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Letter to the Editor

Regarding "Diabetes-Related Factors and Abdominal Aortic Aneurysm Events: The Atherosclerotic Risk in Communities Study"

We read with great interest the recent publication of Kubota et al. that investigated the association between metabolic syndrome and plasma biomarkers with abdominal aortic aneurysm (AAA) risk [1]. Metabolic syndrome is defined by the presence of at least three metabolic disorders including central obesity, low high-density lipoprotein cholesterol, hypertension, hypertriglyceridemia, or abnormal glucose metabolism [2]. Among these metabolic disorders, low high-density lipoprotein cholesterol, obesity, hypertension, and hypertriglyceridemia have been previously identified as risk factors for AAA [3–6]. However, diabetes is paradoxically negatively associated with AAA; the prevalence, the incidence, the AAA size, and the risk of rupture being lower in diabetic patients compared to nondiabetics [7]. The cellular and molecular mechanisms underlying this negative association are complex and not yet fully understood.

In their study, Kubota et al. found that fasting serum glucose was inversely associated with AAA, an observation concordant with other studies revealing an inverse association between short- and long-term blood glucose levels and AAA [1,8,9]. Moreover, no significant association between fasting serum insulin and AAA was observed [1]. Type 2 diabetes, which accounts for almost 90% of diabetic subjects, is characterized by insulin resistance associated with defects in insulin secretion [10]. Although the association between blood glucose and AAA is well known, the link between insulin and AAA has been so far poorly investigated. Interestingly, a study revealed a positive correlation between C-peptide (which reflects endogenous insulin secretion) and AAA diameter in type 2 diabetic patients [11]. We recently found that C-peptide, insulin concentration, and insulin resistance index were significantly higher in patients with large AAA (diameter > 50 mm) compared to patients with smaller AAA (<50 mm) [12]. While the protective effect of diabetes may be, at least partly, due to the impact of hyperglycemia on the aortic wall [7], epidemiological and experimental studies suggest a pathogenic effect of insulin resistance. Indeed, the use of insulin sensitizer drugs such as biguanides and thiazolidinediones is associated with a lower risk of developing aneurysm in human [13]. This was confirmed in several AAA animal models where the administration of these drugs was associated with a decreased aortic dilatation, with a better preservation of the extra-cellular matrix and a decreased inflammatory cell infiltration [14,15].

Interestingly, Kubota et al. found that patients with metabolic syndrome had an increased risk of AAA compared to those without metabolic syndrome [1]. The risk of AAA increased with a greater number of nonglucose metabolic syndrome components. These results are in accordance with the global protective effect of diabetes on AAA pathophysiology [7]. Intriguingly, plasma leptin concentration was inversely associated with AAA occurrence [1]. Elevated leptin concentration is usually associated with obesity [16], and several studies have identified obesity as a risk factor for AAA [4,17]. The authors hypothesize that the inverse association between leptin and AAA occurrence could potentially be explained by the fact that high leptin level predicts increased risk for diabetes [18]. However, after excluding diabetic patients, leptin was sill inversely associated with AAA [1]. It would be of interest for the readers if the authors could provide further explanations on the unexpected inverse association between leptin and AAA.

All in all, the recent publication of Kubota et al. provides new insights in the association between metabolic syndrome and AAA. Metabolic syndrome regroups various metabolic disorders, each potentially having a differential impact on AAA formation. This study confirmed the negative association between hyperglycemia and AAA formation and corroborated the nonglucose parameters of the metabolic syndrome as risk factors of AAA. The link between AAA and insulin resistance is still poorly known, and we truly believe that further studies in the field could provide new insights in AAA pathophysiology and help to identify new therapeutic targets.

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