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An association of metabolic syndrome and chronic kidney disease from a 10-year prospective cohort study

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ABSTRACT

Objective. Although metabolic abnormalities have been considered important risk factors of chronic kidney disease (CKD), the impact of metabolic syndrome (MS) and insulin resistance on renal function deterioration is poorly understood. We investigated the association between MS and incident CKD/rapid decline of estimated glomerular filtration rate (eGFR) in a 10-year population-based longitudinal study.

Material and Methods. Among 10,030 subjects, 6065 without history of CKD or cardiovascular disease at baseline were analyzed using data generated from the Ansan–Ansung cohort of the Korean Genome Epidemiology Study. Participants were categorized into two groups based on the presence of MS at baseline. Incident CKD was defined as eGFR <60 ml/min per 1.73 m^2, and rapid decline of eGFR was defined as >3 ml/min per 1.73 m^2/yr over 10 years.

Results. During the 10-year follow-up period, CKD developed in 893 subjects (14.7%). Compared to subjects without MS, the odds ratio (OR; 95% confidence interval, CI) of incident CKD in those with MS was 1.38 (1.16–1.64) after controlling for confounding factors. The risk of rapid decline of eGFR was also higher in subjects with MS than those without MS (OR: 1.20, 95% CI: 1.04–1.39). In addition, we found that higher levels of homeostatic model

Abbreviations: CKD, chronic kidney disease; MS, metabolic syndrome; DM, diabetes mellitus; HOMA-IR, homeostatic model assessment of insulin resistance; KoGES, Korean Genome Epidemiology Study; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; hsCRP, high sensitivity C-reactive protein.

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assessment of insulin resistance (HOMA-IR) were associated with incident CKD and rapid decline of eGFR independently of traditional CKD risk factors (OR: 1.24, 95% CI: 1.04–1.47).

Conclusion. Both MS and insulin resistance were independent risk factors of incident CKD and rapid decline of eGFR in healthy Korean population.

1. Introduction

Chronic kidney disease (CKD) is not only a precursor of end-stage renal disease, but also an important risk factor of cardiovascular disease, even in the early stage of renal impairment [1]. Additionally, recent population-based studies have shown that CKD is associated with all-cause mortality, premature death, cognitive impairment, and poor quality of life [2]. As the prevalence of CKD has increased globally along with an aging population, it has become a major health problem incurring substantial healthcare costs [3]. Therefore, it is important to investigate the characteristics of subjects who are at higher risk for incident CKD in earlier life.

Metabolic syndrome (MS) is a cluster of medical conditions including central obesity, dyslipidemia, impaired glucose tolerance, and hypertension [4]. A previous study has shown that MS increases the risk of cardiovascular disease and its mortality, as well as the risk of diabetes mellitus (DM) [5]. Moreover, additional study results have indicated that MS is associated with kidney damage [6]. This close relationship between MS and incident CKD might be explained by their common pathogenesis such as chronic inflammation, oxidative stress, and insulin resistance. However, to date, there are few long-term follow-up (≥10 years) cohort studies concerning the relationship between MS and incident CKD. Furthermore, no study has directly demonstrated the link between MS and rapid decline of kidney function.

Insulin resistance is clinically defined as the failure of insulin to maintain glucose homeostasis and is reportedly associated with decline of renal function [7]. Because insulin resistance is considered to play a central role in the pathogenesis of MS, it is suggested as a mediator of MS and deterioration of kidney function. However, only a few studies have examined the impact of insulin resistance on the development of CKD, and the results were inconsistent. For example, Kobayashi et al. evaluated 41 non-diabetic hypertensive individuals and found insulin resistance to be a risk factor of progression of CKD [8]. However, Jing et al. reported that insulin resistance evaluated using the homeostatic model assessment of insulin resistance (HOMA-IR) was not independently associated with chronic kidney disease in the Chinese population [9]. Therefore, a large-scale, long term follow-up prospective study is needed to confirm the relationship between insulin resistance and incident chronic kidney disease in adult population.

Based on the above-mentioned reports, we analyzed whether MS is associated with rapid decline of renal function and incident CKD (eGFR <60 ml/min per 1.73 m^2 with a baseline eGFR of ≥60 ml/min per 1.73 m^2) over a 10-year follow-up period in Korean adults. In addition, we evaluated the independent association between insulin resistance and deterioration of kidney function.

2. Material and Methods

2.1. Study Population and Design

We recruited participants from the Ansung–Ansan cohort study, an ongoing prospective study from 2001 embedded within the Korean Genome Epidemiology Study (KoGES). The Ansung cohort represents the rural community, and the Ansan cohort an urban community. Each cohort consists of a population sample of Korean males and females aged 40–69 years with the same ethnic background. Detailed information regarding KoGES and the methods have been described previously [10,11]. Briefly, 10,030 eligible participants were recruited from 2001 to 2002. Study participants were re-examined at 2-year intervals, and 6238 participated in the sixth follow-up survey. Among them, 100 subjects were excluded for having a glomerular filtration rate < 60 ml/min per 1.73 m^2 at baseline examination. We also excluded subjects with a history of cardiovascular disease (N = 13), use of medications associated with MS and kidney function such as glucocorticoid and diuretics (N = 24) and missing data for MS components (N = 36). After the exclusion of ineligible subjects, 6065 subjects (2820 men and 3,245women) were enrolled for analysis (Fig. 1). At each visit, informed written consent was obtained from all participants. The study protocol was approved by the Ethics Committee of the Korean Center for Disease Control and the Institutional Review

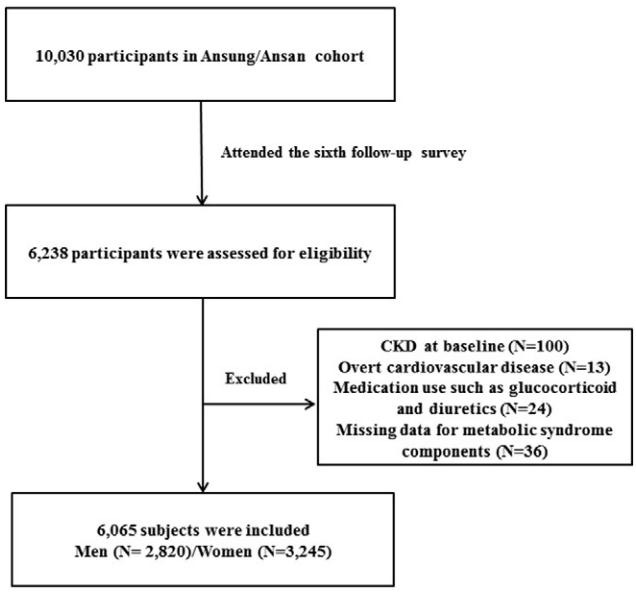

Fig. 1 – Study population.CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; MS, metabolic syndrome.