

SUPPLEMENTAL MATERIALS

S1. Exclusion criteria

A total of 9,117 participants met one or more of the following exclusion criteria at baseline: missing data on body mass index (BMI), creatinine, and urine protein (n=2,496), a history of CVD (n=1,227), a history of kidney disease (n = 3,665), estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m² (n = 315), or proteinuria (n = 1,956). As some individuals met more than one exclusion criterion, the final sample of 113,171 participants was included in the analysis.

S2. Measurements

The following data regarding health behaviors and education level were collected: smoking status (never, former, and current smoker), average alcohol consumption (0, ≤20 and >20 g/day), regular exercise (<3 times/week vs. ≥3 times/week), and education level (less than a college degree or greater or equal to a college degree). A family history of CVD was defined as a self-reported diagnosis of heart disease or stroke in one or more first-degree relatives.

Blood samples were obtained after a fasting period of at least 10 hours. The blood tests included lipid profiles, liver enzymes, glucose, insulin, high-sensitivity C-reactive protein, and creatinine. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as fasting insulin (mg/dL) × fasting glucose (mg/dL) / 405.

S3. Statistical analyses: subgroup analyses

Subgroup analyses were performed stratified by age (<45 vs. ≥45 years), sex (women vs. men), current smoking (no vs. yes), alcohol intake (< 20 vs. ≥ 20 g/day), health enhancing physical activity (no vs. yes), BMI (<25 kg/m² vs. ≥ 25 kg/m²), HOMA-IR (<2.5 vs. ≥2.5),

and hsCRP (<1.0 mg/L vs. \geq 1.0 mg/L), diabetes at baseline (no vs. yes), antidiabetic medication (no vs. yes), hypertension at baseline (no vs. yes), and antihypertensive medication (no vs. yes). The interactions by subgroup characteristics were tested using likelihood ratio tests comparing models with and without multiplicative interaction terms.

S3-1. Statistical analyses: competing risk analyses

To account for the competing risks of CVD and all-cause mortality, HRs and 95% CIs for mortality were estimated using the Fine and Gray proportional hazards regression model with age as the timescale.[1]

S3-2. Statistical analyses: annual CAC progression

To estimate the progression of CAC scores over time in the exposure subgroup, we used linear mixed models with random intercepts and slopes with adjustment for potential confounders. Analyses were performed after the transformation of CAC scores to $\log_e(\text{CAC}+1)$ because the CAC score was right-skewed. Then, the ratios of the annual progression rates of CAC scores (with 95% CIs) were estimated, comparing each eGFR subgroup category with the reference group (normal group). These analyses of CAC progression were performed in all participants and then separately in those with CAC scores of zero and $\text{CAC}>0$ at baseline. Since participants had to have at least two visits, we used inverse probability weights to correct for potential selection bias between participants with a single CAC measurement and those with two or more CAC measurements. Inverse probability weights were obtained from a logistic regression model that included all participants with at least one CAC measurement. Multivariable models were adjusted for smoking status, alcohol consumption, regular exercise, body mass index, education level, history of diabetes, history of hypertension, lipid-lowering medication, eGFR, systolic blood

pressure, total cholesterol, HDL-C, triglyceride, glucose, and HOMA-IR as time-dependent variables and age at baseline, sex, center, year of screening examination, and education level as time-fixed variables.

S4. Results: the role of incident diabetes, hypertension, and hypercholesterolemia

We have further evaluated the role of incident diabetes, hypertension, and hypercholesterolemia at baseline and during follow-up on the associations between CACS and CKD. Over the course of follow-up, the incident cases of hypertension, diabetes, and dyslipidemia (defined as serum LDL cholesterol ≥ 160 mg/dL, serum triglycerides ≥ 150 mg/dL, or serum HDL cholesterol < 40 mg/dL (men) or < 50 mg/dL (women))[2] were 33,517 (29.6%), 5,353 (4.7%), and 48,260 (42.6%), respectively. The association between CACS and incident hypertension in individuals without CKD, proteinuria, or hypertension at baseline showed a positive association with a dose-response pattern (**eTable 4**). The HRs (95% CI) for incident hypertension for CACS 0, $< 0-100$, 101-300, and > 300 were 1.16 (1.11-1.21), 1.10 (0.95-1.26), and 1.42 (1.14-1.77), respectively. A similar pattern was found for incident diabetes, whereas an inverse J-shaped association was observed between increasing CACS and incident dyslipidemia such that the risk increased in CACS $< 0-100$ which then decreased in higher CACS categories. Additionally, when incident hypertension, diabetes, and dyslipidemia during follow-up were further adjusted for in evaluating the association between CACS and CKD (**eTable 5**), the associations between CACS and CKD remained virtually unchanged.

REFERENCES

1. Lau B, Cole SR, Gange SJ. Competing risk regression models for epidemiologic data. *Am J Epidemiol* 2009;170(2):244-256
2. Arnett DK, Blumenthal RS, Albert MA, *et al.* 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2019;140(11):e596-e646

eTable 1. Hazard ratios (95% CI) for chronic kidney disease (CKD) and proteinuria according to coronary artery calcium score (CACs) category using competing risk analysis

CACs categories	Sub-distribution HR ^a (95% CI) while considering CV mortality as a competing event			Sub-distribution HR ^a (95% CI) while considering all-cause mortality as a competing event		
	For CKD (eGFR<60 ml/min/1.73 m ²)	For proteinuria	For all CKD (either eGFR <60 ml/min/1.73 m ² or proteinuria)	For CKD (eGFR<60 ml/min/1.73 m ²)	For proteinuria	For all CKD (either eGFR <60 ml/min/1.73 m ² or proteinuria)
0	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
<0 to 100	1.22 (0.98-1.51)	1.07 (0.98-1.17)	1.10 (1.01-1.19)	1.21 (0.97-1.50)	1.07 (0.98-1.17)	1.10 (1.01-1.19)
101 to 300	1.14 (0.74-1.75)	1.26 (1.01-1.56)	1.29 (1.06-1.56)	1.10 (0.71-1.70)	1.23 (0.99-1.53)	1.26 (1.04-1.53)
>300	1.23 (0.76-1.99)	1.49 (1.09-2.03)	1.61 (1.23-2.10)	1.16 (0.71-1.90)	1.45 (1.06-1.98)	1.57 (1.20-2.05)
P for trend	0.164	0.002	<0.001	0.248	0.004	<0.001
<i>Per 100 increase in CAC score</i>	1.02 (0.97-1.06)	1.05 (1.02-1.08)	1.05 (1.03-1.08)	1.01 (0.96-1.06)	1.05 (1.02-1.08)	1.05 (1.03-1.08)

*Fine and Gray proportional hazard model with age as a time scale was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs).

Multivariable model was adjusted for age (timescale), sex, center, year of screening examination, smoking status, alcohol consumption, regular exercise, body mass index, education level, history of diabetes, history of hypertension, lipid-lowering medication, eGFR, systolic blood pressure, total cholesterol, HDL-C, triglyceride, glucose, and HOMA-IR.

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; HR, hazard ratio

eTable 2. Hazard ratios (95% CI) for chronic kidney disease (CKD) and proteinuria according to coronary artery calcium score (CACs) category among subjects who had at least two or three follow-up

CACs categories	Multivariable-adjusted HR ^a (95% CI) among subjects who had at least two follow-up (n = 91,288)			Multivariable-adjusted HR ^a (95% CI) among subjects who had at least three follow-up (n = 68,942)		
	For CKD (eGFR<60 ml/min/1.73 m ²)	For proteinuria	For all CKD (either eGFR <60 ml/min/1.73 m ² or proteinuria)	For CKD (eGFR<60 ml/min/1.73 m ²)	For proteinuria	For all CKD (either eGFR <60 ml/min/1.73 m ² or proteinuria)
0	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
<0 to 100	1.28 (1.02-1.60)	1.07 (0.97-1.17)	1.10 (1.01-1.20)	1.30 (1.02-1.64)	1.08 (0.98-1.19)	1.12 (1.02-1.22)
101 to 300	1.39 (0.89-2.17)	1.21 (0.97-1.52)	1.26 (1.03-1.54)	1.58 (0.98-2.56)	1.23 (0.97-1.57)	1.27 (1.02-1.59)
>300	1.54 (0.89-2.65)	1.40 (1.002-1.96)	1.51 (1.12-2.02)	1.74 (0.97-3.11)	1.45 (1.01-2.08)	1.55 (1.13-2.14)
P for trend	0.013	0.010	<0.001	0.004	0.006	<0.001
<i>Per 100 increase in CAC score</i>	1.02 (0.98-1.07)	1.05 (1.02-1.08)	1.05 (1.02-1.08)	1.04 (0.99-1.10)	1.06 (1.02-1.09)	1.06 (1.03-1.09)

^a Estimated from Cox proportional hazard models with inverse probability weighting. Multivariable model was adjusted for age, sex, center, year of screening examination, smoking status, alcohol consumption, regular exercise, body mass index, education level, history of diabetes, history of hypertension, lipid-lowering medication, eGFR, systolic blood pressure, total cholesterol, HDL-C, triglyceride, glucose, and HOMA-IR.

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; HR, hazard ratio

eTable 3. Hazard ratios (95% CI) for persistent chronic kidney disease (CKD) and persistent proteinuria according to coronary artery calcium score (CACs) category among subjects who had at least two follow-up (n = 91,288)

CACs categories	For persistent CKD (eGFR<60 ml/min/1.73 m ²)		For persistent proteinuria		For all persistent CKD (either eGFR <60 ml/min/1.73 m ² or proteinuria)	
	Incident case	Multivariable-adjusted HR ^a (95% CI)	Incident case	Multivariable-adjusted HR ^a (95% CI)	Incident case	Multivariable-adjusted HR ^a (95% CI)
0	72	1.00 (reference)	557	1.00 (reference)	625	1.00 (reference)
<0 to 100	36	1.77 (1.14-2.73)	104	1.22 (0.97-1.52)	135	1.27 (1.04-1.56)
101 to 300	8	1.96 (0.90-4.30)	16	1.32 (0.79-2.21)	26	1.60 (1.06-2.41)
>300	4	1.50 (0.50-4.53)	6	1.25 (0.55-2.85)	10	1.45 (0.76-2.76)
P for trend		0.033		0.070		0.003
<i>Per 100 increase in CAC score</i>		1.03 (0.94-1.14)		1.06 (0.99-1.14)		1.06 (1.01-1.12)

^a Estimated from Cox proportional hazard models with inverse probability weighting. Multivariable model was adjusted for age, sex, center, year of screening examination, smoking status, alcohol consumption, regular exercise, body mass index, education level, history of diabetes, history of hypertension, lipid-lowering medication, eGFR, systolic blood pressure, total cholesterol, HDL-cholesterol, triglyceride, glucose, and HOMA-IR at baseline as well as incident hypertension, incident diabetes and incident dyslipidemia during follow up.

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; HR, hazard ratio

eTable 4. Hazard ratios (95% CI) for hypertension, diabetes or dyslipidemia according to coronary artery calcium score category among subjects without CKD and proteinuria as well as each outcome at baseline

CACS categories	Multivariable-adjusted HR ^a (95% CI) for hypertension among subjects without CKD, proteinuria and hypertension at baseline	Multivariable-adjusted HR ^a (95% CI) for diabetes among subjects without CKD, proteinuria and diabetes at baseline	Multivariable-adjusted HR ^a (95% CI) for dyslipidemia among subjects without CKD, proteinuria and dyslipidemia at baseline	Multivariable-adjusted HR ^a (95% CI) for lipid- lowering medication among subjects without CKD, proteinuria and lipid-lowering medication at baseline
0	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
<0 to 100	1.16 (1.11-1.21)	1.11 (1.03-1.20)	1.13 (1.08-1.18)	1.17 (1.11-1.24)
101 to 300	1.10 (0.95-1.26)	1.24 (1.04-1.47)	0.85 (0.75-0.96)	1.58 (1.42-1.77)
>300	1.42 (1.14-1.77)	1.30 (1.003-1.68)	0.64 (0.52-0.79)	1.63 (1.38-1.93)
P for trend	<0.001	<0.001	0.957	<0.001
<i>Per 100 increase in CAC score</i>	1.05 (1.03-1.08)	1.05 (1.02-1.08)	0.93 (0.90-0.95)	1.04 (1.02-1.05)

^a Estimated from Cox proportional hazard models with inverse probability weighting. Multivariable model was adjusted for age, sex, center, year of screening examination, smoking status, alcohol consumption, regular exercise, body mass index, education level, history of diabetes (except for diabetes), history of hypertension (except for hypertension), lipid-lowering medication (except for dyslipidemia and lipid-lowering medication), eGFR, systolic blood pressure (except for hypertension), total cholesterol (except for dyslipidemia), HDL-C (except for dyslipidemia), triglyceride (except for dyslipidemia), glucose (except for diabetes), and HOMA-IR.

Dyslipidemia was defined as serum LDL cholesterol ≥ 160 mg/dl, serum triglycerides ≥ 150 mg/dl, or serum HDL cholesterol < 40 mg/dl (men) or < 50 mg/dl (women).

Abbreviations: CI, confidence interval; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; HR, hazard ratio

eTable 5. Hazard ratios (95% CI) for chronic kidney disease (CKD) and proteinuria according to coronary artery calcium score (CACS) category after further adjustment for incident hypertension, incident diabetes and incident dyslipidemia during follow up

CACS categories	Multivariable-adjusted HR ^a (95% CI)		
	For CKD (eGFR<60 ml/min/1.73 m ²)	For proteinuria	For all CKD (either eGFR <60 ml/min/1.73 m ² or proteinuria)
0	1.00 (reference)	1.00 (reference)	1.00 (reference)
<0 to 100	1.26 (1.01-1.57)	1.05 (0.96-1.15)	1.09 (1.01-1.19)
101 to 300	1.40 (0.94-2.10)	1.25 (1.01-1.55)	1.30 (1.07-1.57)
>300	1.80 (1.12-2.91)	1.53 (1.13-2.06)	1.67 (1.29-2.17)
P for trend	0.003	0.002	<0.001
<i>Per 100 increase in CAC score</i>	1.03 (0.98-1.07)	1.05 (1.02-1.08)	1.06 (1.03-1.08)

^a Estimated from Cox proportional hazard models with inverse probability weighting. Multivariable model was adjusted for age, sex, center, year of screening examination, smoking status, alcohol consumption, regular exercise, body mass index, education level, history of diabetes, history of hypertension, lipid-lowering medication, eGFR, systolic blood pressure, total cholesterol, HDL-cholesterol, triglyceride, glucose, and HOMA-IR at baseline as well as incident hypertension, incident diabetes and incident dyslipidemia during follow up.

Abbreviations: CI, confidence interval; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; HR, hazard ratio

eTable 6. Ratios* (95% CI) of annual progress rates of coronary artery calcium (CAC) scores by stage of chronic kidney disease (CKD) at baseline (n = 42,681)

	eGFR (ml/min/1.73 m ²)		
	<60	60-89	≥90
Number	95	12,267	30,319
Annual rates of CAC progression	1.198 (1.134–1.266)	1.102 (1.097–1.107)	1.077 (1.074–1.079)
Ratio of annual progression rate			
Model 1	1.113 (1.053–1.176)	1.024 (1.019–1.029)	1.000 (reference)
Model 2	1.121 (1.058–1.188)	1.023 (1.018–1.029)	1.000 (reference)

*Annual CAC progression rates and ratios were estimated from mixed models with random intercepts and slopes with natural log(CAC + 1) as the outcome and inverse probability weighting

Multivariable model 1 was adjusted for age at baseline and sex. Model 2 was adjusted for smoking status, alcohol consumption, regular exercise, body mass index, education level, history of diabetes, history of hypertension, lipid-lowering medication, eGFR, systolic blood pressure, total cholesterol, HDL-C, triglyceride, glucose, and HOMA-IR as time-dependent variables and age at baseline, sex, center, year of screening examination, and education level as time-fixed variables.

Abbreviation: CI, confidence interval; eGFR, estimated glomerular filtration rate; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance

eTable 7. Hazard ratio (95% CI) of incident chronic kidney disease (CKD) based on coronary artery calcification (CAC) score category in clinically relevant subgroups

Subgroup	Coronary artery calcification (CAC) score category				<i>P</i> for trend	<i>P</i> for interaction
	0	0< to 100	101 to 300	>300		
Age						0.551
<45 years (n=86,470)	1.00 (reference)	1.14 (1.03-1.27)	1.29 (0.94-1.78)	1.20 (0.66-2.18)	0.003	
≥45 years (n=26,701)	1.00 (reference)	1.09 (0.96-1.24)	1.36 (1.07-1.73)	1.86 (1.39-2.48)	<0.001	
Sex						0.009
Women (n=25,808)	1.00 (reference)	0.71 (0.53-0.95)	1.17 (0.62-2.19)	0.80 (0.26-2.51)	0.136	
Men (n=87,363)	1.00 (reference)	1.15 (1.06-1.25)	1.37 (1.13-1.65)	1.78 (1.30-2.44)	<0.001	
Current smoking						0.827
No (n=83,802)	1.00 (reference)	1.09 (0.98-1.21)	1.21 (0.93-1.56)	1.73 (1.25-2.39)	0.001	
Yes (n=24,509)	1.00 (reference)	1.11 (0.97-1.28)	1.44 (1.06-1.94)	1.61 (1.02-2.53)	0.002	
Alcohol intake						0.256
<20 g/day (n=80,255)	1.00 (reference)	1.12 (1.01-1.24)	1.46 (1.15-1.86)	1.59 (1.11-2.29)	<0.001	
≥20 g/day (n=27,617)	1.00 (reference)	1.08 (0.94-1.24)	0.95 (0.67-1.36)	1.71 (1.15-2.53)	0.051	
HEPA						0.708
No (n=96,029)	1.00 (reference)	1.11 (1.01-1.21)	1.24 (0.99-1.54)	1.56 (1.15-2.12)	<0.001	
Yes (n=14,885)	1.00 (reference)	1.04 (0.84-1.28)	1.29 (0.82-2.05)	2.12 (1.24-3.62)	0.025	
BMI						0.282
<25 kg/m ² (n=69,034)	1.00 (reference)	1.10 (0.96-1.25)	1.40 (1.04-1.90)	2.24 (1.53-3.33)	<0.001	
≥25 kg/m ² (n=44,137)	1.00 (reference)	1.11 (1.00-1.23)	1.25 (0.98-1.60)	1.39 (0.98-1.96)	0.002	
HOMA-IR						0.412
<2.5 (n=92,361)	1.00 (reference)	1.14 (1.03-1.26)	1.46 (1.15-1.83)	1.65 (1.16-2.36)	<0.001	
≥2.5 (n=20,810)	1.00 (reference)	1.05 (0.91-1.20)	1.09 (0.79-1.51)	1.68 (1.16-2.44)	0.034	
hsCRP						0.940
<1.0 mg/L (n=81,687)	1.00 (reference)	1.08 (0.97-1.19)	1.33 (1.05-1.69)	1.70 (1.22-2.38)	<0.001	
≥1.0 mg/L (n=28,945)	1.00 (reference)	1.13 (0.99-1.29)	1.39 (1.01-1.92)	1.60 (1.04-2.47)	0.002	
Diabetes						0.482
No (n=107,818)	1.00 (reference)	1.09 (0.99-1.19)	1.26 (0.99-1.59)	1.54 (1.07-2.20)	0.002	
Yes (n=5,353)	1.00 (reference)	1.21 (1.02-1.45)	1.50 (1.08-2.08)	1.98 (1.36-2.88)	<0.001	
Antidiabetic medication						0.537
No (n=110,540)	1.00 (reference)	1.12 (1.03-1.22)	1.25 (1.00-1.56)	1.75 (1.28-2.39)	<0.001	

Yes (n=2,333)	1.00 (reference)	1.07 (0.83-1.38)	1.66 (1.13-2.45)	1.53 (0.95-2.46)	0.010	
Antihypertensive medication						0.666
No (n=106,209)	1.00 (reference)	1.12 (1.02-1.23)	1.40 (1.10-1.78)	1.96 (1.37-2.82)	<0.001	
Yes (n=6,664)	1.00 (reference)	1.14 (0.95-1.36)	1.26 (0.92-1.71)	1.46 (1.01-2.13)	0.012	
Hypertension						0.654
No (n=97,224)	1.00 (reference)	1.07 (0.96-1.19)	1.24 (0.92-1.67)	1.54 (0.96-2.49)	0.020	
Yes (n=15,946)	1.00 (reference)	1.18 (1.04-1.34)	1.38 (1.07-1.76)	1.76 (1.30-2.40)	<0.001	
Examination time						0.060
Morning (n=100,946)	1.00 (reference)	1.10 (0.85-1.42)	2.56 (1.53-4.29)	2.05 (0.85-4.96)	0.024	
Afternoon (n=12,183)	1.00 (reference)	1.09 (1.00-1.19)	1.21 (0.99-1.48)	1.61 (1.23-2.12)	0.024	

^a Estimated from Cox proportional hazard models. Multivariable model 1 was adjusted for age, sex, center, year of screening examination, smoking status, alcohol consumption, regular exercise, body mass index, education level, history of diabetes, history of hypertension, lipid-lowering medication, eGFR, systolic blood pressure, total cholesterol, HDL-cholesterol, triglyceride, glucose, and HOMA-IR.

Abbreviations: ASM, appendicular skeletal muscle; BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; HEPA, health-enhancing physical activity; HOMA-IR, homeostasis model assessment of insulin resistance; hsCRP, high-sensitivity C-reactive protein