

# Obesity and chronic kidney disease, an important piece in the puzzle of Cardiovascular–Kidney–Metabolic syndrome

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The prevalence and burden of chronic kidney disease (CKD) is increasing worldwide. Approximately 10% of the world's population, or more than 8 million people, have CKD [1,2]. Between 1990 and 2017, the prevalence increased by 29.3% and the associated mortality rate increased by 41.5%, with approximately 1.2 million people dying from CKD in 2017 [3]. According to Health Insurance Review and Assessment Service (HIRA) data, the annual medical cost per CKD patient in Korea in 2021 was 8,369,000 Korean won, making it one of the diseases with the highest medical costs [4]. Moreover, CKD not only leads to end-stage kidney disease but is also an important risk factor for cardiovascular disease (CVD).

To respond to this increasing burden, it is important to elucidate the risk factors and pathophysiology of CKD. Studies have shown that obesity is a risk factor for CKD, along with diabetes, hypertension, old age, family history, genetic factors, smoking, acute kidney injury, nephrotoxins, and low socioeconomic status [5]. In addition, according to the Obesity Fact Sheet of the Korean Society for the Study of Obesity, the prevalence of obesity in Korea reached 37.4% in 2021, a 1.27-fold increase from 30.2% in 2012 [6].

In this setting of increasing obesity and CKD, Song et al. [7] analyzed the association between obesity and incident CKD in 2,711 participants with normal renal function included in the Korean Genome and Epidemiology Study (KoGES), and the results were consistent with previous studies. Obesity, assessed using body mass index or the waist-to-hip ratio, was a risk factor for the development of new

CKD, and this association was maintained regardless of age, sex, diabetes, hypertension, and proteinuria. Of particular interest is that the group whose obesity decreased during the observation period had a lower incidence of CKD than the group whose obesity was maintained. This suggests that CKD can be prevented through active control of obesity. However, this association was not confirmed by multivariate analyses, and the independent association needs to be confirmed in future studies.

Obesity is an important risk factor not only for CKD but also for CVD. CKD is also a risk factor for CVD and increases when CVD is present. There has been a recent movement to develop the relationship among metabolic risk factors obesity, CKD, and CVD into the concept of Cardiovascular–Kidney–Metabolic (CKM) syndrome. CKM syndrome is a systemic disease characterized by the pathophysiological interactions among metabolic risk factors, CKD, and the cardiovascular system, which ultimately results in multi-organ dysfunction and poor cardiovascular outcomes [8]. Excessive dysfunctional adipose tissue is an important pathophysiological factor underlying CKM syndrome. Factors related to inflammation and oxidative stress, mainly secreted from visceral adipose tissue, damage the heart, blood vessels, and kidneys [8].

It is interesting that drugs used in diabetes, CKD, and CVD (such as angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, glucagon-like peptide-1 receptor agonists, sodium-glucose cotransporter-2 inhibitors, and nonsteroidal mineralocorticoid receptor antagonists) have both renal protective and CV risk reduction effects. The widespread use of these drugs is thought to be an important background for the emergence of the concept of

CKM syndrome.

The proposal of CKM syndrome should not be a mere declaration but should be of practical help in clinical practice. This requires future multidisciplinary research and collaboration among experts in various field, including endocrinologists, cardiologists, and nephrologists. The inclusion of renal risk factors, such as the estimated glomerular filtration rate and albuminuria, in recent cardiovascular risk prediction tools may be a good example [9,10].

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