Supplementary Online Content

Zhang H, Li G, Yu X, et al; China Dialysis Calcification Study Group. Progression of vascular calcification and clinical outcomes in patients receiving maintenance dialysis. *JAMA Netw Open*. 2023;6(5):e2310909. doi:10.1001/jamanetworkopen.2023.10909

This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods. Eligibility Criteria, Calcification Measurements, and Laboratory Assessments

Inclusion and exclusion criteria of the CDCS

Inclusion criteria	Exclusion criteria
1. Male or female patients >=18 years old and <75 years old; 2. Patients with ESRD receiving stable HD or PD for at least 6 months; 3. Patient or legally accepted representative willing to sign Consent Form.	1. Patients' life expectancy <6 months; 2. Patients with acute kidney injury, active inflammatory diseases, parathyroidectomy or evident malignancies; 3. Patients with conditions making arterial calcification measurements technically impossible or unreliable, such as cardiac arrhythmias, amputations or severe peripheral vascular lesions; 4. Patients with conditions making arterial calcification measurements technically impossible or unreliable, such as cardiac arrhythmias, amputations or severe peripheral vascular lesions; 5. Concomitant diseases that affect calcium status and soft tissue calcifications (sarcoidosis, multiple myeloma, HIV, amyloidosis); 6. Pregnant or lactating women or women planning to become pregnant in the 6 months following entry into the study.

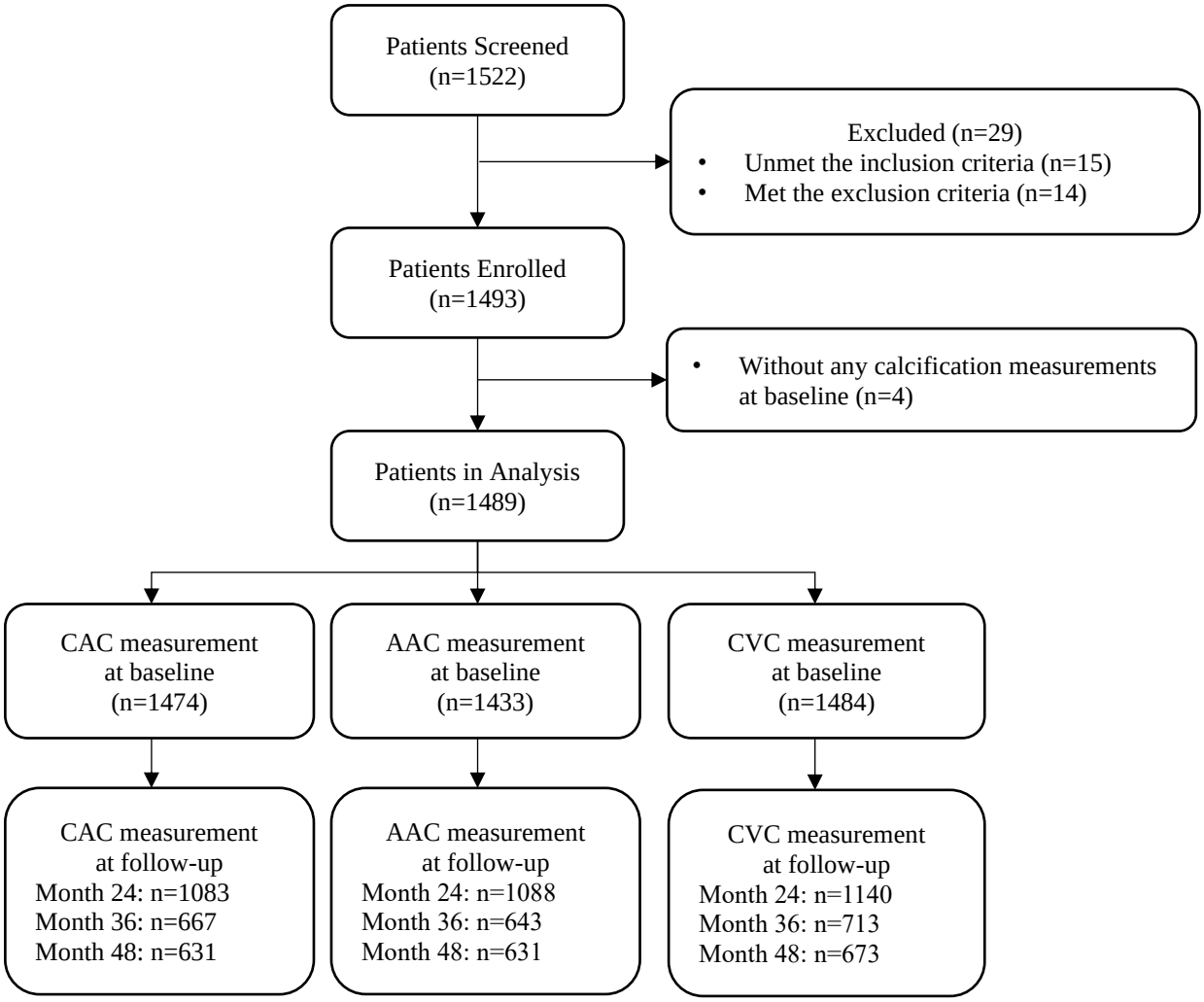
Calcification Measurements

The study patients received assessments of CAC, AAC, and CVC at baseline and during 3 follow-up visits at 24, 36, and 48 months. Baseline physical, laboratory, imaging evaluations and quantitative and semi-quantitative VC scoring have been reported previously[1]. In brief, CAC, AAC, and CVC were measured by electron beam computed tomography (EBCT) or multi-detector computed tomography (MDCT), plain lateral lumbar radiograph, and echocardiography, respectively. CAC score was calculated as a sum of individual calcified lesion scores from 4 arteries (left main, left anterior descending, left circumflex and right coronary), an approach originally proposed by Agatston[2] . AAC score was computed by a validated scoring system to grade individual calcified lesions at both the anterior and posterior walls of the aorta parallel to vertebrae level 1 to level 4, which was first proposed by Kauppila[3]. AAC score ranged from 0-24 points. The presence of CAC and AAC was regarded as a CAC score >0 and a AAC score >0, respectively. CVC was defined as the presence of >1mm of echoes on the aortic valve or mitral cusps or annulus, in which patients were categorized as no valve calcification, single valve calcification, and 2 valves calcification. Total VC was defined as presence of calcification at any 1 of the 3 measurements (CAC score >0, AAC score >0, and/or CVC detected in 1 or 2 valves).

Laboratory Assessments

The laboratory tests for serum calcium (Ca), serum phosphorus (P), iPTH, FGF-23, and 25-OH Vitamin D were measured consecutively over the study period. Serum Ca, serum P, and iPTH were measured at baseline and month 6, 12, 18, 24, 36, and 48, whereas FGF-23 and 25-OH Vitamin D were measured at baseline and month 12 and 24. High-sensitivity C-reactive protein (hsCRP) was collected only at baseline. Intact FGF-23 enzyme-linked immunosorbent assay (ELISA) kit (catalogue no. CY-4000; Kainos Laboratories, Tokyo, Japan) was used to analyze Intact FGF-23 for all the patients from baseline to follow up.

eFigure. Patient Disposition Flowchart



Abbreviations: AAC, abdominal aortic calcification; CAC, coronary artery calcification; CVC, cardiac valve calcification; VC, vascular calcification.

eTable 1. Prevalence of Calcification at Baseline and During 4-Year Follow-up

	Overall		HD		PD	
	n/N	% (95% CI)	n/N	% (95% CI)	n/N	% (95% CI)
CAC						
Baseline	1003/1474	68.0 (65.6-70.4)	831/1157	71.8 (69.1-74.4)	172/317	54.3 (48.6-59.8)
Month 24	824/1083	76.1 (73.4-78.6)	677/853	79.4 (76.5-82.0)	147/230	63.9 (57.3-70.1)
Month 36	540/667	81.0 (77.8-83.9)	426/502	84.9 (81.4-87.9)	114/165	69.1 (61.4-76.0)
Month 48	511/631	81.0 (77.7-84.0)	415/496	83.7 (80.1-86.8)	96/135	71.1 (62.7-78.6)
P trend		<.0001		<.0001		<.0001
AAC						
Baseline	662/1433	46.2 (43.6-48.8)	560/1130	49.6 (46.6-52.5)	102/303	33.7 (28.4-39.3)
Month 24	665/1088	61.1 (58.2-64.0)	551/854	64.5 (61.2-67.7)	114/234	48.7 (42.2-55.3)
Month 36	446/643	69.4 (65.6-72.9)	362/498	72.7 (68.6-76.6)	84/145	57.9 (49.5-66.1)
Month 48	470/631	74.5 (70.9-77.8)	381/504	75.6 (71.6-79.3)	89/127	70.1 (61.3-77.9)
P trend		<.0001		<.0001		<.0001
CVC						
Baseline	430/1484	29.0 (26.7-31.4)	364/1166	31.2 (28.6-34.0)	66/318	20.8 (16.4-25.6)
Month 24	454/1140	39.8 (37.0-42.7)	381/902	42.2 (39.0-45.5)	73/238	30.7 (24.9-37.0)
Month 36	342/713	48.0 (44.2-51.7)	278/544	51.1 (46.8-55.4)	64/169	37.9 (30.5-45.6)
Month 48	308/673	45.8 (42.0-49.6)	250/535	46.7 (42.4-51.1)	58/138	42.0 (33.7-50.7)
P trend		<.0001		<.0001		<.0001
Total VC [a]						
Baseline	1148/1489	77.1 (74.9-79.2)	940/1168	80.5 (78.1-82.7)	208/321	80.5 (78.1-82.7)
Month 24	980/1162	84.3 (82.1-86.4)	798/912	87.5 (85.2-89.6)	182/250	87.5 (85.2-89.6)
Month 36	646/717	90.1 (87.7-92.2)	506/548	92.3 (89.8-94.4)	140/169	92.3 (89.8-94.4)
Month 48	617/680	90.7 (88.3-92.8)	497/542	91.7 (89.0-93.9)	120/138	91.7 (89.0-93.9)
P trend		<.0001		<.0001		<.0001

Abbreviations: AAC, abdominal aortic calcification; CAC, coronary artery calcification; CI, confidence interval; HD, hemodialysis; PD, peritoneal dialysis; CVC, cardiac valve calcification; VC, vascular calcification.

[a] Total VC was defined as calcification presented in any 1 of the 3 measurements (CAC, AAC, and CVC).

eTable 2. Proportions of Patients With Progression of Calcification During 4-Year Follow-up Among Those Without Baseline Calcification

	Overall		HD		PD	
	n/N	**% (95% CI)**	**n/N**	**% (95% CI)**	**n/N**	**% (95% CI)**
Progression of CAC						
Month 24	91/373	24.4 (20.1-29.1)	71/260	27.3 (22.0-33.2])	20/113	17.7 (11.2-26.0)
Month 36	85/244	34.8 (28.9-41.2)	61/161	37.9 (30.4-45.9)	24/83	28.9 (19.5-39.9)
Month 48	102/239	42.7 (36.3-49.2)	80/169	47.3 (39.6-55.1)	22/70	31.4 (20.9-43.6)
P trend		<.0001		<.0001		.0271
Progression of AAC						
Month 24	197/586	33.6 (29.8-37.6)	150/427	35.1 (30.6-39.9)	47/159	29.6 (22.6-37.3)
Month 36	169/359	47.1 (41.8-52.4)	130/260	50.0 (43.8-56.2)	39/99	39.4 (29.7-49.7)
Month 48	210/365	57.5 (52.3-62.7)	162/279	58.1 (52.0-63.9)	48/86	55.8 (44.7-66.5)
P trend		<.0001		<.0001		<.0001
Progression of CVC						
Month 24	185/814	22.7 (19.9-25.8)	146/622	23.5 (20.2-27.0)	39/192	20.3 (14.9-26.7)
Month 36	166/498	33.3 (29.2-37.7)	125/358	34.9 (30.0-40.1)	41/140	29.3 (21.9-37.6)
Month 48	162/484	33.5 (29.3-37.9)	124/373	33.2 (28.5-38.3)	38/111	34.2 (25.5-43.8)
P trend		<.0001		.0003		.0061
Progression of Total VC [a]						
Month 24	126/284	44.4 (38.5-50.4)	87/188	46.3 (39.0-53.7)	39/96	40.6 (30.7-51.1)
Month 36	110/181	60.8 (53.3-67.9)	71/115	61.7 (52.2-70.6)	39/66	59.1 (46.3-71.0)
Month 48	126/184	68.5 (61.2-75.1)	86/126	68.3 (59.4-76.3)	40/58	69.0 (55.5-80.5)
P trend		<.0001		<.0001		.0004

Abbreviations: AAC, abdominal aortic calcification; CAC, coronary artery calcification; CI, confidence interval; HD, hemodialysis; PD, peritoneal dialysis; CVC, cardiac valve calcification; VC, vascular calcification.

N= total number of patients with calcification; n= proportion of patients with calcification progression

[a] Progression of total VC was defined as progression presented in any one of the 3 measurements (CAC, AAC, and CVC)

eTable 3. Proportions of Patients With Progression of Calcification During 4-Year Follow-up

	Overall		HD		PD	
	n/N	**% (95% CI)**	**n/N**	**% (95% CI)**	**n/N**	**% (95% CI)**
Progression of CAC						
Month 24	626/1083	57.8 (54.8-60.8)	515/853	60.4 (57.0-63.7)	111/230	48.3 (41.6-54.9)
Month 36	432/667	64.8 (61.0-68.4)	345/502	68.7 (64.5-72.8)	87/165	52.7 (44.8-60.5)
Month 48	439/631	69.6 (65.8-73.1)	358/496	72.2 (68.0-76.1)	81/135	60.0 (51.2-68.3)
P trend		<.0001		<.0001		.0317
Progression of AAC						
Month 24	554/1088	50.9 (47.9-53.9)	450/854	52.7 (49.3-56.1)	104/234	44.4 (38.0-51.1)
Month 36	427/643	66.4 (62.6-70.1)	347/498	69.7 (65.4-73.7)	80/145	55.2 (46.7-63.4)
Month 48	457/631	72.4 (68.8-75.9)	368/504	73.0 (68.9-76.8)	89/127	70.1 (61.3-77.9)
P trend		<.0001		<.0001		<.0001
Progression of CVC [a]						
Month 24	239/1016	23.5 (20.9-26.3)	194/790	24.6 (21.6-27.7)	45/226	19.9 (14.9-25.7)
Month 36	214/633	33.8 (30.1-37.6)	166/473	35.1 (30.8-39.6)	48/160	30.0 (23.0-37.7)
Month 48	202/604	33.4 (29.7-37.4)	155/474	32.7 (28.5-37.1)	47/130	36.2 (27.9-45.0)
P trend		<.0001		.0006		.0006
Progression of Total VC [b]						
Month 24	861/1162	74.1 (71.5-76.6)	700/912	76.8 (73.9-79.5)	161/250	64.4 (58.1-70.3)
Month 36	601/717	83.8 (80.9-86.4)	472/548	86.1 (83.0-88.9)	129/169	76.3 (69.2-82.5)
Month 48	588/680	86.5 (83.7-89.0)	475/542	87.6 (84.6-90.3)	113/138	81.9 (74.4-87.9)
P trend		<.0001		<.0001		.0001

Abbreviations: AAC, abdominal aortic calcification; CAC, coronary artery calcification; CI, confidence interval; HD, hemodialysis; PD, peritoneal dialysis; CVC, cardiac valve calcification; VC, vascular calcification.

N= total number of patients with calcification; n= proportion of patients with calcification progression; The denominator was the total number of patients who received each calcification measurement during follow-up.

[a] Among those patients without or with 1 baseline CVC (N = 1324).

[b] Progression of total VC was defined as progression presented in any 1 of the 3 measurements (CAC, AAC, and CVC).

eTable 4. Incidence Rates of the Occurrence of Clinical Outcomes

	All-cause death		CV-lead to death		Composite of non-fatal CV events and all-cause death	
	No. (%) of events	**Incidence per 1000 person-years (95% CI)**	**No. (%) of events**	**Incidence per 1000 person-years (95% CI)**	**No. (%) of events**	**Incidence per 1000 person-years (95% CI)**
From baseline to the end of the study						
Overall	195 (13.1)	39.4 (34.2-45.2)	109 (7.3)	22.0 (18.1-26.5)	221 (14.8)	45.2 (39.6-51.4)
HD	181 (15.5)	46.4 (40.1-53.5)	102 (8.7)	26.2 (21.4-31.7)	204 (17.5)	53.1 (46.2-60.7)
PD	14 (4.4)	13.3 (7.3-22.2)	7 (2.2)	6.7 (2.7-13.7)	17 (5.3)	16.2 (9.5-25.9)
From Month 24 to the end of the study						
Overall	110 (9.1)	51.3 (42.4-61.5)	44 (3.6)	20.5 (15.0-27.5)	115 (9.6)	54.5 (45.2-65.0)
HD	102 (10.6)	60.1 (49.3-72.5)	42 (4.4)	24.8 (17.9-33.3)	106 (11.2)	63.6 (52.4-76.5)
PD	8 (3.2)	17.9 (7.7-34.9)	2 (0.8)	4.5 (0.5-16.0)	9 (3.6)	20.2 (9.3-38.0)

Abbreviations: CI, confidence interval; CV, cardiovascular; HD, hemodialysis; PD, peritoneal dialysis.

eTable 5. Association of Progression of Calcification With the Occurrence of Clinical Outcomes

	All-cause death			CV-lead to death			Composite of non-fatal CV events and all-cause death		
	HR	**(95% CI)**	***P* Value**	**HR**	**(95% CI)**	***P* Value**	**HR**	**(95% CI)**	***P* Value**
Progression of CAC									
Univariable model	2.55	(1.52-4.29)	.0004	2.22	(1.01-4.92)	.0483	2.54	(1.53-4.21)	.0003
Multivariable Model 1	1.97	(1.16-3.33)	.0115	1.59	(0.71-3.57)	.2580	1.98	(1.19-3.31)	.0089
Multivariable Model 2	1.89	(1.11-3.21)	.0191	1.58	(0.70-3.59)	.2712	1.91	(1.14-3.21)	.0139
Multivariable Model 3	1.92	(1.11-3.31)	.0200	1.56	(0.67-3.63)	.3026	1.95	(1.14-3.33)	.0143
Multivariable Model 4	1.43	(0.81-2.54)	.2181	1.03	(0.43-2.50)	.9444	1.41	(0.81-2.47)	.2232
Progression of AAC									
Univariable model	1.72	(1.10-2.70)	.0173	3.24	(1.41-7.45)	.0058	1.80	(1.15-2.80)	.0100
Multivariable Model 1	1.09	(0.69-1.72)	.7177	2.10	(0.89-4.95)	.0895	1.13	(0.72-1.78)	.5922
Multivariable Model 2	1.10	(0.70-1.74)	.6759	2.08	(0.88-4.89)	.0938	1.14	(0.72-1.80)	.5692
Multivariable Model 3	1.06	(0.66-1.71)	.7943	1.98	(0.83-4.73)	.1243	1.10	(0.68-1.75)	.7042
Multivariable Model 4	0.97	(0.60-1.57)	.9076	1.80	(0.75-4.32)	.1913	0.99	(0.62-1.59)	.9704
Progression of CVC									
Univariable model	1.53	(0.97-2.42)	.0662	2.33	(1.09-4.98)	.0297	1.47	(0.93-2.30)	.0972
Multivariable Model 1	1.21	(0.76-1.91)	.4197	1.89	(0.88-4.06)	.1039	1.15	(0.73-1.81)	.5501
Multivariable Model 2	1.21	(0.76-1.92)	.4235	1.91	(0.88-4.12)	.1013	1.14	(0.72-1.80)	.5825
Multivariable Model 3	1.13	(0.70-1.83)	.6198	1.71	(0.77-3.79)	.1869	1.04	(0.65-1.67)	.8721
Multivariable Model 4	1.13	(0.70-1.83)	.6195	1.70	(0.77-3.78)	.1897	1.04	(0.65-1.67)	.8709

Abbreviations: AAC, abdominal aortic calcification; BMI, body mass index; CAC, coronary artery calcification; CI, confidence intervals; CV, cardiovascular; CPB, calcium-based phosphate binder; FGF-23, fibroblast growth factor-23; HR, hazards ratio; iPTH, intact parathyroid hormone; P, phosphorus; CVC, cardiac valve calcification

Model 1: Adjust age, sex, and BMI.

Model 2: Adjust factors in Model 1 and smoking status, history of diabetes mellitus, and mean arterial pressure.

Model 3: Adjust factors in Model 2 and Ca, P, iPTH, FGF-23, and use of CPB.

Model 4: Adjust factors in Model 3 and baseline calcification.

eTable 6. Association of Target Achievement With the Progression of Calcification

	CAC progression			AAC progression			CVC progression		
	OR	**(95% CI)**	***P* Value**	**OR**	**(95% CI)**	***P* Value**	**OR**	**(95% CI)**	***P* Value**
Univariable (Ref: All targets)									
No targets vs ref	4.39	(2.35-8.23)	<.0001	1.34	(0.76-2.38)	.3099	1.83	(0.95-3.53)	.0686
1 target vs ref	3.08	(1.96-4.84)	<.0001	1.63	(1.04-2.55)	.0326	2.00	(1.18-3.38)	.0100
2 targets vs ref	2.39	(1.54-3.70)	.0001	1.31	(0.85-2.02)	.2200	1.62	(0.96-2.73)	.0693
Multivariable Model 1 (Ref: All targets)									
No targets vs ref	4.75	(2.65-8.52)	<.0001	1.71	(0.99-2.97)	.0561	2.22	(1.14-4.32)	.0183
1 target vs ref	3.71	(2.35-5.88)	<.0001	2.15	(1.36-3.39)	.0010	2.07	(1.20-3.58)	.0089
2 targets vs ref	2.73	(1.74-4.26)	<.0001	1.61	(1.03-2.50)	.0363	1.76	(1.02-3.02)	.0407
Multivariable Model 2 (Ref: All targets)									
No targets vs ref	4.81	(2.67-8.66)	<.0001	1.71	(0.99-2.97)	.0545	2.21	(1.14-4.29)	.0195
1 target vs ref	3.62	(2.26-5.78)	<.0001	2.10	(1.34-3.28)	.0011	2.09	(1.21-3.61)	.0083
2 targets vs ref	2.69	(1.71-4.25)	<.0001	1.60	(1.04-2.47)	.0330	1.75	(1.02-3.01)	.0426
Multivariable Model 3 (Ref: All targets)									
No targets vs ref	2.76	(1.48-5.16)	.0015	1.05	(0.58-1.88)	.8767	1.57	(0.76-3.21)	.2198
1 target vs ref	2.19	(1.33-3.61)	.0021	1.37	(0.84-2.21)	.2052	1.56	(0.86-2.84)	.1404
2 targets vs ref	1.72	(1.06-2.79)	.0279	1.09	(0.68-1.74)	.7212	1.35	(0.75-2.43)	.3148
Multivariable Model 4 (Ref: All targets)									
No targets vs ref	2.90	(1.45-5.80)	.0026	1.06	(0.59-1.89)	.8463	1.58	(0.77-3.21)	.2111
1 target vs ref	2.51	(1.42-4.42)	.0015	1.42	(0.89-2.27)	.1421	1.57	(0.87-2.84)	.1352
2 targets vs ref	2.08	(1.19-3.62)	.0099	1.17	(0.74-1.84)	.5028	1.35	(0.75-2.42)	.3100

Abbreviations: AAC, abdominal aortic calcification; BMI, body mass index; CPB, calcium-based phosphate binder; CAC, coronary artery calcification; CI, confidence intervals; FGF-23, fibroblast growth factor-23; OR, odds ratio, CVC, cardiac valve calcification.
Model 1: Adjust age, sex, and BMI.
Model 2: Adjust factors in Model 1 and smoking status, history of diabetes mellitus, and mean arterial pressure.
Model 3: Adjust factors in Model 2 and FGF-23, and use of CPB.
Model 4: Adjust factors in Model 3 and baseline calcification and its interaction with time.

eTable 7. Association of Baseline Calcification With the Occurrence of Clinical Outcomes

	All-cause death			CV-lead to death			Composite of non-fatal CV events and all-cause death		
	HR	**(95% CI)**	***P* value**	**HR**	**(95% CI)**	***P* value**	**HR**	**(95% CI)**	***P* value**
Baseline CAC									
Univariable model	1.26	(1.19-1.33)	<.0001	1.29	(1.19-1.39)	<.0001	1.28	(1.22-1.35)	<.0001
Multivariable Model 1	1.16	(1.09-1.23)	<.0001	1.19	(1.10-1.29)	<.0001	1.19	(1.12-1.26)	<.0001
Multivariable Model 2	1.16	(1.09-1.24)	<.0001	1.20	(1.10-1.31)	<.0001	1.19	(1.12-1.26)	<.0001
Multivariable Model 3	1.18	(1.10-1.26)	<.0001	1.22	(1.11-1.34)	<.0001	1.20	(1.13-1.28)	<.0001
Baseline AAC									
Univariable model	1.62	(1.42-1.85)	<.0001	1.54	(1.29-1.85)	<.0001	1.66	(1.46-1.88)	<.0001
Multivariable Model 1	1.26	(1.09-1.46)	.0020	1.24	(1.01-1.50)	.0358	1.31	(1.14-1.50)	.0002
Multivariable Model 2	1.25	(1.07-1.46)	.0042	1.21	(0.99-1.49)	.0687	1.29	(1.12-1.49)	.0005
Multivariable Model 3	1.27	(1.08-1.49)	.0036	1.24	(1.00-1.54)	.0524	1.30	(1.12-1.51)	.0007
Baseline CVC									
Univariable model	1.37	(1.13-1.65)	.0011	1.31	(1.02-1.68)	.0355	1.33	(1.11-1.58)	.0019
Multivariable Model 1	1.07	(0.88-1.31)	.5116	1.06	(0.81-1.39)	.6650	1.04	(0.86-1.26)	.6854
Multivariable Model 2	1.09	(0.89-1.34)	.4014	1.10	(0.83-1.44)	.5154	1.05	(0.86-1.27)	.6481
Multivariable Model 3	1.08	(0.87-1.33)	.4787	1.11	(0.84-1.47)	.4715	1.02	(0.84-1.25)	.8364

Abbreviations: AAC, abdominal aortic calcification; BMI, body mass index; Ca, calcium; CAC, coronary artery calcification; CI, confidence interval; CPB, calcium-based phosphate binder; CV, cardiovascular; FGF-23, fibroblast growth factor-23; HR, hazards ratio; iPTH, intact parathyroid hormone; P, phosphorus; CVC, cardiac valve calcification; VC, vascular calcification.
Model 1: Adjust age, sex, and BMI.
Model 2: Adjust factors in Model 1 and smoking status, history of diabetes mellitus, and mean arterial pressure.
Model 3: Adjust factors in Model 2 and Ca, P, iPTH, FGF-23, and use of CPB.

eReferences

1. Liu ZH, Yu XQ, Yang JW, et al. Prevalence and risk factors for vascular calcification in Chinese patients receiving dialysis: baseline results from a prospective cohort study. Curr Med Res Opin. 2018;34(8):1491-1500.
2. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol. 1990;15(4):827-832.
3. Kauppila LI, Polak JF, Cupples LA, Hannan MT, Kiel DP, Wilson PW. New indices to classify location, severity and progression of calcific lesions in the abdominal aorta: a 25-year follow-up study. Atherosclerosis. 1997;132(2):245-250.