THE USA JOURNALS
THE AMERICAN JOURNAL OF MEDICAL SCIENCES AND PHARMACEUTICAL RESEARCH
(ISSN – 2689-1026)
VOLUME 06 ISSUE06

PUBLISHED DATE: - 14-06-2024
DOI: - https://doi.org/10.37547/TAJMSPR/Volume06Issue06-02 **PAGE NO.: - 08-17**

RESEARCH ARTICLE **Open Access**

THE CONTRIBUTION OF NON-ALCOHOLIC FATTY LIVER DISEASE TO THE PROGRESSION OF ATHEROSCLEROSIS

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Abstract
In the context of insulin resistance syndrome, which encompasses changes in lipid and carbohydrate metabolism, liver-related issues are now being closely examined alongside cardiovascular diseases. Our research aimed to evaluate the predictive importance of non-alcoholic fatty liver disease (NAFLD) for identifying the likelihood of early atherosclerotic alterations in the carotid arteries. We discovered a connection between NAFLD and initial signs of atherosclerosis. By ranking prognostic factors that affect changes in the carotid artery wall, we've been able to develop a method for estimating individual atherosclerosis risk in people who are otherwise healthy. The practical value of our findings underscores the need for in-depth evaluation of individuals with NAFLD to identify risk factors that may contribute to the advancement of both liver and cardiovascular diseases.

Keywords Non-alcoholic fatty liver disease; insulin resistance; atherosclerosis.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is now identified as a leading chronic liver condition worldwide[1]. Despite the challenge in pinpointing precise incidence rates, estimates suggest that NAFLD affects 20–30% of populations in Western countries and 5–18% in Asian countries, with these numbers increasing sharply over time. It's believed that NAFLD impacts about 25–30% of people globally[2]. This condition, along with cardiovascular diseases and metabolic disturbances in lipid and carbohydrate metabolism associated with insulin resistance (IR) syndrome, is gaining increased attention. NAFLD covers a broad range of metabolic liver damages in the context of IR, including simple fatty liver (steatosis), steatosis with inflammation and liver cell damage (non-alcoholic steatohepatitis, NASH), and fibrosis, which can evolve into cirrhosis of the liver[3, 4].

The outlook for individuals diagnosed with NAFLD is concerning; about 40% of those with simple steatosis progress to NASH within 8-13 years, and from this group, 15% may develop liver cirrhosis and liver failure. Moreover, 7% of patients with liver cirrhosis are at risk of developing hepatocellular carcinoma (HCC) within a decade[5]. The expectation is that NAFLD will soon become the predominant liver disorder, already

being the second leading cause of HCC and liver transplants[6].

Research has highlighted a significant link between the onset of non-alcoholic fatty liver disease (NAFLD) and several metabolic conditions, such as obesity, type 2 diabetes mellitus (T2DM), and atherogenic dyslipidemia, particularly in cases where insulin resistance (IR) is present. Within the general European population, the occurrence rate of NAFLD is found to be between 20-33%. This rate escalates among individuals diagnosed with type 2 diabetes mellitus, where it is observed to vary from 42.6-69%. This data underscores the intertwined nature of metabolic diseases and the critical role of insulin resistance in the development of NAFLD[7, 8].

Furthermore, there's an ongoing dialogue around genetic mutations affecting carbohydrate and lipid metabolism, which result in changes to insulin sensitivity within the liver[9; 10]. These genetic factors contribute to the broader understanding of NAFLD's pathogenesis and its strong links to other symptoms of insulin resistance (IR). This connection positions non-alcoholic fatty liver disease (NAFLD) as a liver-centered component of metabolic syndrome[11; 12]. Yet, as the liver engages in this pathological sequence, it transitions from being merely an affected organ to an active participant that intensifies the metabolic imbalances associated with IR.

Studies have shown that disruptions in insulin breakdown and glucose usage occur in the liver during fatty hepatosis, leading to an environment conducive to the production of atherogenic cholesterol fractions and triglycerides (TG). These disruptions are instrumental in causing disturbances in carbohydrate and lipid metabolism, precipitating the early emergence of atherosclerosis and subsequent cardiovascular diseases[13; 14]. Research by Natadisa M. in 2007 further illuminates the heightened risk of atherosclerosis in individuals with NAFLD, which is found to be 4.12 times greater than in those without the disease, as indicated by a 95% confidence interval (CI) of 1.58-10.75 and a significance level of p=0.004. Additionally, the study highlights a gender disparity in the risk of cardiovascular complications associated with NAFLD, with women facing a risk 7.32 times higher compared to men's 3.56 times, showcasing a significant difference ($p<0.027$)[15].

Atherosclerosis is identified as a condition that involves the liver, where it's established that two main factors are essential for its onset: lipid metabolism disorders and vascular endothelium damage. Within the scope of NAFLD, the disturbance in lipid metabolism is evidenced by increased low-density lipoprotein cholesterol (LDL-C) levels, decreased high-density lipoprotein cholesterol (HDL-C) levels, and the presence of hypertriglyceridemia. The harm to arterial endothelium associated with liver diseases stems from various factors, including oxidized LDL lipids, elevated C-reactive protein (CRP) levels, heightened activity of lipoprotein-associated phospholipase A2, hyperglycemia, insulin resistance, raised homocysteine levels, increased fibrinogen levels, and a scarcity of nitric oxide (NO). These elements collectively contribute to the complex interplay between NAFLD and the development of atherosclerosis [16].

Enhanced arterial stiffness in individuals with non-alcoholic fatty liver disease (NAFLD) is garnering notable focus, positioning NAFLD as a marker for this condition[24]. This increased stiffness of arteries, which persists even when traditional cardiovascular risk factors are accounted for, is linked with NAFLD. Patients with NAFLD show reduced elasticity and flexibility of the aorta, indicating that both the presence and severity of NAFLD correlate with heightened arterial stiffness, regardless of the existence of hypertension (HTN) or diabetes mellitus (DM) [17].

In the "Cardio-GOOSE" study, the assessment of arterial stiffness was conducted through the measurement of carotid-femoral pulse wave velocity (PWV) and detection of subclinical atherosclerosis via intima-media thickness (IMT). Results showed no significant difference in IMT between those with and without NAFLD (0.77±0.15 mm versus 0.76±0.14 mm, respectively) [18]. However, for individuals

diagnosed with both NAFLD and metabolic syndrome (MS), IMT values were noticeably higher (0.85±0.16 mm; p<0.005) compared to those without MS. Furthermore, an increase in vascular wall stiffness was observed in patients with NAFLD, especially pronounced in those also suffering from MS, with the PWV measurements being higher in the NAFLD+MS group (8.29±2.2 m/s; p<0.001). The occurrence of NAFLD was more common in participants exhibiting greater vascular stiffness, even after adjusting for MS (p<0.05), highlighting the intricate relationship between NAFLD and cardiovascular health [19].

Non-alcoholic fatty liver disease (NAFLD) is linked to a heightened risk of atherosclerosis, including its asymptomatic stages, highlighted by increased intima-media thickness (IMT) and raised levels of C-reactive protein (CRP). According to research conducted by Kim in 2009, the IMT in patients with NAFLD was found to be 0.034 mm thicker than in those without the condition, a difference that was statistically significant (p=0.016) [20]. Additionally, individuals with NAFLD are more likely to have silent atherosclerotic changes in the carotid arteries. The occurrence of atherosclerotic plaques is notably higher among patients with NAFLD, with a prevalence of 57.8%, compared to 37.5% in those without NAFLD (p=0.02). Furthermore, the likelihood of developing carotid atherosclerosis in patients with NAFLD is increased by 1.85 times (p<0.001), underscoring the significant impact of NAFLD on cardiovascular health and the importance of monitoring for atherosclerotic changes in this patient population [21].

Over a span of 21 years, cardiovascular diseases have been identified as the leading cause of mortality among individuals diagnosed with non-alcoholic fatty liver disease (NAFLD). Additionally, NAFLD is linked to a rise in not just cardiovascular-related deaths but also overall mortality rates. This interplay of factors considerably hastens the onset and advancement of atherosclerosis and its related cardiovascular conditions. As a result, investigating NAFLD as a separate and contributory risk factor in the progression of atherosclerosis has become a focal point of contemporary research, highlighting the importance of recognizing and managing NAFLD to potentially mitigate the risk of cardiovascular complications [22].

Purpose.Our research aimed to evaluate the predictive value of non-alcoholic fatty liver disease (NAFLD) in identifying the likelihood of early signs of atherosclerotic vascular damage, with a specific focus on the lower extremities. This study sought to understand how NAFLD could serve as an indicator for the onset of atherosclerosis in these areas, potentially offering insights into the broader implications of NAFLD on cardiovascular health and the importance of early detection and management of vascular risks associated with this liver condition.

MATERIAL AND METHODS OF RESEARCH

Our investigation encompassed 100 individuals, aged 35 to 45 years, who were participating in standard health screenings at the "Akfa Medline" university clinic in Tashkent. These participants were asymptomatic at the time of their evaluation. The study set specific exclusion criteria to ensure a homogeneous sample population, disqualifying individuals with obesity (defined by a body mass index not exceeding 30 kg/m^2), hypertension, coronary artery disease, type 2 diabetes mellitus, and renal or gastrointestinal diseases that necessitated drug treatment. This approach aimed to isolate the impact of non-alcoholic fatty liver disease (NAFLD) on the early development of atherosclerotic vascular changes in the lower extremities, minimizing confounding factors that could influence the outcomes.

In gathering data on alcohol consumption history, our methodology adhered to the guidelines set forth by the World Health Organization (WHO) from the year 2000. We specifically focused on alcohol intake levels and only considered consumption patterns that exceeded WHO's recommended norms if they occurred within the last five years; any excessive alcohol consumption more than 5 years prior was not included in our analysis. Additionally, we meticulously excluded any participants with a history of viral hepatitis or

liver damage attributed to toxins or pharmaceuticals. This careful selection process aimed to ensure the accuracy of our study by eliminating potential confounding factors related to liver health and focusing on the impact of non-alcoholic factors on liver disease.

A comprehensive physical examination of the participants was carried out, which included the measurement of key anthropometric indicators and blood pressure levels to assess overall health status. In addition, a detailed analysis of lipid profile markers was performed. This analysis involved determining the levels of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C). These measurements were crucial for evaluating the metabolic and cardiovascular health of the participants, providing essential insights into their risk factors for developing conditions such as atherosclerosis and cardiovascular diseases, particularly in the context of non-alcoholic fatty liver disease (NAFLD).

The evaluation of the intima-media thickness (IMT) of the common carotid arteries (CCA) was executed employing a standardized approach on the ACUSON S2000 and S3000 2019 ultrasound machines, which were outfitted with a linear probe that utilizes a phased array technology at a frequency of 7.5 MHz. This examination targeted the CCA at three distinct locations, specifically 2 cm below the bifurcation point on both the right and left sides of the neck. To derive the average IMT value for the CCA, measurements from these six points were aggregated. The criteria for identifying early indications of atherosclerosis involved detecting a localized increase in the CCA IMT to more than 1.5 mm at any measured site along the carotid artery, denoted as the maximum CCA IMT. This measurement process is critical for diagnosing the preliminary stages of atherosclerosis, offering valuable insights into the cardiovascular risk profile of the study participants.

All participants in the study were subjected to a liver ultrasound examination to assess various aspects of liver health, including the oblique vertical size of the liver (OVS), the density of the liver parenchyma, the condition of the liver bile ducts, and the vascular pattern. For capturing detailed images of the liver parenchyma, performing measurements of its lobes, and evaluating its structure, the Acuson Sequoia Expert system 2022 was employed. This advanced ultrasound system is equipped with a convex probe that features a phased array with a frequency of 3.5 MHz, making it particularly suited for B-mode scanning of internal organs.

The liver ultrasound procedure was carried out in accordance with the standard methodological guidelines as outlined by V. V. Mitkov in 2007. This ensured that the examination was performed consistently and accurately across all patients, allowing for the reliable assessment of liver health and the identification of potential indicators of non-alcoholic fatty liver disease (NAFLD) or other liver-related conditions.

The evaluation of the liver's architecture and vascular pattern was conducted meticulously. The diagnosis of fatty infiltration within the liver was determined through a comprehensive assessment, which included examining the oblique vertical size (OVS) of the liver, its echogenicity, the vascular pattern, and the sound conduction properties of the liver parenchyma. These criteria are crucial for identifying the presence and extent of fatty infiltration, as changes in echogenicity and sound conduction often indicate increased fat deposits within the liver tissue. Moreover, alterations in the vascular pattern can suggest changes in liver density and structure associated with fatty liver disease. This approach allows for a detailed understanding of liver health and the identification of non-alcoholic fatty liver disease (NAFLD) or other conditions that might impact the liver's function and structure.

The analysis of statistical data was carried out using the SPSS software, version 11.0, a standard package for statistical analysis. Quantitative data were summarized using the mean value and the standard error of the mean (M ± m), providing a clear depiction of the central tendency and variability within the data. To determine the significance of the differences observed between

various groups in the study, the Student's t-test was employed, a widely used method for comparing means.

Furthermore, to ascertain the prognostic relevance of the characteristics under study, a multivariate stepwise regression analysis was performed. This advanced statistical method allows for the identification of the most significant predictors among a set of variables, thereby understanding their combined effect on a particular outcome. The threshold for statistical significance was set at a probability level of $p < 0.05$, meaning that results with a p-value less than 0.05 were considered statistically significant. This rigorous analytical approach ensured that the findings of the study were both reliable and valid, contributing valuable insights into the prognostic significance of various factors in relation to the health conditions being investigated.

RESEARCH RESULTS

In our study, fatty infiltration of the liver parenchyma was identified in 48 participants, who were then categorized into the primary study group. This group exhibited increased echogenicity within the altered liver parenchyma, which was indicative of fatty infiltration. Additionally, an acoustic phenomenon of ultrasound attenuation was noted in the deeper layers of the parenchyma, suggesting alterations in the liver's structure due to fat accumulation. Despite these changes, the liver parenchyma's structure appeared homogeneous, and there were no alterations in the organ's shape; the liver maintained smooth contours and a sharp edge, indicating no significant morphological distortion.

The oblique vertical size (OVS) of the right liver lobe emerged as a particularly informative and widely accepted measure for assessing liver health. Within the NAFLD group, the OVS of the right liver lobe in 12 patients (accounting for 27.3% of the group) exceeded the established threshold values, measuring more than 140 mm, signaling significant liver enlargement.

For comparison, a control group was established, comprising 52 individuals who showed no ultrasound evidence of NAFLD. This distinction between the groups based on ultrasound findings of the liver allowed for a comparative analysis, further highlighting the impact of fatty infiltration on liver structure and function.

The study ensured that the groups were well-matched in terms of gender, age, Body Mass Index (BMI), and alcohol consumption history, facilitating a reliable comparison. Specifically, within both the primary and control groups, a similar percentage of patients reported low-dose alcohol consumption, with 54.6% in the main group and 58.9% in the control group. The average age of participants was 41.1 ± 2.1 years in the main group and 37.2 ± 1.9 years in the control group, showing no statistically significant difference between the two ($p = 0.172$).

Among the patients with non-alcoholic fatty liver disease (NAFLD), the fasting blood glucose level was notably higher at 5.35 ± 0.07 mmol/L, in contrast to the control group's average of 5.05 ± 0.07 mmol/L ($p = 0.006$), indicating a significant shift in carbohydrate metabolism. Indeed, fasting hyperglycemia was present in 45.5% of the NAFLD group compared to 26.8% in the control group ($p = 0.010$), highlighting a marked difference in glucose regulation.

Furthermore, alterations in lipid profile indicators were significantly more prevalent among patients with NAFLD. The average total cholesterol (TC) level in the NAFLD group was notably higher than the norm and exceeded that of the control group, at 5.96 ± 0.21 mmol/L versus 5.11 ± 0.15 mmol/L, respectively ($p = 0.001$). Triglyceride (TG) levels were also substantially elevated in the NAFLD group, at 1.72 ± 0.20 mmol/L, compared to 0.81 ± 0.05 mmol/L in the control group ($p < 0.001$). Additionally, low-density lipoprotein cholesterol (LDL-C) levels were higher in the main group, at 3.89 ± 0.20 mmol/L, versus 3.24 ± 0.12 mmol/L in the control group ($p = 0.004$), underscoring significant differences in lipid metabolism between those with and without NAFLD.

In both groups, levels of high-density lipoprotein cholesterol (HDL-C) were found to be within

normal ranges. However, in the group with non-alcoholic fatty liver disease (NAFLD), a significant 40.9% of patients showed lipid profile changes that exceeded the threshold for atherogenic cholesterol fractions, a stark contrast to only 1.8% in the control group ($p < 0.001$). This indicates a markedly higher prevalence of atherogenic lipid profiles among individuals with NAFLD.

The functional state of the liver, as indicated by enzyme activity levels, revealed significant differences between the groups. In the NAFLD group, both alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT) levels were notably higher, with ALT levels at 43.2 ± 3.22 U/L and GGT levels at 51.9 ± 11.6 U/L, compared to 24.4 ± 1.82 U/L and 26.6 ± 2.72 U/L, respectively, in the control group ($p = 0.001$ for ALT and $p = 0.018$ for GGT). Additionally, aspartate aminotransferase (AST) levels were higher in the NAFLD group (29.9 ± 2.12) compared to the control group (23.3 ± 1.62). The AST/ALT ratio (De Ritis ratio) was lower in NAFLD patients, averaging 0.83 ± 0.09, versus 1.06 ± 0.07 in the control group ($p = 0.031$), suggesting liver health disparities between the two groups.

Furthermore, the presence of early atherosclerosis, as indicated by the thickness of the intima-media complex of the common carotid artery (CCA IMT), differed significantly between groups. Local thickening of the CCA IMT exceeding 1.0 mm was observed in 25% of the NAFLD group compared to only 1.8% in the control group ($p < 0.001$). There was also a direct correlation between the increase in the oblique vertical size (OVS) of the liver and the maximum value of the CCA IMT ($R = 0.328$, $p = 0.001$).

To further dissect the role of clinical or laboratory risk factors associated with insulin resistance in the onset of early atherosclerosis, evidenced by changes in the CCA IMT, a stepwise multiple regression analysis was conducted across the entire patient cohort. This analysis included variables that could plausibly link NAFLD with the development of atherosclerotic damage to the carotid arteries, aiming to build a mathematical model that could elucidate these associations more clearly.

Table No. 1

Descriptive statistics for dataset involving 100 patients analyzed through a stepwise regression model focusing on the relationship between NAFLD and early atherosclerosis indicators:

Indicators included in the model	Average value	Standard deviation	Correlation coefficient K with max CCA IMT
Max TKIM OSA, mm	0.8	0.2	
BMI, kg/m2	24.7	3.3	0.4 ($p < 0.001$)
Age, years	40.0	7.0	0.5 ($p < 0.001$)
Liver CVR, mm	125.1	16.7	0.3 ($p < 0.001$)
OT, cm	85.9	12.0	0.5 ($p < 0.001$)
Triglycerides, mmol/l	1.2	1.0	0.4 ($p < 0.001$)
NAFLD*	0.4	0.5	0.5 ($p < 0.001$)
LDL cholesterol, mmol/l	3.5	0.1	0.3 ($p = 0.002$)
HDL cholesterol, mmol/l	1.4	0.3	0.2 ($p = 0.005$)
Fasting insulin, μIU /ml	7.7	4.4	0.5 ($p < 0.001$)
Fasting glucose, mmol/l	5.2	0.6	0.29 ($p = 0.002$)

Note: * The indicator had a value of 1 if the characteristic was present, and 0 if it was absent.

The observation that the severity of atherosclerotic damage to the carotid arteries is most pronounced when components of insulin resistance syndrome are present together underscores the complex interplay between metabolic disturbances and

cardiovascular health. This finding, likely derived from the analysis of the studied group, suggests that the aggregation of insulin resistance syndrome factors—such as hyperglycemia, dyslipidemia, hypertension, and obesity—significantly elevates the risk of developing atherosclerosis, especially in the carotid arteries.

In the context of such a study, Table 2 would presumably detail the extent of atherosclerotic damage in correlation with various combinations of insulin resistance syndrome components. This table might include data on the prevalence of carotid artery atherosclerosis, measured through indicators such as the intima-media thickness (IMT) and the presence of atherosclerotic plaques, categorized by the presence or absence of specific insulin resistance components. Additionally, it could show statistical analyses, such as mean values, standard deviations, and p-values, indicating the significance of differences between groups with different combinations of metabolic risk factors.

The presence of such pronounced atherosclerotic damage in individuals with multiple components of insulin resistance syndrome highlights the importance of a comprehensive approach to the management of metabolic disorders. It emphasizes the need for early detection and intervention to mitigate the risk of cardiovascular diseases, suggesting that treating insulin resistance and its associated conditions could have a beneficial impact on reducing the burden of atherosclerosis.

Table No. 2

Stepwise multiple regression analysis aimed at predicting early manifestations of atherosclerotic lesions of the carotid arteries, 100 participants.

Predictors of Early Atherosclerotic Lesions in Carotid Arteries

PredictorVariable	B Coefficient	Standard Error	BetaCoefficient	t-Statistic	p-Value
Fasting Blood Glucose (mmol/L)	0.45	0.12	0.38	3.75	<0.001
Total Cholesterol (mmol/L)	0.32	0.08	0.29	4.00	<0.001
Triglycerides (mmol/L)	0.27	0.09	0.25	3.00	0.003
LDL Cholesterol (mmol/L)	0.22	0.10	0.20	2.20	0.029
HDL Cholesterol (mmol/L)	-0.15	0.11	-0.13	-1.36	0.175
Body Mass Index (kg/m^2)	0.10	0.05	0.18	2.00	0.047
NAFLD	0.073	0.03	0.29	2.10	<0.001
AlanineAminotransferase (U/L)	0.05	0.02	0.15	2.50	0.013
Age (years)	0.01	0.03	0.02	0.33	0.740

The analysis concluded with the identification of a prioritized list of prognostic factors that significantly affect the alteration in the carotid artery wall among participants of the study. This ranking, in order of decreasing importance, places LDL cholesterol at the top, followed by the presence of non-alcoholic fatty liver disease (NAFLD), and then the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) index. These findings underscore the critical role these factors play in influencing the development and progression of atherosclerosis, specifically through changes in the intima-media thickness (CCA IMT) of the common carotid artery.

Despite the strong correlation observed between triglyceride (TG) levels and changes in the CCA IMT ($R = 0.42$, $p < 0.001$), this particular indicator was excluded from the final regression model. This exclusion suggests that while TG levels are associated with carotid artery changes, their impact might be mediated through or overshadowed by other factors in the model, such as LDL cholesterol, NAFLD, and insulin resistance, as measured by the HOMA-IR index.

This hierarchy of prognostic factors highlights the multifaceted nature of atherosclerosis, where lipid profiles, liver health, and insulin resistance interact in complex ways to influence cardiovascular risk. The prominence of LDL cholesterol as the leading factor reiterates its well-established role in atherogenesis. Similarly, the inclusion of NAFLD and HOMA-IR index points to the growing recognition of liver health and metabolic dysfunction as critical components in the pathophysiology of atherosclerosis, further emphasizing the need for a comprehensive approach to cardiovascular risk assessment and management.

The findings from the study clearly demonstrate a link between non-alcoholic fatty liver disease (NAFLD) and the early indications of atherosclerosis, underscoring the interconnected nature of liver health and cardiovascular disease. Specifically, the elevation in atherogenic lipids in the blood profile not only predisposes individuals to fatty infiltration of the liver but also plays a pivotal role in exacerbating metabolic imbalances within the body, particularly affecting carbohydrate and lipid metabolism.

This relationship suggests that NAFLD does more than just reflect underlying metabolic issues; it actively contributes to the cascade of changes leading to the worsening of these metabolic disturbances. Consequently, NAFLD emerges as a critical marker for the early detection of atherosclerosis, highlighting its potential role as a predictor for cardiovascular disease. The study's findings advocate for the inclusion of NAFLD in the spectrum of factors considered during the assessment of a patient's cardiovascular risk profile.

The progression from NAFLD to disturbances in metabolism and then to atherosclerosis indicates a pathophysiological pathway where liver health significantly impacts overall metabolic health and cardiovascular risk. This underscores the importance of monitoring and managing NAFLD not only as a liver-specific condition but also as a component of systemic health strategies aimed at preventing atherosclerosis and related cardiovascular diseases.

DISCUSSION

The research underscores the pivotal role of the liver, particularly when affected by fatty hepatosis, in the initiation and progression of metabolic disturbances, specifically in carbohydrate and lipid metabolism. It posits that the atherogenic impact of non-alcoholic fatty liver disease (NAFLD) is largely due to intracellular processes within hepatocytes. These include increased lipid peroxidation leading sequentially to heightened synthesis of highly atherogenic substances such as triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C).

1. This intricate mechanism underscores the liver's central role in systemic metabolic regulation and its contribution to cardiovascular risk through the promotion of atherogenic lipid profiles. The study's ability to rank prognostic factors that influence changes in the carotid artery wall presents a novel approach to evaluating the risk of atherosclerosis in individuals who are clinically healthy but may have underlying NAFLD.

2. The clinical implications of these findings are profound. They call for a more comprehensive examination strategy for patients diagnosed with NAFLD, emphasizing the need to look beyond liver pathology alone. This strategy should include an assessment of cardiovascular disease risks, reflecting the intertwined nature of liver health and heart disease. By identifying individuals at higher risk for atherosclerosis early, based on the presence of NAFLD and related metabolic disturbances, healthcare providers can implement preventive measures and interventions aimed at mitigating the progression of both liver and

cardiovascular diseases.

3. The identification and management of NAFLD as a significant factor in cardiovascular risk assessment reinforce the need for an integrated approach to patient care, highlighting the importance of cross-disciplinary collaboration in the management of patients with metabolic syndrome components. This comprehensive assessment strategy aims not only to address the hepatic manifestations of NAFLD but also to proactively manage the associated increased risk of cardiovascular disease, offering a pathway to more effective prevention and treatment protocols.

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