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COMMENT

Triglyceride-glucose index is a good indicator for early prediction of future chronic kidney disease development in all blood pressure subtypes

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Hypertension and insulin resistance are known as risk factors for chronic kidney disease (CKD) [1]. Hypertension can be classified into three categories based on the reference values for systolic blood pressure (SBP) and diastolic blood pressure (DBP): isolated diastolic hypertension (IDH), isolated systolic hypertension (ISH), and systolic-diastolic hypertension (SDH). Numerous studies have examined the association between each of these categories and cardiovascular disease (CVD) risk, and have shown that each subtype of hypertension has different characteristics [2, 3]. Therefore, it is important to determine the risk of outcome for each hypertension subtype.

The triglyceride-glucose (TyG) index has been reported as a simple indicator of insulin resistance [4]. TyG is calculated using the formula: TyG = log (fasting triglycerides (TG) (mg/dL) × fasting blood glucose (FBG) (mg/dL)/2) [4]. Previous several studies have investigated the relationship between TyG index and the risk of CKD, and recently a meta-analysis has shown that higher TyG index was associated with increased risk of CKD, independently of established risk factors [5].

The present retrospective cohort study by Sakoda et al. [6] investigates the association between TyG index and new onset of CKD using health checkup data of 41,811 middle-aged Japanese men. Analysis using the COX proportional hazards model reveals that a high baseline TyG index increases the risk of new onset of CKD. In this study, subjects are classified into four groups (IDH, ISH, SDH, and normotensive group) based on their baseline blood pressure (BP) values and the relationship between TyG index and CKD development is analyzed for each hypertension subtype. The results show that high TyG index values are associated with an increased risk of new onset CKD for all BP subtypes. In addition, the TyG index shows a higher hazard ratio than FBG or TG alone for the risk of CKD development, and this result is consistent for all BP subtypes. From the above, TyG index can be a good indicator for early prediction of future CKD development (Fig. 1).

The association between TyG index and CKD have also been recently reported by others [5]. Ren et al. demonstrated that higher TyG index was associated with increased risk of CKD, independently of established risk factors based on the data of longitudinal study including 10498 participants [5]. Furthermore, Ren et al. conducted a meta-analysis including twelve published articles and their study, and confirmed the significant associations between TyG index and CKD [5]. However, no studies have analyzed the association between TyG index and CKD based on BP subtype. For the first time, this study reveals that high TyG levels are associated with new onset of CKD, regardless of BP subtype [6]. Interestingly, this association is also confirmed in IDH and normotensive subjects [6]. IDH is the most common type of hypertension in young to middle-aged men [7] and is often overlooked and unaware as hypertension [8]. It is a very significant finding that high TyG levels are associated with the risk of future CKD development even in people with normal BP and IDH.

As described in the Discussion, the underlying mechanisms of the association between the TyG index and CKD are yet to be fully understood. The TyG index is composed of factors related to lipid metabolism and glucose, which are closely related to insulin resistance. Hyperinsulinemia induces renal vasodilation, which leads to

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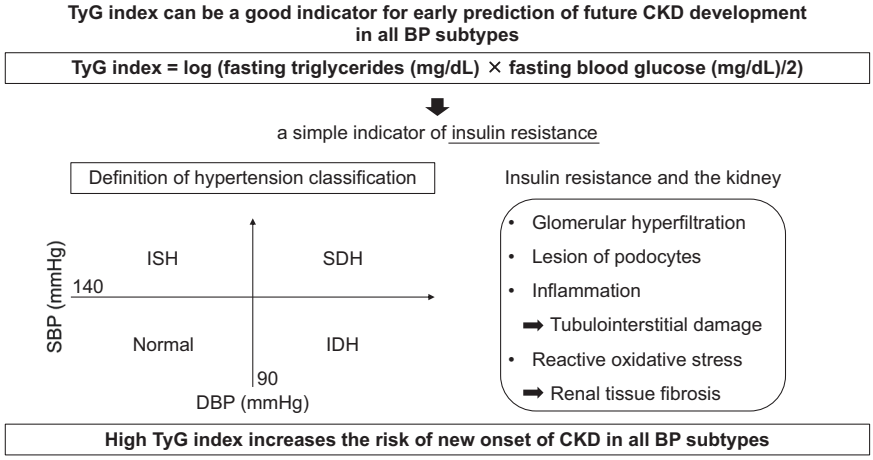

Fig. 1 Relationship between TyG index and the risk of CKD. BP blood pressure, CKD chronic kidney disease, DBP diastolic blood pressure, IDH isolated diastolic hypertension, ISH isolated systolic hypertension, SBP systolic blood pressure, SDH systolic-diastolic hypertension, TyG triglyceride-glucose

glomerular hypertension and hyperfiltration [9]. Glomerular hyperfiltration contributes to glomerulosclerosis and renal impairment. Insulin plays a predominant role in the metabolism and function of podocytes. Hyperinsulinemia could contribute to the lesion of podocytes and proteinuria through some molecular mechanisms [9]. Hyperglycemia can also provoke inflammation, which results in tubulointerstitial damage [9]. Furthermore, Insulin resistance induces overproduction of reactive oxidative stress by activating the mitochondrial electron transport chain, resulting in renal tissue fibrosis.

In recent years, in addition to conventional treatments centered on RAS inhibitors, new treatment options, such as SGLT2 inhibitors and mineralocorticoid receptor antagonists, have emerged for CKD treatment [10]. The TyG index is considered to be a highly significant CKD prediction index for early therapeutic intervention in CKD. As described in the discussion, this study is a retrospective observational study, and the causal relationship is unknown. It has been reported that SGLT2 inhibitors and GLP1 agonists have a renal protective effect as hypoglycemic agents [11]. Conventional fibrates used as TG-lowering therapy are excreted by the kidneys, and their use is contraindicated in patients with severely impaired renal function. Recently, selective PPARα modulator "Pemafibrate", which is excreted by bile, has been released and can now be used in patients with severe renal function decline, and its use in CKD patients is attracting attention [12]. Thus, further studies are necessary to verify whether improving TyG index with these drugs suppresses the onset and progression of CKD.

Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

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