLD (n=75)	p-value
Age (years), mean $\pm$ SD	42.17 $\pm$ 10.19	43.33 $\pm$ 11.25	0.509
Male sex, n (%)	42 (56.0)	37 (49.3)	0.513
BMI (kg/m ²), mean $\pm$ SD	22.45 $\pm$ 1.84	22.01 $\pm$ 1.66	0.128
Waist circumference (cm), mean $\pm$ SD	82.76 $\pm$ 6.86	83.23 $\pm$ 7.49	0.691
Systolic BP (mmHg), mean $\pm$ SD	119.32 $\pm$ 9.75	122.72 $\pm$ 9.45	0.032
Diastolic BP (mmHg), mean $\pm$ SD	76.24 $\pm$ 6.23	76.48 $\pm$ 6.82	0.822
Current smokers, n (%)	16 (21.3)	16 (21.3)	1.000

Parameter	Non-NAFLD (n=75)	NAFLD (n=75)	p-value
Diabetes mellitus, n (%)	5 (6.7)	6 (8.0)	1.000
Hypertension, n (%)	9 (12.0)	24 (32.0)	0.006

Table 1. Baseline demographic and anthropometric characteristics by NAFLD status

Table 2 sets out the biochemical and metabolic profile. Participants with NAFLD had markedly higher AST, ALT, total cholesterol, triglycerides, LDL-cholesterol, fasting blood sugar, HbA1c, and hs-CRP, and markedly lower HDL-cholesterol, than those without NAFLD, all with $p < 0.001$. The size of the hs-CRP difference (3.56 ± 1.20 vs 1.20 ± 0.52 mg/L) stands out given that both groups were free of overt cardiovascular disease, and points to some degree of subclinical systemic inflammation running alongside NAFLD even at a normal BMI.

Parameter	Non-NAFLD (n=75)	NAFLD (n=75)	p-value
AST (U/L)	27.75 ± 5.37	48.79 ± 11.08	<0.001
ALT (U/L)	29.56 ± 6.85	72.53 ± 14.17	<0.001
Total cholesterol (mg/dL)	175.64 ± 16.14	207.89 ± 20.27	<0.001
Triglycerides (mg/dL)	122.47 ± 25.57	187.83 ± 29.24	<0.001
HDL-cholesterol (mg/dL)	54.24 ± 5.80	40.20 ± 4.91	<0.001
LDL-cholesterol (mg/dL)	94.79 ± 15.15	127.03 ± 17.03	<0.001
Fasting blood sugar (mg/dL)	93.71 ± 8.23	109.40 ± 11.84	<0.001
HbA1c (%)	5.32 ± 0.30	6.07 ± 0.45	<0.001
hs-CRP (mg/L)	1.20 ± 0.52	3.56 ± 1.20	<0.001

Table 2. Biochemical and metabolic profile by NAFLD status

Table 3 compares the early atherosclerotic markers. CIMT was much higher in the NAFLD group (0.74 ± 0.09 mm vs 0.53 ± 0.07 mm, $p < 0.001$), as was PWV (9.25 ± 0.82 vs 7.05 ± 0.72 m/s, $p < 0.001$), while FMD was clearly lower ($7.92 \pm 1.53\%$ vs $12.95 \pm 1.35\%$, $p < 0.001$). Carotid plaque turned up in 16 of 75 (21.3%) participants with NAFLD compared with 4 of 75 (5.3%) without ($p = 0.008$). The composite outcome of early atherosclerosis was present in 54 of 75 (72.0%) participants with NAFLD versus 6 of 75 (8.0%) without NAFLD ($p < 0.001$), shown in Figure 3.

Marker	Non-NAFLD (n=75)	NAFLD (n=75)	p-value
CIMT (mm), mean $\pm$ SD	0.53 $\pm$ 0.07	0.74 $\pm$ 0.09	<0.001
Carotid plaque, n (%)	4 (5.3)	16 (21.3)	0.008
PWV (m/s), mean $\pm$ SD	7.05 $\pm$ 0.72	9.25 $\pm$ 0.82	<0.001
FMD (%), mean $\pm$ SD	12.95 $\pm$ 1.35	7.92 $\pm$ 1.53	<0.001
Composite early atherosclerosis, n (%)	6 (8.0)	54 (72.0)	<0.001

Table 3. Early atherosclerotic markers by NAFLD status

Figure 1 shows the mean CIMT, PWV, and FMD values for the two groups, and the direction and size of the vascular difference is consistent across all three markers.

Figure 1. Early Atherosclerotic Markers by NAFLD Status (Mean $\pm$ SD)

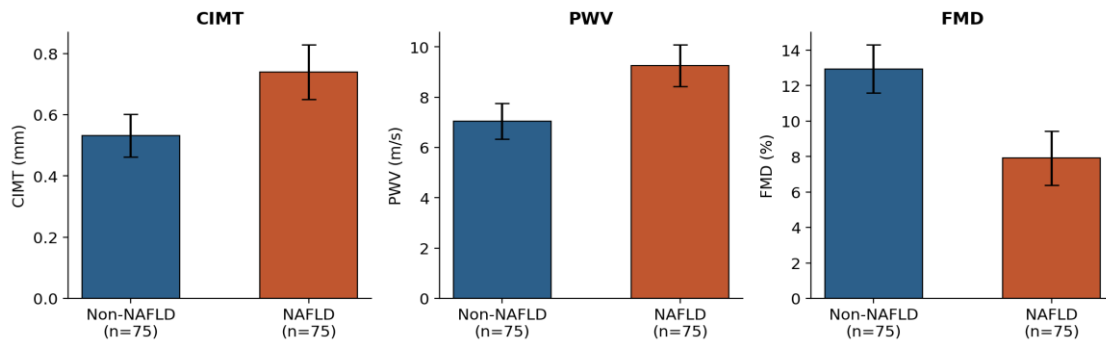


Figure 1. Early atherosclerotic markers by NAFLD status (mean $\pm$ SD)

Table 4 and Figure 2 show that these differences were not just a simple NAFLD present or absent split but tracked with how severe the disease was. CIMT rose from 0.53 mm at Grade 0 to 0.73 to 0.77 mm at Grades I and II, PWV rose in step, and FMD fell in a near mirror pattern, with statistically significant trends across grades for all three markers (all trend $p < 0.001$) and for hs-CRP as well. Interestingly, Grade III participants did not show any further worsening in CIMT, PWV, or FMD beyond Grade II, though the small number of Grade III participants ($n=13$) limits how much can be read into a possible plateau or ceiling effect at more advanced grades.

Marker	Grade 0 (n=75)	Grade I (n=39)	Grade II (n=23)	Grade III (n=13)	ANOVA p	Trend r (p)
CIMT (mm)	0.53 ± 0.07	0.73 ± 0.09	0.77 ± 0.08	0.72 ± 0.11	<0.001	0.68 (<0.001)
PWV (m/s)	7.05 ± 0.72	9.15 ± 0.74	9.64 ± 0.84	8.88 ± 0.81	<0.001	0.69 (<0.001)
FMD (%)	12.95 ± 1.35	8.04 ± 1.55	7.69 ± 1.60	7.97 ± 1.39	<0.001	-0.74 (<0.001)
hs-CRP (mg/L)	1.20 ± 0.52	3.58 ± 1.21	3.53 ± 1.28	3.55 ± 1.13	<0.001	0.66 (<0.001)

Table 4. NAFLD grade-wise trend in early atherosclerotic markers and hs-CRP

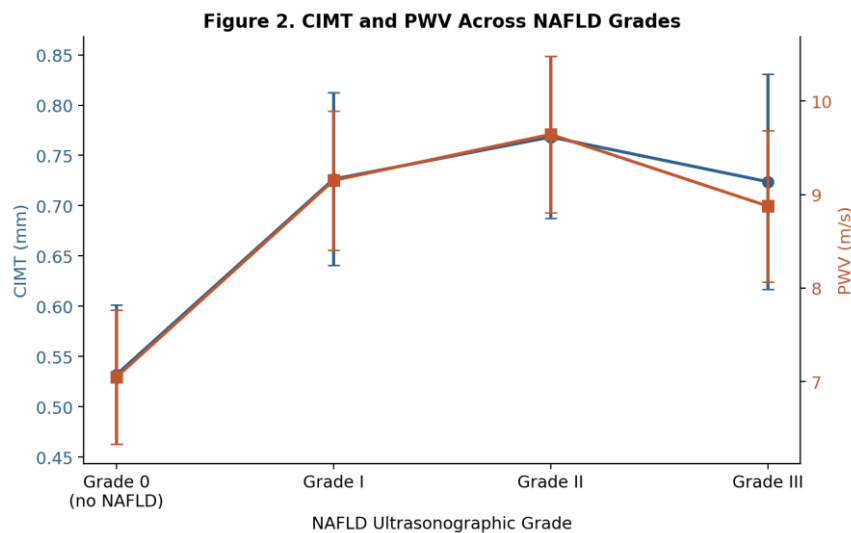


Figure 2. CIMT and PWV across NAFLD grades

Correlation analysis backed up these grade wise patterns. ALT correlated with CIMT ($r=0.73$), PWV ($r=0.72$), and inversely with FMD ($r=-0.74$), all with $p<0.001$, and hs-CRP showed similarly strong correlations with all three vascular markers ($r=0.62$ to -0.71 , all $p<0.001$). By contrast, neither BMI nor waist circumference showed any meaningful correlation with any vascular marker (all absolute r below 0.12 , all p above 0.16), which fits with the narrow, non-obese range of body fat in this cohort, and supports the idea that within this range, liver and inflammatory status carried more vascular information than body measurements did.

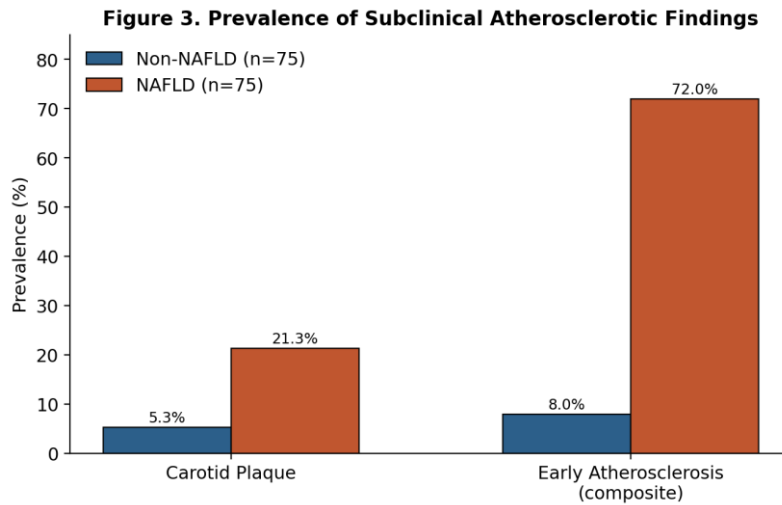


Figure 3. Prevalence of carotid plaque and composite early atherosclerosis by NAFLD status

Table 5 sets out the multivariable logistic regression for composite early atherosclerosis. After adjusting for age, sex, BMI, waist circumference, HbA1c, hs-CRP, and hypertension, NAFLD stayed strongly and independently associated with early atherosclerosis (adjusted OR 48.8, 95% CI 9.1 to 260.4, $p < 0.001$). None of the anthropometric or metabolic covariates reached independent significance in the adjusted model, including BMI (aOR 0.99, 95% CI 0.76 to 1.30, $p = 0.963$), waist circumference (aOR 0.99, 95% CI 0.93 to 1.05, $p = 0.718$), and hs-CRP (aOR 0.73, 95% CI 0.47 to 1.14, $p = 0.167$), which suggests that the effect of NAFLD on early vascular change in this cohort was not simply working through these more familiar risk markers, at least not in a way this sample was powered to pick up individually.

Covariate	Adjusted OR	95% CI	p-value
NAFLD (present vs absent)	48.79	9.14 to 260.39	<0.001
Age (per year)	1.01	0.97 to 1.05	0.606
Sex (male vs female)	1.32	0.52 to 3.31	0.559
BMI (per kg/m ²)	0.99	0.76 to 1.30	0.963
Waist circumference (per cm)	0.99	0.93 to 1.05	0.718
HbA1c (per %)	1.29	0.42 to 3.95	0.659
hs-CRP (per mg/L)	0.73	0.47 to 1.14	0.167
Hypertension (present vs absent)	2.38	0.84 to 6.77	0.104

Table 5. Multivariable logistic regression for composite early atherosclerosis

4. Discussion

This cross-sectional study found that non-obese adults with NAFLD confirmed on ultrasound had a markedly greater carotid intima-media thickness, higher arterial stiffness, and lower endothelial function than their non-obese counterparts without steatosis, and that this pattern grew stronger with increasing NAFLD grade. Importantly, these differences held up after adjusting for BMI, waist circumference, glycaemic status, hs-CRP, and hypertension, and BMI itself showed almost no correlation with any vascular marker within this narrow, non-obese range. Taken together, these findings suggest that in adults who are not obese, fatty liver carries vascular information that a normal BMI or waist circumference simply does not.

These results line up with, and add to, a growing body of literature that questions the assumption that NAFLD's cardiovascular consequences are just a function of accompanying obesity. Comparisons of obese and non-obese NAFLD patients have shown that while overt metabolic syndrome is less common in non-obese NAFLD, the cardiometabolic risk tied to NAFLD in non-obese patients is still much higher than in non-obese people without steatosis^[5,15]. Multicentre Indian data have made a similar point, that NAFLD in lean patients is neither rare nor harmless, and that central body fat, rather than BMI on its own, may better explain why steatosis develops even at an unremarkable body weight in Asian populations^[3,4]. Our finding that waist circumference did not correlate with CIMENT, PWV, or FMD in this cohort should be read with that context in mind. Because our sample was deliberately kept to a narrow band of non-obese body fat, the study was not well placed to pick up a waist circumference gradient that might show up more clearly across a wider range of body composition. The point still stands, though, that within this common and clinically important non-obese range, the presence of fatty liver told risk apart far more clearly than body measurements did.

The gradient seen across NAFLD grades, with CIMENT and PWV climbing, and FMD falling, from Grade 0 through Grade II, matches the internationally reported dose response relationship between how severe hepatic steatosis is and how much vascular injury follows. A tertiary care series from Nepal similarly reported progressively higher CIMENT with rising NAFLD grade, with the highest mean CIMENT seen in Grade II disease, and an overall mean CIMENT across their NAFLD cohort broadly close to the values seen in our NAFLD group^[6]. A more recent cross-sectional study from Iraq, screening patients with ultrasound signs of fatty liver of varying severity, likewise found that most of their NAFLD sample had a CIMENT above the usual 0.08 cm threshold used to flag subclinical atherosclerosis, with the proportion crossing this threshold rising alongside higher fatty liver grade^[7]. Our own composite early atherosclerosis figure of 72.0% among non-obese NAFLD participants sits at the higher end of this range, which may reflect differences in the composite definition used, the specific population studied, or genuine differences in vascular vulnerability among non-obese individuals who still go on to develop steatosis. The apparent plateau, or even slight reversal, of vascular markers at Grade III in the present cohort is interesting but should not be read too far into, given the small subgroup size (n=13). It may reflect a true ceiling effect in ultrasound sensitivity at advanced steatosis, sampling variation, or a Grade III subgroup with a shorter disease duration, and it would benefit from confirmation in a larger, dedicated sample.

The size of the FMD impairment seen here, roughly 5 percentage points lower in NAFLD, fits with pooled estimates from a systematic review and meta-analysis of over twenty studies, which found a large,

consistent drop in FMD among NAFLD patients relative to controls^[9]. Other authors have argued specifically that endothelial dysfunction in NAFLD is not just standing in for coexisting metabolic syndrome, since impaired FMD has been shown even in NAFLD patients without metabolic syndrome, though to a lesser degree than in those with it^[10]. Our multivariable analysis, in which NAFLD stayed a strong independent predictor of early atherosclerosis even after accounting for hs-CRP, HbA1c, and hypertension, broadly agrees with that view. The vascular signal tied to NAFLD in this cohort was not fully explained by the inflammatory and metabolic covariates measured.

Mechanistically, a few pathways have been put forward to link hepatic steatosis to vascular injury independent of general obesity. The steatotic liver is a source of atherogenic dyslipidaemia, low grade systemic inflammation, and altered adipokine and hepatokine secretion, all of which can drive endothelial dysfunction and arterial stiffening even when overall body fat is modest^[10,16]. The raised hs-CRP seen in our NAFLD group, despite similar BMI and waist circumference between groups, fits this pathway, even though hs-CRP itself did not stay independently significant once NAFLD was in the model, a pattern that would be expected if much of the inflammatory signal tied to early atherosclerosis works largely through, rather than alongside, the presence of steatosis itself.

Carotid plaque, a more advanced marker of atherosclerosis than CINT alone, was over four times more common among participants with NAFLD in our cohort. This matches a recent large retrospective analysis focused specifically on lean individuals, which reported a materially higher risk of carotid plaque in lean NAFLD compared with lean individuals without steatosis^[8]. Read alongside our CINT and plaque findings, this suggests that the vascular consequences of NAFLD in non-obese individuals are not limited to early functional change (reduced FMD) but can extend to structural disease as well.

From a clinical point of view, these findings argue against using BMI as a gatekeeper for cardiovascular risk assessment in patients found to have NAFLD, or indeed for NAFLD case finding itself. A meaningful minority of NAFLD in Asian populations turns up below the usual obesity thresholds, and international guidance already recognises that Asian populations face raised metabolic risk at lower BMI values than Western reference ranges suggest^[2]. Our data show that once NAFLD is present, a normal BMI does not mean a normal vascular profile. Nearly three quarters of the non-obese participants with NAFLD in this study already showed evidence of early atherosclerosis. This would support building simple, low cost vascular checks, particularly CINT, which is widely available on the same ultrasound machines already used to diagnose NAFLD, into the evaluation of lean patients found to have fatty liver, rather than reassuring such patients purely on the basis of body weight.

For primary care and community medicine practice specifically, where NAFLD is often picked up by chance on an abdominal ultrasound done for something else entirely, our findings argue for a change in what happens next. A non-obese patient with an incidental finding of fatty liver should probably not be treated as a low cardiovascular priority just because their BMI is normal. A brief carotid ultrasound, where it is locally available, or at the very least closer attention to blood pressure, lipid profile, and blood sugar, may be a reasonable and inexpensive addition to the existing diagnostic pathway, particularly in settings such as ours where advanced imaging options like coronary calcium scoring are not routinely within reach.

It is worth noting that sex distribution did not differ between the NAFLD and non-NAFLD groups, and sex was not an independent predictor of early atherosclerosis in the adjusted model. This argues against

sex specific confounding as an explanation for our findings, although the study was not specifically powered to pick up sex based interaction effects, and larger studies may be better placed to look at whether the vascular impact of non-obese NAFLD differs meaningfully between men and women, particularly around the menopausal transition when vascular risk in women tends to rise.

This study also has some real strengths. It deliberately kept enrolment to a single, narrow, non-obese BMI band rather than treating non-obese participants as a subgroup within a wider, mostly obese cohort, which let the independent contribution of NAFLD be looked at without a wide body fat gradient diluting the picture. It also assessed atherosclerosis through three complementary and mechanistically distinct markers, a structural marker (CIMT and plaque), a stiffness marker (PWV), and a functional marker (FMD), rather than leaning on a single vascular endpoint, and it looked at a dose response relationship across NAFLD grades rather than treating NAFLD as a simple yes or no exposure.

Limitations

A few limitations are worth keeping in mind. First, the cross-sectional design does not allow for cause and effect conclusions. Longitudinal studies are needed to work out whether NAFLD comes before vascular change or whether both share some common upstream driver not fully captured by the covariates measured here. Second, NAFLD diagnosis and grading relied on ultrasound rather than liver biopsy or elastography based quantification, which may have brought in some grading imprecision, particularly at higher grades. Third, although waist circumference was recorded, visceral fat was not directly measured by imaging, and some residual confounding by unmeasured visceral fat cannot be ruled out. Fourth, the modest size of the Grade III subgroup limits how precise the grade wise trend estimates can be at the upper end of disease severity. Finally, since this is a single analysis cross-sectional dataset, the findings should be repeated in larger, multi-centre, and ideally prospective cohorts before firm clinical recommendations are drawn from them.

5. Conclusion

In this cohort of non-obese adults, NAFLD was strongly and independently tied to early markers of atherosclerosis, raised CIMT, higher carotid plaque prevalence, greater arterial stiffness, and reduced endothelial function, and this link held up after adjusting for body fat, glycaemic status, hypertension, and inflammation, and grew stronger with increasing NAFLD grade. These findings suggest that fatty liver, rather than BMI, may be a more useful marker of early cardiovascular risk in lean individuals, and support closer vascular follow-up in non-obese adults found to have NAFLD rather than reassurance based on normal body weight alone. Larger, prospective, multi-centre studies that directly measure visceral fat and track hard cardiovascular endpoints are needed to confirm these findings and to work out what, if any, extra screening pathway non-obese NAFLD patients should be offered in routine practice.

References

1. Exploring diversity in Non-Alcoholic Fatty Liver Disease (NAFLD) among lean, overweight, and obese patients: A Multicenter study from India. PMC, article ID PMC12571367.
2. Gujral UP, Vittinghoff E, Mongraw-Chaffin M, et al. BMI Cut Points to Identify At-Risk Asian Americans for Type 2 Diabetes Screening. *Diabetes Care*. 2015;38(1):150-158. Free article, PMC4392932.
3. Comparison of cardiometabolic risk factors between obese and non-obese patients with nonalcoholic fatty liver disease. PMC, article ID PMC10477254.
4. Prevalence, Metabolic Profile, and Associated Risk Factors of Non-alcoholic Fatty Liver Disease in an Adult Population of India. PMC, article ID PMC9938792.
5. Nonobese NAFLD subjects demonstrate lower risk of metabolic syndrome than obese non-NAFLD subjects: A multicenter cross-sectional study. PMC, article ID PMC12401270.
6. Bom BC, Jaiswal RK, Gupta PK, Paudel R, Subedi RK. Carotid Intima-media Thickness in Patients with Non-alcoholic Fatty Liver Disease Attending a Tertiary Care Center: A Descriptive Cross-sectional Study. *Journal of Nepal Medical Association*. 2021. Free article, PMC8673453.
7. Association Between Non-Alcoholic Fatty Liver Disease and Subclinical Atherosclerosis: A Study of Carotid Intima-Media Thickness. *Al-Rafidain Journal of Medical Sciences*. 2025;9(2):103-108. Open access.
8. Higher risk of carotid plaque among lean individuals with non-alcoholic fatty liver disease: A retrospective study. *PLOS One*. 2025. Open access.
9. Endothelial Dysfunction in Nonalcoholic Fatty Liver Disease: A Systematic Review and Meta-Analysis. PMC, article ID PMC9144621.
10. Endothelial Dysfunction, a Marker of Atherosclerosis, Is Independent of Metabolic Syndrome in NAFLD Patients. PMC, article ID PMC7382713.
11. Relationship Between Aspartate Aminotransferase-to-Platelet Ratio Index and Carotid Intima-Media Thickness in Obese Adolescents with Non-Alcoholic Fatty Liver Disease. PMC, article ID PMC3814245.
12. National Workshop on Fatty Liver and Alcoholic Liver Disease, Chinese Society of Hepatology. Guidelines for the prevention and treatment of nonalcoholic fatty liver disease, 2018 update. Free article, PMC12769340.
13. Touboul PJ, Hennerici MG, Meairs S, et al. Mannheim carotid intima-media thickness and plaque consensus (2004 to 2006 to 2011). *Cerebrovascular Diseases*. 2012;34:290-296. Free PMC article.
14. Assessment of Endothelial Function by Means of Flow-Mediated Changes Using Pulse Wave Velocity. PMC, article ID PMC8673162.
15. Kumar R, Rastogi A, Sharma MK, et al. Clinicopathological characteristics and metabolic profiles of non-alcoholic fatty liver disease in Indian patients with normal body mass index. *Indian Journal of Endocrinology and Metabolism*. Open access, PMC3743367.

16. Duseja A, Singh SP, Saraswat VA, et al. Non-alcoholic Fatty Liver Disease and Metabolic Syndrome, Position Paper of the Indian National Association for the Study of the Liver, Endocrine Society of India, Indian College of Cardiology and Indian Society of Gastroenterology. Journal of Clinical and Experimental Hepatology. 2015;5(1):51-68. Free article, PMC4415196.
17. Prevalence of normal weight obesity and its associated cardio-metabolic risk factors, results from the baseline data of the Kerala Diabetes Prevention Program. PMC, article ID PMC7446975.