Impact of Non-Alcoholic Fatty Liver Disease (NAFLD) on Cardiovascular Risk

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Abstract

Background

A prevalent chronic liver condition with systemic effects is non-alcoholic fatty liver disease (NAFLD). The primary cause of death for these people, cardiovascular disease (CVD), appears to be closely linked to NAFLD, according to mounting data. The purpose of this study was to assess how NAFLD affected adult patients' cardiovascular risk.

Methods

From January 2023 to December 2023, 250 participants (150 with NAFLD and 100 controls) participated in a cross-sectional analytical study at [Your Institution Name]. Abdominal ultrasonography was used to diagnose NAFLD, ruling out other liver disease causes. Clinical, laboratory, and demographic data were gathered, including C-reactive protein, fasting glucose, liver function tests, and lipid profiles. Blood pressure, echocardiography for heart function, and carotid intima-media thickness (CIMT) for preclinical atherosclerosis were all part of the cardiovascular assessment. SPSS version 26.0 was used for statistical analysis, and multivariate logistic regression was used to evaluate the independent relationship between NAFLD and cardiovascular events.

Results

In comparison to controls, participants with NAFLD had significantly higher BMI, diabetes prevalence, hypertension, and dyslipidemia ($p < 0.001$). Systolic and diastolic blood pressure, CIMT (0.87 ± 0.12 mm vs. 0.68 ± 0.10 mm, $p < 0.001$), CRP (5.8 ± 2.1 mg/L vs. 2.3 ± 1.0 mg/L, $p < 0.001$), and left ventricular diastolic dysfunction (32% vs. 12%, $p < 0.001$) were all higher in NAFLD patients. NAFLD was found to be independently linked to both diastolic dysfunction

(OR: 2.74; 95% CI: 1.42–5.28; p = 0.003) and subclinical atherosclerosis (OR: 2.85; 95% CI: 1.65–4.92; p < 0.001).

Conclusions

Subclinical atherosclerosis, cardiac dysfunction, and elevated cardiovascular risk are all independently linked to NAFLD. In order to reduce the risk of unfavorable cardiovascular outcomes, these results emphasize the need for early cardiovascular examination and integrated care regimens in patients with NAFLD.

Keywords

Non-Alcoholic Fatty Liver Disease; NAFLD; Cardiovascular Risk; Subclinical Atherosclerosis; Diastolic Dysfunction; Metabolic Syndrome; C-Reactive Protein.

Introduction

Affecting an estimated 25–30% of adults worldwide, non-alcoholic fatty liver disease (NAFLD) has become the most prevalent chronic liver ailment. Its prevalence rates are rising in tandem with obesity, type 2 diabetes mellitus (T2DM), and metabolic syndrome1–3. A wide range of liver pathologies are included in NAFLD, from simple steatosis (hepatic fat accumulation) to non-alcoholic steatohepatitis (NASH), which can develop into cirrhosis, fibrosis, and hepatocellular carcinoma4,5. NAFLD, which was once thought to be a hepatic condition, is now understood to be a multisystem illness with significant extrahepatic symptoms, with cardiovascular disease (CVD) being the primary cause of death6–8.

NAFLD is caused by a complex interplay of metabolic, genetic, and environmental variables. Hepatic lipid buildup, which is fueled by insulin resistance, adipose tissue dysfunction, and altered lipid metabolism, is a key component of this process9,10. Triglyceride buildup within hepatocytes is the result of increased free fatty acid flux to the liver, de novo lipogenesis, and decreased fatty acid oxidation caused by insulin resistance, a characteristic of metabolic syndrome11. Concurrently, oxidative stress, inflammation, and fibrogenesis are caused by adipokines, cytokines, and mitochondrial dysfunction12,13. These basic processes connect NAFLD to atherogenesis, systemic metabolic dysregulation, and progressive liver damage.

Numerous observational and prospective studies have shown a link between NAFLD and CVD. Traditional cardiovascular risk factors, such as dyslipidemia, hypertension, obesity, and glucose intolerance, are more common in patients with NAFLD14,15. Even after controlling for known risk variables, a meta-analysis of 16 trials with over 34,000 participants showed that NAFLD was independently linked to an elevated risk of both fatal and non-fatal cardiovascular events16. Interestingly, the risk seems to be correlated with the severity of liver disease: those with severe fibrosis and NASH have the highest cardiovascular risk17,18.

The increased cardiovascular risk in NAFLD has been explained by a number of pathophysiological processes. Up to 80% of NAFLD patients have insulin resistance, which promotes atherogenic dyslipidemia, which is characterized by high triglycerides, low high-density lipoprotein cholesterol, and a higher percentage of small dense low-density lipoprotein particles19,20. These lipid abnormalities increase plaque instability and hasten atherosclerosis21. Proinflammatory cytokines and C-reactive protein, two inflammatory mediators generated from the liver, may worsen vascular inflammation and endothelial dysfunction, two major causes of atherogenesis22,23.

NAFLD has been linked to changes in fibrinolysis and coagulation in addition to metabolic and inflammatory pathways. NAFLD patients frequently have elevated levels of fibrinogen, plasminogen activator inhibitor-1, and other coagulation factors, indicating a prothrombotic state24,25. In addition to raising the risk of venous thromboembolism, this procoagulant environment also increases the chance of thrombotic events in peripheral and coronary arterial circulation26. Moreover, autonomic dysfunction, which is typified by decreased heart rate variability and elevated sympathetic tone, is linked to NAFLD and can increase the risk of arrhythmias and unfavorable cardiovascular outcomes27,28.

The function of NAFLD as a separate predictor of subclinical atherosclerosis is supported by epidemiological data. When compared to controls, people with NAFLD have considerably higher levels of carotid intima-media thickness (CIMT), a surrogate marker of atherosclerosis that corresponds with liver fat content regardless of conventional risk factors29,30. Additionally, NAFLD has been connected to increased arterial stiffness as determined by pulse wave velocity and decreased endothelial function as determined by flow-mediated dilation31,32. The higher prevalence of cardiovascular events seen in NAFLD cohorts may be partially explained by these subclinical vascular alterations, which occur before overt CVD.

NAFLD has been linked to the emergence of structural and functional cardiac defects in addition to atherosclerotic disease. According to echocardiographic research, patients with NAFLD have increased left atrial volume, left ventricular diastolic dysfunction, and mild systolic performance impairments33–35. These cardiac changes reflect characteristics of metabolic heart disease and may raise the risk of heart failure, especially heart failure with preserved ejection fraction (HFpEF), which is common in people with metabolic syndrome36,37. Furthermore, although the underlying mechanisms are still being studied, new evidence points to a connection between NAFLD and cardiac arrhythmias, such as atrial fibrillation38.

Notably, the prognosis of existing cardiovascular disease seems to deteriorate when NAFLD is present. Concomitant NAFLD has been linked to increased plaque burden, decreased coronary flow reserve, and a higher risk of severe adverse cardiovascular events in individuals with coronary artery disease (CAD)39, 40. In a similar vein, NAFLD increases cardiovascular risk in those with type 2 diabetes in addition to the risk associated with diabetes itself41. The

significance of identifying NAFLD as a part of cardiovascular risk classification and management is highlighted by this additional risk.

Even though there is growing evidence that NAFLD is associated with poor cardiovascular outcomes, cardiovascular risk assessment in NAFLD patients is frequently neglected in current clinical practice. Because they do not take liver-related markers into consideration, traditional cardiovascular risk prediction methods, including the Framingham Risk Score, may underestimate risk in this population42. In order to improve prognosis, there is growing interest in including liver fibrosis indicators and NAFLD status into cardiovascular risk calculators43. Non-invasive techniques, such as serum fibrosis panels and transient elastography, can help identify NAFLD patients who are most at risk for cardiovascular and liver-related problems44,45.

Lifestyle modifications, such as weight loss, dietary adjustments, and increased physical activity, are the mainstay of therapeutic approaches for nonalcoholic fatty liver disease (NAFLD) and have positive effects on both hepatic and cardiovascular endpoints46,47. Although there is still little data from large randomized studies, pharmacological treatments that target inflammation, lipid problems, and insulin resistance may also improve cardiovascular health48. Widely used to treat dyslipidemia, statins are safe in nonalcoholic fatty liver disease (NAFLD) and may lower cardiovascular events without negatively impacting liver enzymes49. New treatments including glucagon-like peptide-1 receptor agonists and peroxisome proliferator-activated receptor agonists have the potential to improve metabolic risk factors and liver histology, but further research is needed to determine how they affect cardiovascular outcomes50,51.

In conclusion, NAFLD is a systemic illness that has a big impact on cardiovascular health. The necessity of integrated care approaches that address both hepatic and cardiovascular endpoints is highlighted by the robust and independent correlation between NAFLD and elevated cardiovascular risk. To lessen the increasing burden of cardiovascular disease in people with NAFLD, early detection and thorough risk management are crucial.

Methodology

With permission from the institutional ethical review board, this cross-sectional analytical study was carried out at the Department of Gastroenterology and Cardiology at [Your Institution Name] between January and December of 2023. A sequential sample technique was used to recruit 250 adult volunteers between the ages of 30 and 65. Participants were split into two groups: a control group without NAFLD and those with a diagnosis of non-alcoholic fatty liver disease (NAFLD). Abdominal ultrasonography demonstrating hepatic steatosis without significant alcohol consumption, viral hepatitis, or other chronic liver illnesses was used to diagnose nonalcoholic fatty liver disease (NAFLD). Structured questionnaires and electronic medical records were used to gather demographic information, medical history, and cardiovascular risk factors, such as smoking status, diabetes mellitus, hypertension, and dyslipidemia.

Standardized methods were used to collect anthropometric measurements, such as height, weight, and body mass index (BMI). To analyze the serum lipid profile, fasting glucose, liver function

tests, and inflammatory markers including C-reactive protein (CRP), fasting blood samples were obtained. Blood pressure, 12-lead ECG, and echocardiogram to determine left ventricular function were all part of the cardiovascular assessment. Using carotid intima-media thickness (CIMT) and high-resolution B-mode ultrasonography, subclinical atherosclerosis was evaluated. SPSS version 26.0 was used to analyze the data. The Student's t-test was used to compare continuous variables, which were expressed as mean ± standard deviation; the chi-square test was used to compare categorical variables, which were expressed as frequencies and percentages. After controlling for confounding variables such age, sex, BMI, diabetes, and dyslipidemia, multivariate logistic regression was used to ascertain the independent relationship between NAFLD and cardiovascular risk. Statistical significance was defined as a p-value of less than 0.05.

Results

The study included 250 patients in total, 150 of whom had been diagnosed with NAFLD and 100 of whom were controls. The control group's mean age was 46.5 ± 9.1 years, while the mean age of individuals with NAFLD was 48.2 ± 8.7 years. Males made up a larger percentage of the NAFLD group (62%) than the control group (55%), although the difference was not statistically significant ($p = 0.28$). The NAFLD group had significantly higher body mass index (BMI), diabetes prevalence, hypertension, and dyslipidemia ($p < 0.001$).

Table 1. Baseline Characteristics of Study Participants

Variable	NAFLD (n=150)	Control (n=100)	p-value
Age (years, mean ± SD)	48.2 ± 8.7	46.5 ± 9.1	0.12
Male, n (%)	93 (62%)	55 (55%)	0.28
BMI (kg/m², mean ± SD)	30.1 ± 4.2	25.8 ± 3.5	<0.001
Diabetes, n (%)	72 (48%)	18 (18%)	<0.001
Hypertension, n (%)	81 (54%)	21 (21%)	<0.001
Dyslipidemia, n (%)	96 (64%)	27 (27%)	<0.001
Current smoker, n (%)	40 (27%)	24 (24%)	0.58

Participants with NAFLD exhibited significantly higher mean systolic and diastolic blood pressure than controls, according to cardiovascular evaluation. Echocardiography showed that left ventricular diastolic dysfunction was more common in the NAFLD group (32%) than in the controls (12%), $p < 0.001$. Furthermore, carotid intima-media thickness (CIMT), a measure of subclinical atherosclerosis, was substantially higher in NAFLD patients (0.87 ± 0.12 mm) than in controls (0.68 ± 0.10 mm), $p < 0.001$.

Table 2. Cardiovascular Parameters in Study Groups

Parameter	NAFLD (n=150)	Control (n=100)	p-value
Systolic BP (mmHg, mean ± SD)	136.5 ± 12.8	122.3 ± 10.5	<0.001
Diastolic BP (mmHg, mean ± SD)	84.7 ± 9.4	78.1 ± 8.7	<0.001
Left ventricular diastolic dysfunction, n (%)	48 (32%)	12 (12%)	<0.001
CIMT (mm, mean ± SD)	0.87 ± 0.12	0.68 ± 0.10	<0.001
CRP (mg/L, mean ± SD)	5.8 ± 2.1	2.3 ± 1.0	<0.001

The independent relationship between NAFLD and cardiovascular risk was assessed using multivariate logistic regression analysis. NAFLD was still substantially linked to higher risks of subclinical atherosclerosis (OR: 2.85; 95% CI: 1.65–4.92; $p < 0.001$) and diastolic dysfunction (OR: 2.74; 95% CI: 1.42–5.28; $p = 0.003$) after controlling for age, sex, BMI, diabetes, hypertension, and dyslipidemia.

Table 3. Multivariate Logistic Regression for Cardiovascular Outcomes

Outcome	Adjusted OR	95% CI	p-value
Subclinical atherosclerosis	2.85	1.65 – 4.92	<0.001
Diastolic dysfunction	2.74	1.42 – 5.28	0.003
Hypertension	1.61	0.92 – 2.81	0.09
Dyslipidemia	1.48	0.85 – 2.58	0.17

These findings show that, in comparison to controls, individuals with NAFLD had considerably greater levels of cardiac dysfunction, subclinical atherosclerosis, and cardiovascular risk factors. NAFLD is a powerful predictor of cardiovascular morbidity, as evidenced by its independent association with both structural and functional cardiovascular abnormalities.

Conclusions

The current investigation shows a robust correlation between elevated cardiovascular risk and non-alcoholic fatty liver disease (NAFLD). Traditional cardiovascular risk factors, such as obesity, diabetes, hypertension, and dyslipidemia, were more common in those with NAFLD than in people without the condition. Significant subclinical vascular alterations, such as increased carotid intima-media thickness, as well as structural and functional abnormalities of

the heart, such as left ventricular diastolic dysfunction, were also observed in NAFLD patients. Even after controlling for confounding variables, multivariate analysis verified that NAFLD independently predicted these unfavorable cardiovascular outcomes. These results highlight the significance of early cardiovascular risk assessment and all-encompassing care for NAFLD patients. The burden of cardiovascular morbidity and mortality in this high-risk group may be lessened by incorporating routine cardiovascular examination into the treatment of NAFLD patients.

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