

[EDITORIAL]

Obesity Indices and the Risk of CKD

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Alongside the worldwide epidemic of obesity, obesity-related complications have emerged as increasing socioeconomic problems (1). The kidney is one of the target organs for obesity-related health disorders. Obesity is recognized as not only a risk factor for the progression of chronic kidney disease (CKD), but also as an independent risk factor for the development of CKD (2). That is, obesity-related kidney impairment can occur independently of obesity-associated comorbidities, including hypertension, dyslipidemia and impaired glucose tolerance. Although the mechanisms for the development of CKD associated with a “pure” obesity state in the absence of obesity-related comorbidities are incompletely understood, several plausible factors, including structural metabolic, and hemodynamic alterations of the kidney may be involved (3).

Previous studies have demonstrated that adipocytes in visceral fat rather than subcutaneous fat may serve as the source of inflammatory cytokines and may be associated with injuries in systemic organs, including the kidneys (4). Accordingly, the clinical significance of body size indices indicating visceral obesity, including the waist circumference (WC) and the waist-to-height ratio (WtHR) have been emphasized, rather than those defined by weight and height, such as the body mass index (BMI). However, the current information on indices that best predict the development of CKD is limited, since BMI has been an exclusively used as an obesity index in previous studies on CKD. Another important aspect of the obesity index is the sex difference in the distribution of fat accumulation. In general, females have more abundant subcutaneous fat in comparison to males. Thus, in females, the measurement of the WC is less likely to reflect the visceral fat accumulation in comparison to males.

In this issue of Intern Med, Yamasaki et al. reported the results of a cohort study of Japanese middle-aged workers (male, $n=1,725$; female, $n=1,186$) (5). The relationships between obesity indices, including BMI, WC and WtHR, and the development of CKD were examined separately in men

and women by analyzing their annual health check-up records over a 6-year period. The new development of CKD was defined based on the occurrence of an estimated GFR (eGFR) decline to <60 mL/min/1.73 m² or dipstick urinary protein scores of 1+ or more. Among the obesity indices, BMI, WC and WtHR were significantly associated with the new development of CKD in men, even after adjustment for potential confounding factors, including age, smoking status, alcohol consumption, regular exercise, the presence of high blood pressure, dyslipidemia, and high fasting plasma glucose at baseline. In contrast, the associations between the development of CKD and all three obesity indices in women were weaker in comparison to those in men, suggesting a sex difference in the utility of these obesity indices as indicators for the development of CKD. Interestingly, BMI showed a stronger association with the development of CKD than WC or WtHR, and the observed relationships between BMI and the incidence of CKD were found to be linear in both men and women in some statistical models. Of note, the participants included in the study were middle-aged relatively healthier workers and the majority of participants showed BMI values that were within the normal-range; the mean BMI values were 23.6 kg/m² in men and 22.3 kg/m² in women. This population did not include participants with severe disease-associated body weight loss, and thus fairly excluded physical states potentially leading to a “J-shaped” distribution between body size and the development of CKD (6).

Despite an advancement in the studies on kidney injuries potentially occurring in the presence of obesity, it remains unclear why only a limited number of obese individuals actually develop CKD. In addition, the renal characteristics of injuries associated with severe obesity can be similarly detected in individuals with relatively mild obesity (7). Thus, it is conceivable that obesity is not the sole factor causing this type of kidney injury and that there may be additional predisposing factors. The structural diversity of the kidneys may produce differences in the susceptibility to kidney in-

jury among individuals (8). Some individuals with a low kidney functional reserve may exhibit renal symptoms more easily in response to increases in metabolic or hemodynamic demands, even if they do not fulfil the criteria for obesity. Based on this point of view, the findings of a linear association between BMI and the development of CKD, irrespective of obesity - as reported by Yamasaki et al. - may provide important implications regarding the pathogenesis of CKD.

The author states that he has no Conflict of Interest (COI).

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