

# **SUPPLEMENTAL MATERIAL**

**Table S1. Baseline characteristics according to CKD stages.**

	<b>Total (n=1741)</b>	<b>Stage 1 (n=579)</b>	<b>Stage 2 (n=627)</b>	<b>Stage 3 (n=323)</b>	<b>Stage 4 (n=141)</b>	<b>Stage 5 (n=71)</b>	<b>P for trend**</b>
<b>Age (years)</b>	60.8 ± 11.4	55.9 ± 10.7	63.6 ± 0.4	62.3 ± 11.4	59.3 ± 12.7	57.9 ± 11.7	<0.001
<b>Men (%)</b>	953 (54.7)	300 (51.8)	359 (57.3)	192 (59.4)	71 (50.4)	31 (43.7)	0.866
<b>Body mass index (kg/m<sup>2</sup>)</b>	25.3 ± 3.8	25.4 ± 4.2	25.5 ± 3.4	25.3 ± 3.8	24.8 ± 4.1	23.6 ± 3.4	0.017
<b>Waist to hip ratio</b>	0.93 ± 0.07	0.92 ± 0.06	0.93 ± 0.07	0.94 ± 0.07	0.93 ± 0.08	0.92 ± 0.08	<0.001
<b>ECW/TBW</b>	0.386 ± 0.016	0.384 ± 0.020	0.385 ± 0.014	0.388 ± 0.013	0.391 ± 0.018	0.392 ± 0.018	<0.001
<b>ECW/TBW ≥0.390</b>	518 (29.8)	107 (27.1)	170 (27.1)	124 (38.4)	77 (54.6)	40 (56.3)	<0.001
<b>ECW/TBW ≥0.400</b>	110 (6.3)	16 (2.8)	26 (4.1)	25 (7.7)	27 (19.1)	16 (22.5)	<0.001
<b>Pulse pressure (mmHg) *</b>	48.7 ± 22.9	38.6 ± 21.3	42.0 ± 22.8	44.4 ± 21.8	49.7 ± 21.6	53.7 ± 18.8	<0.001
<b>Diabetes (%)</b>	730 (42.1)	214 (37.1)	266 (42.8)	160 (49.5)	63 (44.7)	27 (28.6)	0.019
<b>Hypertension (%)</b>	1474 (85.0)	460 (79.7)	541 (87.0)	288 (89.2)	124 (87.9)	61 (85.9)	0.001
<b>Cardiovascular disease (%)‡</b>	750 (43.3)	281 (48.7)	341 (54.8)	95 (29.4)	22 (15.7)	11 (15.9)	<0.001
<b>Smoking (%)</b>	781 (45.0)	249 (43.2)	287 (45.8)	163 (50.8)	57 (40.7)	25 (35.2)	0.871
<b>CACS †</b>	22.0 (0.0 – 189.3)	0.0 (0.0 – 80.5)	43.7 (0.0 – 256.5)	45.2 (0.0 – 267.0)	42.1 (0.0 – 255.7)	20.1 (0.0 – 132.0)	<0.001
<b>CAC (%)§</b>	251 (14.4)	41 (7.1)	104 (16.6)	68 (21.1)	24 (17.0)	14 (19.7)	<0.001
<b>Laboratory findings</b>							
eGFR (mL•min-1•1.73 m <sup>-2</sup> )	72.2 ± 28.6	100.6 ± 7.9	77.4 ± 8.7	46.5 ± 8.8	22.7 ± 4.3	10.8 ± 2.7	<0.001
Hemoglobin (g/dL)	13.5 ± 2.0	14.3 ± 1.5	14.0 ± 1.7	13.2 ± 2.0	11.3 ± 1.3	10.4 ± 1.4	<0.001
Total cholesterol (mg/dL)	174.1 ± 38.2	176.5 ± 38.8	172.3 ± 34.0	173.7 ± 41.7	177.8 ± 43.6	166.5 ± 38.8	0.070
LDL (mg/dL)	96.2 ± 30.9	98.2 ± 32.2	94.8 ± 29.3	94.3 ± 29.8	100.5 ± 34.8	90.4 ± 19.2	0.165
HDL (mg/dL)	49.5 ± 13.5	51.5 ± 13.5	50.8 ± 12.6	48.1 ± 14.5	45.5 ± 12.7	41.5 ± 12.7	<0.001
Triglyceride (mg/dL)	139.2 ± 79.9	134.7 ± 79.4	136.9 ± 76.7	148.5 ± 92.0	144.7 ± 63.3	146.2 ± 80.5	<0.001
Albumin (g/dL)	4.2 ± 0.3	4.3 ± 0.3	4.3 ± 0.3	4.2 ± 0.4	4.0 ± 0.4	3.9 ± 0.4	<0.001
Calcium (mg/dL)	9.15 ± 0.46	9.17 ± 0.38	9.22 ± 0.42	9.16 ± 0.46	8.95 ± 0.54	8.65 ± 0.68	<0.001
Phosphate (mg/dL)	3.63 ± 0.55	3.61 ± 0.48	3.52 ± 0.50	3.60 ± 0.52	3.86 ± 0.51	4.38 ± 0.93	<0.001
Sodium (mmol/L)	141.4 ± 2.2	141.2 ± 2.2	141.5 ± 2.2	141.6 ± 2.4	141.5 ± 2.4	140.9 ± 3.1	0.028
Potassium (mmol/L)	4.6 ± 0.5	4.4 ± 0.4	4.5 ± 0.4	4.7 ± 0.5	5.0 ± 0.5	4.9 ± 0.5	<0.001
Chloride (mmol/L)	105.3 ± 4.8	102.7 ± 2.7	103.1 ± 2.5	104.3 ± 3.4	106.5 ± 3.3	105.3 ± 4.8	<0.001

hs-CRP (mg/L) <sup>†</sup>	0.8 (0.5 – 1.5)	0.8 (0.5 – 1.5)	0.8 (0.5 – 1.4)	0.9 (0.6 – 1.7)	0.8 (0.5 – 2.3)	0.8 (0.5 – 1.8)	0.016
uACR (mg/gCr) <sup>†</sup>	4.8 (1.1 – 37.9)	1.5 (0.7 – 7.2)	2.6 (0.9 – 9.5)	14.2 (3.1 – 57.8)	64.8 (26.5 – 154.0)	82.2 (36.8 – 186.2)	<0.001
<b>Medications</b>							
Antihypertensive drugs <sup>  </sup>	1335 (76.7)	407 (70.3)	483 (77.0)	261 (80.8)	122 (86.5)	62 (87.3)	<0.001
Lipid lowering agents <sup>#</sup>	955 (54.9)	319 (55.1)	384 (61.2)	156 (48.3)	65 (46.1)	31 (43.7)	0.002
Diuretics	429 (24.6)	109 (18.8)	173 (27.6)	80 (24.8)	42 (29.8)	25 (35.2)	<0.001
Antithrombotic agents <sup>**</sup>	667 (38.3)	199 (34.4)	284 (45.3)	114 (35.3)	47 (33.3)	23 (32.4)	0.540
Oral calcium	22 (1.3)	0 (0.0)	5 (0.8)	6 (1.9)	3 (2.1)	8 (11.3)	<0.001
Calcium-based phosphate binder	6 (0.3)	0 (0.0)	0 (0.0)	1 (0.3)	2 (1.4)	3 (4.2)	<0.001
Non-Ca-based phosphate binder	1 (0.1)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0.429
Phosphate binders <sup>†</sup>	7 (0.4)	0 (0.0)	0 (0.0)	2 (0.6)	2 (1.4)	3 (4.2)	<0.001

\*Mean value of pulse pressure measured by 24-hour ambulatory blood pressure monitoring, <sup>†</sup>Kruskal-Wallis test, <sup>\*</sup>Cardiovascular diseases included coronary occlusive disease, ischemic heart disease, congestive heart failure, arrhythmia, atherosclerosis, and cerebrovascular disease., <sup>§</sup>A total CACS  $\geq$  400 was defined as CAC., <sup>||</sup> Antihypertensive drugs included angiotensin receptor blockers, angiotensin-converting enzyme inhibitors, calcium channel blocker,  $\beta$ -blocker, and  $\alpha$ -blocker., <sup>#</sup> Lipid lowering agents included statin, fibrate, and nicotinic acid., <sup>\*\*</sup>Antithrombotic agents included aspirin, other anti-platelets and anti-coagulants., <sup>†</sup> Phosphate binders included both calcium-based and non-calcium-based phosphate binders, and <sup>\*\*†</sup>P values by the Mantel–Haenszel’s linear by linear association method or Jonckheere–Terpstra test

ECF/TBW, extracellular water to total body water ratio; CKD, chronic kidney disease; CACS, coronary artery calcium score; CAC, coronary artery calcification; eGFR, estimated glomerular filtration rate; LDL, low density lipoprotein cholesterol; HDL, high density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; uACR, urine albumin to creatinine ratio

**Table S2. Univariate linear regression analysis of variables associated with extracellular fluid status.**

	$\beta$	95% CI	<i>P</i>
<b>Age (per 1 year)</b>	0.029	0.023 – 0.036	<0.001
<b>Men (vs. Women)</b>	-0.509	-0.660 – -0.359	<0.001
<b>Body mass index (per 1 kg/m<sup>2</sup>)</b>	-0.043	-0.063 – -0.023	<0.001
<b>Waist to hip ratio (per 0.01)</b>	0.012	0.001 – 0.023	0.037
<b>Pulse pressure (per 1 mmHg)<sup>†</sup></b>	0.005	0.002 – 0.008	0.004
<b>Hypertension</b>	-0.026	-0.238 – 0.189	0.815
<b>Diabetes</b>	0.431	0.277 – 0.583	<0.001
<b>Cardiovascular diseases<sup>‡</sup></b>	-0.046	-0.197 – 0.108	0.556
<b>Smoking history</b>	-0.484	-0.635 – -0.332	<0.001
<b>CACS (per 1 log)<sup>*</sup></b>	0.352	0.250 – 0.453	<0.001
<b>Laboratory findings</b>			
eGFR (per 1 mL•min <sup>-1</sup> •1.73 m <sup>-2</sup> )	-0.009	-0.012 – -0.006	<0.001
Hemoglobin (per 1 g/dL)	-0.254	-0.293 – -0.215	<0.001
Total cholesterol (per 1 mg/dL)	-0.002	-0.004 – 0.000	0.024
LDL (per 1 mg/dL)	-0.002	-0.004 – 0.001	0.157
HDL (per 1 mg/dL)	0.003	-0.003 – 0.009	0.355
Triglyceride (per 1 mg/dL)	-0.002	-0.003 – -0.001	<0.001
Albumin (per 1 g/dL)	-1.073	-1.292 – -0.853	<0.001
Calcium (per 1 mg/dL)	-0.475	-0.641 – -0.309	<0.001
Phosphate (per 1 mg/dL)	0.238	0.102 – 0.379	0.001
Sodium	0.032	-0.005 – 0.069	0.091
Potassium	0.177	-0.002 – 0.358	0.054
Chloride	0.064	0.037 – 0.091	<0.001
hs-CRP (per 1 log) <sup>*</sup>	0.224	-0.493 – 0.960	0.544
uACR (per 1 log) <sup>*</sup>	0.232	0.021 – 0.441	0.031
<b>Medications</b>			
Antihypertensive drugs <sup>§</sup>	-0.132	-0.311 – 0.049	0.150
Lipid lowering agents <sup>  </sup>	-0.016	-0.168 – 0.138	0.834
Diuretics	-0.161	-0.016 – 0.336	0.073
Antithrombotic agents <sup>#</sup>	0.028	-0.126 – 0.186	0.723
Oral calcium	0.280	-0.401 – 0.960	0.420
Phosphate binders <sup>**</sup>	0.656	-0.545 – 1.857	0.284

\* Log transformed, <sup>†</sup> Mean value of pulse pressure measured by 24-hour ambulatory blood pressure monitoring, <sup>‡</sup> Cardiovascular diseases included coronary occlusive disease, ischemic heart disease, congestive heart failure, arrhythmia, atherosclerosis, and cerebrovascular disease., <sup>§</sup> Antihypertensive drugs included angiotensin receptor blockers, angiotensin-converting enzyme inhibitors, calcium channel blocker,  $\beta$ -blocker, and  $\alpha$ -blocker., <sup>||</sup> Lipid lowering agents included statin, fibrate, and nicotinic acid., <sup>#</sup> Antithrombotic agents included aspirin, other anti-platelets and anti-coagulants., <sup>\*\*</sup> Phosphate binders included both calcium-based and non-calcium-based phosphate binders.

CI, confidence interval; CACS, coronary artery calcium score; eGFR, estimated glomerular filtration rate; LDL, low density lipoprotein cholesterol; HDL, high density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; uACR, urine albumin to creatinine ratio

**Table S3. Univariable logistic regression analyses for presence of coronary artery calcification\*.**

	Univariable		
	OR	95% CI	P
<b>Age (per 1 year)</b>	1.055	1.040 – 1.070	<0.001
<b>Men (vs. Women)</b>	1.944	1.463 – 2.583	<0.001
<b>Body mass index (per 1 kg/m<sup>2</sup>)</b>	1.000	0.965 – 1.035	0.989
<b>Waist hip ratio (per 0.01)</b>	1.054	1.033 – 1.075	<0.001
<b>Pulse pressure (per 1 mmHg) ‡</b>	1.007	1.000 – 1.013	0.035
<b>Hypertension</b>	1.287	0.861 – 1.923	0.218
<b>Diabetes</b>	2.459	1.867 – 3.238	<0.001
<b>Cardiovascular diseases §</b>	1.315	1.005 – 1.720	0.046
<b>Smoking history</b>	1.703	1.299 – 2.231	<0.001
<b>ECW/TBW (per 0.01)</b>	1.297	1.147 – 1.467	<0.001
<b>Laboratory findings</b>			
eGFR (per 1 mL•min <sup>-1</sup> •1.73 m <sup>-2</sup> )	0.988	0.983 – 0.992	<0.001
Hemoglobin (per 1 g/dL)	0.879	0.820 – 0.942	<0.001
Total cholesterol (per 1 mg/dL)	0.991	0.987 – 0.995	<0.001
LDL (per 1 mg/dL)	0.988	0.983 – 0.993	<0.001
HDL (per 1 mg/dL)	0.987	0.977 – 0.998	0.021
Triglyceride (per 1 mg/dL)	0.999	0.997 – 1.001	0.411
Albumin (per 1 g/dL)	0.538	0.371 – 0.779	0.001
Calcium (per 1 mg/dL)	1.184	0.884 – 1.586	0.258
Phosphate (per 1 mg/dL)	0.923	0.722 – 1.181	0.524
hs-CRP (per 1 log) †	0.835	0.255 – 3.097	0.788
uACR (per 1 log) †	1.273	0.921 – 1.760	0.144
<b>Medications</b>			
Antihypertensive drugs ‖	1.232	0.886 – 1.712	0.215
Lipid lowering agents #	1.346	1.025 – 1.769	0.033
Diuretics	1.300	0.966 – 1.750	0.083
Antithrombotic agents **	1.813	1.386 – 2.371	<0.001
Oral calcium	1.324	0.444 – 3.946	0.614
Phosphate binders ††	4.494	1.000 – 20.200	0.050

\*A total Agatston coronary artery calcium score  $\geq 400$  was defined as coronary artery calcification., †log transformed, ‡ Mean value of pulse pressure measured by 24-hour ambulatory blood pressure, § Cardiovascular diseases included coronary occlusive disease, ischemic heart disease, congestive heart failure, arrhythmia, atherosclerosis, and cerebrovascular disease., ‖ Antihypertensive drugs included angiotensin receptor blockers, angiotensin-converting enzyme inhibitors, calcium channel blocker,  $\beta$ -blocker, and  $\alpha$ -blocker., # Lipid lowering agents included statin, fibrate, and nicotinic acid., \*\* Antithrombotic agents included aspirin, other anti-platelets and anti-coagulants., †† Phosphate binders included both calcium-based and non-calcium-based phosphate binders.

OR, odds ratio; CI, confidence interval; ECW/TBW, extracellular water to total body water ratio; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; LDL, Low density lipoprotein cholesterol; HDL, high density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; uACR, urine albumin to creatinine ratio

**Table S4. Reclassification improvement for presence of coronary artery calcification \* by extracellular fluid status.**

		Basic clinical model <sup>†</sup> + ECW/TBW			Reclassification	
		<10%	10 – 20%	≥20%	Up	Down
<b>Non-CAC (CAC &lt;400, n =1490)</b>						
<b>Basic clinical model<sup>†</sup></b>	<10%	751	11	3		
	10 – 20%	40	373	9	23	64
	≥20%	0	24	279		
<b>CAC (CACS ≥400, n =251)</b>						
<b>Basic clinical model<sup>†</sup></b>	<10%	36	2	0		
	10 – 20%	4	63	10	12	6
	≥20%	0	2	134		

\* A total Agatston coronary artery calcium score ≥ 400 was defined as coronary artery calcification

† Adjusted for age, sex, waist to hip ratio, hypertension, diabetes, cardiovascular disease, smoking status, pulse pressure, estimated glomerular filtration rate, hemoglobin, low-density lipoprotein cholesterol, albumin, calcium, phosphate, and use of lipid lowering agents, antithrombotic agents, and phosphate binders

ECW/TBW, extracellular water to total body water ratio; NRI, net reclassification improvement; IDI, integrated discrimination improvement

**Table S5. Unadjusted and adjusted linear regression analyses of extracellular fluid status for the coronary artery calcium scores\*.**

	$\beta$	95% CI	<i>P</i>
<b>ECW/TBW (per 0.01 increase)</b>	0.074	0.052 – 0.095	<0.001
<b>Model 1<sup>†</sup></b>	0.053	0.032 – 0.073	<0.001
<b>Model 2<sup>‡</sup></b>	0.038	0.017 – 0.060	<0.001
<b>Model 3<sup>§</sup></b>	0.040	0.019 – 0.061	<0.001

\* Log transformed coronary artery calcium scores

<sup>†</sup> Adjusted for age, sex, waist to hip ratio, hypertension, diabetes, cardiovascular disease, smoking status, and pulse pressure

<sup>‡</sup> Adjusted for model 1 + estimated glomerular filtration rate, hemoglobin, low-density lipoprotein cholesterol, albumin, calcium, and phosphate

<sup>§</sup> Adjusted for model 2 + use of lipid lowering agents, antithrombotic agents, and phosphate binders

ECW/TBW, extracellular water to total body water ratio; OR, odds ratio; CI, confidence interval

**Table S6. Association of ECF status for the presence of coronary artery calcification\* after additional adjustment of NT-proBNP.**

	<b>OR</b>	<b>95% CI</b>	<b>P</b>
<b>ECW/TBW (per 0.01 increase)</b>	1.941	1.474 – 2.554	<0.001
<b>Model 1<sup>†</sup></b>	1.530	1.099 – 2.129	0.012
<b>Model 2<sup>‡</sup></b>	1.645	1.113 – 2.432	0.013
<b>Model 3<sup>§</sup></b>	1.690	1.139 – 2.507	0.009

\* A total Agatston coronary artery calcium score  $\geq 400$  was defined as coronary artery calcification

<sup>†</sup> Adjusted for age, sex, waist to hip ratio, hypertension, diabetes, cardiovascular disease, smoking status, and pulse pressure

<sup>‡</sup> Adjusted for model 1 + estimated glomerular filtration rate, hemoglobin, low-density lipoprotein cholesterol, albumin, calcium, phosphate, and log transformed NT-proBNP

<sup>§</sup> Adjusted for model 2 + use of lipid lowering agents, antithrombotic agents, and phosphate binders

ECW/TBW, extracellular water to total body water ratio; OR, odds ratio; CI, confidence interval



**Table S7. Subgroup analysis.**

	Hypertension group (CAC/total N=65/767)			DM with albuminuria group (CAC/total N=152/730)			CVD group* (CAC/total N=8/95)		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
<b>ECW/TBW (per 0.01)</b>	1.589	1.212 – 2.083	0.001	1.794	1.476 – 2.181	<0.001	0.795	0.273 – 2.313	0.673
<b>Model 1<sup>†</sup></b>	1.355	0.967 – 1.900	0.078	1.821	1.469 – 2.256	<0.001	1.284	0.322 – 5.123	0.724
<b>Model 2<sup>‡</sup></b>	1.875	1.183 – 2.971	0.007	1.869	1.411 – 2.476	<0.001	2.183	0.398 – 11.981	0.369
<b>Model 3<sup>§</sup></b>	2.036	1.271 – 3.261	0.003	1.867	1.409 – 2.473	<0.001	2.843	0.383 – 21.115	0.307

\* CVD group include asymptomatic peripheral vascular disease, atrial fibrillation, and heart failure patients without diabetes.

<sup>†</sup> Adjusted for age, sex, waist to hip ratio, hypertension, diabetes, cardiovascular disease, smoking status, and pulse pressure

<sup>‡</sup> Adjusted for model 1 + hemoglobin, lipid profiles, albumin, and estimated glomerular filtration rate

<sup>§</sup> Adjusted for model 2 + use of lipid lowering agents and antithrombotic agents

DM, diabetes mellitus; CVD, cardiovascular disease; ECW/TBW, extracellular water to total body water ratio; OR, odds ratio; CI, confidence interval

**Table S8. Unadjusted and adjusted odds ratios of extracellular fluid status for the presence of coronary artery calcification\* stratified by the severity of chronic kidney disease.**

	CKD stage 12 (n = 145/1206)			CKD stage 3-5 (n = 106/535)		
	OR	95% CI	P	OR	95% CI	P
<b>ECW/TBW (per 0.01 increase)</b>	1.094	1.014 – 1.182	0.021	1.820	1.475 – 2.246	<0.001
<b>Model 1<sup>†</sup></b>	1.098	1.014 – 1.188	0.021	1.722	1.402 – 2.240	<0.001
<b>Model 2<sup>‡</sup></b>	1.109	1.021 – 1.205	0.014	2.166	1.580 – 2.970	<0.001
<b>Model 3<sup>§</sup></b>	1.113	1.024 – 1.209	0.011	2.238	1.627 – 3.078	<0.001

\* A total Agatston coronary artery calcium score  $\geq 400$  was defined as coronary artery calcification

<sup>†</sup> Adjusted for age, sex, waist to hip ratio, hypertension, diabetes, cardiovascular disease, smoking status, and pulse pressure

<sup>‡</sup> Adjusted for model 1 + estimated glomerular filtration rate, hemoglobin, low-density lipoprotein cholesterol, albumin, calcium, and phosphate

<sup>§</sup> Adjusted for model 2 + use of lipid lowering agents, antithrombotic agents, and phosphate binders

ECW/TBW, extracellular water to total body water ratio; OR, odds ratio; CI, confidence interval

**Table S9. Association of ECF status for the presence of coronary artery calcification\* depending on diuretic use.**

	Diuretics non-user			Diuretics user		
	OR	95% CI	P	OR	95% CI	P
<b>ECW/TBW (per 0.01 increase)</b>	1.171	1.053 – 1.304	0.004	1.643	1.321 – 2.043	<0.001
<b>Model 1<sup>†</sup></b>	1.143	1.054 – 1.239	0.001	1.474	1.156 – 1.878	0.002
<b>Model 2<sup>‡</sup></b>	1.135	1.051 – 1.225	0.001	2.024	1.365 – 3.002	<0.001
<b>Model 3<sup>§</sup></b>	1.137	1.054 – 1.228	0.001	2.232	1.478 – 3.371	<0.001

\* A total Agatston coronary artery calcium score  $\geq 400$  was defined as coronary artery calcification

<sup>†</sup> Adjusted for age, sex, waist to hip ratio, hypertension, diabetes, cardiovascular disease, smoking status, and pulse pressure

<sup>‡</sup> Adjusted for model 1 + estimated glomerular filtration rate, hemoglobin, low-density lipoprotein cholesterol, albumin, calcium, and phosphate

<sup>§</sup> Adjusted for model 2 + use of lipid lowering agents, antithrombotic agents, and phosphate binders

ECW/TBW, extracellular water to total body water ratio; OR, odds ratio; CI, confidence interval