

Editorial

Nafld and Increased Risk of Cardiac Complications: Myth or Realty?

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EDITORIAL

Nonalcoholic fatty liver disease (NAFLD) is increasingly worldwide and is the most common chronic liver disease observed in clinical practice, affecting approximately one-third of general population and up to 70% of patients with Type 2 diabetes [1]. Over the past decades, accumulating evidence strongly suggests that there is an increased risk of cardiovascular disease (CVD) in patients with NAFLD [1-3]. For example, many epidemiological studies have reported the existence of a link among NAFLD and coronary heart disease (CHD) and other functional and structural myocardial alterations (e.g., left ventricular dysfunction, left ventricular hypertrophy, aortic valve sclerosis, mitral annulus calcification, atrial fibrillation, QTc interval prolongation) in both non-diabetic and diabetic individuals [1-3]. Notably and importantly, these associations seem to be independent of traditional cardiovascular risk factors and features of metabolic syndrome across a wide range of patient populations, including patients with diabetes (for a detailed review on this topic please see reference 2). Moreover, experimental studies have examined the putative biological mechanisms that could explain this association, suggesting that fatty and inflamed liver (especially when nonalcoholic steatohepatitis [NASH] develops) could contribute to the development and progression of atherosclerotic plaques and to structural and electrical remodeling of myocardium through the release into bloodstream of many pro-inflammatory (e.g., c-reactive protein, interleukin-1, interleukin-6, tumor necrosis factor- α), pro-coagulant (e.g., plasminogen activator inhibitor-1, factor VIII, endothelin-1, tumor growth factor- β), pro-oxidant molecules from hepatocytes, Ito cells and Kupffer cells [1-3].

Therefore, in view of these data, several Authors have suggested that NAFLD might have a causal role in the development and progression of CVD and that patient with NAFLD might benefit from more careful surveillance and early treatment interventions to decrease the risk of vascular and cardiac complications.

However, despite all these data and considerations, two important key questions remain still unsolved. Firstly, what is the exact prognostic role of NAFLD in risk stratification for CVD? Secondly, is the prognostic role of NAFLD in the development and

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progression of CHD/cardiac diseases restricted to NASH or is also associated with simple steatosis?

To note, in this field of research, as suggested by Bonora and Targher [1], there are some important problems that complicate the study of the role of NAFLD in the development of cardiac complications and the attempt to answer these important key questions. As shown in **Table 1**, the main challenges are: (a) NAFLD is not a single entity, but encompasses a spectrum of pathological conditions, including simple steatosis, NASH and cirrhosis that may, sometimes, progress to hepatocellular carcinoma (HCC); (b) NAFLD is a diagnosis of exclusion and it is not always easy to exclude patients who have an excessive alcohol consumption (a threshold of 20 g/die for women and 30 g/die for men is conventionally adopted) through medical history

Table 1: Main challenges and certainties in studying causal role of NAFLD in the development of CVD (1).

Challenges	Certainties
NAFLD is not a single entity, but encompasses a spectrum of pathological conditions (simple steatosis, NASH and cirrhosis).	The relationship between NAFLD and CVD seems to be quite consistent in non-diabetic and diabetic individuals.
The exclusion of patients with excessive alcohol consumption is not so easy.	The relationship between NAFLD and the risk of CVD seems to have temporality.
NAFLD is associated with several cardio-metabolic risk factors.	NASH appears to be more strongly associated with CVD than simple steatosis.
Statistical associations do not imply a relationship of cause-effect.	Several possible mechanisms linking NAFLD and CVD have been proposed and are biologically plausible.
Residual or unmeasured confounding factors might weaken the association.	
If the development of CVD can be partly prevented in NAFLD patients through an improvement in the degree of hepatic steatosis, inflammation and fibrosis has not yet been elucidated.	

Abbreviations: CVD, cardiovascular disease; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis.

and specific questionnaires; (c) NAFLD patients have often concurrently several cardio-metabolic risk factors that make the interpretation of data very difficult; (d) statistical associations do not necessarily imply a relationship of cause-effect; (e) residual and/or unmeasured confounding factors could weaken the association; and (f) the reversibility of such association through an improvement of liver steatosis, inflammation and fibrosis has not yet been demonstrated.

Therefore, further large longitudinal studies are urgently needed to establish whether adding NAFLD to the currently available risk scoring systems will improve CHD/CVD risk prediction and more research is necessary to gain mechanistic insights into the pathophysiology linking NAFLD with CHD and cardiac alterations.

Finally, specific mediators of “*hepato-cardiac axis*” need to be further investigated in order to discover innovative drugs and treatments to decrease the risk of vascular and cardiac complications in these patients.

I sincerely hope that the coming years will be very productive in this important and interesting research area in order to establish definitively the pathological role of NAFLD in the development and progression of cardiac complications.

It is time to answer two key questions.

REFERENCES

1. Bonora E, Targher G. Increased risk of cardiovascular disease and chronic kidney disease in NAFLD. *Nat Rev Gastroenterol Hepatol*. 2012; 9: 372-381.
2. Mantovani A, Ballestri S, Lonardo A, Targher G. Cardiovascular Disease and Myocardial Abnormalities in Nonalcoholic Fatty Liver Disease. *Digestive Diseases and Sciences*. 2016; 61: 1246-1267.
3. Targher G, Day CP, Bonora E. Risk of cardiovascular disease in patients with nonalcoholic fatty liver disease. *N Engl J Med*. 2010; 363: 1341-1350.

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