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Original Article

ORIGINAL ARTICLE

Risk of incident chronic kidney disease among patients with urolithiasis: a nationwide longitudinal cohort study

Jae Young Kim[1,2], Jae Kwang Lee[3], Jung Tak Park[2] and Tae Ik Chang[1]

[1]Department of Internal Medicine, National Health Insurance Service Ilsan Hospital, Goyangshi, Gyeonggi-do, Republic of Korea, [2]Department of Internal Medicine, College of Medicine, Institute of Kidney Disease Research, Yonsei University, Seoul, Republic of Korea and [3]Research and Analysis Team, National Health Insurance Service Ilsan Hospital, Goyangshi, Gyeonggi-do, Republic of Korea

Correspondence to: Tae Ik Chang; E-mail: kidneyjang@gmail.com

ABSTRACT

Background. Urolithiasis has been infrequently implicated to have a causal association with chronic kidney disease (CKD). Recently, several studies have demonstrated the relationship between urolithiasis and CKD. However, the generalizability of their results is limited. This study aimed to investigate the association between urolithiasis and the risk of incident CKD.

Methods. This longitudinal cohort study used the National Health Insurance Service data, including 219 570 Korean adults with incident urolithiasis requiring procedural interventions and without prior kidney disease and 219 570 age- and sex-matched controls without urolithiasis between 1 January 2002 and 31 December 2020. Primary outcome was the development of CKD, defined by an estimated glomerular filtration rate <60 ml/min/1.73 m^2 for at least two consecutive measurements at least 90 days apart. The risk for incident CKD was further examined using the outcome defined by newly occurring diagnostic codes indicating CKD.

Results. Over a mean follow-up of 6 years, 12 338 (2.8%) primary outcome events of CKD were observed (incidence rate 4.6/1000 person-years). Per multivariable Cox analysis, urolithiasis was associated with a higher risk of incident CKD [adjusted hazard ratio 1.41 (95% confidence interval 1.36–1.46)]. This association remained consistent across all clinically relevant subgroups and when the CKD outcome was defined based on the diagnostic codes in the sensitivity analysis.

Conclusions. In this large national cohort study, patients with urolithiasis were associated with a higher risk of incident CKD than those without urolithiasis. Further studies are warranted to establish the benefits of preventing urolithiasis in reducing CKD development.

Keywords: chronic kidney disease, urolithiasis

INTRODUCTION

Urolithiasis is a common clinical condition and its prevalence and incidence have increased globally in recent decades not only in Western society [1, 2], but also in Korea [3, 4]. Urolithiasis is presumed to be a systemic disorder associated with various co-morbidities, including hypertension [5], diabetes [6], metabolic syndrome [7, 8] and cardiovascular disease [9, 10].

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KEY LEARNING POINTS

What was known:

- Urolithiasis has been implicated to have a causal relationship with the development of chronic kidney disease (CKD).

This study adds:

- In this nationwide longitudinal cohort study, patients with urolithiasis had a higher risk of incident CKD than those without urolithiasis.

Potential impact:

- Urolithiasis is an important potential contributor to the risk of CKD and patients with a history of urolithiasis must be considered at increased risk for adverse renal outcomes.

Although the prevalence of chronic kidney disease (CKD) is increasing with considerable socio-economic effects in Western society [11] and Korea [12], urolithiasis has been infrequently implicated to have a causal relationship with CKD. Recently, several epidemiological studies and meta-analyses have demonstrated an association between the presence of urolithiasis and the development of CKD and eventually end-stage renal disease (ESRD). However, the generalizability of these results might be limited owing to the relatively small sample sizes [13, 14] or the composition of study populations, which mainly included Western populations in some studies [15–18]. Consequently, the association between urolithiasis and CKD has not been adequately established across different populations and ethnical backgrounds.

Considering that urolithiasis is common and potentially preventable and that the burden of kidney disease is sharply increasing despite dedicated efforts to control diabetes and hypertension, the long-term effects of urolithiasis need to be clarified to inform health interventions for high-risk individuals. Therefore, this study aimed to investigate the association between urolithiasis and the risk of incident CKD using a large nationwide population-based cohort using data from the Korean National Health Insurance Service (NHIS) database.

MATERIALS AND METHODS

Data source and study population

This nationwide longitudinal cohort study used data obtained from an anonymized database provided by the NHIS, which includes all medical claims records of all citizens in Korea, as the NHIS covers compulsory health insurance as a single-payer national health system [19, 20]. This data source was described in previous studies [21, 22]. This study complied with the Declaration of Helsinki and the study protocol was approved by the Institutional Review Board of NHIS Ilsan Hospital (NHIMC 2022-11-030), which waived the requirement for informed consent owing to the use of de-identified administrative data.

A total of 1 017 772 patients treated for urolithiasis between 1 January 2002 and 31 December 2020 were identified. The occurrence of urolithiasis requiring treatment was defined when a diagnostic code related to urolithiasis [*International Statistical Classification of Disease and Related Health Problems Tenth Revision* (ICD-10): N200, N201, N202, N209, N210, N211, N218, N219, N228] was confirmed along with the relevant claims data regarding the treatment for urolithiasis, such as shock wave lithotripsy, ureteroscopy and percutaneous or open procedures (Supplementary Table S1). If there were multiple claims for the treatment of urolithiasis, the date of the first treatment was defined as the index date. Patients <19 years of age ($n = 9003$) or those who died within 90 days from the index date ($n = 15\,856$) were excluded. To detect incident urolithiasis, we further excluded 213 563 patients diagnosed with urolithiasis before 1 January 2009, when serum creatinine levels began to be measured during the national health examination. Next, 425 070 patients without health examination visits at baseline or during subsequent follow-ups were further excluded, while the last record was used as the baseline if a participant underwent multiple examinations during the 2-year period preceding the index date. Participants with diagnostic codes of CKD or ESRD or having received regular dialysis treatments during the 2-year look-back period ($n = 760$) or with an estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2 at baseline ($n = 16\,255$) were considered patients with pre-existing kidney disease and further excluded. After excluding study participants with incomplete covariable information ($n = 33\,141$), for each patient with urolithiasis, we randomly matched one control by age and sex who did not have a diagnosis of urolithiasis throughout the study period, wherein a randomly assigned index date was drawn from the corresponding date of the case with urolithiasis. A final analytical sample was constructed with 219 570 patients with urolithiasis and 219 570 controls whose eGFR measurements were confirmed twice or more during the follow-up (Fig. 1).

Data collection and measurements

Baseline sociodemographic information was obtained on the index date. The presence of comorbidities was established using insurance claims data, which were ascertained by the presence of diagnostic codes confirmed at least once during hospitalization or at least twice during outpatient visits during a 2-year look-back period. Clinical and biochemical parameters were obtained from routine biennial NHIS health examinations provided to all Korean adults. Details of the Korean health examinations have been previously described [23]. eGFR was determined according to the Chronic Kidney Disease Epidemiology Collaboration equation for creatinine [24] and the presence of proteinuria was defined as higher than a trace level from dipstick urine test results. For follow-up measurements of subsequent eGFR measurements to determine the occurrence of outcome events, only eGFR results measured 90 days after urolithiasis treatment were included in the analyses to ensure a temporal association between urolithiasis and CKD. A detailed description of data collection is provided in the Supplementary Methods.

Exposure and outcomes

The exposure of interest was the first diagnosis of urolithiasis that required a procedure, such as ureteroscopy, shock wave

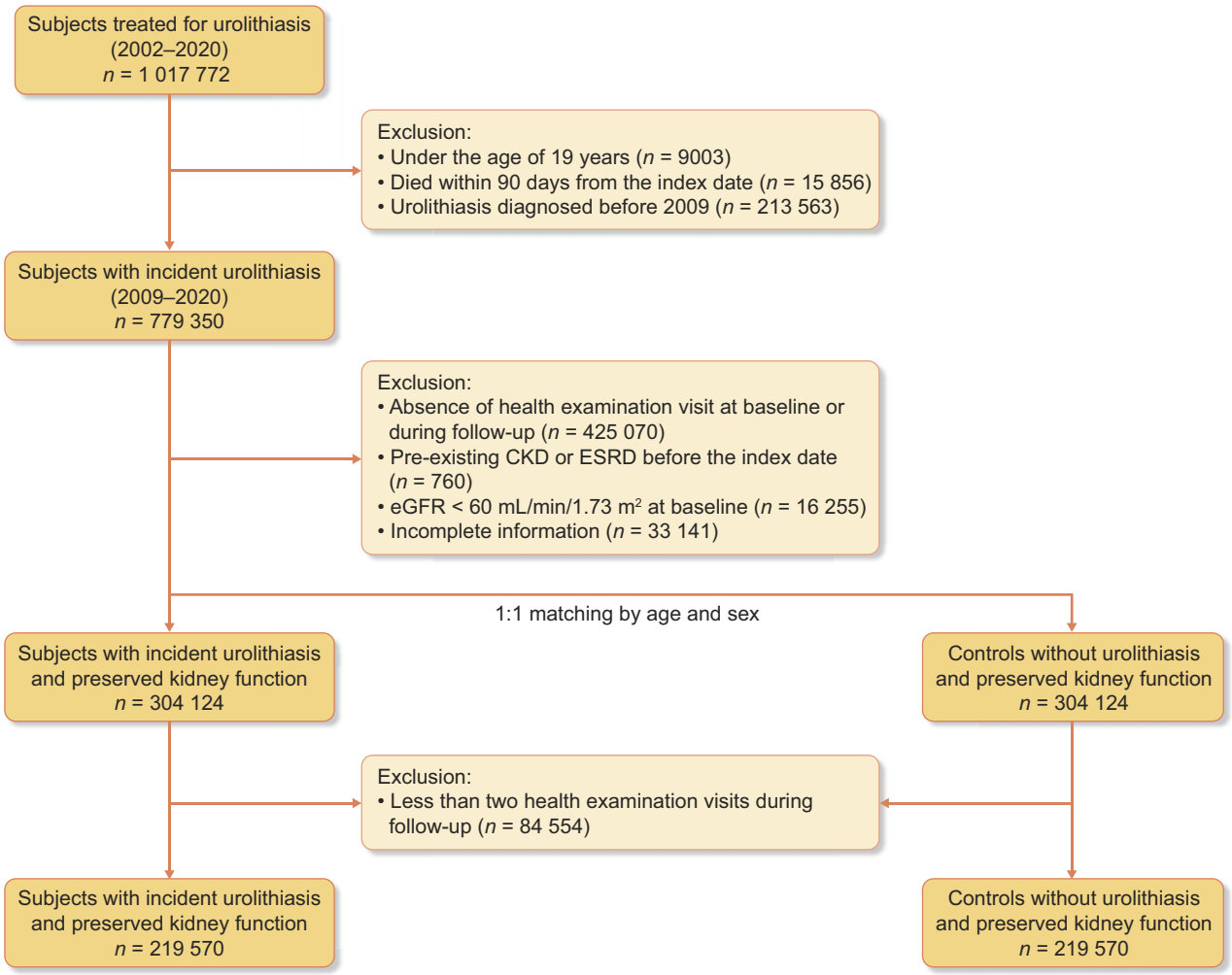

Figure 1: Flow diagram of study participants.

lithotripsy or percutaneous or operative removal of urolithiasis. If a participant experienced more than one event during the follow-up period, the first event was considered as the main exposure. An interval of ≥180 days between claims was assumed to represent separate episodes of urolithiasis; claims occurring within 180 days of each other were classified as a result of a single stone episode [25]. The primary outcome of interest was the de novo development of incident CKD, defined as eGFR <60 ml/min/1.73 m^2 for at least two consecutive measurements at least 90 days apart, according to the definition of CKD in the clinical practice guidelines [26]. In the latter sensitivity analyses, to assess the robustness of our findings, the risk of incident CKD was further examined using outcomes defined using several strategies as follows: eGFR <60 ml/min/1.73 m^2 on at least one instance and a newly occurring diagnostic code indicating CKD (ICD-10: N18) confirmed at least once during hospitalization or at least twice at outpatient visits, assessed separately. The accuracy of the definition of CKD based on diagnostic codes has been previously validated [27]. Participants who did not experience any outcome events were censored either on the date of death, last follow-up or 31 December 2020, whichever occurred first. Deaths were ascertained by linking to the national registry using resident registration numbers.

Statistical analyses

Baseline characteristics are presented as mean ± standard deviation (SD), median [interquartile range (IQR)] or number (percentage), as appropriate. The incidence rates of CKD events were calculated as the number of events per 1000 person-years of follow-up. Hazard ratios (HRs) with 95% confidence intervals (CIs) for the risk of each outcome were calculated using the Cox proportional hazards model. Covariables for the adjustment of HRs were selected a priori on the basis of their possible associations with urolithiasis and CKD. The cumulative incidence of incident CKD was estimated using the Kaplan–Meier curve method and differences among groups were compared using the logrank test. The association between urolithiasis and incident CKD was further investigated in subgroups stratified by age (<65 versus ≥65 years); sex; body mass index (BMI; <25 versus ≥25 kg/m^2); comorbidities of hypertension, diabetes, gout, cardiovascular disease and malignancy (presence versus absence); baseline eGFR (<90 versus ≥90 ml/min/1.73 m^2) and proteinuria (presence versus absence). In the sensitivity analyses for CKD outcomes with different definitions, we further included study participants with health examination visits at least once during the study period while retaining matching by age and sex (304 124 patients with urolithiasis and 304 124

Table 1: Baseline characteristics of the study participants with and without urolithiasis.

Characteristics	Overall (n = 439 140)	Urolithiasis (n = 219 570)	Controls (n = 219 570)
Demographic data			
Age (years), median (IQR)	50 (41–58)	50 (41–58)	50 (41–58)
Male, *n* (%)	423 852 (69.7)	211 926 (69.7)	211 926 (69.7)
Residential area, *n* (%)			
Metropolitan	202 198 (33.2)	105 232 (34.6)	96 966 (31.9)
Large city	130 060 (21.4)	67 666 (22.2)	62 394 (20.5)
Small city and rural area	275 990 (45.4)	131 226 (43.1)	144 764 (47.6)
Household income quartiles, *n* (%)			
First (lowest)	112 989 (18.6)	55 877 (18.4)	57 112 (18.8)
Second	113 245 (18.6)	56 722 (18.7)	56 523 (18.6)
Third	168 839 (27.8)	85 237 (28.0)	83 602 (27.5)
Fourth (highest)	213 175 (35.0)	106 288 (34.9)	106 887 (35.1)
Smoking status, *n* (%)			
Never	302 751 (49.8)	152 891 (50.3)	149 860 (49.3)
Past	127 479 (21.0)	63 529 (20.9)	63 950 (21.0)
Current	178 018 (29.3)	87 704 (28.8)	90 314 (29.7)
Alcohol consumption, *n* (%)			
None	418 041 (68.7)	215 177 (70.8)	202 864 (66.7)
1–2 times/week	144 309 (23.7)	67 338 (22.1)	76 971 (25.3)
≥3 times/week	45 898 (7.5)	21 609 (7.1)	24 289 (8.0)
Exercise frequency, *n* (%)			
None	195 191 (32.1)	101 550 (33.4)	93 641 (30.8)
1–2 times/week	175 291 (28.8)	87 246 (28.7)	88 045 (29.0)
≥3 times/week	237 766 (39.1)	115 328 (37.9)	122 438 (40.3)
Systolic BP (mmHg), mean ± SD	123.9 ± 14.2	124.4 ± 14.1	123.3 ± 14.3
Diastolic BP (mmHg), mean ± SD	77.4 ± 9.8	77.9 ± 9.8	77.0 ± 9.8
BMI (kg/m^2), mean ± SD	24.5 ± 3.3	24.9 ± 3.3	24.2 ± 3.2
Comorbidities, *n* (%)			
Ischaemic heart disease	13 109 (2.2)	7561 (2.5)	5548 (1.8)
Cerebrovascular disease	10 509 (1.7)	5975 (2.0)	4534 (1.5)
Heart failure	3680 (0.6)	2101 (0.7)	1579 (0.5)
Peripheral vascular disease	91 176 (15.0)	48 896 (16.1)	42 280 (13.9)
Hypertension	137 113 (22.5)	75 892 (25.0)	61 221 (20.1)
Diabetes	70 410 (11.6)	40 808 (13.4)	29 602 (9.7)
Gout	7691 (1.3)	4509 (1.5)	3182 (1.0)
Dementia	10 182 (1.7)	5051 (1.7)	5131 (1.7)
Chronic pulmonary disease	170 596 (28.0)	88 694 (29.2)	81 902 (26.9)
Connective tissue disease	43 442 (7.1)	23 527 (7.7)	19 915 (6.5)
Peptic ulcer disease	286 979 (47.2)	151 922 (50.0)	135 057 (44.4)
Liver disease	63 279 (10.4)	35 088 (11.5)	28 191 (9.3)
Hemiplegia	3962 (0.7)	2007 (0.7)	1955 (0.6)
Malignancy	56 096 (12.8)	30 823 (14.0	25819 (11.8)
Acquired immune deficiency syndrome	225 (0.0)	103 (0.0)	122 (0.0)
Laboratory parameters			
eGFR (ml/min/1.73 m^2), mean ± SD	91.9 ± 15.7	91.9 ± 15.8	91.8 ± 15.6
Proteinuria, *n* (%)	31 006 (5.1)	17 063 (5.6)	13 943 (4.6)
Haemoglobin (g/dl), mean ± SD	14.5 ± 1.5	14.5 ± 1.5	14.5 ± 1.5
Fasting blood glucose (mg/dl), mean ± SD	100.6 ± 24.3	101.2 ± 24.4	99.9 ± 24.2
Total cholesterol (mg/dl), mean ± SD	198.1 ± 37.5	199.2 ± 37.9	197.0 ± 37.1
Procedures, *n* (%)			
Ureteroscopy		25 534 (8.4)	
Shock wave lithotripsy		274 683 (90.3)	
Other		3907 (1.3)	

controls). Differences were considered statistically significant at $P < .05$. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA) and Stata version 15.1 (StataCorp, College Station, TX, USA).

RESULTS

Baseline characteristics of the study population

The baseline characteristics of the study participants are presented in Table 1. The median age of the 439 140 participants

Table 2: Association between the risk of incident CKD and urolithiasis.

Variables	Person-years	Events (%)	Incidence rate per 1000 person-years (95% CI)	HR (95% CI)	P-value
Overall	2 648 100.8	12 238 (2.8)	4.6 (4.5–4.7)		
Control	1 328 105.9	4842 (2.2)	3.6 (3.5–3.7)	Reference	
Urolithiasis	1 319 994.9	7396 (3.4)	5.6 (5.5–5.7)	1.41 (1.36–1.46)	<.001

All models are adjusted for age; sex; household income quartile; tobacco smoking; alcohol consumption; exercise frequency; systolic and diastolic BP; BMI; presence of comorbidities, including ischaemic heart disease, cerebrovascular disease, heart failure, peripheral vascular disease, hypertension, diabetes, gout, dementia, chronic pulmonary disease, connective tissue disease, peptic ulcer disease, liver disease, hemiplegia, malignancies and acquired immune deficiency syndrome; and laboratory parameters, including eGFR, proteinuria, haemoglobin, fasting blood glucose and total cholesterol at baseline.

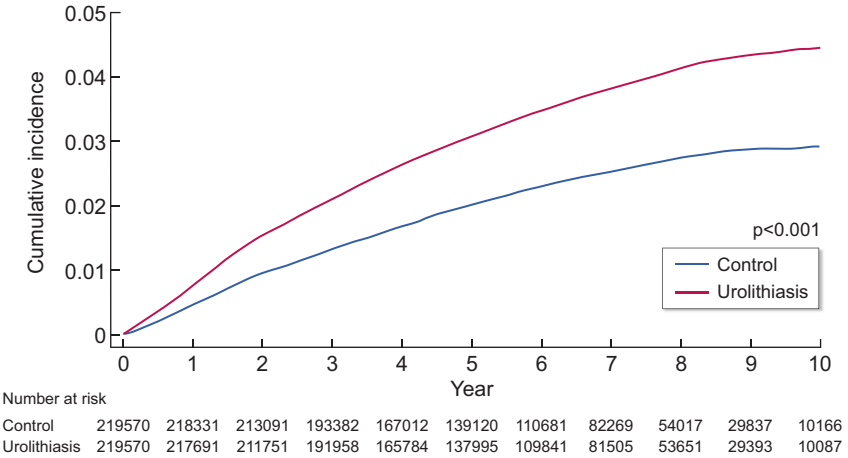

Figure 2: Kaplan–Meier curves for the cumulative incidence of the incident CKD. The cumulative incidence rate of CKD events was significantly higher in patients with urolithiasis than in controls. Statistical analysis was performed using the logrank test.

in the NHIS data was 50 years and 69.7% were men. Patients with urolithiasis lived more often in a metropolitan area or large cities, exercised less frequently, had higher systolic and diastolic blood pressure (BP) and BMI, more comorbidities, higher prevalence of proteinuria and higher fasting glucose and total cholesterol levels compared with controls without urolithiasis. There was no significant difference in the eGFR at baseline between the groups. Among the patients with urolithiasis, 8.4% and 90.3% were treated with ureteroscopy and shock wave lithotripsy, respectively.

Urolithiasis and risk of incident CKD

During a mean follow-up of 6.0 years (2 648 100.8 person-years), 12 238 (2.8%) primary outcome events of incident CKD were recorded, with an incidence rate of 4.6/1000 person-years. While there were 4842 (2.2%) incident CKD events in controls, 7396 (3.4%) events were observed in patients with urolithiasis (Table 2). Incidence rates per 1000 person-years of controls and patients with urolithiasis were 3.6 (95% CI 3.5–3.7) and 5.6 (95% CI 5.5–5.7), respectively ($P < .001$). Patients with urolithiasis were associated with a higher risk of incident CKD compared with controls, with a multivariable-adjusted HR of 1.41 (95% CI 1.36–1.46). The cumulative incidence rate of CKD events was also significantly higher in patients with urolithiasis than in controls (Fig. 2). In the additional analysis, the number of episodes of urolithiasis was observed to have a graded association with the risk of incident CKD, as adjusted HRs for individuals with a single episode and with multiple episodes of urolithiasis were 1.40 (95% CI 1.35–1.45) and 1.45 (95% C, 1.37–1.54), respectively, when compared with controls (Supplementary Table S2).

Subgroup analyses

Given the potential heterogeneity of the study population, we also examined the association between urolithiasis and the risk of the primary outcome of incident CKD across clinically relevant subgroups (Fig. 3). Overall, the aforementioned pattern of association was robust and generally consistent across prespecified subgroups stratified by age; sex; BMI; presence of comorbidities such as hypertension, diabetes, gout, cardiovascular disease and malignancy; eGFR; and presence of proteinuria. Notably, the magnitudes of risk increase were greater in subgroups of participants who were <65 years of age, male, without hypertension and with an eGFR ≥90 ml/min/1.73 m^2 and no proteinuria at baseline.

Sensitivity analyses

Additional sensitivity analyses were performed using CKD outcomes defined by several strategies. While comparison of baseline characteristics of the analytical cohort revealed a similar pattern of differences between the groups as in the main analysis, there was no significant difference in baseline eGFR between the groups as in the main analysis (Supplementary Table S3). Outcome events of eGFR <60 ml/min/1.73 m^2 at least once during follow-up were observed in 45 880 participants, with an incidence rate of 15.0/1000 person-years, which was higher than

Groups	Subgroups	N	Events (%)	HR (95% CI)	P for interaction
Age (years)	< 65	391 610	7 216 (1.8)	1.50 [1.42–1.57]	< 0.001
	≥ 65	47 530	5 022 (10.6)	1.30 [1.23–1.38]	
Sex	Male	312 304	8 559 (2.7)	1.52 [1.45–1.59]	< 0.001
	Female	126 836	3 679 (2.9)	1.18 [1.10–1.26]	
BMI (kg/m²)	<25	261 639	6 292 (2.4)	1.37 [1.31–1.45]	0.22
	≥25	177 501	5 946 (3.3)	1.44 [1.37–1.52]	
Hypertension	Absent	345 220	6 009 (1.7)	1.47 [1.40–1.55]	0.009
	Present	93 920	6 229 (6.6)	1.34 [1.27–1.41]	
Diabetes	Absent	391 903	8 621 (2.2)	1.37 [1.31–1.43]	0.07
	Present	47 237	3 617 (7.7)	1.50 [1.40–1.61]	
Gout	Absent	434 043	11 943 (2.8)	1.40 [1.35–1.46]	0.42
	Present	5 097	295 (5.8)	1.61 [1.25–2.07]	
Cardiovascular disease	Absent	415 251	10 602 (2.6)	1.42 [1.37–1.48]	0.08
	Present	23 889	1 636 (6.8)	1.31 [1.18–1.45]	
Malignancy	Absent	402 462	10 625 (2.6)	1.40 [1.35–1.46]	0.67
	Present	26 678	1 613 (6.0)	1.45 [1.30–1.60]	
eGFR (ml/min/1.73 m²)	≥ 90	237 483	1 606 (0.7)	1.53 [1.38–1.70]	0.03
	< 90	201 657	10 632 (5.3)	1.39 [1.34–1.45]	
Proteinuria	Absent	417 820	10 986 (2.6)	1.44 [1.38–1.49]	0.001
	Present	21 320	1 252 (5.9)	1.19 [1.06–1.33]	

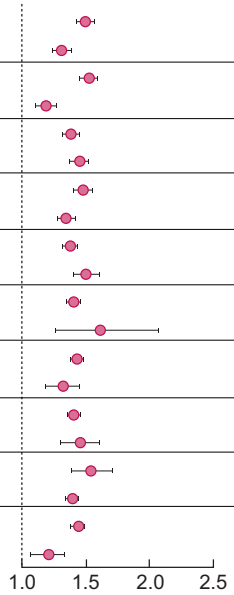

Figure 3: Forest plot for subgroup analysis. The association between urolithiasis and an increased risk of incident CKD was consistent across all clinically relevant subgroups. Cardiovascular disease includes ischaemic heart disease, cerebrovascular disease and heart failure. All models are adjusted for age; sex; household income quartile; tobacco smoking; alcohol consumption; exercise frequency; systolic and diastolic BP; BMI; presence of comorbidities, including ischaemic heart disease, cerebrovascular disease, heart failure, peripheral vascular disease, hypertension, diabetes, gout, dementia, chronic pulmonary disease, connective tissue disease, peptic ulcer disease, liver disease, hemiplegia, malignancies and acquired immune deficiency syndrome; and laboratory parameters, including eGFR, proteinuria, haemoglobin, fasting blood glucose and total cholesterol at baseline.

in the main analysis (Supplementary Table S4). Patients with urolithiasis were consistently associated with a higher risk of eGFR decline compared with controls, with an adjusted HR of 1.23 (95% CI 1.21–1.26). Furthermore, incident CKD, defined by diagnostic codes, was observed in 4518 participants, with an incidence rate of 1.2/1000 person-years. Similarly, patients with urolithiasis were significantly associated with a 70% higher risk of the incident CKD [HR 1.70 (95% CI 1.60–1.81)].

DISCUSSION

We hypothesized that there was a causal relationship between urolithiasis and a risk of incident CKD. In this nationwide longitudinal cohort study of Korean adults, we found a significant association between urolithiasis requiring procedural treatment and an increased risk of incident CKD. This association was generally consistent irrespective of the various definitions of CKD outcomes based on laboratory results of eGFR decline or diagnostic codes and across all clinically relevant subgroups. Thus our findings suggest that urolithiasis adversely affects kidney health.

Although several population-based studies were mostly consistent in showing a trend for a greater risk of CKD in patients with urolithiasis as did our findings [16, 28, 29], this association was not observed in certain populations or subgroups. Some suspected reasons for this discrepancy between study results may include differences in the definitions of CKD as an outcome (i.e. whether it was defined based on laboratory results of eGFR or diagnostic codes, with proteinuria being counted as an outcome). Urolithiasis was found to induce a transient increase in serum creatinine levels, which subsequently resolved, indicating acute kidney injury [30]. Therefore, we defined renal outcomes by two consecutive laboratory results of decreased eGFR >90 days apart and measured them 90 days after the urolithiasis event in the main analysis to investigate the long-term risk due to urolithiasis and avoid overestimation of the prevalence of CKD that can result from a single measurement of eGFR [31, 32]. This association remained consistent even when further sensitivity analysis was performed with CKD outcomes defined by diagnostic codes referring to CKD. In addition, to prevent possible misidentification that might have been implied in several previous studies that defined urolithiasis based on diagnostic codes or through a questionnaire-based survey [13, 16, 28, 33], we restricted cases to symptomatic urolithiasis in which the diagnostic code was confirmed along with the concomitant treatment codes of relevant procedures. Another possible reason for the differences between study results might be attributable to the substantial heterogeneity or small sample size of the study populations [33–35]. Interestingly, while a recent meta-analysis investigating the risk of CKD in patients with urolithiasis showed that the pooled results of two studies conducted in Asian populations were statistically insignificant [18], the findings of this nationwide cohort study of healthy Korean adults with relatively fewer comorbidities provided further evidence to support this association.

Although the mechanism underlying urolithiasis being a risk factor for CKD is unclear, the putative correlation is likely multifactorial. The most plausible pathogenesis involves obstructive uropathy that leads to progressive scarring of the kidney [36, 37]. Crystal deposition in the Bellini duct and inner medullary collecting ducts can lead to inflammatory changes and subsequent fibrotic damage [38, 39]. In addition, metabolic disorders associated with both CKD and urolithiasis have been reported as risk factors identified among patients with urolithiasis who

developed CKD [40]. Secondary infection following obstruction or struvite stones can also lead to the loss of kidney function. Although a significant association between urolithiasis and CKD was observed in our study, further mechanistic studies are required to verify whether urolithiasis causes permanent renal parenchymal damage.

Our study has several strengths. This study comprised the largest cohort of patients with symptomatic urolithiasis and age- and sex-matched controls whose outcomes were precisely and longitudinally determined by accessing national claims data with detailed medical records on diagnostic codes and procedures. Moreover, the sensitivity analyses based on various definitions of CKD outcomes allowed for a comprehensive review of the effects of urolithiasis on kidney function loss. However, our findings should be interpreted considering some limitations. First, owing to the nature of an observational study, a causal association between urolithiasis and CKD could not be established and potential residual confounding factors might not have been thoroughly controlled despite the rigorous adjustment of measured variables, such as demographic, clinical and laboratory parameters. In particular, the effect of urologic procedures as a treatment for urolithiasis on the renal function could not be investigated. In addition, due to the lack of information on hereditary disease, the effect of the presence of preexisting genetic disorders on the association between the development of urolithiasis and the risk of incident CKD could not be determined. Second, we were unable to determine the composition or location of urolithiasis and thus could not assess the specific risk associated with different stone types or stone locations. Third, although the effects of obesity determined by BMI and questionnaire-based details on health-related behaviours, such as smoking status and alcohol consumption, were considered throughout the analyses, other lifestyle risk factors, including daily fluid intake or dietary patterns, that could have affected the development of urolithiasis and CKD could not be fully accounted for owing to a lack of information. Finally, because the study cohort consisted entirely of Koreans, the results obtained in this study should be interpreted with caution when applied to other populations.

This cohort study suggests that urolithiasis is an important potential contributor to the risk of CKD and that patients with a history of urolithiasis must be considered at increased risk for adverse renal outcomes. Further studies are required to determine the mechanisms underlying this association and assess the benefits of urolithiasis prevention in reducing CKD development.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

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AUTHORS' CONTRIBUTIONS

J.Y.K. and T.I.C. were responsible for the study concept and design and drafting of the manuscript. They had full access to all data in the study and are responsible for the integrity of the data and accuracy of the analysis. J.Y.K. J.K.L. and T.I.C. were responsible for the acquisition, analysis and interpretation of data. J.Y.K. and J.K.L. were responsible for the statistical analyses. J.K.L. was responsible for administrative, technical and material support. J.Y.K., J.T.P. and T.I.C. were responsible for study supervision. All authors were responsible for critical revision of the manuscript for important intellectual content.

DATA AVAILABILITY STATEMENT

The technical appendix and statistical code for data sharing are available from T.I.C. (email: kidneyjang@gmail.com). All data are available through approval and oversight by the Korean National Health Insurance Service at the National Health Insurance Data Sharing Service (https://nhiss.nhis.or.kr/bd/ab/bdaba000eng.do).

CONFLICT OF INTEREST STATEMENT

All authors declare no relevant conflicts of interest.

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