Association Between Sonographically Diagnosed Nephrolithiasis and Subclinical Coronary Artery Calcification in Adults

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Background: Although recent studies suggest an association between nephrolithiasis and clinical cardiovascular events, this association has been underexplored.

Study Design: Cross-sectional study.

Setting & Participants: 62,091 asymptomatic adults without known coronary heart disease who underwent a screening health examination that included cardiac tomography.

Predictor: Nephrolithiasis.

Outcome: Coronary artery calcification (CAC).

Measurements: Nephrolithiasis assessed using ultrasonography of the abdomen. CAC scoring assessed using cardiac computed tomography.

Results: The prevalence of CAC scores > 0 was 13.1% overall. Participants with nephrolithiasis had a higher prevalence of coronary calcification than those without (19.1% vs 12.8%). In Tobit models adjusted for age and sex, the CAC score ratio comparing participants with nephrolithiasis with those without nephrolithiasis was 1.56 (95% CI, 1.19-2.05). After further adjustment for screening center, year of screening examination, physical activity, alcohol intake, smoking status, education level, body mass index, family history of cardiovascular disease, total energy intake, glucose concentration, systolic blood pressure, triglyceride concentration, high-density lipoprotein cholesterol concentration, uric acid concentration, and estimated glomerular filtration rate, the CAC score ratio was attenuated, but remained significant (CAC score ratio, 1.31; 95% CI, 1.00-1.71).

Limitations: Computed tomographic diagnosis of nephrolithiasis was unavailable.

Conclusions: Nephrolithiasis was associated with the presence of CAC in adults without known coronary heart disease, supporting the hypothesis that these 2 health conditions share a common pathophysiology.

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Coronary heart disease (CHD) is a major cause of death in the United States and accounts for 1 in 4 deaths.[1] Considering the increasing economic and social burden, greater efforts are needed to control mortality and morbidity from CHD.[2] The identification of individuals with increased risk for CHD is crucial for effective intervention through preventative lifestyle modifications and medical treatment.[3]

Nephrolithiasis is common throughout the world and has increased in prevalence in recent years. According to a recent study from NHANES (National Health and Nutrition Examination Survey), the prevalence of self-reported kidney stones was estimated at ~8.8% in the United States.[4] When diagnosed, half these patients have kidney stone recurrence within 5 to 10 years.[5] The increasing prevalence and high recurrence rate of nephrolithiasis contribute to an increasing economic and social burden. Recent studies have suggested that nephrolithiasis is recognized as a systemic disorder related to multiple chronic morbidity, including obesity, diabetes, hypertension, and metabolic syndrome,[6-8] all of which are also cardiovascular risk factors. Furthermore, studies have reported an association between nephrolithiasis and clinical cardiovascular events such as CHD or stroke.[9,10] Recently, several studies supported a relationship between nephrolithiasis and subclinical atherosclerosis, including carotid atherosclerosis, increased arterial stiffness, and abdominal aortic calcification.[11-14]

Several mechanisms for the occurrence of nephrolithiasis have been suggested by studies, including vascular calcification.[15] Calcification can occur in almost any other vessel, including the coronary artery. Coronary artery calcification (CAC) is a useful marker of subclinical coronary atherosclerosis, as well as an independent predictor of future cardiovascular events.[16,17] Therefore, we evaluated the association of nephrolithiasis with CAC score in a large cohort of Korean adults who participated in a health screening examination.

Methods

Study Population

This cross-sectional study was part of the Kangbuk Samsung Health Study, which is a cohort study of Korean men and women 18 years or older who underwent a comprehensive annual or biennial health examination at Kangbuk Samsung Hospital Total Healthcare Centers in Seoul and Suwon, South Korea.[18,19] More than 80% of participants consisted of employees of various companies and local governmental organizations and their spouses. In South Korea, the Industrial Safety and Health Law requires annual or biennial health screening examinations of all employees, without

charge. Other participants voluntarily had screening examinations at the health examination center. Ultrasonography of the abdomen is a routine part of the health checkup program. Coronary artery calcium multidetector computed tomography (CT) was performed if participants wanted to know their estimated risk for cardiovascular disease (CVD). In Korea, CAC scoring has become a common CVD screening test.[18,20] The present study included the subset of Kangbuk Samsung Health Study participants who underwent cardiac CT to measure CAC scores as part of a comprehensive health examination from 2011 through 2014 (n = 67,834).

Among them, 5,743 participants were excluded at baseline for the following reasons: missing ultrasonography of the abdomen data (n = 235); history of CVD (n = 925); history of malignancy (n = 1,701); history of kidney and bladder disease including nephrolithiasis (n = 2,727); polycystic kidney disease, deformity, hypoplasia, dysgenesis, renal tumor, renal cancer, kidney transplantation, or postsurgical status on initial sonographic examination (n = 255); and estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 (n = 280). Because some participants met more than 1 exclusion criterion, the total number of participants included in the final analysis was 62,091 (Fig 1). The study was approved by the Institutional Review Board of Kangbuk Samsung Hospital, which waived the requirement for informed consent due to the use of de-identified data obtained as part of routine health screening examinations (2015-07-033).

Measurements

All health examinations were performed at Kangbuk Samsung Hospital Health Screening Center clinics in Seoul and Suwon. Data for demographic characteristics, physical activity, alcohol consumption, smoking status, education level, and medical history of hypertension, diabetes, CVD, malignancy, kidney disease (including kidney stones), and medication use were collected by standardized self-administered questionnaires as previously described.[18,21] Physical activity was assessed using the validated Korean version of the International Physical Activity Questionnaire (IPAQ) short form.[22] Health behaviors and education levels were categorized as follows: physical activity (inactive, minimally active, and health-enhancing physically active),[22] alcohol consumption (categorized as ≤20 and >20 g/d), smoking status (never, former, and current smokers), and education level (less than college graduate or college graduate or more).

Height and weight were measured by trained nurses.[19] Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared, and obesity was defined as BMI ≥ 25 kg/m^2, the proposed cutoff for the diagnosis of obesity in Asians.[23] Blood pressure (BP) was measured using an automated oscillometric device (53000; Welch Allyn) while individuals were seated with the arm supported at heart level. Hypertension was defined as either systolic BP ≥ 140 mm Hg, diastolic BP ≥ 90 mm Hg, or use of antihypertensive medication.

Blood samples were taken from the antecubital vein after at least a 10-hour fast. Blood tests included total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, aspartate aminotransferase, alanine transaminase, γ-glutamyltransferase, fasting glucose, hemoglobin A_{1c}, uric acid, high-sensitivity C-reactive protein (hsCRP), and creatinine.[18] eGFR was calculated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) creatinine equation.[24] The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as fasting insulin (in mg/dL) multiplied by fasting glucose (in mg/dL), divided by 405.[25] Diabetes was defined as fasting serum glucose concentration ≥ 126 mg/dL, hemoglobin A_{1c} concentration ≥ 6.5%, history of diabetes, or current use of antidiabetic medication.

Ultrasonography of the abdomen was performed by experienced radiologists who were unaware of the aim of the study using a Logic Q700 MR 3.5-MHz transducer (GE). All participants underwent ultrasonography of the abdomen in the supine position with the right arm raised above the head. Nephrolithiasis was

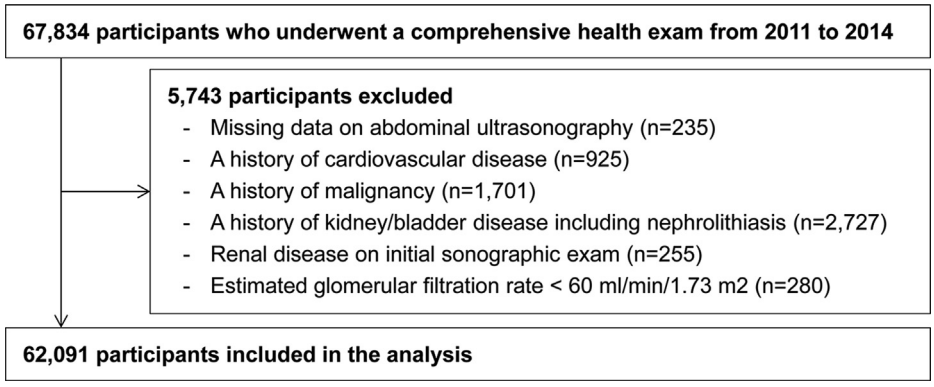

Figure 1. Flow chart of included participants.