Editorial

The Mediterranean diet and nonalcoholic fatty liver disease in individuals at high cardiovascular risk

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Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in the world, affecting about 30% of the world's adult population (1,2). The disease ranges from simple steatosis (SS) to nonalcoholic steatohepatitis (NASH) (3). The prevalence of NAFLD is higher in patients with cardio metabolic risk and cardiac metabolic conditions are associated with increased risk of cardiovascular disease and type 2 diabetes. It is found in 50% of people with hypertension, 70% of diabetics and 90% of obese people (4). According to the "multiple-hit" theory of insulin resistance, lipotoxicity, nutritional factors, gastrointestinal microbiome, epigenetic and genetic factors are widely involved in the pathogenesis of this disease (5). As a result of obesity, visceral adipose tissue secretes adipokines, such as TNF-α and interleukins, which lead to vascular inflammation and insulin resistance (6). The first physiological event in NAFLD is insulin resistance. The severity of insulin resistance is associated with the severity of liver injury, from benign steatosis to advanced NASH and fibrosis (7).

Lifestyle changes such as nutritional intervention and physical activity are recommended to reduce intrahepatic fat and improve NAFLD (8). The Mediterranean diet (MD) has been shown to reduce the incidence and about 33% risk of mortality rate of cardiovascular disease (7,9). This plant-based diet has a high MUFA to SFA ratio of 30-40% of daily energy (10). MD is a model of consuming fruits and vegetables, olive oil, nuts, whole grains, fish, low-fat dairy products, limited consumption of red meat (7). The protective effects of MD are provided by extra virgin olive oil (EVOO), which contains polyphenol, tocopherol and carotenoids, which increase hepatic steatosis by increasing lipid oxidation and inhibiting lipogenesis (4). It also plays a role in improving NAFLD by improving lipid profiles, insulin resistance and obesity-induced inflammation (4). Olive oil-rich MD reduces liver fat up to 40% in NAFLD patients in clinical trials (3).

In the article published in Journal of Nutrition in issue 11, November 2019, Pintó *et al.* showed that EVOO-rich MD reduced the prevalence of NAFLD in people with high cardiovascular risk (11). This study was performed on a subgroup of PREvenciónconDIeta MEDiterránea (PREDIMED) trials designed in a multicenter, randomized controlled, parallel fashion. The PREDIMED cohort aimed at the effect of MD on primary prevention of cardiovascular disease continued from 2003 to 2011. This study, unlike other interventional studies, provided the same opportunity for long-term follow-up in people with cardiovascular risk under Mediterranean conditions (12).

In the study of Pintó *et al.*, 109 individuals at risk for cardiovascular disease including type 2 diabetes and having at least 3 cardiovascular risk factors but without CVD were included. Subjects were divided into three intervention groups including MD + EVOO receiving EVOO one liter per week, MD + nuts receiving 30 g walnut, almond and hazelnut daily, and control group (advice to reduce all dietary fat) for 3 years. Cardio metabolic risk was similar in all three intervention groups. Hepatic steatosis, evaluated with NMR, was significantly different between the groups (P=0.027) and was 8.8% in the MD + EVOO group compared to 3.33% in the other groups. The ratio of 12

(S)-hydroxyeicosatetraenoic acid (12-HETE) to creatinine indicating inflammatory status and oxidative stress was lower in the MD + EVOO group than in the other two groups. Adherence to diet improved in both MD groups over three years but decreased in the control group (11).

In some clinical trials, the effect of MD on fat loss and weight-independent steatosis has been observed (3,13). In Pintó *et al.* study, the effect of MD + EVOO without energy restriction and no significant reduction changes over three years resulted in NAFLD improvement. Although BMI changes were significant between the two groups with and without steatosis, no clinically significant differences were observed (11). In spite of no significant differences in HOMA-IR among groups, the level of fasting glucose was better to be mentioned and discussed.

Although it is not clear which components of MD are the major responsible for these effects, the beneficial role of polyphenols and EVOO has been reported (14).

Finally, by changing the components of the MD diet, we can see its beneficial effects on steatosis as a major NAFLD criterion, but further studies are needed to identify the mechanism of these effects on other metabolic factors.

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