Coronary Artery Calcification Score and the Progression of Chronic Kidney Disease

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Supplemental contents

A. All CKD patients B. Patients without CKD progression. C. Patients with CKD progression. Each dot represents the CACS of an individual patient. Red, blue, and green dots indicate CACS of 0, 1–100, and >100 AU, respectively. In boxplots, the horizontal line inside the box represents the median. The bottom and top lines of the box represent the first and third quartiles. The whiskers reflect the within 1.5 times the interquartile range of CACS.
Abbreviation: CKD, chronic kidney disease; CACS, coronary artery calcification score; AU, Agatston unit

Supplemental Table 1. The number of imputed missing data

Variable	Missing n (%)
Education level	2 (0.10)
Body mass index	1 (0.05)
Blood pressure	2 (0.10)
Total cholesterol	14 (0.72)
HDL-cholesterol	36 (1.86)
LDL-cholesterol	34 (1.76)
hs-CRP	89 (4.59)
Phosphate	8 (0.41)
Intact PTH	43 (2.22)
FGF-23	75 (3.87)

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein; hs-CRP, high-sensitive C-reactive protein; PTH, parathyroid hormone; FGF-23, fibroblast growth factor-23.

Supplemental Table 2. Subdistribution hazard model for the risk of composite kidney outcome

CACS	Model 1	Model 2	Model 3	Model 4
0	Reference	Reference	Reference	Reference
0–100	1.53 (1.27–1.86)	1.46 (1.20–1.83)	1.39 (1.13–1.71)	1.32 (1.06–1.64)
>100	1.89 (1.54–2.31)	1.77 (1.39–2.28)	1.60 (1.24–2.09)	1.47 (1.16–1.89)

Note: The composite kidney outcome was defined as the first occurrence of a 50% decline in eGFR from the baseline value, or the onset of kidney failure with replacement therapy.
Model 1: a crude analysis without adjustment
Model 2: adjusted for sex, age, CCI, smoking status, education level, body mass index, and etiology of kidney disease.
Model 3: Model 2 + blood pressure, eGFR, total cholesterol, HDL-cholesterol, LDL-cholesterol, hs-CRP, and medications (anti-hypertensive drugs and lipid-lowering drugs)
Model 4: Model 3 + phosphate, intact-parathyroid hormone, FGF-23, and urinary protein to creatinine ratio.
Abbreviations: CACS, coronary artery calcification score; SD, standard deviation; CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hs-CRP, high-sensitive C-reactive protein; FGF-23, fibroblast growth factor-23.

Supplemental Table 3. Time-varying model for risk of composite kidney outcome according to coronary artery calcification score

CACS	Events, n (%)	Person-years	Incidence rate 1000 person-years	Model 1	Model 2	Model 3	Model 4
0	231 (24.2)	3452	6.6	Reference	Reference	Reference	Reference
1–100	190 (34.4)	1953	9.7	1.34 (1.11–1.63)	1.43 (1.17–1.77)	1.42 (1.15–1.75)	1.31 (1.07–1.60)
>100	161 (37.8)	1339	12.0	1.74 (1.42–2.13)	1.92 (1.52–2.42)	1.89 (1.49–2.40)	1.46 (1.16–1.85)
Per 1 SD log of CACS	582 (30.0)	6744	8.6	1.22 (1.13–1.32)	1.27 (1.16–1.39)	1.24 (1.13–1.35)	1.12 (1.02–1.23)
HRs for Non-fatal CVE				1.41 (1.04–1.89)	1.46 (1.18–1.89)	1.33 (1.09–1.63)	1.25 (1.02–1.79)

Note: The composite kidney outcome was defined as the first occurrence of a 50% decline in eGFR from the baseline value, or the onset of kidney failure with replacement therapy. The non-fatal cardiovascular event (n=118) which was defined as myocardial infarction, stable, unstable angina, heart failure, and stroke before the composite kidney outcome was treated as a time-varying covariate. Other repeated variables such as blood pressure, body mass index, urinary protein to creatinine ratio, and estimated glomerular filtration rate was also treated as time-varying covariates.

Model 1: a crude analysis without adjustment

Model 2: adjusted for sex, age, CCI, smoking status, education level, body mass index, and etiology of kidney disease.

Model 3: Model 2 + blood pressure, eGFR, total cholesterol, HDL-cholesterol, LDL-cholesterol, hs-CRP, and medications (anti-hypertensive drugs and lipid-lowering drugs)

Model 4: Model 3 + phosphate, intact-parathyroid hormone, FGF-23, and urinary protein to creatinine ratio.

Abbreviations: CACS, coronary artery calcification score; SD, standard deviation; CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hs-CRP, high-sensitive C-reactive protein; FGF-23, fibroblast growth factor-23.

Supplemental Table 4. Hazard ratios for the risk of 50% estimated glomerular filtration rate decline and kidney failure with replacement therapy according to coronary artery calcification score

CACS	Events, n (%)	Person-years	Incidence rate 1000 person-years	Model 1	Model 2	Model 3	Model 4
50% eGFR decline							
0	168	4440	3.7	Reference	Reference	Reference	Reference
1–100	123	2526	4.8	1.30 (1.03–1.64)	1.28 (0.99–1.65)	1.29 (1.04–1.63)	1.28 (0.99–1.64)
>100	99	1748	5.6	1.57 (1.22–2.01)	1.59 (1.18–2.13)	1.39 (1.07–1.62)	1.34 (1.00–1.80)
Per 1 SD log of CACS	390	8716	4.4	1.17 (1.06–1.29)	1.16 (1.03–2.30)	1.14 (1.02–1.27)	1.15 (1.03–1.29)
Kidney failure with replacement therapy							
0	182	4410	4.1	Reference	Reference	Reference	Reference
1–100	143	2419	5.9	1.45 (1.16–1.80)	1.29 (1.01–1.63)	1.19 (0.93–1.52)	1.19 (0.94–1.52)
>100	143	1641	8.7	2.20 (1.76–2.74)	1.88 (1.45–2.44)	1.44 (1.11–1.88)	1.54 (1.17–2.02)
Per 1 SD log of CACS	468	8471	5.5	1.35 (1.24–1.47)	1.26 (1.14–1.39)	1.16 (1.05–1.28)	1.19 (1.07–1.32)

Model 1: a crude analysis without adjustment

Model 2: adjusted for sex, age, CCI, smoking status, education level, body mass index, and etiology of kidney disease.

Model 3: Model 2 + blood pressure, eGFR, total cholesterol, HDL-cholesterol, LDL-cholesterol, hs-CRP, and medications (anti-hypertensive drugs and lipid-lowering drugs)

Model 4: Model 3 + phosphate, intact-parathyroid hormone, FGF-23, and urinary protein to creatinine ratio.

Abbreviations: CACS, coronary artery calcification score; SD, standard deviation; CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hs-CRP, high-sensitive C-reactive protein; FGF-23, fibroblast growth factor-23.

Supplemental Table 5. Hazard ratios for the risk of all-cause mortality according to coronary artery calcification score

CACS	Events, n (%)	Person-years	Incidence rate 1000 person-years	Model 1	Model 2	Model 3	Model 4
0	20 (2.1)	4851	0.4	Reference	Reference	Reference	Reference
1–100	16 (2.9)	2795	0.5	1.40 (0.73–2.71)	1.24 (0.92–1.89)	1.13 (0.86–1.69)	1.07 (0.82–1.59)
>100	49 (11.5)	1955	2.5	6.43 (3.82–10.8)	2.48 (1.37–4.50)	2.28 (1.23–4.23)	2.34 (1.24–4.42)
Per 1 SD log of CACS	85 (4.3)	9601	0.8	2.16 (1.77–2.64)	1.60 (1.27–2.03)	1.61 (1.26–2.07)	1.65 (1.28–2.12)

Model 1: a crude analysis without adjustment

Model 2: adjusted for sex, age, CCI, smoking status, education level, body mass index, and etiology of kidney disease.

Model 3: Model 2 + blood pressure, eGFR, total cholesterol, HDL-cholesterol, LDL-cholesterol, hs-CRP, and medications (anti-hypertensive drugs and lipid-lowering drugs)

Model 4: Model 3 + phosphate, intact-parathyroid hormone, FGF-23, and urinary protein to creatinine ratio.

Abbreviations: CACS, coronary artery calcification score; SD, standard deviation; CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hs-CRP, high-sensitive C-reactive protein; FGF-23, fibroblast growth factor-23.

Supplemental Table 6. Hazard ratios for the risk of composite kidney outcome according to coronary artery calcification score in patients with eGFR ≥ 15.0 ml/min/1.73m^2

CACS	Events, n (%)	Person-years	Incidence rate 1000 person-years	Model 1	Model 2	Model 3	Model 4
0	195	4151	4.6	Reference	Reference	Reference	Reference
1–100	157	2266	6.9	1.50 (1.21–1.84)	1.41 (1.12–1.78)	1.28 (1.01–1.62)	1.27 (1.01–1.60)
>100	133	1515	8.7	1.97 (1.58–2.45)	1.85 (1.42–2.41)	1.45 (1.10–1.90)	1.43 (1.08–1.89)
Per 1 SD log of CACS	485	7934	6.1	1.30 (1.20–1.42)	1.25 (1.13–1.39)	1.15 (1.03–1.27)	1.13 (1.02–1.26)

Note: The composite kidney outcome was defined as the first occurrence of a 50% decline in eGFR from the baseline value, or the onset of kidney failure with replacement therapy.

Model 1: a crude analysis without adjustment

Model 2: adjusted for sex, age, CCI, smoking status, education level, body mass index, and etiology of kidney disease.

Model 3: Model 2 + blood pressure, eGFR, total cholesterol, HDL-cholesterol, LDL-cholesterol, hs-CRP, and medications (anti-hypertensive drugs and lipid-lowering drugs)

Model 4: Model 3 + phosphate, intact-parathyroid hormone, FGF-23, and urinary protein to creatinine ratio.

Abbreviations: CACS, coronary artery calcification score; SD, standard deviation; CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hs-CRP, high-sensitive C-reactive protein; FGF-23, fibroblast growth factor-23.

Supplemental Table 7. Hazard ratios for the risk of composite kidney outcome in patients with previous coronary artery disease

CACS	Events, n (%)	Person-years	Incidence rate 1000 person-years	Model 1	Model 2	Model 3	Model 4
0	232 (24.2)	4251	5.4	Reference	Reference	Reference	Reference
1–100	204 (35.6)	2532	8.0	1.50 (1.27–1.77)	1.35 (1.11–1.64)	1.28 (1.06–1.56)	1.28 (1.05–1.57)
>100	205 (42.5)	1929	10.6	2.01 (1.69–2.37)	1.84 (1.48–2.28)	1.61 (1.35–1.94)	1.59 (1.29-1.96)
Per 1 SD log of CACS	641 (31.8)	8712	7.4	1.32 (1.21-1.43)	1.25 (1.14–1.37)	1.19 (1.07–1.31)	1.18 (1.06–1.29)

Note: Patients with a previous history of coronary artery disease, but without prior coronary artery stenting were added to the analysis (n=77). The composite kidney outcome was defined as the first occurrence of a 50% decline in eGFR from the baseline value, or the onset of kidney failure with replacement therapy.

Model 1: a crude analysis without adjustment

Model 2: adjusted for sex, age, CCI, smoking status, education level, body mass index, and etiology of kidney disease.

Model 3: Model 2 + blood pressure, eGFR, total cholesterol, HDL-cholesterol, LDL-cholesterol, hs-CRP, and medications (anti-hypertensive drugs and lipid-lowering drugs)

Model 4: Model 3 + phosphate, intact-parathyroid hormone, FGF-23, and urinary protein to creatinine ratio.

Abbreviations: CACS, coronary artery calcification score; SD, standard deviation; CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hs-CRP, high-sensitive C-reactive protein; FGF-23, fibroblast growth factor-23.

Supplemental Table 8. Hazard ratios for the risk of composite kidney outcome in patients without calcium-based phosphate binder

CACS	Events, n (%)	Person-years	Incidence rate 1000 person-years	Model 1	Model 2	Model 3	Model 4
0	190	3884	4.8	Reference	Reference	Reference	Reference
1–100	169	2153	7.8	1.63 (1.32–2.00)	1.53 (1.22–1.92)	1.32 (1.05–1.67)	1.33 (1.05–1.68)
>100	144	1504	9.5	2.03 (1.63–2.52)	1.86 (1.44–2.42)	1.34 (1.03–1.75)	1.43 (1.09–1.87)
Per 1 SD log of CACS	503	7542	6.6	1.30 (1.20–1.42)	1.24 (1.12–1.37)	1.10 (1.00–1.22)	1.12 (1.01–1.24)

Note: The composite kidney outcome was defined as the first occurrence of a 50% decline in eGFR from the baseline value, or the onset of kidney failure with replacement therapy.

Model 1: a crude analysis without adjustment

Model 2: adjusted for sex, age, CCI, smoking status, education level, body mass index, and etiology of kidney disease.

Model 3: Model 2 + blood pressure, eGFR, total cholesterol, HDL-cholesterol, LDL-cholesterol, hs-CRP, and medications (anti-hypertensive drugs and lipid-lowering drugs)

Model 4: Model 3 + phosphate, intact-parathyroid hormone, FGF-23, and urinary protein to creatinine ratio.

Abbreviations: CACS, coronary artery calcification score; SD, standard deviation; CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hs-CRP, high-sensitive C-reactive protein; FGF-23, fibroblast growth factor-23.

Supplemental Table 9. Hazard ratios for the risk of 50% estimated glomerular filtration rate decline and kidney failure with replacement therapy according to different coronary artery calcification score categories

CAC score	Events, n (%)	Person-years	Incidence rate 1000 person-years	Model 1	Model 2	Model 3	Model 4
0	231 (24.2)	4248	5.4	Reference	Reference	Reference	Reference
1–400	280 (35.5)	3177	8.8	1.65 (1.39–1.97)	1.53 (1.26–1.87)	1.38 (1.15–1.67)	1.34 (1.08–1.64)
>400	73 (38.0)	407	10.3	1.98 (1.52–2.57)	1.77 (1.30–2.39)	1.62 (1.19–2.20)	1.55 (1.13–2.12)
0	231 (24.2)	4248	5.4	Reference	Reference	Reference	Reference
1–100	191 (34.5)	2312	8.2	1.53 (1.27–1.86)	1.41 (1.14–1.75)	1.32 (1.07–1.64)	1.29 (1.04–1.61)
101–400	89 (37.9)	865	10.2	1.95 (1.53–2.50)	1.78 (1.35–2.34)	1.39 (1.06–1.94)	1.36 (1.03–1.82)
>400	73 (38.0)	704	10.3	1.98 (1.52–2.57)	1.67 (1.24–2.27)	1.53 (1.12–2.09)	1.50 (1.09–2.08)

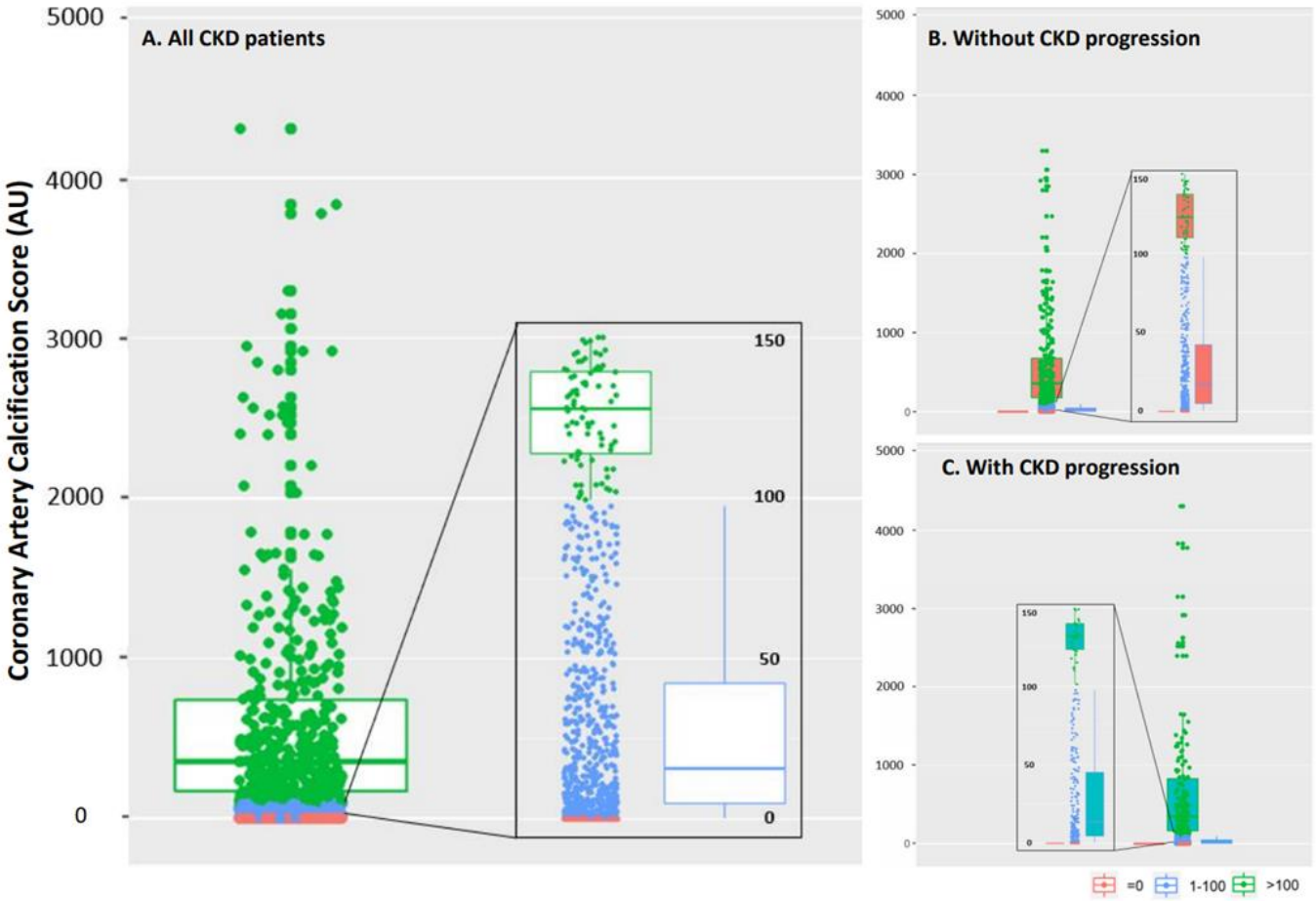
Model 1: a crude analysis without adjustment

Model 2: adjusted for sex, age, CCI, smoking status, education level, body mass index, and etiology of kidney disease.

Model 3: Model 2 + blood pressure, eGFR, total cholesterol, HDL-cholesterol, LDL-cholesterol, hs-CRP, and medications (anti-hypertensive drugs and lipid-lowering drugs)

Model 4: Model 3 + phosphate, intact-parathyroid hormone, FGF-23, and urinary protein to creatinine ratio.

Abbreviations: CACS, coronary artery calcification score; SD, standard deviation; CCI, Charlson comorbidity index; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; hs-CRP, high-sensitive C-reactive protein; FGF-23, fibroblast growth factor-23.



Supplemental Figure 1. Distribution of coronary artery calcification score

A. All CKD patients B. Patients without CKD progression. C. Patients with CKD progression. Each dot represents the CACS of an individual patient. Red, blue, and green dots indicate CACS of 0, 1–100, and >100 AU, respectively. In boxplots, the horizontal line inside the box represents the median. The bottom and top lines of the box represent the first and third quartiles. The whiskers reflect the within 1.5 times the interquartile range of CACS.

Abbreviation: CKD, chronic kidney disease; CACS, coronary artery calcification score; AU, Agatston unit