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## Editorial

# The effect of moderate alcohol consumption on nonalcoholic fatty liver disease

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Nonalcoholic fatty liver disease (NAFLD) has emerged as a major cause of chronic liver disease worldwide since its first description in 1980 by Jurgen Ludwig and colleagues.<sup>1</sup> The global prevalence has increased steadily over the last decade, reaching 25–30%.<sup>2</sup> NAFLD is interlinked with features of metabolic dysfunction including obesity, insulin resistance, type 2 diabetes mellitus, and dyslipidemia.<sup>3</sup> Diagnostic tests such as the fibrosis-4 index, as a first-line test, transient elastography, and blood testing can be used to differentiate high risk subjects in NAFLD patients.<sup>4</sup> The exclusion of significant alcohol consumption (more than 30 g/day in men and 20 g/day in women) is a prerequisite criterion for NAFLD diagnosis. Significant alcohol consumption typically follows the threshold suggested in guidelines of scientific association recommendations,<sup>5,6</sup> and the distinction between NAFLD and alcoholic liver disease relies on patient statements concerning alcohol consumption. This artificial classification is far from perfect because widespread issue of mild to moderate alco-

hol intake exists with metabolic derangements in patients diagnosed with “NAFLD”. The interaction between NAFLD and alcohol consumption has remained controversial over the last few years, in particular, the effects of moderate alcohol consumption on NAFLD is ill-defined.<sup>7</sup>

The definition of moderate alcohol consumption slightly differed from study to study, usually suggested as drinking in excess of the recommended limits for safe alcohol consumption. The safe levels of alcohol consumption suggested by the European Association for the Study of the Liver (EASL) and the American Association for the Study of the Liver (AASLD) are 30 g/day in men and 20 g/day in women, whereas, the Asian Pacific for the Study of the Liver (APASL) proposed a more cautious threshold of <20 g/day and 10 g/day in men and women, respectively.<sup>8,9</sup> However, with regards to the risk for advanced liver disease, prospective studies from the general population suggest that no safe limit of alcohol use exists.<sup>10,11</sup> In addition to alcohol quantity, alcoholic beverage type, drinking patterns, lifestyle patterns, and dietary constituents are important in NAFLD. These confounding factors provide complexity in the interpretation of previous studies.

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There have been some studies suggesting a beneficial effect of moderate alcohol consumption with the occurrence and progression of NAFLD.<sup>12-14</sup> However, most of these studies are cross-sectional studies and therefore cannot address the temporal relationship or causality between moderate alcohol consumption and NAFLD.

Looking at relatively well-characterized longitudinal cohort studies, Ekstedt et al.<sup>15</sup> assessed weekly alcohol consumption at baseline and follow-up. In addition, heavy episodic drinking defined as >60 g/day in men and >48 g/day in women more than once a month was assessed. Although the study group was small (71 participants), they were biopsy-proven NAFLD patients and follow-up histology was investigated on an average of 13.8 years after the initial biopsy. They observed that heavy episodic drinking was independently associated with significant fibrosis progression, suggesting that low levels of alcohol consumption may cause fibrosis progression in NAFLD, especially when the drinking pattern exhibits intermittent ingestion of a significant amount of alcohol. With a similar aim, Ajimera et al. conducted a longitudinal cohort study using a NAFLD population taken from the nonalcoholic steatohepatitis clinical research network (CRN) trials.<sup>16</sup> A total of 285 patients were included in the study, and the changes in NAFLD histology were evaluated using paired liver biopsies collected on an average of 3.9 years later. Modest alcohol consumption (defined as  $\leq 2$  drinks/day) was associated with less improvement in steatosis and aspartate transaminase levels and lower odds of non-alcoholic steatohepatitis resolution compared with consistent nondrinking individuals. In both the Ekstedt and Ajimera studies, 'moderate drinkers' included very low levels of alcohol consumption. Furthermore, a significant number of patients with NASH at baseline was present with this proportion being over 50% in both studies. Therefore, further studies are necessary to clarify the effect of "standardized" moderate alcohol consumption on a general NAFLD population. The study by Chang is valuable as the research meets these requirements. This prospective cohort study was performed in 58,927 young and middle-aged Korean adults with NAFLD and low fibrosis scores who were followed for a median of 4.9 years. Moderate drinkers were defined as 10–29.9 g/

day and 10–19.9 g/day for men and women, respectively. The progression of NAFLD was assessed using noninvasive blood-based markers such as the NAFLD fibrosis score and Fibrosis-4 Index. They demonstrated that moderate alcohol consumption was independently associated with worsening fibrosis markers.<sup>17</sup> There is another longitudinal study using the Finnish National Health Surveys (FINRISK, Health 2000) cohort.<sup>18</sup> Åberg et al.<sup>18</sup> determined that in subjects with fatty liver disease (defined as a fatty liver index  $\geq 60$ ), consuming 10–19 g/day of alcohol in general or 0–9 g/day as nonwine alcoholic beverages increased the risk for future advanced liver disease. Additionally, only among nonsmoking subjects, moderate alcohol consumption was associated with a reduced risk for cardiovascular disease events.

Based on the latest available longitudinal data, any amount of alcohol, even at low levels, cannot be encouraged in NAFLD patients. However, individual susceptibility to alcohol induced liver injury is substantially variable and the alcohol dose required to impact the disease course at individual patient levels may differ. Therefore, further investigations are required to enable individualized counseling regarding alcohol intake for each patient with NAFLD.

### Authors' contribution

Ji-Won Park contributed to write the manuscript. Ki Tae Suk contributed to study concept and revision.

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### Conflicts of Interest

The authors have no conflicts to disclose.

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#### Abbreviations:

NAFLD, nonalcoholic fatty liver disease; EASL, European Association for the Study of the Liver; AASLD, American Association for the Study of the Liver; APASL, Asian Pacific for the Study of the Liver; CRN, clinical research network

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