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Trajectories of atherosclerotic cardiovascular disease risk scores as a predictor for incident chronic kidney disease

Hye Sun Lee[1], Hong Il Lim[2], Tae Ju Moon[2], So Young Lee[2] and Jun-Hyuk Lee[3*]

Abstract

Background The relationship between atherosclerosis and renal function is well established. Atherosclerotic cardiovascular disease (ASCVD) risk scores reflect atherosclerotic burden, which changes over time. We investigated the association between ASCVD risk trajectories and incident chronic kidney disease (CKD) using data from a large community-based Korean cohort with up to 16 years of follow-up.

Methods We analyzed data from 5032 participants without CKD from the baseline survey of the Korean Genome and Epidemiology Study Ansan-Ansung cohort. Participants were categorized into stable or increasing ASCVD risk groups based on the revised ASCVD risk pooled cohort equation over a median period of exposure of 5.8 years. Incident CKD was defined as two consecutive events of an estimated glomerular filtration rate < 60 mL/min/1.73 m^2.

Results During a median 9.9 years of event accrual period, 449 (8.92%) new-onset CKD cases were identified. Multiple Cox proportional regression analyses showed that the hazard ratio (95% confidence interval) for incident CKD in the increasing group, compared to the stable group, was 2.13 (1.74–2.62) in the unadjusted model and 1.35 (1.02–1.78) in the fully-adjusted model. Significant relationships were maintained in subgroups of individuals in their 50s, without diabetes mellitus or hypertension. The prevalence of proteinuria was consistently higher in the increasing group than that in the stable group.

Conclusions An increasing trend in ASCVD risk scores independently predicted adverse renal outcomes in patients without diabetes mellitus or hypertension. Continuous monitoring of ASCVD risk is not only important for predicting cardiovascular disease but also for predicting CKD.

Keywords Atherosclerotic cardiovascular disease, Trajectory, Chronic kidney disease, Incidence, Prospective cohort

Introduction

Atherosclerosis is an important contributor to cardiovascular disease (CVD), including myocardial infarction, ischemic stroke, and peripheral vascular disease [1, 2]. Atherosclerotic cardiovascular disease (ASCVD) risk scores have been developed to estimate an individual's risk of CVD [3, 4]. Among them, the revised ASCVD pooled cohort equations, in particular, provide race- and sex-specific 10-year ASCVD risk estimates, highlighting the variability in risk factor prevalence, associated risks,

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and underlying ASCVD event rates among different groups [3].

There is an inter-relationship between atherosclerosis and renal function [5, 6]. The pathological process of atherosclerosis can stimulate intrarenal atherogenesis through the mediation of oxidative stress and inflammation, subsequently leading to a decline in renal function [5]. Concurrently, a decrease in renal function, especially as seen in chronic kidney disease (CKD), can exacerbate the production of uremic toxins, free radicals, and pro-inflammatory cytokines [6]. Previous research has also suggested that 10-year ASCVD risk scores have predictive power beyond those of conventional cardiovascular risk predictors in determining cardiovascular events in patients with CKD [7–11]. However, ASCVD risk score changes over time. If temporal trends in ASCVD risk scores can serve as significant predictors of CKD, they could provide additional information for clinicians to identify individuals at risk of CKD, in addition to those at risk of CVD, allowing for the application of cost-effective early interventions. Therefore, this study aimed to investigate the association between the trajectories of ASCVD risk scores and incident CKD using a large community-based prospective Korean cohort.

Methods

Study population

The analysis utilized data from the Ansan-Ansung cohort of the KoGES, which is a community-based, prospective cohort study conducted by the KCDA [12]. In the initial survey conducted in 2001–2002, a total of 10,030 participants aged 40–69 years who had been living in urban (Ansan) and rural (Ansung) areas for at least 6 months were recruited and followed up biennially for a maximum duration of 16 years, until 2017–2018. The period from the baseline survey to six years was defined as the exposure period, whereas the period from six to 16 years was defined as the event accrual period.

Figure 1 shows a flowchart of the study population selection. Among a total of 10,030 participants at baseline survey of the KoGES_Ansan and Ansung study, we analyzed data from a total of 5032 participants without CKD during the exposure period by applying the exclusion criteria as follows:1) Missing data for assessing 10-year ASCVD risk scores at baseline ($n=136$), 2) Prevalent CKD at baseline ($n=220$), 3) Use of diuretics or steroid medications ($n=22$), 4) Newly developed CKD during the exposure period ($n=209$), 5) Never followed up during the exposure period ($n=1158$), and 6) Never followed up during the event accrual period ($n=3253$).

The Korean Genome and Epidemiology Study (KoGES) Ansan-Ansung cohort protocol was reviewed and approved by the institutional review board of the Korea Centers for Disease Control Agency (KCDA). Written informed consent was obtained from all participants. The study protocol conformed with the ethical guidelines of the 1964 Declaration of Helsinki and its subsequent amendments. This study was approved by the institutional review board of Nowon Eulji Medical Center (institutional review board number:2023–02-023).

Measurements

Height (m) and weight (kg) were measured, and the body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were calculated as the average of the last two of three measurements. The mean blood pressure (MBP) was calculated. Smoking status was divided into never smoked, ex/ intermittent smokers, and daily smokers. Alcohol consumption status was divided into current drinkers and non-drinkers. Physical activity was measured in metabolic equivalents of task (MET)-hours per day (MET-h/day), based on the

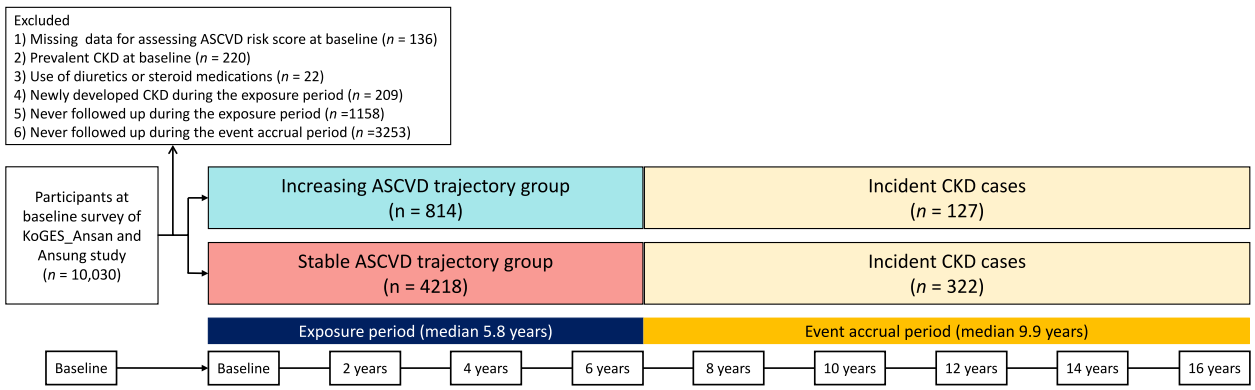


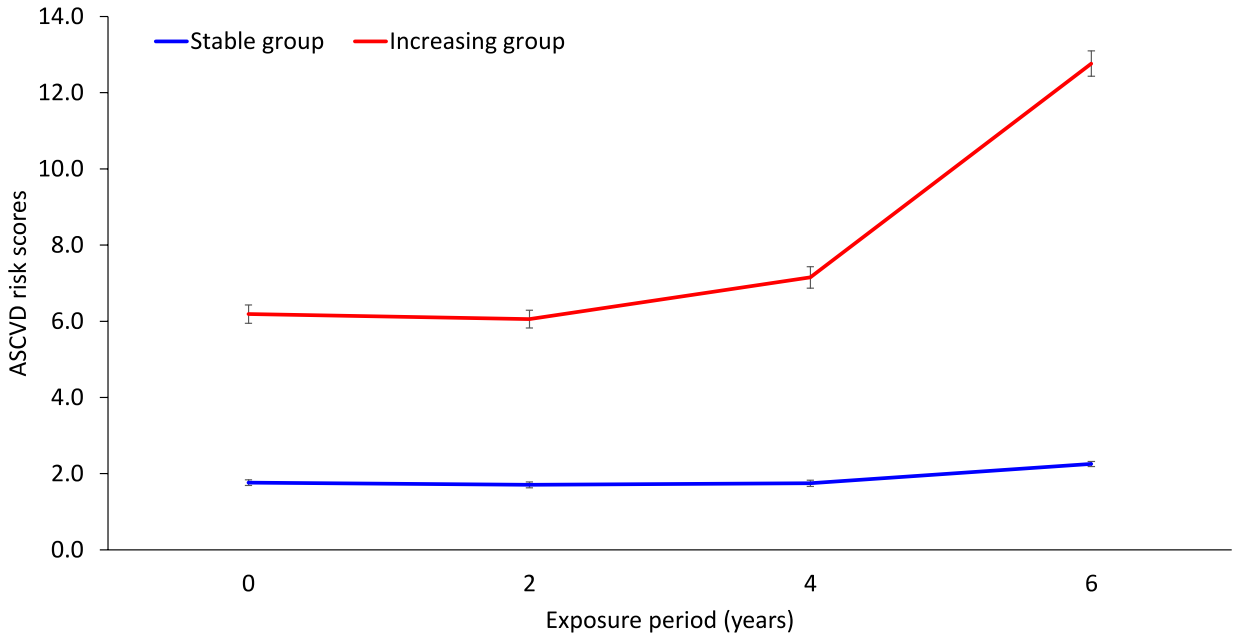
Fig. 1 Flowchart of the study population

International Physical Activity Questionnaire, and was divided into low-intensity (<7.5 MET-h/day), moderate-intensity (7.5–30 MET-hr/day), and high-intensity (>30 MET-h/day) groups. The total energy intake (kcal/day) was calculated using a 103-item food frequency questionnaire. Blood samples were collected from each participant after at least 8-h fasting. Fasting plasma glucose (FPG), glycosylated hemoglobin (HbA1c), serum creatinine, total cholesterol, and C-reactive protein (CRP) levels were measured. Estimated glomerular filtration rates (eGFR) were calculated using the CKD-Epidemiology Collaboration equation [13]. The presence of protein traces of 1+, 2+, 3+, or 4+was considered indicative of proteinuria based on the results of a urinary dipstick test.

Diabetes mellitus (DM) was defined as a FPG level of 126 mg/dL or higher, a 2-h glucose level of 200 mg/dL or higher after a 75 g oral glucose tolerance test, HbA1c of 6.5% or higher, or the use of antidiabetic medication or insulin therapy [14]. Hypertension (HTN) was defined as a SBP of 140 mmHg or higher, DBP of 90 mmHg or higher, or the use of antihypertensive medication [15].

ASCVD risk trajectories assessment

The main exposure in the current study was the change in ASCVD risk over time. The cardiovascular risk assessment was estimated by using the revised 10-year ASCVD pooled cohort equations [16]. Using baseline and temporal measurements of the 10-year ASCVD risk scores during the median period of exposure of 5.8 years, we performed trajectory modelling by using R package "lcmm," which was used for latent variable mixture modelling [17, 18]. Latent variable mixture modeling enabled the identification of potential variability in the patterns of continuous variables such as 10-year ASCVD risk scores across different periods. Models with two to five trajectories were constructed by considering the individual as a random effect and time as a fixed effect [19, 20]. The optimal number of groups of ASCVD risk trajectories was two groups (stable group and increasing group; Fig. 2), based on the lowest Bayesian information criterion value and the number of participants in each trajectory (≥5% of the total population), as shown in Supplementary Table 1. Finally, we classified the participants into stable



	Median ASCVD risk scores			
	0	**2**	**4**	**6**
Stable group	1.8	1.7	1.7	2.3
Increasing group	6.2	6.1	7.2	12.8

Fig. 2 Trajectory modeling with the revised ASCVD risk pooled cohort equation using the latent variable mixture model. Red line: increasing ASCVD risk trajectory group, blue line: stable ASCVD risk trajectory group. Abbreviation: ASCVD, atherosclerotic cardiovascular disease

($n=4218$) and increasing ($n=814$) ASCVD risk trajectory groups.

Renal outcome assessment

The primary outcome of the study was incident CKD, which was defined as the occurrence of two consecutive events with an eGFR of < 60 mL/min/1.73m^2 [21, 22]. Participants who did not experience an incident CKD event during the exposure period were followed up from the end of the exposure period until the occurrence of an incident CKD event, the end of the study, or the last date of contact with the participant that provided informative data. The number of new CKD events during the accrual period was also recorded.

Statistical analysis

Data are presented as mean ± standard deviation for continuous variables and number (percentage, %) for categorical variables. The student's t-test was used to compare the differences between the increasing and stable ASCVD risk trajectory groups for continuous variables, whereas the chi-square test was used for categorical variables.

A Kaplan–Meier curve was drawn to compare the cumulative incidence rate of CKD between the stable and increasing ASCVD risk trajectory groups using the log-rank test. Multiple Cox proportional hazard regression analysis was used to estimate the hazard ratio (HR) with a 95% confidence interval (CI) for incident CKD in the increasing ASCVD risk trajectory group compared with the stable group. In Model 1, we adjusted for age, BMI, total energy intake, smoking status, alcohol consumption status, and physical activity. In Model 2, we adjusted for the variables used in Model 1 plus MBP, FPG, serum total cholesterol, and CRP levels. In Model 3, we further adjusted for baseline ASCVD risk scores and baseline eGFR. We illustrated a forest plot showing subgroup analyses based on sex, age groups, DM, HTN, and high ASCVD risk (≥ 10%) status, adjusting for variables used in Model 3. The prevalence of proteinuria in the two ASCVD risk trajectory groups at each time point was compared using the chi-squared test. Sensitivity analysis was also performed for participants who were consistently followed-up during the exposure period.

All statistical analyses were performed using SAS statistical software (version 9.4; SAS Institute Inc., Cary, NC, USA), SPSS statistical software (version 25.0; SPSS Inc., Chicago, IL, USA), and R software (version 4.2.1; R Foundation for Statistical Computing, Vienna, Austria). Statistical significance was set at $p < 0.05$.

Results

Clinical characteristics of the study population based on the different ASCVD risk trajectory groups

Table 1 presents the baseline characteristics of the study population based on ASCVD risk trajectory groups. Compared with the stable ASCVD risk trajectory group, the increasing group had a higher proportion of men, individuals aged 50 to 69 years, ex-smokers, intermittent smokers, daily smokers, current drinkers, individuals with high-level physical activity, lower baseline eGFR, higher MBP, FPG, serum total cholesterol level, CRP level, and baseline ASCVD risk scores. The prevalence of DM and HTN was significantly higher in the group with increasing ASCVD risk trajectory compared to the stable group (both $p < 0.001$).

Association of ASCVD risk trajectory groups with incident CKD during the event accrual period

During the median 9.9 years of the event accrual period, a total of 449 (8.92%) newly developed CKD cases occurred. The incidence rate of CKD per 1000 person-years was 9.35.

Figure 3 shows the Kaplan–Meier curves for the cumulative incidence rate of CKD during the event accrual period according to the two different ASCVD risk trajectory groups. The increasing ASCVD risk trajectory group showed a persistently higher cumulative incidence of CKD than the stable group (p for log-rank test < 0.001). Table 2 presents the Cox proportional hazard regression analysis for incident CKD in the increasing ASCVD risk trajectory group compared with the stable group. In the unadjusted model, the HR (95% CI) for incident CKD in the increasing ASCVD risk trajectory group compared with that in the stable group, was 2.13 (1.74–2.62). Additionally, the adjusted HR (95% CI) for incident CKD in the increasing ASCVD risk trajectory group, compared to stable group, was 1.39 (1.06–1.82) in Model 1, 1.35 (1.02–1.77) in Model 2, and 1.35 (1.02–1.78) in Model 3. Subgroup analysis revealed a significant association between ASCVD risk trajectories and incident CKD in individuals in their 50s without DM and HTN (Fig. 4).

Prevalence of proteinuria between the increasing and stable ASCVD risk trajectory groups

Table 3 presents the prevalence of proteinuria based on the ASCVD risk trajectory groups during the event accrual period. The prevalence of proteinuria was consistently and significantly higher in the increasing ASCVD risk trajectory group than that in the stable group during the event accrual period.

Table 1 Baseline characteristics of the study population

Variables	Total population	ASCVD trajectory groups		
		Stable	Increasing	P^*
	(*n* = 5032)	(*n* = 4218)	(*n* = 814)	
Male sex, n (%)	2365 (47.0%)	1776 (42.1%)	589 (72.4%)	< 0.001
Age groups, n (%)				< 0.001
40s	2580 (58.4%)	2363 (62.5%)	217 (34.2%)	
50s	1434 (32.5%)	1166 (30.8%)	268 (42.2%)	
60s	403 (9.1%)	253 (6.7%)	150 (23.6%)	
BMI, kg/m^2	24.6 ± 3.0	24.6 ± 3.0	24.7 ± 3.1	0.244
MBP, mmHg	95.9 ± 12.8	95.2 ± 12.9	99.8 ± 11.8	< 0.001
Smoking status, n (%)				< 0.001
Never smoker	3165 (62.9%)	2849 (67.5%)	316 (38.8%)	
Ex-smoker	755 (15.0%)	596 (14.1%)	159 (19.5%)	
Intermittent smoker	111 (2.2%)	81 (1.9%)	30 (3.7%)	
Daily smoker	1001 (19.9%)	692 (16.4%)	309 (38.0%)	
Current drinker, n (%)		1957 (46.6%)	455 (56.0%)	< 0.001
Physical activity, n (%)				< 0.001
Low	326 (6.7%)	273 (6.7%)	53 (6.8%)	
Moderate	2953 (60.7%)	2572 (63.0%)	381 (48.8%)	
High	1586 (32.6%)	1239 (30.3%)	347 (44.4%)	
Total energy intake, kcal/day	1970.3 ± 697.7	1969.4 ± 699.2	1975.2 ± 690.3	0.830
Baseline eGFR, mL/min/1.73m^2	93.7 ± 12.6	94.2 ± 12.6	90.7 ± 12.2	< 0.001
FPG, mg/dL	86.4 ± 19.1	85.8 ± 18.5	89.9 ± 21.4	< 0.001
Total cholesterol, mg/dL	190.1 ± 34.3	189.4 ± 34.2	193.8 ± 34.5	< 0.001
CRP, mg/dL	0.14 [0.06;0.23]	0.13 [0.06;0.23]	0.16 [0.08;0.27]	< 0.001
Baseline ASCVD risk, %	2.3 [0.7;5.5]	1.8 [0.5; 4.4]	6.2 [3.4;10.7]	< 0.001
DM, n (%)	542 (10.8%)	402 (9.5%)	140 (17.2%)	< 0.001
HTN, n (%)	1810 (36.0%)	1432 (33.9%)	378 (46.4%)	< 0.001

* *P*-values were derived from Student's t-test or Mann–Whitney test for continuous variables and chi-square test for categorical variables to compare differences in variables between groups. A *p*-value of less than 0.05 was considered statistically significant

Abbreviations: *ASCVD* atherosclerotic cardiovascular disease, *BMI* body mass index, *MBP* mean blood pressure, *eGFR* estimated glomerular filtration rate, *FPG* fasting plasma glucose, *CRP* C-reactive protein, *DM* diabetes mellitus, *HTN* hypertension

Sensitivity analysis with participants who were consistently followed up during the exposure period

During the exposure period, 4634 participants were consistently followed up. Among these, 411 cases (8.87%) of newly developed CKD were identified. Supplementary Table 2 demonstrates a higher risk of incident CKD in the increasing compared to the stable ASCVD risk trajectory group, with fully-adjusted HR of 1.36 and 95% CI of 1.03–1.81. The prevalence of proteinuria was consistently higher in the increasing ASCVD risk trajectory group than that in the stable group (Supplementary Table 3).

Discussion

To the best of our knowledge, this is the first study to investigate the association between ASCVD risk trajectory and incident CKD. Previous studies have concentrated mainly on evaluating ASCVD risk in individuals with pre-existing CKD [23–25]. However, the identification of individuals at a higher risk of CKD through early detection and implementation of early interventions can be a potentially cost-effective approach to reducing the burden of CKD. In the current study, the ASCVD risk trajectory group had a 2.13 times higher risk of incident CVD than the stable group, regardless of the ASCVD risk at baseline. Moreover, the increasing group consistently showed a higher prevalence of proteinuria than did the stable group during the event accrual period. Mean eGFR was consistently lower in the increasing than in the stable ASCVD risk trajectory group.

Ren et al. [8] found that individuals with higher ASCVD risk scores showed lower eGFR and more severe renal interstitial inflammation among 218 patients with type 2 DM and biopsy-proven CKD and suggested that an ASCVD risk of 14.1% was an independent indicator of

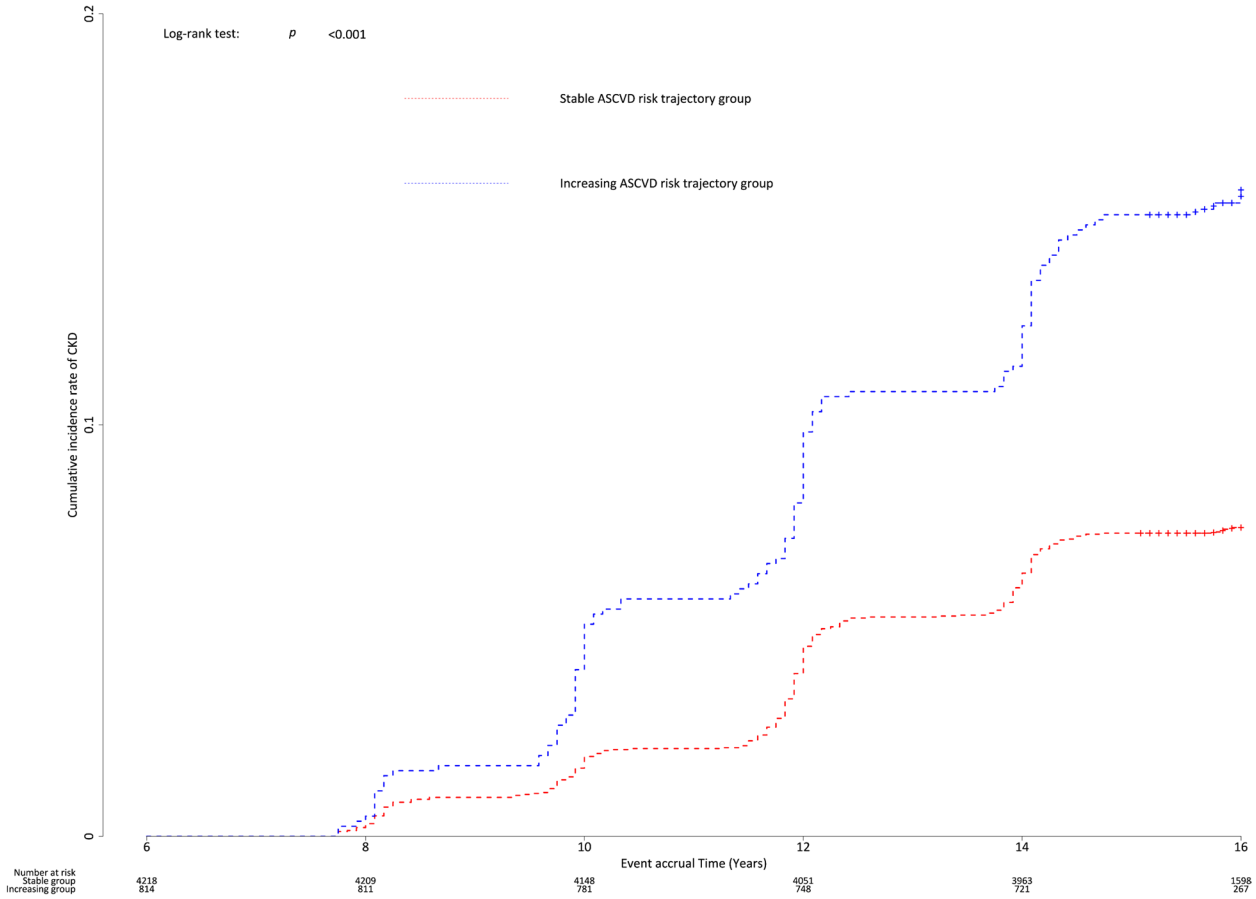


Fig. 3 Kaplan–Meier curves showing the cumulative incidence rates of CKD based on the ASCVD risk trajectory groups. Abbreviations: CKD, chronic kidney disease; ASCVD, atherosclerotic cardiovascular disease

Table 2 Cox proportional hazard regression analysis showing the relationship of ASCVD risk trajectories with incident chronic kidney disease

	Stable ASCVD risk	Increasing ASCVD risk		
Total cases, n	4218	814		
Incident CKD cases, n	322	127		
Follow-up time, person-year	40,492.7	7536.8		
Incident rate per 1000 person-year	7.95	16.85		
		HR	95% CI	*p*
Unadjusted	1 (reference)	2.13	1.74–2.62	< 0.001
Model 1	1 (reference)	1.39	1.06–1.82	0.016
Model 2	1 (reference)	1.35	1.02–1.77	0.033
Model 3	1 (reference)	1.35	1.02–1.78	0.033

Model 1: Adjusted for sex, age groups, BMI, total energy intake, smoking status, alcohol drinking status, and physical activity

Model 2: Adjusted for variables used in Model 1 plus MBP, FPG, serum total cholesterol, and CRP levels

Model 3: Adjusted for variables used in Model 2 plus baseline ASCVD risk scores and baseline eGFR

Abbreviations: *ASCVD* atherosclerotic cardiovascular disease, *CKD* chronic kidney disease, *BMI* body mass index, *MBP* mean blood pressure, *FPG* fasting plasma glucose, *CRP* C-reactive protein, *eGFR* estimated glomerular filtration rate, *HR* hazard ratio, *CI* confidence interval

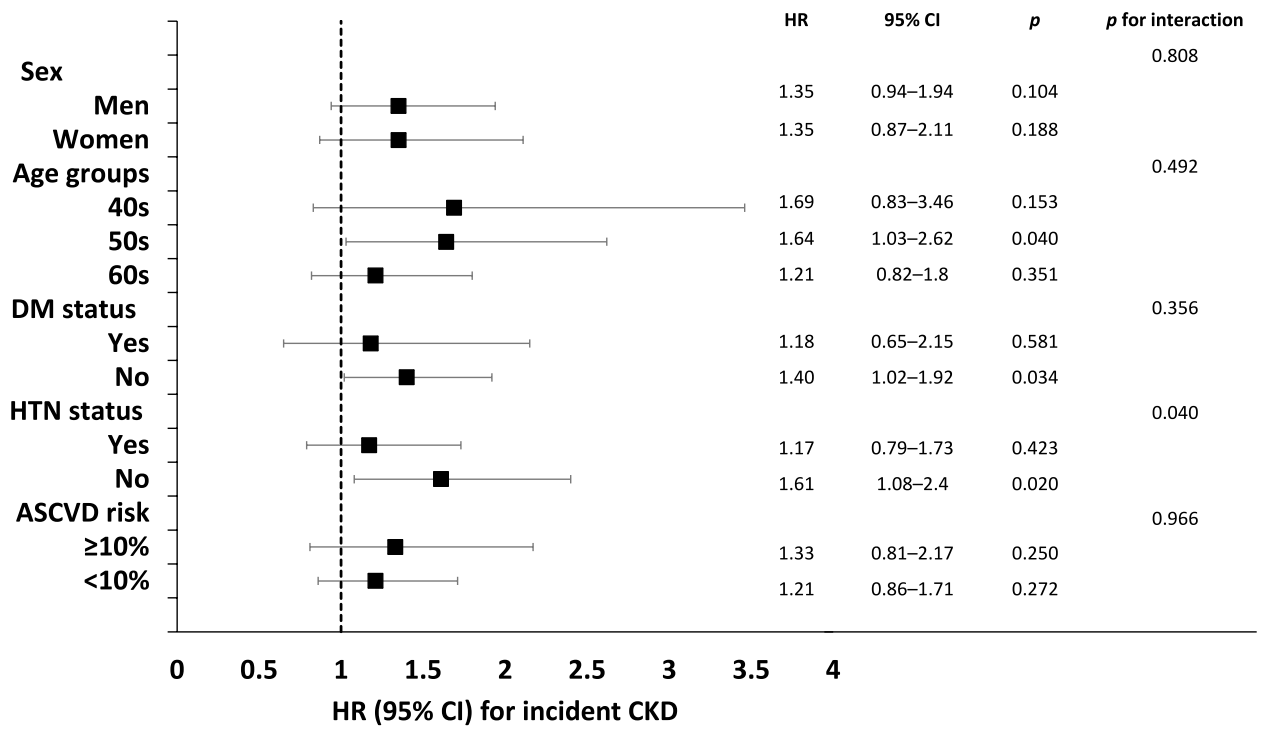


Fig. 4 A forest plot illustrating the subgroup analysis of ASCVD risk trajectory groups and their association with the risk of incident CKD. Abbreviations: ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease

Table 3 The prevalence of proteinuria according to the ASCVD risk trajectory groups

	ASCVD risk trajectory groups		
Prevalence of proteinuria (%)	**Stable**	**Increasing**	***p***
At 8 years	1.90	4.02	0.004
At 10 years	1.75	3.46	0.015
At 12 years	3.40	5.71	0.013
At 14 years	4.03	8.31	< 0.001
At 16 years	6.73	9.94	0.005

Abbreviations: *ASCVD* atherosclerotic cardiovascular disease

renal dysfunction. At the end of the exposure period of the current study, the median ASCVD risk score in the increasing ASCVD risk trajectory group was 12.8. As we investigated the risk of development of CKD in the future using participants without CKD, the ASCVD risk score for predicting renal dysfunction may be lower than that suggested previously.

The risk of incident CKD was associated with ASCVD risk trajectories in the subgroups of patients in their 50s, those without DM, and those without HTN. Particularly, the interaction for the HTN subgroup was significant, suggesting that the presence of HTN should be prioritized when evaluating the risk of CKD using ASCVD risk trajectories. This finding highlights the critical need to incorporate HTN status into the assessment models, emphasizing its substantial impact on the progression and risk evaluation of CKD within individualized patient care strategies. The incidence of CVD is approximately 40% in the age group of 40–59 years and 75% in the age group of 60–79 years [26]. In a study that tracked middle-aged men over a period of 40 years, the influence of traditional CVD risk factors declined with age and only low-density lipoprotein cholesterol consistently affected CVD risk, while BMI and FPG had an impact on heart failure, regardless of age [27]. Given that age in itself is a significant risk factor for both CVD and CKD, the lack of a significant correlation between the increase in ASCVD risk score in individuals in their 60 s and the risk of incident CKD in our study could suggest that age may have played a vital role in the development of CKD. In contrast, the incidence rates of CKD per 100,000 population years were 132 for mild CKD, 33 for moderate CKD, and 15 for severe CKD in individuals aged 20 to 64 years [28]. Participants from the current study aged 40–49 years may not have been able to demonstrate the impact of changes in the ASCVD risk score on the incidence of CKD due to low CKD rates even after a period of 16 years, given that they remained below the age of 65 at completion of the

study. In contrast, we hypothesized that, in individuals aged 50–59 years, we were able to establish a significant correlation between alterations in ASCVD risk scores and the incidence of CKD. This is likely related to their reaching an increased risk of CKD during the substantial 16-year follow-up period, whereas the effects of CVD risk factors did not diminish with age. In patients with DM, those individuals with DM at baseline could have already developed CKD to a sufficient extent during the exposure period, given that it takes approximately 7–10 years for CKD to develop [29]. The rapid decline in renal function was observed particularly in patients with DM with high SBP [30]. Similarly, in patients with HTN, an analysis using data from a total of 43,305 patients with HTN from the United States revealed that time-varying SBP is a factor for a rapid decline in eGFR, with every 10 mmHg increase in SBP leading to a 0.2 mL/min/1.73 m^2 decline in eGFR [31]. As a consequence, individuals exhibiting an upward trajectory in ASCVD risk scores may have been excluded due to the premature development of CKD. Furthermore, given that the formula for calculating ASCVD risk scores incorporates both DM and SBP, this inclusion could potentially diminish the observed association between variations in ASCVD risk scores and the onset of CKD during the period of event accumulation in patients diagnosed with either DM or HTN. The absence of a significant association between ASCVD risk score changes and CKD onset in the DM and HTN subgroups in this study could be due to this factor.

We suggest several explanations for these findings, as well as providing the exact underlying mechanism for the significant relationship between ASCVD risk trajectory groups and incident CKD. First, it is possible that individuals in the group with increased ASCVD risk experience comorbidities such as HTN, DM, and dyslipidemia [32], leading to an increased risk of CKD. At the molecular level, a recent study suggested that microRNAs (miRNAs) mediate homeostasis of the vascular wall and are involved in vasculature pathologies [33]. miR-155 and miR-223 play a role in the imbalance of calcium and phosphate in the vessels, which leads to the loss of these minerals from the bones and their accumulation in the vascular wall, contributing to vascular calcification. Additionally, miR-21 is upregulated in endothelial cells from atheroma plaques and progenitor cells from patients with coronary artery disease and is associated with the physiological proliferation of vascular smooth muscle cells and kidney fibrosis [30]. Second, an increase in ASCVD risk could reflect a more active atherosclerotic disease process, thus leading to higher susceptibility to renal damage and subsequent CKD [5, 34]. Cigarette smoking can exacerbate endothelial dysfunction and facilitate the infiltration of inflammatory cells into the vascular wall, thus promoting the formation of atherosclerotic plaques. In the current study, a higher proportion of daily smokers and elevated CRP levels were seen in the group with increasing ASCVD risk trajectory than that in the stable group. This could contribute to the observed association between an increased ASCVD risk trajectory and CKD incidence. Additionally, other lifestyle factors such as physical inactivity and alcohol consumption may contribute to the progression of ASCVD, which may lead to renal damage over time.

This study had several limitations. First, the exclusion of individuals with new-onset CKD during the exposure period may have limited the ability of our trajectory modeling to fully reflect the risk of CKD onset. Second, the risk of CKD may have been underestimated in the increasing ASCVD risk trajectory group. Additionally, a more accurate definition of CKD could have been achieved if not only the GFR category but also the cause and albuminuria category had been utilized. However, due to the limitations of the cohort, including a lack of information on the cause of CKD and the potential inaccuracy of proteinuria measurements in individuals taking antihypertensive medications, our study defined CKD based solely on the GFR category. Third, our results may not be applicable to other ethnicities because the KoGES consists only of Koreans. Finally, we focused solely on changes in ASCVD risk scores over time and did not account for the dynamic effects of other important variables such as BMI, blood pressure, plasma glucose level, lipid profiles, and lifestyle factors. Further studies incorporating these factors and their time-dependent effects will provide valuable insights into the development and progression of CKD.

Conclusion

In conclusion, our study provides evidence that an increasing trend in ASCVD risk scores serves as an independent predictor of adverse renal outcomes such as new-onset CKD and the presence of proteinuria, in patients without DM or HTN. Our findings underscore the importance of continuous monitoring and effective control of ASCVD risk factors, not only for cardiovascular health but also for the prevention and management of CKD. Further research is needed to validate these findings and elucidate the precise mechanisms underlying this association.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12882-024-03583-1.

Supplementary Material 1.

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Authors' contributions
Hye Sun Lee: study concept and design; methodology; acquisition, analysis, and interpretation of data; drafting the manuscript; Hong Il Lim: interpretation of data; Tae Ju Moon: interpretation of data; So Young Lee: interpretation of data; methodology; Jun-Hyuk Lee: study concept and design; methodology; interpretation of data; supervision; revising the manuscript; All authors approved the final manuscript.

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Availability of data and materials
The dataset used in this study can be provided after a KCDA review and evaluation of the research plan (https://www.nih.go.kr/ko/main/contents.do?menuNo=300563).

Declarations

Ethics approval and consent to participate
The KoGES_Ansan_Ansung cohort protocol was reviewed and approved by the Institutional Review Board (IRB) of the KCDA. All the participants read and signed a written informed consent form. The study protocol conformed to the ethical guidelines of the 1964 Declaration of Helsinki and its later amendments. This study was approved by the IRB of the Nowon Eulji Medical Center (IRB number: 2023–02-023).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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