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Risk factors for and a preliminary prediction model of coronary artery calcification in patients beginning hemodialysis

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Abstract

Background and hypothesis Vascular calcification (VC) is an important risk factor for cardiovascular events in patients undergoing maintenance hemodialysis (MHD); however, there is limited data on VC-related factors in patients beginning hemodialysis. Thus, this study aimed to determine the risk factors of VC and to establish a prediction model for evaluating VC progression in new patients undergoing hemodialysis.

Methods This study selected 86 patients who initiated in-center MHD between March 2021 and November 2022. Demographic characteristics, medical history, and laboratory data were collected. Coronary artery calcification (CAC) was assessed based on the Agatston vascular score determined via computed tomography. Serum levels of the VC inhibitors fetuin-A was quantified via enzyme-linked immunosorbent assays. Univariate and multivariate regression analyses were conducted to determine the risk factors for VC, and a neural network-based approach was adopted to construct a VC prediction model.

Results The average age of the patients was 56.74 ± 12.79 years, and 65.1% were male. CAC was observed in 72.09% of patients. Age, body mass index, diabetes, the comorbidity index, and the number of coronary artery branches with calcification were positively correlated with the CAC score, whereas plasma fetuin-A levels was negatively correlated. The multivariate logistic regression analysis revealed that age [odds ratio (OR) 1.07, 95%CI 1.00–1.14], the comorbidity index [OR 1.72, 95%CI 1.16–2.57], diabetes [OR 3.97, 95%CI 1.16–13.58] were independent risk factors for CAC; these factors were used to establish a simple scoring model to predict VC risk.

Conclusion Age, the comorbidity index, diabetes were identified as independent risk factors for CAC in patients beginning hemodialysis, and the new VC prediction model based on these factors may help identify VC in patients undergoing MHD, facilitating clinical interventions.

Keywords Calcium-phosphorus metabolism, Fetuin-a, Hemodialysis, Vascular calcification

Introduction

Chronic kidney disease (CKD) is a global health epidemic that can lead to anemia and bone disease, and it may increase the risk of infection, accelerate the development or progression of cardiovascular disease, and heighten the risk of death [1]. In patients with CKD, cardiovascular events are the primary factor responsible for high hospitalization and mortality rates in the later stages of the disease. In a cohort study published in 2011 [2], vascular calcification (VC) was considered to be a marker of vascular injury as well as a strong predictor of cardiovascular events. Various domestic and international centers have reported a significantly higher incidence of VC in patients with CKD

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and in those undergoing maintenance hemodialysis (MHD) compared to that of healthy individuals of the same age, including coronary artery calcification (CAC) and cardiac valve calcification [3].

VC refers to the pathological deposition of minerals in blood vessels, including various forms of calcium and phosphate [4], with endometrial calcification and medial calcification being two examples [5]. Endometrial calcification mainly occurs within the vascular intima, where endothelial cell dysfunction is implicate. This form of calcification is primarily associated with dyslipidemia and, under the influence of inflammatory mediators, is highly susceptible to plaque rupture. Medium calcification is the result of phenotypic transformation of vascular smooth muscle cell into osteoblast-like cells and localized inflammatory responses. Under conditions of mineral dysregulation, these cells transform into an active synthetic phenotype. This phenotypic alteration of VSMC combined with elastin rupture is the starting point of medium calcification. CKD in particular is characterized by medial calcification. Over time, studies have confirmed that many molecular substances play a role in the development of VC, and an imbalance between factors that inhibit and promote calcification is considered to be one of the main mechanisms that drive VC development [6].

Fetuin-A, a negatively charged polymer protein produced by the liver, has a higher inhibitory effect on VC, which is mainly achieved through competitive inhibition of phosphate deposition, thereby reducing calcium ion levels, affecting the bone morphogenic protein (BMP) signaling pathway, reducing osteoblast generation [7], and inhibiting VSMC apoptosis [8, 9]. In patients with CKD, the synthesis and secretion of fetuin-A are inhibited, negatively impacting its ability to combat VC.

In clinical practice, the early assessment and diagnosis of VC are important to prevent the progression of calcification. The coronary artery calcification score (CACS) is an important tool for assessing the risk of coronary artery disease, with the Agatston scoring system being the most widely used [10]. However, because of the adverse effects of radiation exposure from computed tomography (CT) examinations and its singular use in determining the degree of VC based on CT scores, many researchers are committed to identifying suitable circulating biomarkers that can be used to evaluate VC.

The aims of the present study were to evaluate the degree of CAC in patients beginning hemodialysis for the first time, to screen risk factors for VC, and to establish a preliminary prediction model of VC to develop useful tools for early prognostic assessment and clinical interventions in patients undergoing hemodialysis.

Materials and methods

Study design and participants

This study included patients with end-stage kidney disease who received treatment at the Blood Purification Center of Second Xiangya Hospital of Central South University between March 2021 and November 2022. All participants were at least 18 years of age and had been undergoing regular hemodialysis for less than 3 months. Patients with malignant tumors and those who have undergone dialysis for more than 3 months were excluded from the study. The reporting of this study conforms to Strengthening and Reporting of Observational Studies in Epidemiology (STROBE) guidelines, and the protocol was approved by the Ethics Committee of Second Xiangya Hospital, Central South University (2021 C067). All patients provided written informed consent after obtaining detailed information about the study protocol.

Definition of VC

Patients underwent coronary artery multi-detector computed tomography (MDCT) imaging to determine the CACS at the time of initiation of regular hemodialysis. The Agatston score was calculated by two fixed radiologists. The scanned area of each calcification point was multiplied by the density factor to obtain a single calcification score, and the total CACS was calculated as the sum of all the calcification point scores. VC was defined as the presence of calcification in any coronary artery branch (CACS >0).

Risk factors and covariates of interest

All risk factors and covariates were selected based on literature reviews and clinical knowledge. Patients' baseline demographic and clinical characteristics, including age, sex, body mass index (BMI), blood pressure, smoking status, and history of diabetes were collected, as were laboratory values, including the estimated glomerular filtration rate (eGFR) and the levels of hemoglobin (Hb), serum albumin (ALB), serum creatinine (Scr), uric acid (UA), serum calcium (Ca), serum phosphorus (P), C-reactive protein (CRP), whole parathyroid hormone (iPTH), total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and 25-hydroxyvitamin.

Blood samples were collected to quantify the levels of fetuin-A via enzyme-linked immunosorbent assays (Mlbio, Shanghai, China). The aforementioned indicators were assessed before patients initiated regular dialysis treatment in our hospital. The total serum calcium level was adjusted if the concentration of serum ALB was <4 g/dL to better reflect the free calcium level as follows: corrected total calcium (mmol/L) = total calcium (mmol/L) $+0.02 \times [40 -$ serum ALB (g/L)]. The Charlson

Comorbidity Index (CCI) was calculated for each patient using the medical data recorded at the time of MHD initiation.

Statistical analysis

Measurement data with a normal distribution were expressed as the mean ± standard deviation (± s), and intergroup comparisons were performed using independent samples *t*-tests or multivariate analysis of variance (MANOVA). Measurement data with a skewed distribution were expressed as the median (M) and interquartile range, and intergroup comparisons were performed using the Kruskal–Wallis test or Mann–Whitney *U* test. Count data were expressed as the frequency or quantile, and the chi square test was used for intergroup comparisons. Spearman correlation analysis was conducted to assess correlations between relevant clinical indicators and the CACS. Normality was verified for all datasets. Data conforming to a normal distribution were analyzed using Spearman's method, whereas data not conforming to a normal distribution were analyzed using Pearson's method. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive value of the indicators. Univariate and multivariate logistic regression analyses were conducted to screen for independent risk factors. All statistical analyses were performed using SPSS software (version 25.0), and P values ≤ 0.05 indicated statistical significance. A prediction model was constructed using a neural network-based method, assessed using Python software. The precision and recall rate were used as indicators to assess the effectiveness of the model.

Results

Participant characteristics

A total of 110 patients received regular hemodialysis at our blood purification center between March 2021 and November 2022. After excluding patients who had been receiving hemodialysis for more than 3 months, those under 18 years old, individuals with malignant tumors, and patients with incomplete data, 86 participants were enrolled in the study. Of these 86 patients, there were 56 males (65.1%) and 30 females (34.9%), with a sex ratio of 1.87:1. The average age was 56.74 ± 12.79 years. In terms of etiology, 35 patients (40.7%) had diabetic kidney disease (DKD), 31 (36.0%) had primary glomerular disease, 14 (16.3%) had hypertensive nephropathy, and six (7.0%) had other primary diseases. The median of CACS was 51.25 score. A summary of patients' demographic and clinical characteristics is provided in Table 1.

Comparison of patients with and without calcification

Among the 86 patients, 62 developed CAC; thus, the calcification rate was 72.09%. According to the coronary MDCT results, the participants were divided into a non-calcification group (CACS = 0) and a calcification group (CACS > 0) (Table 1). The median of CACS in calcification group was 137.2 score. There were significant differences between the two groups in terms of the age, BMI, diabetes, CCI, and fetuin-A levels, and the number of branches exhibiting CAC ($P < 0.05$). There were no intergroup differences in terms of the sex, smoking status, blood pressure, eGFR, or the levels of Hb, ALB, Scr, UA, Ca, corrected Ca, P, CRP, TG, TC, LDL, iPTH, and 25 hydroxyvitamin D ($P > 0.05$). The imaging characteristics of the different degrees of CAC presented at the most prominent level are shown in Fig. 1.

Analysis of risk factors affecting VC

To screen for the risk factors related to VC, univariate and multivariate logistic regression analyses were conducted. The multivariate logistic analysis revealed that age (odds ratio (OR) = 1.069, 95% confidence interval (CI): 1.001–1.142, $P = 0.006$), diabetes (OR = 3.972, 95% CI 1.162–13.58, $P = 0.028$), and the CCI (OR = 1.722, 95% CI 1.155–2.568, $P = 0.008$) were independent risk factors for VC in patients beginning hemodialysis (Table 2). The multivariate logistic analysis was presented by adjusted the BMI, Scr, P, number of CAC branches and serum levels of fetuin-A.

Analysis of correlations between clinical indicators and CACS

The correlation analysis (Table 3) of the CACS and clinical indicators revealed that the age, BMI, diabetes, CCI, and the number of branches affected by CAC were positively correlated with the CACS. The CACS was negatively correlated with fetuin-A ($r = -0.876$, $P < 0.001$) levels, with the former exhibiting a stronger negative correlation with the CACS than the latter.

Establishment of a preliminary prediction model for VC in patients beginning MHD

The previous analyses revealed that the age, BMI, diabetes, CCI, and the levels of the calcification inhibitory factors fetuin-A significantly differed between the patients with and without VC. Those factors were selected as predictive factors for the model, as were iPTH and P levels based on clinical experience (Table 4).

The 86 patients undergoing MHD were randomly divided into a derivation queue (51 cases, 60%) and a validation queue (35 cases, 40%) based on the neural network binary classification method. The corresponding integrals

Table 1 Comparison of patients with and without calcification

Classification	Value (%/Q1, Q3)	Non-calcification group (*N* = 24)	Calcification group (*N* = 62)	F/X2/Z	*P*
Age	56.74 ± 12.79	47.88 ± 15.61	60.18 ± 11.67	− 4.42	< 0.001
Male (*N*, %)	56 (65.1%)	12 (50%)	44 (71%)	3.35	0.081
BMI (kg/m^2)	22.77 (20.72, 26.39)	21.12 (19.06, 23.52)	24.15 ± 3.64	− 2.74	0.006
Diabetes (*N*, %)	35 (40.7%)	4 (16.7%)	31 (50%)	7.97	0.005
Smoke (*N*, %)	21 (24.7%)	3 (12.5%)	19 (30.6%)	2.68	0.102
CCI	4.67 ± 1.98	3 (2, 4.75)	5 (1, 7)	− 3.88	< 0.001
Systolic pressure (mmHg)	148 (135, 158.25)	144.71 ± 23.46	150.45 ± 19.0	− 1.18	0.243
Diastolic pressure (mmHg)	85.76 ± 15.02	89.38 ± 15.61	84.35 ± 14.67	1.4	0.166
Hb (g/L)	80 (75.75, 92.25)	78.54 ± 15.92	83.06 ± 16.2	− 1.17	0.247
ALB (g/L)	34.1 (31.19, 37.65)	34.08 ± 5.49	34.0 ± 4.52	0.07	0.946
Scr (μmol/L)	842.5 (633.4, 1150.98)	971.84 ± 288.44	846.67 ± 336.02	1.61	0.111
eGFR (mL/min/1.73 m^2)	8.08 ± 2.83	7.25 ± 1.51	7.47 (6.21, 9.64)	− 1.29	0.197
UA (μmol/L)	434.1 (348.80, 510.00)	477.33 ± 144.19	424.05 ± 120.72	1.74	0.086
Ca (mmol/L)	1.95 ± 0.25	2.02 (1.85, 2.20)	1.96 (1.86, 2.07)	− 1.14	0.256
Corrected Ca (mmol/L)	2.09 (1.97, 2.22)	2.17 (1.98, 2.25)	2.07 (1.97, 2.22)	− 1.26	0.207
P (mmol/L)	1.90 ± 0.68	1.81 ± 0.56	1.8 (1.47, 2.21)	− 0.23	0.817
CRP (mg/L)	11.20 ± 19.41	4.83 (1.4, 7.9)	5.15 (2.54, 10.67)	− 1.18	0.236
TC (mmol/L)	3.80 ± 1.13	3.86 ± 1.28	3.59 (3.08, 4.34)	− 0.01	0.996
TG (mmol/L)	1.45 ± 0.93	1.45 ± 0.53	1.18 (0.81, 1.68)	− 1.22	0.223
LDL (mmol/L)	2.25 ± 0.98	2.09 (1.55, 2.93)	1.99 (1.62, 2.51)	− 0.26	0.16
iPTH (pg/mL)	298.56 ± 242.85	291.2 (138.5, 513.7)	216.3 (91.6, 366.5)	− 1.41	0.16
25 Hydroxyvitamin D (nmol/L)	43.72 ± 23.89	38.5 (27, 50.75)	35.5 (28, 57.5)	− 0.03	0.977
Fetuin-A (pg/mL)	816.77 (594.08, 949.36)	953.0 (923.9, 981.4)	661.0 (528.4, 887.5)	− 5.05	< 0.001
CACS	51.25 (0, 223.3)	0	137.2 (31.5, 451.35)	− 7.24	< 0.001
Number of CAC branches	1.76 ± 1.42	0	2 (1, 3)	− 6.78	< 0.001

BMI body mass index, *CCI* Charlson Comorbidity Index, *Hb* Hemoglobin, *ALB* serum albumin, *Scr* serum creatinine, *eGFR* estimated glomerular filtration rate, *iPTH* Intact parathyroid hormone, *TC* total cholesterol, *TG* triglyceride, *LDL* low density lipoprotein-cholesterol, *CRP* C-reactive protein, *CACS* coronary artery calcification score

were assigned based on the contribution of each factor in the neural network; the integrals were adjusted based on clinical experience to generate the model (Table 4).

The effectiveness of the prediction model

As shown in Table 5, the area under the curve (AUC) (0.87, 0.84) of the model was significant, with consistent sensitivity (85%, 84%) and specificity (78%, 78%) in both the derivation and validation queues, respectively. As shown in Fig. 2, through the precision, accuracy, and recall rate in the neural network indicated that the model's predictive performance was reliable. The cut-off point (6.5 points) was subsequently determined according to the best Youden's J statistic (0.62 points). Patients with a score below 6.5 points were considered to be at low risk of VC, whereas those with a score exceeding 6.5 points were considered to be at high risk of developing VC (Table 5).

Due to the fact that fetuin-A levels are not routinely quantified in clinical practice, the scoring system was modified to exclude the fetuin-A levels, and the new model was retested. As shown in Table 6, the AUC (0.74, 0.74) of the modified model remained significant, with stable sensitivity (72%, 83%) and specificity (70%, 64%). In the new model, the cut-off was 4.5 points according to the Youden's J statistic. The modified model is likely to be more convenient for clinical use.

Discussion

In the present study, the CAC rate among patients who had recently initiated MHD was 72.09%, which was higher than the 60% rate in patients with CKD that was reported in a meta-analysis of 47 studies [11]. That meta-analysis showed that as the calcification score increases, the incidence of cardiovascular events and all-cause hospitalization and mortality rates will increase by 2–4 times; in the present study, the levels of the VC inhibitory factors fetuin-A were significantly lower in the group with calcification than in the group without it, and they were negatively correlated with the CACS. The multivariate also revealed that age, the CCI, and diabetes

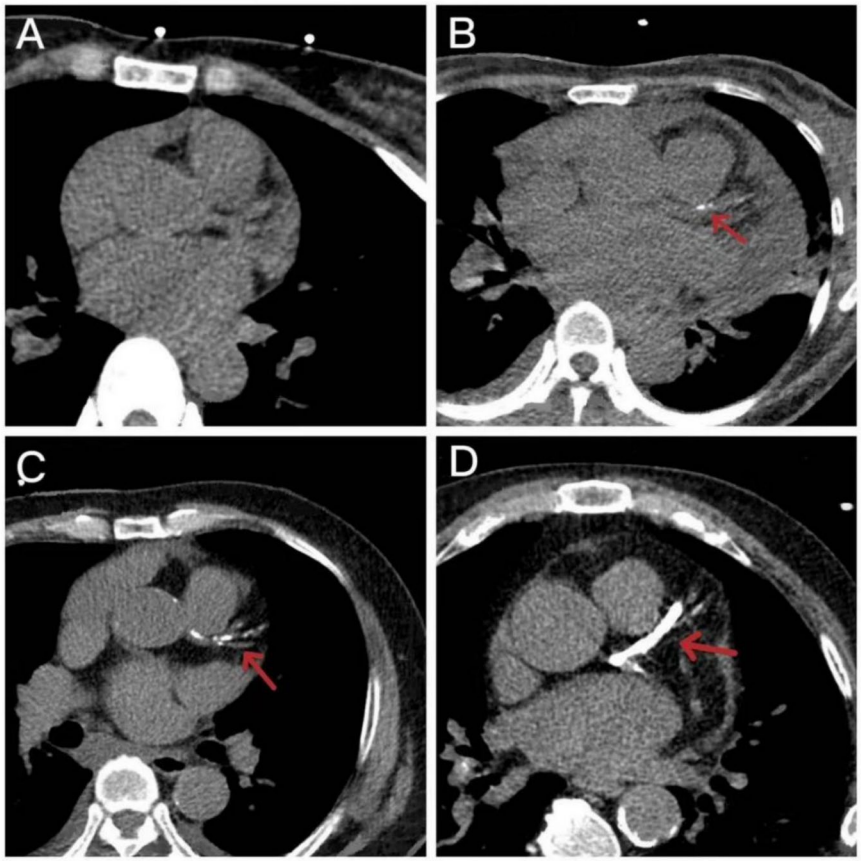

Fig. 1 MDCT imaging characteristics of different degrees of CAC. **A** Shows the CT image of a patient with CACS = 0, indicating no coronary calcification; **B** CACS = 145.3 points, high-density calcification shadows can be observed; **C** CACS = 901.2 points, indicating calcification in multiple coronary arteries; **D** CACS = 2842.5 points, which was the highest CACS patient in this study. Large areas of coronary calcification are visible, indicating poor cardiovascular prognosis may occur in the later stage. Red arrow, imaging of calcified vascular)

Table 2 Logistic regression analysis of VC in participant

Variable	Univariate logistic			Multivariate logistic		
	OR	95%CI	P	OR	95%CI	P
Age	1.09	1.04–1.14	< 0.001	1.069	1.001–1.142	0.006
Diabetes	1.609	1.53–16.3	0.008	3.972	1.162–13.58	0.028
CCI	1.807	1.31–2.49	< 0.001	1.722	1.155–2.568	0.008

CCI Charlson Comorbidity Index

were independent risk factors for VC in this patient population.

Previous studies have shown that an imbalance between factors that promote and inhibit calcification is one of the predominant mechanisms driving VC [6]. In this study, fetuin-A levels also differed significantly between groups and were negatively correlated with the CACS. Fetuin-A is a serum glycoprotein that is mainly secreted by the liver. It is a biologically diverse substance that participates in many processes, including bone and lipid metabolism, and it is involved in central nervous system disorders. Fetuin-A can directly bind with calcium and phosphorus in the circulation, forming low-activity complexes that prevent calcification progression [12]. These substances are called fetal globulin mineral complexes or calcium protein particles, and they prevent premature and rapid ectopic calcification at the physiological level [13]. Fetuin-A binds to calcium ions

Table 3 Correlation analysis between CACS and related clinical indicators

Variable	*r*	*P*
Age	0.381	< 0.001
BMI (kg/m^2)	0.274	0.011
CCI	0.368	< 0.001
Diabetes	0.383	< 0.001
Number of CAC branches	0.590	< 0.001
Fetuin-A (pg/mL)	− 0.876	< 0.001

CCI Charlson Comorbidity Index

Table 4 Corresponding integrals of 8 factors in the prediction model

Predictive factor	Classification	Point
Age	≤ 45	0
	45–65	1
	≥ 65	2
BMI (kg/m^2)	< 24	0
	≥ 24	1
Diabetes	Yes	2
	No	0
CCI	< 5	1
	≥ 5	2
P (mmol/L)	< 1.78	0
	≥ 1.78	2
iPTH (pg/mL)	< 600	0
	≥ 600	1
Fetuin-A (pg/mL)	< 700	1
	≥ 700	0

Risk model formula: calcification risk score = age + BMI + diabetes + CCI + P + iPTH + fetuin-A

to form stable colloidal calcium protein particles, but it can also bind to calcium phosphate crystals, thereby delaying mineral deposition [14]. Kettler et al. reported lower fetuin-A levels in patients receiving hemodialysis or peritoneal dialysis than in healthy people [15]. A multicenter, prospective, cohort study involving 987 patients undergoing dialysis demonstrated a link between fetuin-A levels and mortality [16]. However, another study of 93 patients receiving dialysis found no significant correlation between fetuin-A levels and CAC [17]. Thus, more experimental data are required to better assess whether fetuin-A can be used to predict VC in patients undergoing MHD.

DKD has become the main cause of end-stage renal disease, and some studies have shown that in the past 20 years, diabetic angiopathy has increased the global mortality rate to 37.9% in patients with diabetes [18]. In this study, 40.7% patients had DKD, and the subgroup analysis revealed a higher incidence and greater severity of VC in patients with diabetes, with higher numbers of affected vascular branches, which was consistent with previous findings. VC in patients with DKD is a complex process with many causal factors, including advanced glycation end product accumulation [19, 20] and an imbalance between nitric oxide bioavailability and reactive oxygen species accumulation, leading to endothelial dysfunction [21]. In diabetes, hyperglycemia and insulin resistance can induce endoplasmic reticulum stress, which involves impaired Ca^{2+} handling and the accumulation of unfolded proteins. The increase in reactive oxygen species (ROS) enhances the permeability of the mitochondrial outer membrane, further promoting cellular apoptosis. Additionally, excessive Ca^{2+} uptake leads to Ca^{2+} overload, opening the mitochondrial permeability transition pore, which also contributes to cell apoptosis. These processes are mediated by multiple regulatory factors and pathways, including the BMP2/SMADs, RAGE/JAK2, and Wnt/β-catenin [22]. Diabetes is known to damage blood vessels; therefore, it is beneficial for patients undergoing hemodialysis to maintain stability and control disease progression.

The age-corrected CCI is a scoring system proposed by Charlson et al. that considers age and multiple systemic comorbidities, and it is widely used to evaluate patients with tumors and those in the intensive care unit [23]. The CCI was shown to be correlated with and could consistently predict other survival analysis indicators such as the Kaplan–Feinstein index, and its sensitivity has been repeatedly confirmed, facilitating a comprehensive assessment of the body's state before initiating disease treatment [24]. Because patients undergoing MHD patients always experience many complications, especially cardiac and cerebrovascular disease, which may be related to VC, it was included as a disease status indicator for patients beginning hemodialysis in this study. The

Table 5 Predictive performance of queues in neural networks (model 1)

	Jorden index	Cut-off point	Sensitivity (%)	Specificity (%)	AUC
Derivation queue (*N* = 51)	0.62	6.5	85	78	0.87
Validation queue (*N* = 35)	0.62	6.5	84	78	0.84

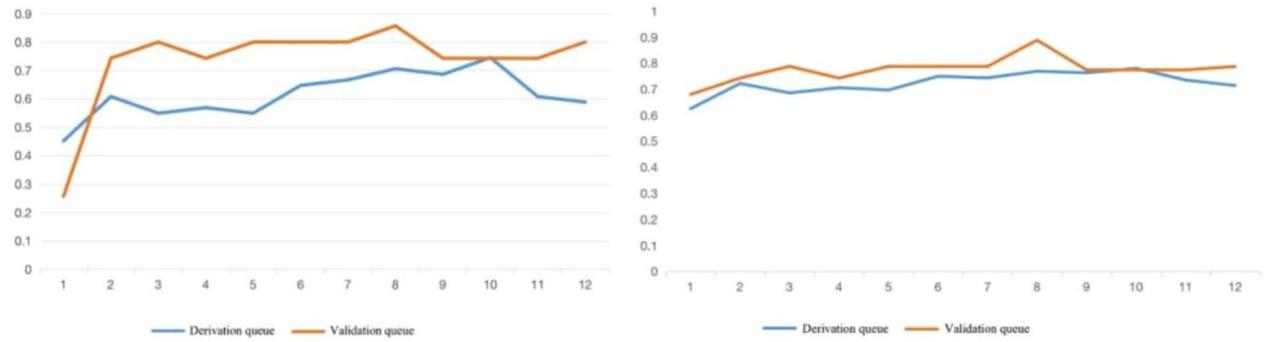

Fig. 2 Precision and recall curves for derivation and validation queues

Table 6 Predictive performance of queues in new model excluding fetuin-A (model 2)

	Jorden index	Cut-off point	Sensitivity (%)	Specificity (%)	AUC
Derivation queue ($N = 51$)	0.48	4.5	72	70	0.74
Validation queue ($N = 35$)	0.48	4.5	83	64	0.74

CCI was one of the risk factors for CAC and could be used to predict in this patient population.

Neural networks can predict the development and prognosis of diseases, helping doctors formulate more effective treatment plans [25]. Neural networks represent a computational model that simulates the structure of neurons in the human brain, extensively applied to tasks such as classification, regression, and time series sequencing. They excel in addressing complex and nonlinear problems, are adaptable to a variety of data types, and can be effectively utilized in clinical settings. Many scholars have utilized neural networks or improved neural network structures to enhance the predictive accuracy of classifications. For example, algorithms based on neural networks have been used to classify benign and malignant solitary pulmonary nodules. The present study adopted such an approach to construct and validate a VC prediction model. The precision, accuracy, and recall rate in the neural network indicated that the model's predictive performance was reliable. A score greater than 6.5 indicated a high risk of VC. Model 2 excluded fetuin-A levels, and scores greater than 4.5 indicated a high risk of VC. Model 2 will be more convenient for clinical use when fetuin-A levels cannot be quantified. However, the neural network fitting method demands substantial data and may pose a risk of overfitting, along with limited interpretability. Therefore, the clinical applicability of this model necessitates further research for validation.

It is worth mentioning that the level of iPTH in non-calcification group was higher than calcification group. However, iPTH was one of the important indicators for evaluating CKD-MBD in clinical practice. In response to this result, we considered that this study was based on real world research, so that iPTH was not significant in this research.

Ultimately, this study showed that VC is affected by many factors in patients initiating MHD, including age, the CCI, diabetes. The prediction model established using neural networks in this study has the potential to become a risk stratification tool for VC in patients undergoing MHD; however, this scoring system must be validated in additional cohorts. The purpose of this study is to provide guidance for the long-term prognosis of new hemodialysis patients, try to find more appropriate indicators to predict vascular calcification in MHD patients, and look forward to clinical data with larger sample data and longer follow-up time to support.

Limitation

This study has some limitations. First, it is a single-center study with a limited sample size, potential bias, and the results must be validated through multicenter, comprehensive studies with more participants. The sample size of this study is too small, and the obtained model is only preliminary, which is also one of the limitations of this study. Second, there were some factors that had not been considered, such as excessive calcium intake, dialysate calcium, hypomagnesemia, calcitriol, using antiplatelet drugs et al. Because of FGF 23 was an acknowledged factor related to VC, so that it was not selected to the study. Then, CACS exhibits certain limitations, including its inability to assess non-calcified plaques, limited

sensitivity to early-stage lesions, and incapacity to determine the necessity for therapeutic intervention. Consequently, there is an anticipation for the development and clinical application of additional vascular calcification assessment methodologies. Finally, the predictive model may not have incorporated every useful indicators, affecting its accuracy.

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Author contributions
HX and FY designed the research. JS and YY collected the data. HX and FY analyzed the data and drafted the manuscript. CS and CW provided help during the research. All author have read and approved the manuscript.

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Data availability statement
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This trial has been approved by the second Xiangya hospital of central south university ethics committee. All participants have signed informed consent forms before entering this trial. The ethical code was LYF2022227. The results presented in this paper have not been published previously in whole or part.

Informed consent
All participants have signed informed consent forms before entering this trial.

Competing interest
The authors declare no competing interests.

The IRB number
LYF2022227.

Animal studies
Not applicable.

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