Supplemental Materials

Supplemental Appendix 1. Supplemental methods

At study enrollment, baseline demographics and clinical data including comorbidities, cause of CKD, economic status, educational level, and medications were collected by a well-trained research coordinator. An 8-hour fasting blood and the second voided or random urine were used to measure serum creatinine, intact parathyroid hormone, and urinary protein-to-creatinine ratios at the central laboratory (Lab Genomics, Seoul, Korea). Other laboratory variables were measured at the hospital laboratory of each participating center. Estimated glomerular filtration rate was calculated using the CKD Epidemiology Collaboration equation[1] and CKD stage 1–5 (non-dialysis) was classified according to the Kidney Disease Improving Global Outcomes guideline.[2]

Reference

1. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, 3rd, Feldman HI, et al.: A new equation to estimate glomerular filtration rate. Ann Intern Med 150:604-612, 2009.

2. Chapter 1: Definition and classification of CKD. Kidney Int Suppl (2011) 3:19-62, 2013.

Supplemental Table 1. The prevalence of CAC based on smoking status between men and women

	Men (*n*=1141)			Women (*n*=773)		
	No. of Events (%)	[1]Prevalence ratio (95% CI)	P-value	No. of Events (%)	[1]Prevalence ratio (95% CI)	P-value
Never smoker	142/280 (51)	1.00		269/710 (38)	1.00	
Former smoker	337/554 (60)	1.10 (0.99 to 1.23)	0.09	9/38 (24)	0.88 (0.54 to 1.43)	0.6
Current smoker	181/307 (59)	1.21 (1.07 to 1.38)	0.002	14/25 (56)	1.54 (1.10 to 2.17)	0.01

[1]Model was adjusted for age, diabetes mellitus, economic status, educational level, body mass index, systolic blood pressure, statin use, calcium-phosphate products, eGFR, and UPCR.

Abbreviations: CAC, coronary artery calcification; CI, confidence interval; eGFR, estimated glomerular filtration rate; UPCR, urinary protein-to-creatinine ratio.

Supplemental Table 2. Categorization of former smokers based on smoking load and cessation duration

	Former smokers (N=592)
Smoking load, median [IQR], pack-years	15 [7 to 30]
0.1 to <10 pack-years (*n*=190)	3 [1 to 6]
10 to <20 pack-years (*n*=136)	13 [10 to 15]
≥20 pack-years (*n*=266)	30 [25 to 40]
[1]Cessation duration, median [IQR], years	12 [7 to 20]
0.5 to <10 years (*n*=190)	5 [2 to 8]
10 to <20 years (*n*=183)	14 [12 to 17]
≥20 years (*n*=122)	27 [23 to 33]

[1]Cessation duration was available in 495 former smokers.

Supplemental Table 3. Prevalence rate for CAC in four combination groups based on smoking dose and cessation duration in 495 former smokers

	Light smoking (0.1 to <10 pack-years)	Heavy smoking (≥10 pack-years)
Short quitting (0.5 to <10 years), *n*(%)	8/40 (20)	97/150 (65)
Long quitting (≥10 years), *n*(%)	61/130 (47)	118/175 (67)

Abbreviations: CAC, coronary artery calcification.

Supplemental Table 4. The prevalence of CAC for former smokers among CKD stage 3−5 participants

	Former vs. never smoker		Former vs. current smoker	
	[1]Prevalence ratio (95% CI)	P-value	[1]Prevalence ratio (95% CI)	P-value
Never smoker (*n*=645)	1.00		−	
[2, 3]Former smoker (*n*=362)				
Light smoking-short quitters (*n*=21)	1.05 (0.59 to 1.87)	0.88	0.71 (0.39 to 1.27)	0.24
Heavy smoking-short quitters (*n*=108)	1.04 (0.88 to 1.24)	0.63	0.86 (0.73 to 1.02)	0.09
Light smoking-long quitters (*n*=99)	0.98 (0.81 to 1.20)	0.9	0.76 (0.63 to 0.93)	0.01
Heavy smoking-long quitters (*n*=134)	1.00 (0.88 to 1.17)	0.9	0.84 (0.73 to 0.97)	0.02
Current smoker (*n*=222)	−		1.00	

[1]Model was adjusted for age, diabetes mellitus, economic status, educational level, body mass index, systolic blood pressure, statin use, calcium-phosphate products, eGFR, and UPCR.

[2]According to 10 pack-years of smoking dose, former smokers were categorized into light (<10 pack-years) and heavy (≥10 pack-years) smokers.

[3]According to 10 years of cessation duration, former smokers were categorized into short (<10 years) and long (≥10 years) quitters.

Abbreviations: CAC, coronary artery calcification; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; UPCR, urinary protein-to-creatinine ratio.

Supplemental Table 5. The prevalence of CAC for former smokers compared with current smokers using different CAC cutoff values

	CAC score >10 AU		CAC score >100 AU	
	[1]Prevalence ratio (95% CI)	P-value	[1]Prevalence ratio (95% CI)	P-value
Current smoker	1.00		1.00	
[2, 3]Former smoker				
Light smoking-short quitters	0.59 (0.29 to 1.20)	0.14	1.42 (0.56 to 3.56)	0.45
Heavy smoking-short quitters	0.87 (0.72 to 1.04)	0.13	1.06 (0.81 to 1.39)	0.66
Light smoking-long quitters	0.64 (0.50 to 0.82)	<0.001	0.88 (0.63 to 1.21)	0.43
Heavy smoking-long quitters	0.74 (0.62 to 0.88)	0.001	0.69 (0.52 to 0.91)	0.01

[1]Model was adjusted for age, diabetes mellitus, economic status, educational level, body mass index, systolic blood pressure, statin use, calcium-phosphate products, eGFR, and UPCR.

[2]According to 10 pack-years of smoking dose, former smokers were categorized into light (<10 pack-years) and heavy (≥10 pack-years) smokers.

[3]According to 10 years of cessation duration, former smokers were categorized into short (<10 years) and long (≥10 years) quitters.

Abbreviations: AU, Agatston unit; CAC, coronary artery calcification; CI, confidence interval; eGFR, estimated glomerular filtration rate; UPCR, urinary protein-to-creatinine ratio.

Supplemental Table 6. Comparison of baseline characteristics in patients with and without follow-up CAC measurements

Variables	Patients with repeated CAC score (n=755)	Patients without repeated CAC score (n=811)	P-value
Smoking status, *n* (%)			0.01
Never smokers	393 (52)	432 (53)	
Former smokers	251 (33)	220 (27)	
Current smokers	111 (15)	159 (20)	
Baseline CAC, *n* (%)	334 (44)	392 (48)	0.11
Age, median [IQR], yr	53 [43 to 61]	54 [45 to 63]	0.10
Men, *n* (%)	445 (59)	482 (59)	0.88
Diabetes mellitus, *n* (%)	151 (20)	258 (32)	<0.001
Economic status, *n* (%)			0.29
High (>4,500 $/m)	193 (26)	181 (22)	
Middle (1,500–4,500 $/m)	425 (56)	469 (58)	
Low (<1,500 $/m)	137 (18)	161 (20)	
Educational level, *n* (%)			0.9

≤6 years	83 (11)	89 (11)	
7-12 years	345 (46)	374 (46)	
≥13 years	327 (43)	348 (43)	
BMI, mean (SD), kg/m^2	24.3 (3.3)	24.8 (3.5)	0.002
Systolic BP, mean (SD), mmHg	126 (15)	126 (16)	0.32
Medications, *n* (%)			
RAAS blocker	639 (85)	697 (86)	0.48
Lipid-lowering agents	340 (45)	375 (46)	0.9
Ca-based P binders	49 (6)	64 (8)	0.33
eGFR, median [IQR], mL/min/1.73 m^2	60 [40 to 86]	50 [33 to 79]	<0.001
UPCR, median [IQR], g/g	0.34 [0.11 to 0.88]	0.50 [0.15 to 1.35]	0.003
Hemoglobin, mean (SD), g/dL	13 (3)	13 (2)	0.1
Albumin, mean (SD), g/dL	4.3 (0.3)	4.2 (0.4)	0.32
Triglyceride, median [IQR], mg/dL	124 [87 to 181]	134 [94 to 201]	0.05
Total cholesterol, mean (SD), mg/dL	176 (34)	176 (39)	0.9
LDL cholesterol, mean (SD), mg/dL	99 (29)	99 (32)	0.9

HDL cholesterol, mean (SD), mg/dL	51 (15)	50 (16)	0.06
Ca x P products, mean (SD), mg^2/dL^2	32 (5)	33 (6)	0.25
Intact PTH, median [IQR], pg/mL	43 [29 to 64]	43 [28 to 76]	0.1

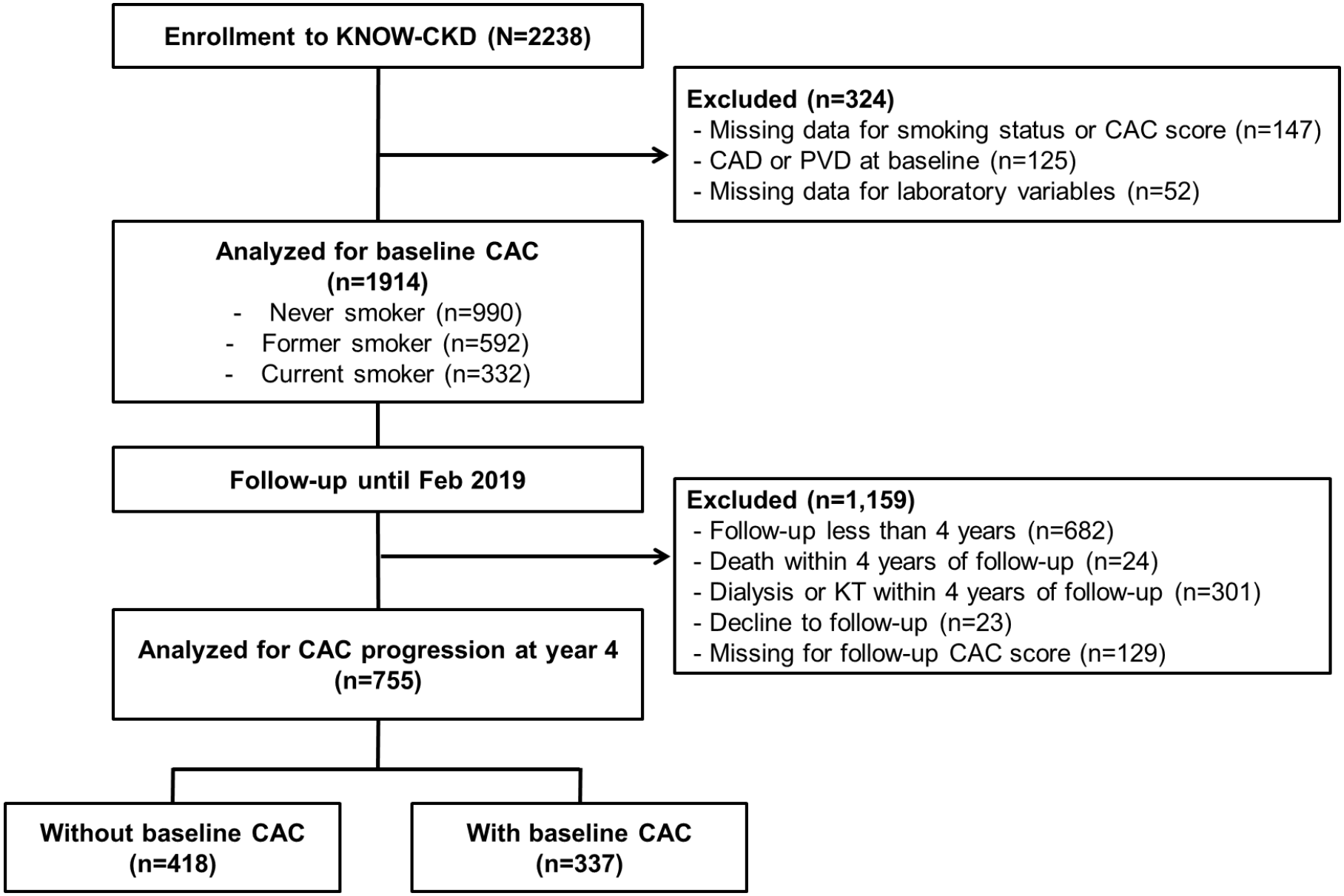
Abbreviations: BP, blood pressure; BMI, body mass index; Ca, calcium; CAC, coronary artery calcification; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; IQR, interquartile range; LDL, low-density lipoprotein; P, phosphate; PTH, parathyroid hormone; RAAS, renin-angiotensin-aldosterone system; SD, standard deviation; UPCR, urinary protein-to-creatinine ratio

Supplemental Table 7. Associations of smoking with CAC progression using different definitions in patients with baseline CAC

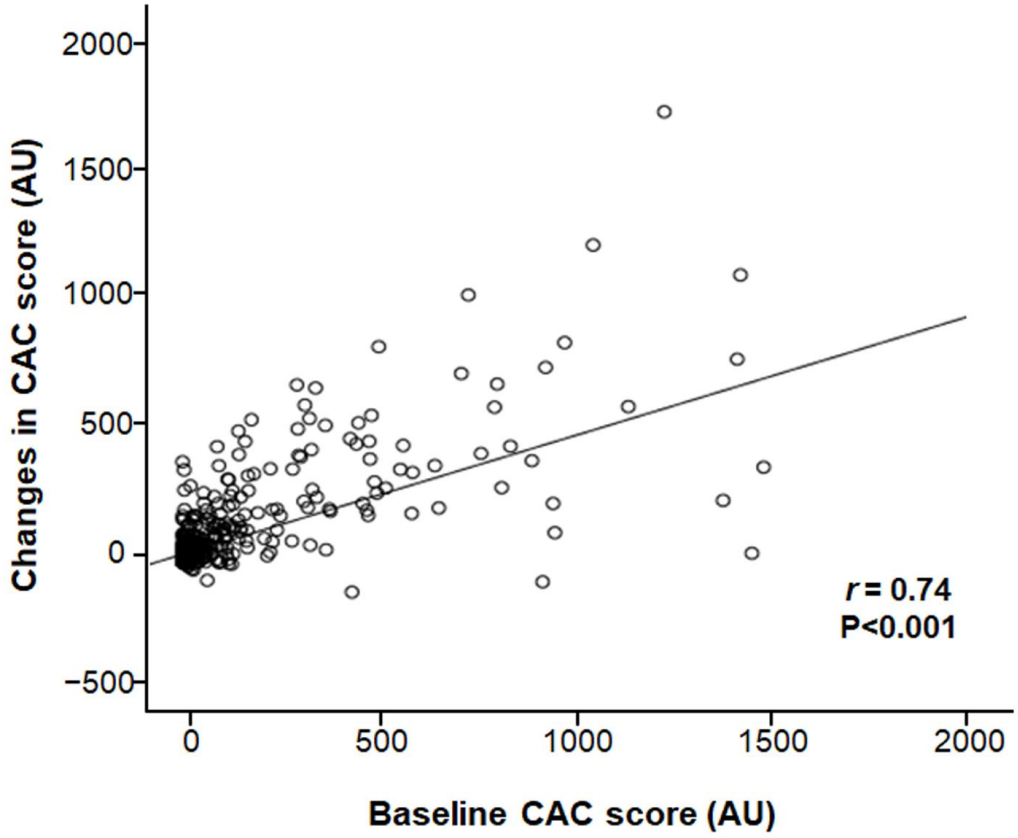
Definitions	Never smokers			Former smokers			Current smokers		
	No. of Events (%)	[1]RR (95% CI)	P-value	No. of Events (%)	[1]RR (95% CI)	P-value	No. of Events (%)	[1]RR (95% CI)	P-value
ΔCAC score ≥100 AU/year	9/142 (6)	1.00		19/135 (14)	0.95 (0.35 to 2.58)	0.9	6/60 (10)	0.83 (0.25 to 2.74)	0.76
ΔCAC score ≥15%/year	82/142 (58)	1.00		60/135 (59)	1.04 (0.80 to 1.35)	0.79	48/60 (80)	1.43 (1.12 to 1.82)	0.004

[1]Model was adjusted for age, diabetes mellitus, economic status, educational level, body mass index, systolic blood pressure, statin use, calcium-phosphate products, eGFR, and UPCR.

Abbreviations: AU, Agatston unit; CAC, coronary artery calcification; CI, confidence interval; eGFR, estimated glomerular filtration rate; RR, relative risk; UPCR, urinary protein-to-creatinine ratio.

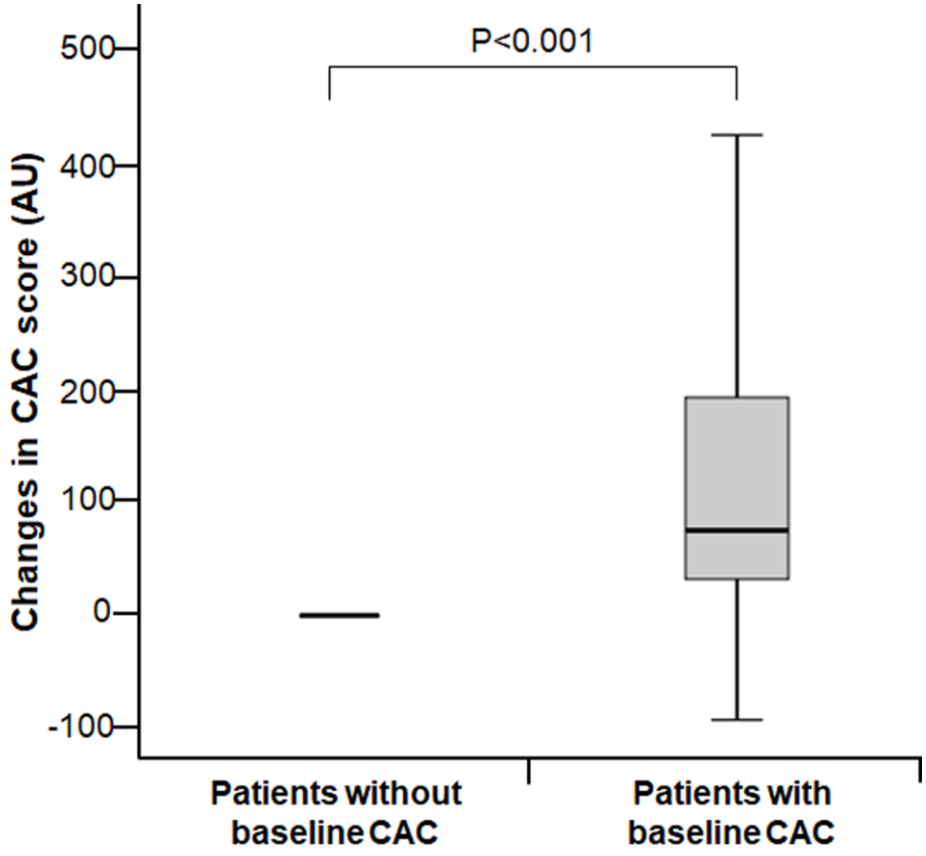

Enrollment to KNOW-CKD (N=2238)
Excluded (n=324)
- Missing data for smoking status or CAC score (n=147)
- CAD or PVD at baseline (n=125)
- Missing data for laboratory variables (n=52)
Analyzed for baseline CAC (n=1914)
- Never smoker (n=990)
- Former smoker (n=592)
- Current smoker (n=332)
Follow-up until Feb 2019
Excluded (n=1,159)
- Follow-up less than 4 years (n=682)
- Death within 4 years of follow-up (n=24)
- Dialysis or KT within 4 years of follow-up (n=301)
- Decline to follow-up (n=23)
- Missing for follow-up CAC score (n=129)
Analyzed for CAC progression at year 4 (n=755)
Without baseline CAC (n=418)
With baseline CAC (n=337)

Supplemental Figure 1. Study participants. Among initially enrolled 2241 participants from the KNOW-CKD, 1914 participants were analyzed for the presence of CAC. For analysis of CAC progression, 755 participants who underwent repeated CAC measurements were analyzed. Abbreviations: CAC, coronary artery calcification; CAD, coronary artery disease; KNOW-CKD, KoreaN Cohort Study for Outcome in Patients With Chronic Kidney Disease; KT, kidney transplantation; PVD, peripheral vascular disease



Supplemental Figure 2. Correlation of baseline CAC score and CAC score changes.

Abbreviations: AU, Agatston unit; CAC, coronary artery calcification



Supplemental Figure 3. Comparison of CAC score changes between patients with and without baseline CAC. Abbreviations: CAC, coronary artery calcification