Editorial

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Comparing the Mortality Risk between Metabolic Dysfunction-Associated Fatty Liver Disease and Non-Alcoholic Fatty Liver Disease

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Non-alcoholic fatty liver disease (NAFLD) comprises a spectrum of diseases ranging from non-alcoholic fatty liver to cirrhosis [1]. Diagnosis of NAFLD is based on exclusion of secondary causes of hepatic steatosis, such as excess alcohol intake, use of steatogenic drugs, viral hepatitis, and autoimmune liver disease [1]. Recently, the nomenclature of NAFLD has been criticized for disregarding the synergistic effects of these components and the involvement of metabolic variables [2]. To address this issue, a group of experts from the European Liver Patients' Association recommended in 2020 metabolic dysfunction-associated fatty liver disease (MAFLD) as a better term for liver disease caused by metabolic dysfunction [3]. A proposed diagnostic criterion for MAFLD was accumulation of liver fat in conjunction with obesity, diabetes mellitus, or metabolic dysfunction indices independent of heterogeneous etiology [3].

The transition from NAFLD to MAFLD has sparked a heated debate about resulting improvement in clinical practice and medication research [4]. Emerging evidence suggests that MAFLD outperforms NAFLD as an indicator of poor clinical manifestations [4,5]. In a Japanese cohort of 765 individuals with fatty liver, those with MAFLD had a stiffer liver than those with NAFLD, as determined by elastography (7.7 kPa vs. 6.8 kPa) and better sensitivity for identifying significant fibrosis (93.9% vs. 73%) [6]. Similarly, an analysis of the Third National Health and Nutrition Examination Survey (NHANES-III) revealed that MAFLD was better than NAFLD at distinguishing high-risk individuals for advanced fibrosis [7]. Notably, MAFLD also seems to better explain the risk of extrahepatic illnesses than NAFLD [5]. According to NHANES-III data, the prevalence of chronic kidney disease (CKD) was greater when MAFLD criteria were applied instead of NAFLD criteria [8]. In Korea and Japan, risk of CKD was greater in patients with MAFLD than those with hepatic steatosis but no metabolic dysfunction [9,10]. In addition, MAFLD was able to identify more people with impaired lung function or colorectal adenoma than NAFLD [11,12].

Mortality is clinically the most significant of many outcome factors. Particularly, cardiovascular complications are the leading cause of mortality in individuals with MAFLD [13]. Previous analyses of NHANES-III data reported greater mortality with MAFLD compared to NAFLD [14,15]. MAFLD was related with a 17% increased risk of all-cause mortality over a median follow-up period of 23 years, whereas NAFLD was not associated with an increased risk [14]. The cumulative incidence of all-cause mortality was significantly higher in the MAFLD-only group (26.2%) compared to patients with both NAFLD and MAFLD (21.1%) and the NAFLD-only group (10.6%) [15]. Similar results were reported for deaths due to cardiovascular disease and other causes [14,15]. Nevertheless, more recent data are needed given that the NHANES-III dataset was collected between 1988 and 1994 [14,15]. Meanwhile, a population-based cohort study of the National Health Insurance Service (NHIS) in Korea revealed that those with only

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MAFLD had a greater risk of incident cardiovascular disease than those with only NAFLD (1.43 vs. 1.09) [16]. However, the presence of hepatic steatosis was determined solely by the fatty liver index rather than using imaging devices or histology [16]. In another study with biopsy-confirmed fatty liver, cardiovascular disease was more common in MAFLD than in NAFLD (20.1% vs. 12.8%), but the difference was not statistically significant, possibly due to a small sample size [17].

In this background of insufficient knowledge, Kim et al. [18] updated the evidence of increased mortality risk with MAFLD using a large health examination cohort. Almost 400,000 individuals from two medical centers in Korea participated and were followed for a median of 5.7 years [18]. The MAFLD-only group, which accounted for 4.29% of the total population, showed the poorest all-cause and cardiovascular survival among normal participants, those with both MAFLD and NAFLD, MAFLD-only, and NAFLD-only individuals [18]. After adjusting for age, the all-cause and cardiovascular mortality risks of the MAFLD-only group were 35% and 90% higher than those of the normal control group, even though the statistical significance was lost after additional adjustment for drinking, smoking, physical activity, total cholesterol, and use of statins [18]. In contrast, the all-cause and cardiovascular mortality of the NAFLD-only group did not differ from the control group [18]. Finally, the authors indicated that patients who meet more criteria for metabolic dysfunction may have a higher mortality risk [19].

This study confirms prior results that people with MAFLD faced an increased risk of death from all-cause and cardiovascular disease [14-18]. Furthermore, MAFLD, an updated term for hepatic steatosis accompanied by metabolic dysregulation, better explained mortality risk than did NAFLD [14-18]. Compared to previous research using the NHANES-III data, this study included more recent data gathered between 2002 and 2012 [14,15,18]. Kim et al. [18] evaluated MAFLD using all diagnostic criteria and liver ultrasonography, which had a high level of reliability between and within examiners.

However, there are some limitations that should be considered before generalizing this finding. As mentioned by the authors, the study participants were apparently healthy adults who received regular medical checkups and were relatively young, with a mean age of 39.6 years [18]. Although both investigations were performed in Korea, the prevalence of MAFLD and NAFLD in this study (24.9% vs. 22.2%) was lower than in the NHIS study (37.3% vs. 28.0%), which consisted of people aged 40 to 64 years [16,18]. Distinct characteristics of participants in this study could have affected the mortality rates and risks of MAFLD. Second, the presence of fatty liver was classified as either normal or steatosis using a dichotomous scale [18]. A gradual increase in mortality rates proportional to fibrosis stage was demonstrated in patients with NAFLD [19]. Since the severity of fibrosis is the most critical prognostic factor for MAFLD [20], further study on the mortality risk in relation to the level of hepatic inflammation is essential.

Despite its limitations, this study validated the all-cause and cardiovascular mortality of MAFLD individuals in comparison to those with NAFLD as well as the normal population by thoroughly examining every diagnostic criterion of MAFLD. Based on the current findings, MAFLD should be recognized as a significant risk indicator of mortality.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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