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Metabolically Healthy Obesity is Associated with Incident Chronic Kidney Disease in the General Population.

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Objectives : Obesity and metabolic abnormalities have become a growing concern in the general population. Recent studies have suggested that obese individuals without metabolic abnormalities exhibit a low cardiovascular risk similarly to non-obese healthy individuals. However, it is unknown on the relationship between such different phenotypes and the development of chronic kidney disease (CKD).

Methods : The Korean Genome and Epidemiology Study (KoGES) is a prospective cohort study to deal with public health issues in Korean population between 2001 and 2014. A total of 10,030 participants were recruited from two cities in Gyeonggi province. After excluding 227 participants who had estimated glomerular filtration rate (eGFR) of < 60 ml/min per 1.73 m², 9,803 were included in the analysis. We used five clinical categories to define metabolic status; 1) HbA1c $\geq 6.5\%$, history of diabetes, fasting blood sugar ≥ 125 mg/dL or homeostatic model assessment-insulin resistance $\geq 2.5\%$, 2) triglyceride ≥ 150 mg/dL, 3) high-density lipoprotein cholesterol ≤ 40 mg/dL in men or ≤ 50 mg/dL in women, 4) high-sensitivity C-reactive protein ≥ 1 mg/L, or 5) history of hypertension, systolic or diastolic blood pressure $\geq 140/90$ mmHg. Participants who met ≥ 3 categories were considered metabolically unhealthy. Obesity was defined as a body mass index of ≥ 25.0 kg/m². Based on the criteria of metabolic abnormality and obesity, participants were classified into 4 groups; 1) metabolically healthy non-obesity [(MHNO, n=4,904 (418%)), 2) metabolically abnormal non-obesity [(MANO, n=1,462 (14.9%)), 3) metabolically healthy obesity [(MHO, n=2,055 (21.0%)), and 4) metabolically abnormal obesity [(MAO, n=2,193 (22.4%)]. The study endpoint was an onset of incident CKD, which was defined as an eGFR of ≤ 60 ml/min per 1.73 m² for at least ≥ 2 measurements during follow-up period.

Results : The mean age was 52.0 years and 4,666 (47.6 %) were males. During a mean follow-up duration of 8.36 years, primary endpoint occurred in 843 (8.5%) participants; 279 (12.7%), 151 (13.1%), 151 (7.3%), and 220 (5.3%) in MAO, MANO, MHO, and MHNO groups, respectively (P < 0.001). In a

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multivariable Cox regression after adjustment of confounding factors, MAO [hazard ratio (HR), 1.511; 95% confidence interval (CI), 1.22–1.85; $P < 0.001$] and MANO (HR, 1.511; 95% CI, 1.22–1.86; $P < 0.001$) phenotypes were associated with increased risks of incident CKD as compared to MHNO phenotype. In addition, MHO group had a higher risk of CKD development (HR, 1.294; 95% CI, 1.04–1.60; $P = 0.017$) than MHNO group, but comparable risk to MAO and MANO groups.

Conclusions : This study showed that metabolically abnormal phenotypes irrespective of obesity portend a worse prognosis for newly developed CKD. In addition, MHO phenotype is also associated with incident CKD, raising a concern against previous notion that MHO is ‘healthy’ in the general population.

Keywords : Metabolic abnormalities, obesity, chronic kidney disease