

## Editorial



# Non-alcoholic Fatty Liver Disease, Cardio-metabolic Syndrome and Hypertension: One Concept Fits Multi-systemic Presentations

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Metabolic syndrome (MetS) is a complex condition in which several interrelated risk factors for cardiovascular diseases (CVD) and type 2 diabetes mellitus (T2DM) co-exist. Clinically, MetS can be diagnosed if at least 3 of the following conditions are present: abdominal obesity, high blood pressure, high blood glucose, high serum triglycerides, and low serum high-density lipoprotein.<sup>1)</sup> Excessive adiposity, insulin resistance, dysglycemia, hypertension and CVD have been traditionally treated as a separate disease. However, the association between such diseases can be reasonably explained within the concept of MetS.<sup>2)</sup>

Non-alcoholic fatty liver disease or non-alcoholic steatohepatitis (NAFLD/NASH) is a hepatic manifestation of MetS.<sup>3)</sup> In world-wide pandemic of obesity and T2DM, NAFLD/NASH affects over 25% of general population including 10% of American children.<sup>4)</sup> It has emerged as a major cause of chronic liver disease and now the second leading indication for liver transplantation in the United States.<sup>5)</sup> Among the adiposity-based chronic organ dysfunctions, ectopic fat infiltration of the liver has particular significance because it is closely associated with increased CVD.<sup>6)</sup> In the setting of obesity-related MetS, hepatic production of triglyceride and glucose is increased and hepatic clearance of low-density lipoprotein (LDL) cholesterol is decreased. The East Asian ethnicity appears to be particularly vulnerable to obesity-related metabolic derangement and CVD.<sup>7)8)</sup>

In this issue, the probable association between NAFLD/NASH and hypertension was presented in general population using national health check-up data.<sup>9)</sup> Fatty liver index (FLI) was used as a surrogate marker of NAFLD/NASH, in which FLI was calculated with the formula including triglyceride, gamma-glutamyl transferase (GGT), waist circumference and body mass index. The authors concluded that higher FLI was associated with the increased risk of newly developed hypertension after 2 years. In detail, individuals with pre-existing hypertension, diabetes, cardiovascular diseases and on lipid-lowering medications at baseline were excluded. The endpoint of study was a diagnosis of hypertension at a later health check-up. In the higher FLI quartile, the percentage of male, systolic blood pressure, current smoker rate, and the amount of alcoholic consumption were significantly higher. Fasting blood glucose, total cholesterol, LDL-cholesterol and GGT were also significantly higher.

There are some limitations that careful interpretation is required. Since GGT increased in alcoholic liver disease, alcoholic etiology of fatty liver disease could not be excluded. The percentage of current smokers was significantly higher in fourth quartile group (Q4), but, current smoking was independent of newly developed hypertension. It is probable that the current smoking rate was high in younger ages. Analysis to determine if there were differences between genders were not provided. In the higher quartiles, the values of estimate glomerular filtration rate was higher, which is likely due to the higher male percentage. Since three of the four FLI components were the indices of MetS, FLI intrinsically reflected the probability of MetS rather than a marker of liver disease. As liver imaging data was not included, FLI had a fundamental limitation as a marker of NAFLD/NASH although FLI showed good correlation with ultrasonographic fatty liver disease.<sup>10)</sup> As the severity of hepatic steatosis, there was no information on the threshold for FLI, especially in the case of non-alcoholic etiology, at high risk for new development of hypertension. The data showed that FLI reflects lifestyle factors including alcohol consumption, and at the same time the risk of MetS and hypertension. In addition, the effect of age on the occurrence of hypertension was not trivial. Nevertheless, the result was interesting and valuable enough. It confirmed that NAFLD/NASH as assessed by FLI is a risk factor for hypertension in Korean population as in western study.<sup>11)</sup> In addition the authors provided meaningful domestic evidence to establish CVD prevention strategy by using national big data set.

Although the understanding of MetS is still ongoing, new conceptual framework about cardiometabolic disease model is notable.<sup>2)12)</sup> As a chronic progressive disease, cardio-MetS progresses from the early risk factor stage to end-point clinical CVD stage. Chronic metabolic derangement can be derived by adiposity-based and dysglycemia-based. These terms are introduced in place of the previous “obesity-based” and “diabetes-based”, respectively. It is an attempt to provide a more scientific and actionable approach to MetS.<sup>2)</sup>

In the context of MetS, although apparent clinical presentation is specific organs other than cardiovascular, patients with NAFLD/NASH should be provided comprehensive CVD management as well as surveillance of hepatic cirrhosis and tumor. A paradigm shift occurs in the drug treatment strategy of T2DM, a prototype of MetS, from a blood glucose control to a CVD prevention based on real-world evidence. It is expected that the story of diabetes treatment, in which CVD management will be more important than blood sugar, will continue in NAFLD/NASH.

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