EDITORIAL

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Non-alcoholic Fatty Liver Disease and Cardiovascular Disease: a Close Relationship

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Non-alcoholic fatty liver disease (NAFLD) has become one of the most common chronic liver diseases, affecting about one-quarter of the population worldwide with an ever-increasing incidence [1]. NAFLD is characterized by a clinical picture ranging from simple steatosis with accumulation of fat in the hepatocytes, to non-alcoholic steatohepatitis (NASH) up to cirrhosis. The NAFLD onset and progression are related to the increasing presence of the metabolic syndrome, obesity, sedentary lifestyle and easy access to hypercaloric food [2]. In this context it has been observed that NAFLD is associated with not only liver-related mortality, but also with increased cardiovascular disease (CVD) mortality [3]. In fact, CVD is the main cause of death in NAFLD patients from data observed in the USA, Europe, and Asia [4]. NAFLD patients' evidence a higher CVD risk, according to the Framingham risk score, and different meta-analyses support this association [5-7].

To detect the patients with high risk of NAFLD early, a simple and non-invasive surrogate score for mass screening has been proposed. Fatty liver index (FLI) is an algorithm that combines four variables' measures, including body mass index, waist circumference, triglycerides and gamma-glutamyl-transferase blood levels [8].

Therefore, Chung et al. [9] in the current issue of the Journal of Gastrointestinal and Liver Diseases, examined the association between FLI and CVD risk in a Korean population apparently healthy as determined by the Framingham risk score. The authors found that FLI was positively and independently associated with a Framingham 10-year CVD risk in the general population and suggested that the FLI might be considered an indicator of CVD events.

The relationship between NAFLD and CVD risk is suggested by common pathophysiological pathways [10]. NAFLD is now considered the hepatic border of the metabolic syndrome [11]. Insulin resistance is the central pathogenic step underlying the metabolic syndrome, which can lead the development of a low-grade systemic inflammation [12]. In this context, the subclinical inflammation with the production of cytokines, such as interleukins and interferons, can regulate free radical-mediated processes with the promotion of CVD events mediated by atherosclerosis [13]. Patients with NAFLD also present a more "atherogenic" lipid profile characterized to the decrease of high-density lipoprotein and increased of triglycerides and low-density lipoproteins, that facilitate the early development of atherosclerosis [14]. Also, clinical studies have confirmed a pro-coagulant imbalance in NAFLD patients in close relationship with the severity of the liver disease [15].

These data support the recommendation of both the American Association for the Study for Liver Diseases (AASLD) and the European Association of the Study of the Liver (EASL), to assess and monitor the risk of CVD in patients with NAFLD [16, 17]. Three central questions ongoing NAFLD clinical trials are to be done in the next near future, in particular: 1) when is it indicated to screen CVD in NAFLD patients? 2) how does the severity of liver disease increases the risk in developing CVD? and 3) what is the impact of the association between these two conditions in clinical practice?

The prevention and management of CVD risk factors in subjects with NAFLD could significantly decrease CVD events, morbidity and mortality [10]. Considering these clinical and pathogenetic aspects, the cross-sectional study of Chung et al. [9] found consistent findings on the positive association between FLI and the increased CVD risk in adult populations.

In conclusion, the relationship between NAFLD and CVD remains under investigation. Actually, many challenges are faced by NAFLD patients and by physicians and scholars involved in its management. The deep bidirectional association

between these clinical pictures, warrants clinical intervention to modify the metabolic risk factors in NAFLD patients. NAFLD patients with a high CVD risk assessed by the Framinghan risk score, should undergo a careful screening to detect the possible presence of underlying CVD.

Conflicts of interest: None to declare.

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