

Non-Alcoholic Fatty Liver disease. Who and how to treat to reduce Cardiometabolic Risk

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The prevalence of nonalcoholic fatty liver disease (NAFLD) is increasing world-wide and 25 percent of the general adult population in the world is affected by NAFLD. In Western countries 3 to 10 percent of all children and about 70 percent of obese children are considered to have NAFLD. This increase in the prevalence of NAFLD is accompanying the increasing prevalence of the non-communicable diseases type 2 diabetes, cardiovascular disease, obesity- and type 2 diabetes-associated cancer and advanced liver diseases, such as hepatic cirrhosis and hepatic cancer.

Subjects with NAFLD often are obese and/or have impaired glucose and lipid metabolism with characteristics of metabolically unhealthy normal weight or obesity, insulin resistance, prediabetes and/or type 2 diabetes. Therefore, it remains unclear to what extent specifically the prevention and treatment of NAFLD may reduce morbidity and mortality in these subjects. Furthermore, NAFLD is a very heterogeneous disease, which can be categorized histologically into nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH) and which has a somewhat different risk of progression to advanced stages of liver disease. In addition, the increased cardiometabolic risk in NAFLD varies among these different stages of NAFLD and is very high in the presence of advanced stages of NAFLD, such as NASH with moderate to advanced fibrosis.

Lifestyle intervention is the primary therapeutic approach in NAFLD. However, while a mean weight loss of ~5% considerably reduces liver fat content, more than 10% of weight loss is thought to effectively reduce hepatic inflammation. Finally, even such a large weight loss appears not to considerably improve hepatic fibrosis in most patients with NAFLD. Thus, in addition to the lifestyle intervention, pharmacological intervention becomes necessary in many patients with advanced stages of NAFLD. However, results from pharmacological clinical trials in patients with NAFLD revealed that each agent tested has a broad spectrum of effects in respect to their anti-inflammatory, anti-fibrotic and cardiometabolic efficacy. Thus, a tailored therapeutic approach based on precise phenotyping of the hepatic and cardiometabolic risk is necessary to provide personalized treatment to our patients with NAFLD.