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COMMENT

Fatty liver index has potential as a predictor of hypertension in the Japanese general population

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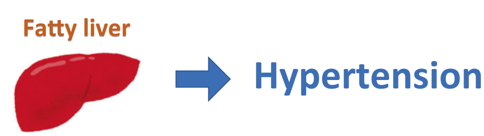
Non-alcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide and the leading cause of liver-related morbidity and mortality [1]. Emerging evidence has shown that NAFLD is strongly associated with an increased risk of incident hypertension and cardiovascular diseases [2, 3]. However, the role of NAFLD in the development of hypertension is still unclear and is highly overlooked by the general public. Although the gold standard test to diagnose fatty liver is liver biopsy, fatty liver is usually diagnosed by imaging tests, such as abdominal ultrasound in clinical practice. Another method used to assess fatty liver is the fatty liver index (FLI), which is based on body mass index (BMI), waist circumference (WC), fasting serum triglycerides (TG), and gamma-glutamyl transferase (GGT) [4], and its utility has been proven. Several studies have reported FLI as a good predictor of incident hypertension; [5, 6] however, whether this applies in the absence of dysglycemia has yet to be determined.

In the current issue of *Hypertension Research*, Wu et al. [7] reported an observational study to determine whether FLI was independently associated with an increased risk of incident hypertension in individuals with and without dysglycemia. In their study, Wu et al. [7] enrolled 3114 patients (1036 males and 2078 females) without hypertension who underwent a Specific Health Checkup in the fiscal year 2013 and were followed up until 2018. They evaluated the incidence of hypertension by dividing the participants into six groups based on FLI tertiles (low, moderate, or high) and whether they had dysglycemia. During the mean follow-up period of 2.8 years, 160 of the 3114 participants developed hypertension. Using the low FLI group with normoglycemia as a reference, the hazard ratio (HR) for incident hypertension was increased in the high FLI group with and without dysglycemia in both sexes after adjusting for confounders except systolic blood pressure (SBP), HR [95% confidence interval (CI)]: male: 1.52 [1.06–2.07] in normoglycemia and 2.05 [1.43–2.92] in dysglycemia, and female: 1.86 [1.43–2.42] in normoglycemia and 2.98 [2.19–4.07] in dysglycemia (Fig. 1). After adjusting for SBP, the risk of developing hypertension was no longer significant in males in the high FLI group with normoglycemia (HR [95% CI]: 1.27 [0.89–1.81]). Meanwhile, it remained unchanged in females in the high FLI group with normoglycemia (HR [95% CI]: 1.51 (1.16–1.98)) and both males and females (male: 1.60 [1.12–2.28] and female: 2.20 [1.61–3.00]) in the high FLI groups with dysglycemia. It is



Male

	Normoglycemia			Dysglycemia		
	Low FTI	Middle FTI	High FTI	Low FTI	Middle FTI	High FTI
Male	1	1.01 (0.71-1.42)	1.52 (1.06-2.17)	1.11 (0.71-1.74)	1.58 (1.05-2.39)	2.05 (1.43-2.92)

Female

	Normoglycemia			Dysglycemia		
	Low FTI	Middle FTI	High FTI	Low FTI	Middle FTI	High FTI
Female	1	1.12 (0.86-1.46)	1.86 (1.43-2.42)	1.56 (0.97-2.49)	1.06 (0.65-1.71)	2.98 (2.19-4.07)

Hazard ratios (95% CIs)

Fig. 1 Hazard ratios and 95% confidence intervals of fatty liver index tertile groups with and without dysglycemia for the development of hypertension which was demonstrated by Wu et al. [7]. CI confidence interval, FLI fatty liver index

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interesting to note that the hazard ratio is consistently higher for females than for males.

As for the mechanism by which NAFLD causes hypertension, NAFLD may promote hypertension by (1) initiating systemic inflammation via secreted cytokines, (2) inducing insulin resistance, which are critical pathophysiological mechanisms leading to the development of hypertension by increasing vasoconstriction and water-sodium retention, (3) increasing oxidative stress in accelerated vascular aging in hypertension, (4) directly increasing vasoconstriction and decreasing vasodilation via increased levels of circulating asymmetrical dimethylarginine, which is an endogenous inhibitor of nitric oxide synthase [1]. Given the close association between NAFLD and hypertension, much attention should be paid to the overlapping management approaches. At present, the fundamental management approach for both NAFLD and hypertension focuses on lifestyle modifications, including consuming a healthy balanced diet, weight reduction, and regular physical activity [1, 8]. Therefore, FLI might be a useful predictor of hypertension in the Japanese general population regardless of the presence of dysglycemia, as described by Wu et al. [7].

Furthermore, Wu et al. [7] did not adopt the conventional classification of FLI ≥ 60 or FLI < 30, which is used in most studies of Westerners [9] but adopted tertiles of FLI by gender. Although the prevalence of obesity is lower in Asians than in other ethnic groups, the prevalence of fatty liver is not lower [10]. Therefore, in Asian populations, the cut-off values for FLI to identify fatty liver may be lower than in other ethnic groups, e.g., FLI ≥ 35 in men and FLI ≥ 20 in women in Taiwan [11]. As a result, they found that higher FLI, even if the cut-off values are lower than the conventional values, is associated with an increased risk for the development of hypertension in Asians. Further studies will be needed to determine the optimal cut-off value of FLI in Asian populations for predicting the development of hypertension and cardiovascular diseases.

In conclusion, the study of Wu et al. on Japanese community dwellers showed that higher FLI was associated with an increased risk of the development of hypertension among individuals with or without dysglycemia, suggesting that those with high FLI, even if normoglycemic, should be managed for the prevention of hypertension. Future studies are needed to assess the association between higher FLI and the development of hypertension and cardiovascular diseases for healthy longevity in the Japanese general population.

Compliance with ethical standards

Conflict of interest The author declares no competing interests.

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