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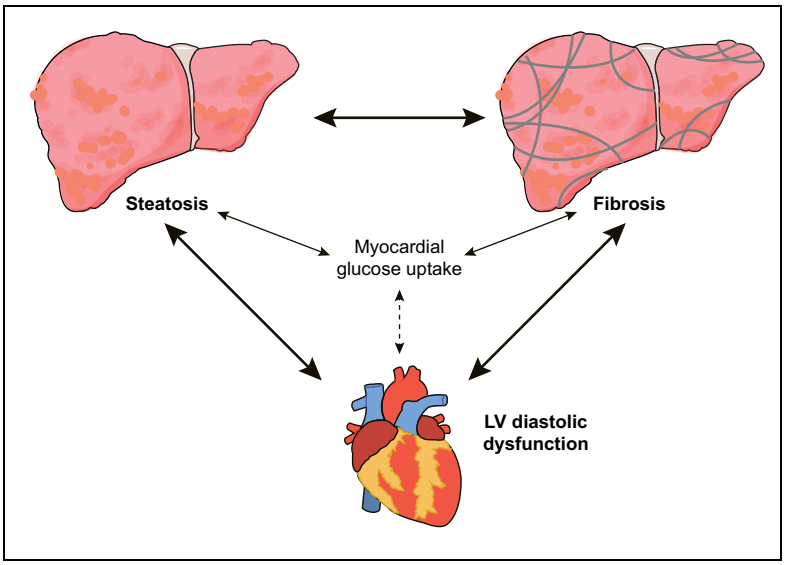
Association of non-alcoholic steatohepatitis with subclinical myocardial dysfunction in non-cirrhotic patients

Graphical abstract



Highlights

- Patients with NAFLD had alterations in cardiac remodeling.
- Hepatic steatosis and fibrosis are associated with diastolic heart dysfunction.
- Those without NAFLD were more likely to have higher myocardial glucose uptake.
- Hepatic fibrosis was correlated with decreased myocardial glucose uptake.

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Lay summary

Non-alcoholic fatty liver disease is associated with an increased risk of cardiovascular disease. More severe forms of non-alcoholic fatty liver disease, where hepatic fibrosis occurs, are linked to increased mortality. In this study, we have shown that hepatic steatosis and fibrosis are associated with subclinical myocardial dysfunction. This association is linked to altered myocardial glucose uptake.

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Association of non-alcoholic steatohepatitis with subclinical myocardial dysfunction in non-cirrhotic patients

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See Editorial, pages 640–642

Background & Aims: Non-alcoholic fatty liver disease (NAFLD) is associated with increased cardiovascular risk. Among categories of NAFLD, hepatic fibrosis is most likely to affect mortality. Myocardial function and its energy metabolism are tightly linked, which might be altered by an insulin resistant condition such as NAFLD. We investigated whether hepatic steatosis and fibrosis were associated with myocardial dysfunction relative to myocardial glucose uptake.

Methods: A total of 308 patients (190 without NAFLD, 118 with NAFLD) were studied in a tertiary care hospital. Myocardial glucose uptake was evaluated at fasted state using [^{18}F]-fluorodeoxyglucose-positron emission tomography (^{18}FDG-PET). Hepatic steatosis and fibrosis were assessed by transient liver elastography (Fibroscan®) with controlled attenuation parameter, which quantifies hepatic fat and by surrogate indices (fatty liver index and NAFLD fibrosis score). Cardiac structure and function were examined by echocardiogram.

Results: Compared to those without NAFLD, patients with NAFLD had alterations in cardiac remodeling, manifested by increased left ventricular mass index, left ventricular end-diastolic diameter, and left atrial volume index (all p <0.05). Hepatic steatosis was significantly associated with left ventricular filling pressure (E/e' ratio), which reflects diastolic dysfunction (p for trend <0.05). Those without NAFLD were more likely to have higher myocardial glucose uptake compared to those with NAFLD. Significant hepatic fibrosis was also correlated with diastolic dysfunction and impaired myocardial glucose uptake. Using multivariable linear regression, E/e' ratio was independently associated with hepatic fibrosis (standardized β = 0.12 to 0.27; all p <0.05). Association between hepatic steatosis and E/e' ratio was also significant (standardized β = 0.10 to 0.15; all p <0.05 excluding the model adjusted for adiposity).

Conclusions: Hepatic steatosis and fibrosis are significantly associated with diastolic heart dysfunction. This association is linked with myocardial glucose uptake evaluated by ^{18}FDG-PET.

Lay summary: Non-alcoholic fatty liver disease is associated with an increased risk of cardiovascular disease. More severe forms of non-alcoholic fatty liver disease, where hepatic fibrosis occurs, are linked to increased mortality. In this study, we have shown that hepatic steatosis and fibrosis are associated with subclinical myocardial dysfunction. This association is linked to altered myocardial glucose uptake.

Introduction

Non-alcoholic fatty liver disease (NAFLD) has become a common metabolic liver disease worldwide, with an estimated prevalence ranging from 25% to 45% in Asian as well as Western countries.[1,2] NAFLD is defined as accumulation of lipids, mainly triglycerides, in ≥5% of hepatocytes with no evidence of excessive alcohol consumption or other secondary causes.[3] The NAFLD spectrum ranges from simple steatosis, a benign disease with absence of hepatic inflammation and fibrosis, to non-alcoholic steatohepatitis (NASH), an aggressive condition that can develop into cirrhosis, hepatocellular carcinoma, and liver-related mortality.[4,5] A recent meta-analysis reported that in patients with NASH, 35% progressed to cirrhosis in an average of seven years, often followed by liver-related complications.[6]

Surprisingly, the most common cause of death in patients with NAFLD is cardiovascular disease, not liver-associated complications.[7] Individuals with NASH showed much higher risk of coronary artery disease-related mortality (12% to 16%)[8,9] compared to those with NAFLD (1% to 3%),[10,11] indicating a dose-dependent relationship between severity of NAFLD and risk of cardiovascular disease mortality. There are several possible mechanisms to explain cross-talk between the heart and liver. Small studies previously demonstrated that fatty liver was associated with insulin resistance in myocardium,[12] altered left

Keywords: Diastolic heart dysfunction; Liver fibrosis; Non-alcoholic fatty liver disease; Obesity; Insulin resistance; Positron emission tomography.
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