

Chest CT-Estimated Aortic Arch Calcification and Its Prognostic Value for Cardiovascular and All-Cause Mortality in Maintenance Hemodialysis Patients

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Abstract

Background

Cardiovascular complications are the leading cause of death in hemodialysis patients, and vascular calcification, particularly aortic arch calcification (AoAC), is an independent predictor of cardiovascular and all-cause mortality. However, chest X-ray, a commonly used method for assessing AoAC may underestimate calcium deposition. This study aimed to evaluate the prognostic value of AoAC assessed by chest computed tomography (CT) for predicting cardiovascular and all-cause mortality in maintenance hemodialysis (MHD) patients.

Methods

A retrospective cohort study was conducted, including 205 hemodialysis patients who underwent chest CT scans between January and December 2019. Patients were followed up until August 31, 2024, with a median follow-up duration of 61 months. AoAC scores (AoACS) were calculated using the Agatston-type method. Cox proportional hazards models and Kaplan-Meier survival analysis were used for statistical evaluation.

Results

Higher AoACS was associated with increased mortality risk and significantly reduced cardiovascular and overall survival rates ($p < 0.001$). Multivariable analysis revealed that $\log(\text{AoACS} + 1)$ was independently associated with cardiovascular mortality (HR 1.935, 95%CI 1.148–3.263, $p = 0.013$) and all-cause mortality (HR 1.641, 95%CI 1.156–2.329, $p < 0.006$). Diabetes and serum albumin levels were also independent predictors of mortality.

Conclusions

AoACS derived from routine chest CT is a novel and promising marker for risk stratification in MHD patients.

Trial Registration

This study was registered at the Chinese Clinical Trial Registry (ChiCTR2500098576) on March 11, 2025.

Background

Cardiovascular complications, including coronary artery disease, heart failure, arrhythmias, and sudden cardiac death, remain highly prevalent among patients with end-stage kidney disease (ESKD), even after the initiation of hemodialysis[1]. Notably, cardiovascular events represent the leading cause of mortality in this patient population[2]. Vascular calcification (VC) has been established as both an independent risk factor and a robust predictor of cardiovascular disease in hemodialysis patients[3]. VC arises from a complex interplay of mineral metabolism, chronic inflammation, and vascular smooth-muscle cell plasticity, with emerging roles for autophagy and micro-RNA signaling[4].

Calcification commonly occurs in the heart valves, coronary arteries, aortae, and other locations[5]. Aortic arch calcification (AoAC), as measured by chest X-ray, is a simple method for assessing vascular calcification in maintenance hemodialysis (MHD) patients and has been associated with cardiovascular events and all-cause mortality[6]. However, chest X-ray measurements may underestimate the true extent of calcium deposition in the aortic wall, thereby limiting the clinical utility of chest X-ray for predicting mortality in hemodialysis patients[7]. In contrast, computed tomography (CT) remains the gold standard and most sensitive method for detecting and quantifying vascular calcification. Despite its widespread use, the value of using chest CT to evaluate AoAC in MHD patients remains to be elucidated. In this study, we retrospectively analyzed multi-slice chest spiral CT (MSCT) images from MHD patients to calculate AoAC score (AoACS). Our goal was to explore the relationship between AoACS levels and long-term patient outcomes. To our knowledge, this is the first study to evaluate the prognostic utility of CT-quantified AoACS in MHD patients, while prior comparative studies—though not replicated herein—have suggested CT’s greater sensitivity than chest X-ray for detecting AoAC.

Methods

Study population

This retrospective cohort study included MHD patients who received hemodialysis treatment at Ningbo Medical Center Lihuli Hospital between January 2019 and December 2019, inclusive. A total of 317 patients were identified through the hospital’s electronic health records (EHR). Patients were eligible for inclusion if they met the following criteria: (1) dialysis duration > 6 months and underwent stable regular hemodialysis using bicarbonate dialysate; (2) availability of complete medical records during the study period, including demographic data, laboratory results, and treatment history; (3) had undergone laboratory tests and a chest CT scan within 1 month before or after the laboratory tests for the purpose of regular health check-ups or to detect lung and mediastinal abnormalities at our hospital. Patients with acute infection or malignant tumor, prior myocardial infarction, and prior stroke were excluded. Ultimately, 205 patients were enrolled in the study. Among the 205 patients, 159 (77.6%) underwent chest CT for routine health check-ups and 46 (22.4%) for suspected thoracic disease; baseline characteristics were comparable between the two indications (all $p > 0.05$). (Supplementary Table S1)

Data collection was performed using a combination of EHR and telephone consultations. Baseline demographic and clinical characteristics, laboratory results, and treatment history were extracted from the EHR. Follow-up information was obtained through regular hemodialysis sessions, outpatient visits, or telephone follow-ups, with the last follow-up date being August 31, 2024. The median follow-up duration was 61 months (interquartile range: 51–63 months). For patients who were transferred to other dialysis units, additional information was obtained through review of medical records or contact with the receiving institutions.

Assessment of aortic arch calcification

Inter- and intra-observer reproducibility of AoACS measurements were assessed in 30 randomly selected CT scans. Intraclass correlation coefficients (ICC) values were 0.97 (95% CI: 0.95–0.99) for inter-observer and 0.99 (95% CI: 0.98–1.00) for intra-observer agreement, indicating excellent reliability.

Chest CT scans were performed using a PHILIPS Ingenuity Flex 16-slice spiral CT scanner with a standardized non-contrast protocol. Scan parameters included a tube voltage of 120 kV, a tube current of 114 mA, a slice thickness of 5 mm, and an interslice interval of 5 mm.

CT images were imported into MANGO image analysis software (Research Imaging Institute, UTHSCSA; available at <https://mangoviewer.com/>) to measure AoACS (Fig. 1). The aortic arch region was defined using the following anatomical landmarks[8]: the anterior-inferior border was situated at the level of the superior border of the second sternocostal joint; the posterior-inferior border corresponded to the level of the inferior border of the fourth thoracic vertebra; and the superior border was demarcated by the origins of the brachiocephalic trunk, left common carotid artery, and left subclavian artery. All CT slices within this region were evaluated.

The following measures of calcium were obtained: volume, area (volume ÷ CT slice thickness), density [CT attenuation of the hyperdense foci (HU)], density factor [ordinal score corresponding to the attenuation of the foci: 1 = 130–199 HU; 2 = 200–299 HU; 3 = 300–399 HU; 4 = ≥ 400 HU], and an Agatston-type score (area × density factor) was calculated for the aortic arch. Although the original Agatston method[9] was defined for coronary arteries, the same algorithm was applied to the aortic arch region. The sum of the Agatston-type scores across all CT slices within the aortic arch region was defined as the AoACS, which was calculated as detailed in the Supplementary Methods. This metric provides a comprehensive assessment of AoAC, reflecting both the extent and density of calcified deposits. As no established cutoffs exist for AoACS in MHD patients, we first isolated those without any calcification (Grade 0). The remaining patients were then split by the median AoACS into Grade 1 (below median) and Grade 2 (above median).

Laboratory measurements

Blood was drawn just before starting a dialysis session while patients were in a fasting state. The following laboratory parameters were measured: hemoglobin, total protein, serum albumin, hypersensitive C-reactive protein (hs-CRP), creatinine, uric acid, urea, glucose, triglyceride, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, blood calcium, blood phosphorus, blood magnesium, intact parathyroid hormone (iPTH), alkaline phosphatase and Kt/V (HD adequacy). Serum corrected calcium (mg/dL) was calculated using the formula: Corrected Ca (mg/dL) = Measured total Ca (mg/dL) + 0.8 × [4.0 – Albumin (g/dL)].

Clinical outcomes

In the present study, cardiovascular death was defined as death attributable to acute myocardial infarction, heart failure, sudden cardiac death, or other cardiac causes; cerebrovascular events were not included.

Statistical analysis

Measurement data with normal distribution were expressed as mean±standard deviation, while those with non-normal distribution were presented as median (interquartile range). Counting data were stated as number of cases (percentage). For normally distributed data, group differences were compared using ANOVA; for non-normally distributed data, the Kruskal-Wallis test was used; and for counting data, the χ^2 test was applied. Variables related to survival were identified through univariate Cox proportional hazards analysis. Significant

variables were then entered into multivariate Cox proportional hazard models for further analysis. In the Cox analysis, AoACS values were log-transformed after adding 1 to all scores to handle zero values [$\log(\text{AoACS} + 1)$] due to their highly skewed distribution. Survival probabilities were estimated using the Kaplan-Meier method, and survival differences between groups based on different degrees of AoAC were compared using the log-rank test. A priori sample-size calculation (G*Power 3.1.9.2, one-way ANOVA, 3 groups, effect size $f = 0.25$, $\alpha = 0.05$, power = 0.80) indicated a minimum of 159 participants; our cohort of 205 exceeded this requirement. All analyses except discrimination and reclassification metrics were performed using SPSS 26.0; the latter were computed in R 4.5.1 using standard packages. A two-sided p -value < 0.05 was considered statistically significant.

Multicollinearity was assessed by calculating variance inflation factors (VIFs) for all variables in the final multivariable models; all VIFs were < 2 , indicating no significant collinearity (Supplementary Table S2).

Study design and procedures

The overall study design and procedures are summarized in Fig. 2.

Results

Baseline characteristics

The study population included 205 patients with a mean age of 58.2 ± 14.5 years. The median duration of dialysis was 43.0 months (interquartile range: 21.5–72.0 months). Male patients accounted for 59.0% of the cohort. The underlying causes of ESKD were diabetes ($n = 47$), chronic glomerulonephritis ($n = 68$), hypertension ($n = 27$), polycystic kidney disease ($n = 19$), interstitial nephritis ($n = 17$), and unknown etiology ($n = 27$). Overall, 38.5% of the patients had diabetes.

Patients were categorized into three groups based on the severity of AoAC: Grade 0 (AoACS = 0), Grade 1 (AoACS 1–490) and Grade 2 (AoACS ≥ 491). The cut-off of 490 corresponds to the median Agatston score among patients with detectable calcification. Table 1 displays the baseline characteristics of the hemodialysis patients.

Table 1
Baseline characteristics of the maintenance hemodialysis patients

Patient, ^c n(%)	Grade 0	Grade 1	Grade 2	All	p-value
	57(27.8)	74(36.1)	74(36.1)	205(100)	
Dialysis vintage, ^b months	35.0(12.5,52.0)	40.5(20.8,75.3)	53.5(26.0,87.0)	43.0(21.5,72.0)	0.005*
Age, ^a years	47.2 ± 12.0	59.0 ± 13.0	66.0 ± 12.3	58.2 ± 14.5	< 0.001*
Gender, M/F	36/21	42/32	43/31	121/84	0.746
BMI, ^a kg/m ²	22.4 ± 4.1	22.5 ± 3.8	21.8 ± 3.8	22.3 ± 3.9	0.506
Kt/V	1.5 ± 0.3	1.5 ± 0.3	1.4 ± 0.3	1.5 ± 0.3	0.580
CHD, ^c n(%)	2(3.5)	6(8.1)	9(12.2)	17(8.3)	0.204
Hypertension, ^c n(%)	50(87.7)	69(93.2)	68(91.9)	187(91.2)	0.524
Diabetes, ^c n(%)	14(24.6)	29(39.2)	36(48.6)	79(38.5)	0.019*
Hemoglobin, ^a g/dl	10.9 ± 1.8	11.2 ± 1.7	10.7 ± 1.7	10.9 ± 1.7	0.189
hs-CRP, ^b mg/l	1.0(0.1,3.0)	1.1(0.1,4.4)	2.8(0.7,6.7)	1.4(0.3,5.0)	0.007*
Total protein, ^a g/dl	6.4 ± 0.7	6.5 ± 0.6	6.3 ± 0.6	6.4 ± 0.6	0.447
Albumin, ^a g/dl	3.9 ± 0.5	3.8 ± 0.5	3.7 ± 0.5	3.8 ± 0.5	0.031*
Creatinine, ^a mg/dl	10.3 ± 3.2	9.4 ± 3.5	8.3 ± 3.0	9.3 ± 3.3	0.002*
Uric acid, ^a mg/dl	6.1 ± 1.8	5.9 ± 1.6	5.8 ± 2.1	5.9 ± 1.8	0.735
BMI body mass index; CHD coronary heart disease; hs-CRP hypersensitive C-reactive protein; LDL-C low-density lipoprotein cholesterol; HDL-C high-density lipoprotein cholesterol; iPTH intact parathyroid hormone.					
^a Data are presented as mean ± SD for normally distributed continuous variables. ^b median (IQR) for non-normally distributed continuous variables. ^c n (%) for categorical variables.					
Normality of continuous variables was assessed using the Shapiro-Wilk test. Variables with $p < 0.05$ in the Shapiro-Wilk test were considered non-normally distributed.					
* $p < 0.05$					

Patient, ^c n(%)	Grade 0	Grade 1	Grade 2	All	<i>p</i> - value
	57(27.8)	74(36.1)	74(36.1)	205(100)	
Urea, ^a mg/dl	123.7 ± 41.8	121.3 ± 44.1	120.3 ± 45.1	121.6 ± 43.7	0.909
Corrected calcium, ^a mg/dl	9.3 ± 0.9	9.6 ± 0.7	9.5 ± 0.7	9.5 ± 0.8	0.037*
Phosphorus, ^a mg/dl	5.5 ± 1.4	5.2 ± 1.4	5.1 ± 1.7	5.2 ± 1.5	0.298
Magnesium, ^a mg/dl	2.4 ± 0.3	2.4 ± 0.3	2.3 ± 0.3	2.4 ± 0.3	0.770
Glucose, ^b mg/dl	108.2(84.7,139.5)	104.2(86.1,147.7)	97.4(83.8,146.3)	103.5(85.5,143.4)	0.746
Total cholesterol, ^a mg/dl	148.1 ± 36.5	150.4 ± 48.2	144.3 ± 44.4	147.6 ± 43.7	0.694
Triglyceride, ^b mg/dl	131.9(92.1,201.4)	132.4(87.4,233.5)	124.0(85.4,192.4)	130.2(89.4,205.4)	0.566
LDL-C, ^a mg/dl	81.4 ± 25.8	84.4 ± 33.9	80.7 ± 29.4	82.2 ± 30.1	0.729
HDL-C, ^a mg/dl	38.3 ± 12.4	39.3 ± 14.7	37.0 ± 13.0	38.2 ± 13.5	0.587
Alkaline phosphatase, ^b U/l	78.0(61.0,105.0)	89.5(73.5,110.5)	93.0(68.8,134.3)	89.0(66.5,116.0)	0.069
iPTH, ^b pg/ml	205.2(109.0,374.9)	173.5(64.4,317.2)	174.0(92.8,425.6)	193.0(92.4,383.8)	0.220
Calcium-free phosphate binders, ^c n(%)	29(50.9)	39(52.7)	30(40.5)	98(47.8)	0.288
Calcium- based phosphate	6(10.5)	2(2.7)	7(9.5)	15(7.3)	0.148
BMI body mass index; CHD coronary heart disease; hs-CRP hypersensitive C-reactive protein; LDL-C low-density lipoprotein cholesterol; HDL-C high-density lipoprotein cholesterol; iPTH intact parathyroid hormone.					
^a Data are presented as mean ± SD for normally distributed continuous variables. ^b median (IQR) for non-normally distributed continuous variables. ^c n (%) for categorical variables.					
Normality of continuous variables was assessed using the Shapiro-Wilk test. Variables with <i>p</i> < 0.05 in the Shapiro-Wilk test were considered non-normally distributed.					
* <i>p</i> < 0.05					

Patient, ^c n(%)	Grade 0	Grade 1	Grade 2	All	p-value
	57(27.8)	74(36.1)	74(36.1)	205(100)	
binders, ^c n(%)					
Active vitamin D3, ^c n(%)	20(35.1)	15(20.3)	25(33.8)	60(29.3)	0.103
BMI body mass index; CHD coronary heart disease; hs-CRP hypersensitive C-reactive protein; LDL-C low-density lipoprotein cholesterol; HDL-C high-density lipoprotein cholesterol; iPTH intact parathyroid hormone.					
^a Data are presented as mean ± SD for normally distributed continuous variables. ^b median (IQR) for non-normally distributed continuous variables. ^c n (%) for categorical variables.					
Normality of continuous variables was assessed using the Shapiro-Wilk test. Variables with $p < 0.05$ in the Shapiro-Wilk test were considered non-normally distributed.					
* $p < 0.05$					

Comparisons among the groups revealed that patients with higher AoACS (Grade 2) were significantly older than those with no calcification (Grade 0; $p < 0.001$) and had a significantly longer duration of dialysis ($p = 0.005$). A proportional increase in diabetes with an increasing severity of calcification was noted ($p = 0.019$). No significant differences were observed in gender distribution or the presence of hypertension among the groups. Dialysis adequacy, as assessed by Kt/V, did not significantly differ among the groups. Patients with higher AoACS had significantly higher hs-CRP levels ($p = 0.007$) and corrected calcium levels ($p = 0.002$), but significantly lower creatinine levels ($p = 0.002$) and serum albumin levels ($p = 0.031$) compared to other groups. No significant differences were found in serum levels of phosphorus or iPTH. The lipid profile did not significantly differ among the groups. There were no significant differences in the prescription of phosphate binders or active vitamin D3.

Risk factors associated with mortality

During the observation period until August 31, 2024, a total of 56 deaths (27.3%) were recorded in the study population. Cardiovascular death was the most common cause, accounting for 28 deaths (13.7%), which represented 50.0% of all deaths. Other causes included infectious disease (30.4%), cerebrovascular event (8.9%), malignancy (7.1%), and gastrointestinal bleeding (3.6%). As shown in Table 2, univariate Cox regression analysis identified age, diabetes, serum creatinine levels, and Log(AoACS + 1) as significant factors associated with cardiovascular mortality. Multivariable Cox regression analysis further revealed that age and Log(AoACS + 1) were independently associated with cardiovascular mortality. Table 3 presents the factors associated with all-cause mortality. Univariate Cox regression analysis identified age, diabetes, serum levels of albumin, creatinine, urea, fasting glucose, alkaline phosphatase, prescription of active vitamin D3, and Log(AoACS + 1) as significant factors associated with all-cause mortality. Multivariable Cox regression analysis identified that age, diabetes, serum albumin levels, and Log(AoACS + 1) were independent factors related to all-cause mortality.

Table 2
Univariate and multivariate Cox proportional hazards analysis for cardiovascular mortality

	Univariate			Multivariate		
	HR	95%CI	p-value	HR	95%CI	p-value
Dialysis vintage, months	1.000	0.991–1.008	0.944			
Age, years	1.071	1.040–1.104	< 0.001*	1.044	1.007–1.083	0.021*
Male gender, M/F	1.217	0.562–2.637	0.618			
BMI, kg/m ²	0.997	0.905–1.100	0.957			
Kt/V	0.549	0.140–2.159	0.391			
CHD, yes/no	2.161	0.749–6.234	0.154			
Hypertension, yes/no	1.303	0.309–5.490	0.718			
Diabetes, yes/no	3.463	1.596–7.515	0.002*	2.084	0.938–4.628	0.071
Hemoglobin, g/dl	1.011	0.989–1.033	0.337			
hs-CRP, mg/l	1.019	0.962–1.079	0.528			
Total protein, g/dl	0.968	0.914–1.026	0.274			
Albumin, g/dl	0.952	0.883–1.025	0.190			
Creatinine, mg/dl	0.998	0.997–1.000	0.014*	1.000	0.998–1.001	0.520
Uric acid, mg/dl	1.001	0.997–1.004	0.723			
Urea, mg/dl	0.995	0.944–1.048	0.838			
Corrected calcium, mg/dl	3.326	0.441–25.058	0.244			
Phosphorus, mg/dl	0.814	0.374–1.772	0.604			
Magnesium, mg/dl	0.908	0.059–13.998	0.945			
Glucose, mg/dl	1.104	0.966–1.224	0.060			
Total cholesterol, mg/dl	1.181	0.866–1.610	0.294			
Triglyceride, mg/dl	1.153	0.986–1.348	0.074			
LDL-C, mg/dl	1.276	0.808–2.017	0.296			
HDL-C, mg/dl	1.014	0.348–2.958	0.980			
Alkaline phosphatase, U/l	1.001	0.998–1.004	0.678			
* $p < 0.05$						

	Univariate			Multivariate		
	HR	95%CI	<i>p</i> -value	HR	95%CI	<i>p</i> -value
iPTH, pg/ml	1.000	0.999–1.002	0.746			
Calcium-free phosphate binders, yes/no	0.675	0.316–1.441	0.309			
Calcium-based phosphate binders, yes/no	2.220	0.770–6.401	0.140			
Active vitamin D3, yes/no	0.599	0.243–1.479	0.267			
Log(AoACS + 1)	2.478	1.518–4.046	< 0.001*	1.935	1.148–3.263	0.013*
* $p < 0.05$						

Table 3
Univariate and multivariate Cox proportional hazards analysis for all-cause mortality

	Univariate			Multivariate		
	HR	95%CI	p-value	HR	95%CI	p-value
Dialysis vintage, months	1.002	0.996–1.007	0.533			
Age, years	1.070	1.047–1.093	< 0.001*	1.033	1.006–1.061	0.017*
Male gender, M/F	0.836	0.493–1.415	0.504			
BMI, kg/m ²	0.977	0.911–1.048	0.517			
Kt/V	0.635	0.242–1.663	0.355			
CHD, yes/no	1.892	0.857–4.179	0.115			
Hypertension, yes/no	1.765	0.551–5.648	0.339			
Diabetes, yes/no	3.529	2.041–6.102	< 0.001*	2.432	1.276–4.634	0.007*
Hemoglobin, g/dl	0.993	0.978–1.008	0.334			
hs-CRP, mg/l	1.027	0.989–1.067	0.164			
Total protein, g/dl	0.962	0.924–1.002	0.062			
Albumin, g/dl	0.916	0.869–0.966	0.001*	0.917	0.861–0.976	0.007*
Creatinine, mg/dl	0.998	0.997–0.999	< 0.001*	0.999	0.997–1.000	0.058
Uric acid, mg/dl	0.999	0.997–1.001	0.449			
Urea, mg/dl	0.949	0.911–0.988	0.011*	0.993	0.943–1.045	0.781
Corrected calcium, mg/dl	2.004	0.483–8.312	0.338			
Phosphorus, mg/dl	0.577	0.325–1.026	0.061			
Magnesium, mg/dl	0.751	0.108–5.210	0.772			
* $p < 0.05$						

	Univariate			Multivariate		
	HR	95%CI	p-value	HR	95%CI	p-value
Glucose, mg/dl	1.107	1.030–1.189	0.005*	1.057	0.972–1.149	0.197
Total cholesterol, mg/dl	0.995	0.785–1.263	0.969			
Triglyceride, mg/dl	0.965	0.809–1.151	0.689			
LDL-C, mg/dl	1.041	0.740–1.464	0.817			
HDL-C, mg/dl	1.089	0.518–2.289	0.822			
Alkaline phosphatase, U/l	1.002	1.000-1.003	0.010*	1.002	1.000-1.003	0.077
iPTH, pg/ml	1.000	0.999–1.001	0.677			
Calcium-free phosphate binders, yes/no	0.776	0.457–1.318	0.348			
Calcium-based phosphate binders, yes/no	1.613	0.692–3.763	0.269			
Active vitamin D3, yes/no	0.476	0.240–0.943	0.033*	0.782	0.376–1.628	0.511
Log(AoACS + 1)	2.145	1.570–2.930	< 0.001*	1.641	1.156–2.329	0.006*
* $p < 0.05$						

Survival analysis

The Kaplan–Meier survival curves of different groups according to the severity of AoAC, as assessed by the AoACS, are presented in Fig. 3. Panel A shows that patients with higher AoACS had significantly lower cardiovascular survival than those with lower AoACS ($p < 0.001$). Panel B displays the survival analysis for all-cause mortality; similarly, patients with higher AoACS had significantly lower overall survival than those with lower AoACS ($p < 0.001$).

Discussion

In this retrospective cohort study of 205 MHD patients followed for a median of 61 months, we found that the CT-derived AoACS was strongly and independently associated with both cardiovascular and all-cause mortality. After adjustment for traditional risk factors, each log-unit increment in AoACS conveyed an approximately 2-fold higher risk of cardiovascular death (HR = 1.94, 95% CI 1.15–3.26) and a 64% higher risk of all-cause death (HR = 1.64, 95% CI 1.16–2.33). Kaplan-Meier curves confirmed a graded, inverse relationship between AoACS groups and survival, with patients in the highest AoACS group (≥ 491) experiencing the worst outcomes. These data establish CT-quantified AoACS as a novel and promising prognostic biomarker in MHD patients.

In MHD patients, AoAC develops through a complex interplay of disordered calcium-phosphate metabolism, secondary hyperparathyroidism, underlying comorbidities, dialysis vintage and ageing[10–12]. Consistent with observations in the general population, the present study demonstrated that greater AoAC severity was positively associated with advancing age and longer dialysis duration, and was further accentuated in individuals with concomitant diabetes mellitus. Chronic hyperglycaemia accelerates the accumulation of advanced glycation end-products, which, via their cognate receptors, potentiate cardiovascular calcification[13]. Serum creatinine and albumin concentrations were inversely related to AoAC severity, corroborating the findings of Lee et al[14]. Moreover, patients with extensive AoAC exhibited elevated hs-CRP levels, suggesting a milieu of chronic inflammation and protein-energy wasting. Malnutrition and persistent inflammation are recognised to depress albumin and creatinine levels[15, 16], and constitute pivotal drivers of disturbed calcium-phosphate homeostasis and accelerated vascular calcification[17, 18].

Consistent with prior work, higher AoACS independently predicted cardiovascular and all-cause mortality[19]. The Agatston score captures both calcium load and its downstream effects—arterial stiffening, greater cardiac workload[20], and recurrent intradialytic hypotension that can trigger ischaemia or arrhythmia[21]. Thus, in long-term dialysis, AoAC is both a cumulative marker of mineral stress and a direct driver of haemodynamic instability. Serum albumin inversely correlated with AoAC severity, yet lost independent predictive power for cardiovascular death after adjustment for $\log(\text{AoACS} + 1)$, age and diabetes, supporting the idea that hypoalbuminaemia influences outcome via a calcification-mediated mechanism[15, 18]. Age, and AoACS jointly determined both cardiovascular and all-cause mortality, whereas diabetes and hypoalbuminaemia were linked solely to all-cause death. This divergence points to distinct pathways: AoAC and age accelerate cardiovascular demise through arterial stiffening and myocardial fibrosis, whereas diabetes and hypoalbuminaemia operate mainly via non-cardiovascular routes—sepsis, malignancy and the malnutrition–inflammation–atherosclerosis (MIA) syndrome[22, 23]. Interestingly, the Age $\times$ $\log(\text{AoACS} + 1)$ interaction was significant only for all-cause mortality ($p = 0.031$), with a hazard ratio of 1.836 (95% CI 1.123–3.002, $p = 0.007$) per 1-log increase in AoACS in patients ≥ 60 years, whereas no interaction was observed for cardiovascular death ($p = 0.345$). Medial calcification increases arterial stiffness, elevating left-ventricular after-load and coronary shear stress while reducing renal, cerebral and mesenteric perfusion, thereby precipitating non-cardiovascular events such as infection, bleeding and malnutrition that inflate the all-cause endpoint[24, 25]. The modest number of adjudicated cardiac events limits power to detect a similar interaction on cardiovascular mortality. Thus, AoACS functions as a systemic vulnerability marker whose deleterious impact is amplified by ageing across a broad spectrum of death pathways, not solely through acute coronary events. Finally, although some studies report survival benefits with either active vitamin D₃ or phosphate binders[26, 27], we observed none; residual confounding by indication, single-point exposure data, and limited power to separate binder subclasses may account for the discrepancy. Prospective trials are required to clarify any true effect of both interventions.

VC is characterised by pathological deposition of calcium- and phosphate-rich hydroxyapatite within the vessel wall. Based on the dominant site of mineral deposition, VC is broadly classified as intimal or medial calcification, each governed by distinct pathobiological mechanisms[28]. In patients with ESKD, aortic calcification is driven not only by the chronic progression of endothelial atheromatous plaques but also by an active, medial-layer mineralizing process[29]. The prevailing mechanism involves dedifferentiation of vascular smooth muscle cells (VSMCs) into osteoblast- or chondrocyte-like phenotypes, triggered by hyperphosphataemia, possibly elevated iPTH levels, and oxidative stress[30]. Hyperphosphataemia up-regulates the sodium-dependent phosphate cotransporters PiT-1 and PiT-2[31], enhancing phosphate influx into VSMCs and inducing gene programmes

associated with matrix mineralization[32, 33]. Both hypercalcaemia and hyperphosphataemia augment the release of VSMC-derived matrix vesicles, thereby promoting hydroxyapatite deposition[34].

Owing to its unique anatomical curvature and sustained exposure to high pulsatile stress, the aortic arch is particularly vulnerable to structural damage and calcification, rendering it a sensitive surrogate for global aortic calcification burden. VC can be quantified by X-ray photodensitometry, ultrasonography, CT, MRI, or scintigraphy, each modality offering distinct advantages and technical limitations[35–37]. Although the present study did not perform a direct head-to-head comparison, existing evidence underscores the superior sensitivity of CT: a meta-analysis of chest X-ray studies reported AoAC detection rates of only 23–58% in MHD cohorts[38], whereas CT-based imaging in the current series identified calcification in 72% of participants. This 30–50% absolute sensitivity gap aligns with a direct comparative study showing that chest radiography missed 40% of thoracic aortic calcifications detected by CT[39].

Dedicated imaging for vascular calcification refers predominantly to electrocardiogram-gated, thin-slice CT for coronary artery calcium (CAC) scoring—is resource-intensive, demands strict heart-rate control, and remains unavailable in many centers. Recognising these constraints, studies over the past decade have explored whether routine, non-gated chest CT can serve as a pragmatic alternative. Among several confirmatory reports, Groen et al. demonstrated excellent agreement between non-gated chest CT and ECG-gated CT for CAC quantification (pooled $r = 0.96$; 95% CI 0.92–0.98, $p < 0.001$)[40]; when considered alongside earlier cohort data, these findings informed the BSCI/BSCCT consensus to endorse incidental CAC detected on low-dose, non-gated thoracic CT for risk-guided preventive therapy (Class IIa, Level B)[41]. Specifically for the aortic arch, two anatomical features strengthen this substitution: the larger vessel diameter and thicker wall foster voluminous calcified plaques, rendering them less susceptible to partial-volume effects even with standard 5 mm slice thickness, while the arch’s anatomical distance from the cardiac center of motion makes ECG-gating of minimal added value. Consistent with this, Golub et al. reported that non-gated chest CT yields reproducible quantification of AoAC (intraclass correlation coefficient 0.96–0.97)[42].

In this study, CT scans were not acquired for vascular-calcification scoring. We performed a secondary analysis of existing, non-contrast chest CT scans obtained during routine health screening or clinical care, adding neither radiation nor cost. National data support the practicality of this opportunistic approach: the Chinese National Renal Data System (CNRDS, 2024) reports that approximately 1.18 million patients are on maintenance dialysis, and published Chinese studies indicate that more than 60% of these patients undergo at least one chest or abdominal CT scan annually. KDIGO 2017 guidelines recommend lateral lumbar radiography (Kauppila AACS 0–24) for vascular-calcification screening in CKD G3a–G5D[43]. Because no head-to-head outcome studies have compared incidental CT-based assessment with lumbar X-ray in this population, the magnitude of any substitution remains uncertain. Assuming—pending such evidence—equivalent prognostic value and unchanged reimbursement, modeling suggests that widespread use of existing CT datasets could theoretically obviate several hundred thousand additional X-ray examinations and yield nationwide annual savings in the tens of millions of RMB.

This study has several limitations. Its single-centre retrospective design and the exclusion of patients with prior myocardial infarction, stroke or malignancy probably selected a relatively healthier cohort, so the findings should be generalised cautiously. Residual confounding is possible because serial mineral-metabolite trends, residual renal function, dialysis prescription details, cardioprotective drugs such as statins and under-ascertained comorbidities were not captured in the final model. These limitations highlight the need for prospective,

multicentre cohorts that capture complete medication and biochemical data to reduce selection and confounding biases, and within which CT-quantified AoACS can be validated using other calcium-scoring algorithms, directly compared against X-ray calcification assessment, and used to perform segment-specific analyses of the ascending aorta, aortic arch, and descending aorta to determine their respective prognostic impacts.

Conclusion

CT-quantified AoACS independently predicts cardiovascular and all-cause mortality in MHD patients. These findings support opportunistic use of routine chest CT for vascular calcification assessment and encourage larger prospective studies to confirm AoACS as a prognostic indicator.

Abbreviations

AoAC Aortic arch calcification

AoACS Aortic arch calcification scores

BMI Body mass index

CAC Coronary artery calcium

CT Computed tomography

EHR Electronic health records

ESKD End-stage kidney disease

Hs-CRP Hypersensitive C-reactive protein

HDL-C High-density lipoprotein cholesterol

IPTH Intact parathyroid hormone

LDL-C Low-density lipoprotein cholesterol

MHD Maintenance hemodialysis

MSCT Multi-slice chest spiral CT

VC Vascular calcification

VSMCs Vascular smooth muscle cells

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Ningbo Medical Center Lihuili Hospital (approval number: LHL-2025-081) and registered with the Chinese Clinical Trial Registration Center (ChiCTR2500098576;

<http://www.chictr.org.cn>). The requirement for written informed consent was waived due to the retrospective design and use of anonymized data. All procedures were performed in accordance with the Declaration of Helsinki.

Availability of data and materials

The data that support the findings of this study are not openly available due to privacy restrictions protecting research participant confidentiality. Data are located in controlled access data storage at Ningbo Medical Center Lihuili Hospital and are available from the corresponding author, Pengjie Xu, upon reasonable request.

Competing interests

The authors have no conflicts of interest to declare.

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Author Contributions

GY and DK contributed to the conception and design of the study, as well as the analysis and interpretation of data. GY and DK drafted the paper. XP revised the manuscript for intellectual content and approved the final version for publication. All authors participated in data acquisition. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work.

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Figures

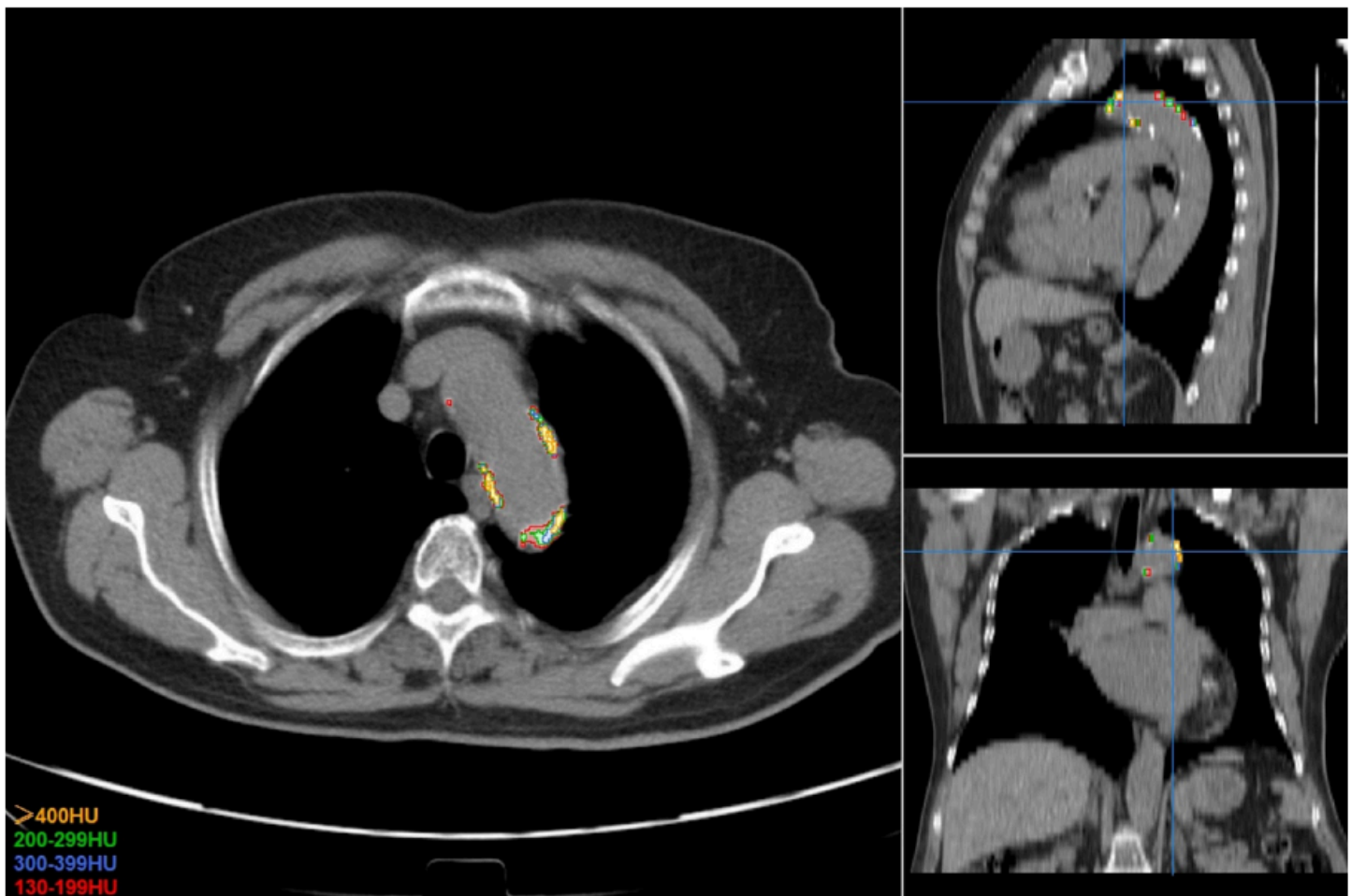


Figure 1

Color overlay image of the aortic arch ROI showing voxel distribution by CT attenuation: 130–199 HU (red), 200–299 HU (green), 300–399 HU (blue), ≥ 400 HU (yellow). Voxel statistics are provided in Supplementary Table S3.

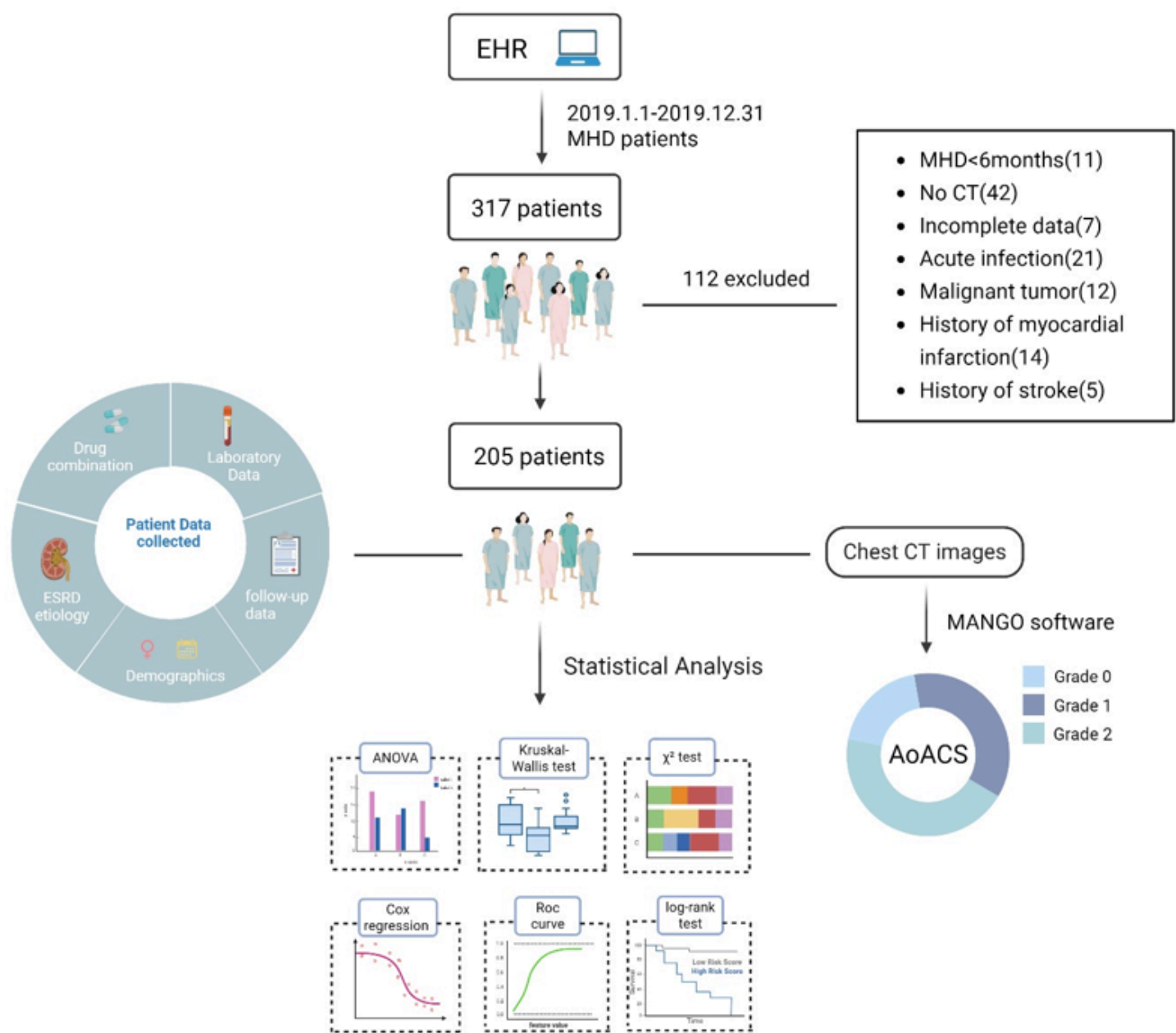


Figure 2

Flowchart of study design and patient selection process. EHR: electronic health records; MHD: maintenance hemodialysis; CT: computed tomography; AoACS: aortic arch calcification score.

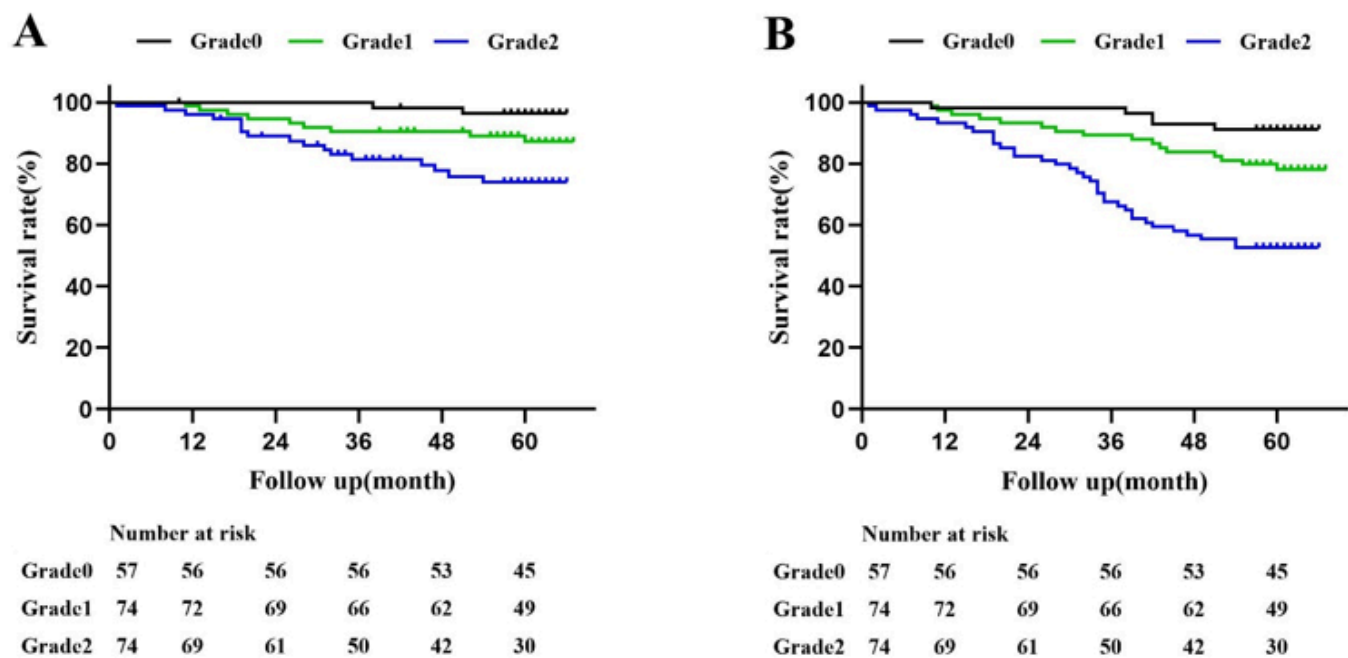


Figure 3

Kaplan-Meier survival curves for 205 maintenance hemodialysis patients, showing (A) cardiovascular mortality and (B) all-cause mortality according to AoACS groups. The log-rank test p -values for pairwise comparisons are as follows: (A) Gr. 0 vs. Gr. 1: $p = 0.072$, Gr. 0 vs. Gr. 2: $p < 0.001$, Gr. 1 vs. Gr. 2: $p = 0.047$; (B) Gr. 0 vs. Gr. 1: $p = 0.048$, Gr. 0 vs. Gr. 2: $p < 0.001$, Gr. 1 vs. Gr. 2: $p = 0.001$.

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