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Is fatty liver a risk marker for heart failure?

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Nonalcoholic fatty liver disease (NAFLD) is often an obesity-related condition with an estimated prevalence of 10-30% worldwide and 70-90% among obese persons undergoing bariatric surgery(1). NAFLD is a spectrum of diseases that includes isolated hepatic steatosis, nonalcoholic steatohepatitis (NASH; steatosis plus hepatocyte injury), and fibrosis/cirrhosis that can lead to liver cancer, liver failure and need for transplantation(1). NAFLD is an asymptomatic disease and a diagnosis of exclusion made by documenting the presence of fat on imaging after exclusion of other potential causes of liver fat (e.g., alcohol)(1). In contrast, NASH, which is the more severe form of NAFLD, requires liver biopsy for diagnosis.

Cardiovascular disease (CVD) is the most common cause of death in NAFLD, but whether NAFLD is a driver or merely a passenger biomarker for the development of CVD remains to be determined(1, 2). Several small studies have demonstrated that both imaging-based and biopsy-proven NAFLD are associated with subclinical changes in myocardial structure and function in both children and adults(3, 4, 5). More recently, investigators from the Coronary Artery Risk Development in Young Adults (CARDIA) study, a large prospective population-based cohort of biracial adults, demonstrated that computed tomography (CT)-diagnosed NAFLD in mid-life (mean age 50) was associated with subclinical myocardial remodeling independent of traditional heart failure (HF) risk factors or adiposity measures, providing pathophysiologic insight into the potential link between NAFLD and HF(2). To date, no studies have demonstrated whether biopsy-proven NASH *per se* is associated with differential risk for underlying cardiac abnormalities.

In the current issue, Simon et al. demonstrate for the first time that histological NASH is associated with increased left atrial volume index, left ventricular concentric remodeling and impaired diastolic function among a retrospective cohort of bariatric surgery patients. Adverse structural remodeling of the heart is a pivotal process in the progression of HF(6), and is, therefore, emerging as a therapeutic target in HF prevention(7). Better understanding of potential mediators in the developmental pathways towards abnormal myocardial

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geometry, such as NAFLD/NASH, may offer important potential therapeutic targets in order to prevent and treat the HF epidemic.

Several limitations of the current work warrant mention and temper enthusiasm for the study findings. First, this is a very small single-center retrospective cross-sectional study with only 11 patients having histologic confirmed NASH. Thus, neither temporal nor causal relationships can be inferred. Second, the authors lacked measurement of cardiac hemodynamics. Clinically, patients with obesity and HF often have high cardiac output compared to non-obese patients with HF. The increase in cardiac output associated with obesity may be due to increased body size alone, but other causes of a high output state, most notably subclinical liver disease, may play a role. Cirrhosis is a high cardiac output state(8); thus it is plausible that subclinical hepatic dysfunction, perhaps mediated by NASH, may contribute to high cardiac output in some patients with obesity. Finally, several of the observed differences in echocardiographic parameters (e.g., E:A ratio 1.03 vs. 1.16), though statistically significant, may not represent a clinically significant difference. Thus, the study findings illuminate potential pathophysiologic mechanisms of the association between NASH and HF, and do not demonstrate a direct link to clinical HF. Future prospective study to determine the impact of the full histologic spectrum of NAFLD on a full range of echocardiographic parameters, including hemodynamic measurement, and on subsequent risk for clinical HF is needed.

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References

1. Chalasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, et al. The diagnosis and management of non-alcoholic fatty liver disease: Practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. *Hepatology* (Baltimore, Md). 2012; 55:2005–2023.
2. VanWagner LB, Wilcox JE, Colangelo LA, Lloyd-Jones DM, Carr JJ, Lima JA, et al. Association of nonalcoholic fatty liver disease with subclinical myocardial remodeling and dysfunction: A population-based study. *Hepatology* (Baltimore, Md). 2015
3. Fotbolcu H, Yakar T, Duman D, Karaahmet T, Tigen K, Cevik C, et al. Impairment of the left ventricular systolic and diastolic function in patients with non-alcoholic fatty liver disease. *Cardiol J*. 2010; 17:457–463. [PubMed: 20865675]
4. Karabay CY, Kocabay G, Kalayci A, Colak Y, Oduncu V, Akgun T, et al. Impaired left ventricular mechanics in nonalcoholic fatty liver disease: a speckle-tracking echocardiography study. *Eur J Gastroenterol Hepatol*. 2014; 26:325–331. [PubMed: 24161963]
5. Pacifico L, Di Martino M, De Merulis A, Bezzi M, Osborn JF, Catalano C, et al. Left ventricular dysfunction in obese children and adolescents with nonalcoholic fatty liver disease. *Hepatology* (Baltimore, Md). 2014; 59:461–470.
6. Cohn JN, Ferrari R, Sharpe N. Cardiac remodeling—concepts and clinical implications: a consensus paper from an international forum on cardiac remodeling. *J Am Coll Cardiol*. 2000; 35:569–582. [PubMed: 10716457]
7. Konstam MA, Kramer DG, Patel AR, Maron MS, Udelson JE. Left Ventricular Remodeling in Heart Failure: Current Concepts in Clinical Significance and Assessment. *JACC: Cardiovascular Imaging*. 2011; 4:98–108. [PubMed: 21232712]

8. Mehta PA, Dubrey SW. High output heart failure. QJM. 2009; 102:235–241. [PubMed: 18990720]

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