

'A fatty liver may result in a broken heart,' according to new research

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Cardiovascular disease (CVD) is primarily the cause of death of patients with nonalcoholic fatty liver disease (NAFLD). The extent to which NAFLD itself, rather than associated conditions such as diabetes, obesity, or atherogenic dyslipidemia, is responsible for increased cardiovascular death has been a matter of debate. In a new study, investigators from the Pitié-Salpêtrière Hospital, Pierre and Marie Curie University conclude that NAFLD is an independent risk factor for atherosclerosis and therefore CVD. Their findings, published in the *Journal of Hepatology*, recommend strict monitoring of cardiovascular health and metabolic complications in patients with NAFLD.

NAFLD is an increasingly common condition in patients with obesity, type 2 diabetes, atherogenic dyslipidemia and arterial hypertension. "Evidence indicates that the fatty and inflamed liver expresses several pro-inflammatory and procoagulant factors, as well as genes involved in accelerated atherogenesis," explained lead investigator Raluca Pais, MD, PhD, of the Pierre and Marie Curie University, INSERM, and the CDR Saint Antoine, Institute of Cardiometabolism and Nutrition (ICAN), Paris, France. "This raises the possibility that the link between NAFLD and cardiovascular mortality might not simply be mediated by shared, underlying, common risk factors, but rather that NAFLD independently contributes to increasing this risk," added senior author Professor Vlad Ratziu, MD, PhD.

Investigators undertook a large retrospective study of close to 6,000 patients referred to the Primary Cardiovascular Prevention Center at

Pitié-Salpêtrière Hospital, Paris between 1995 and 2012 to assess whether NAFLD is incidental to or is the cause of atherosclerosis of the carotid arteries, the major blood vessels in the neck that supply blood to the brain, neck, and face.

All patients were examined using carotid ultrasound with measurement of carotid intima-media thickness and carotid plaques. Using the Fatty Liver Index (FLI) a well-validated biomarker panel, researchers observed that steatosis (fatty liver) is associated with carotid intima-media thickness (C-IMT), a pre-atherosclerotic lesion that predicts cardiovascular events. C-IMT increased proportionally with FLI, and this association was independent of traditional cardiometabolic risk factors.

Steatosis predicted C-IMT better than diabetes or dyslipidemia, after adjustment for metabolic syndrome and cardiovascular risk factors, in 5,671 patients. Long-term follow-up in 1,872 patients after eight years added a further critical piece of information by confirming that patients with fatty liver were more likely to develop carotid plaque over time. Steatosis occurred in 12% and carotid plaques in 23% of these patients. C-IMT increased in patients with steatosis, but did not change in those who stayed free of steatosis. Steatosis at baseline predicted the occurrence of carotid plaques independent of age, sex, type-2 diabetes, tobacco use, and other cardiovascular risk factors.

The team concluded that in patients with metabolic syndrome at risk for cardiovascular events, NAFLD contributes to early atherosclerosis and its progression, independent of traditional cardiovascular risk factors.

"Regardless of the mechanisms involved, the clinical implications are of critical importance since patients at cardiovascular risk presenting with one or more metabolic syndrome characteristics are at even greater risk if they have steatosis," noted Dr. Pais. "We also found that patients with steatosis, but not overweight, not type 2 diabetic, or without arterial

hypertension are at higher risk of developing these complications than individuals without steatosis. This indicates that NAFLD is a precursor of [metabolic syndrome](#). It follows that the diagnosis of steatosis is extremely important and therefore a thorough cardiovascular and metabolic work-up and strict monitoring of CVD or metabolic complications are needed in the clinical management of NAFLD."

"Taken as a whole, the bulk of evidence suggests NAFLD increases cardiovascular risk, although this relationship may be modified by other factors. The clinical implications of this paradigm may alter the decision to institute primary prevention strategies with anti-platelet, lipid lowering or anti-hypertensive drugs. A further intriguing thought is whether fatty liver can be a therapeutic target for cardiovascular risk reduction," commented noted experts Leon Adams, PhD, of the University of Western Australia, and Quentin M. Anstee, PhD, of Newcastle University, UK, in an accompanying editorial.

"Clinicians should be aware of the increased [cardiovascular risk](#) in [patients](#) with NAFLD and consequently screen for conventional [cardiovascular risk factors](#) and use accepted risk calculators to make decisions regarding preventative pharmacotherapy, including statins," emphasized Dr. Adams and Dr. Anstee.

More information: *Journal of Hepatology*, [DOI: 10.1016/j.jhep.2016.02.023](#)

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