Study on the Prevalence of Vascular Calcification in Different Types of Arteries and Influencing Factors in Maintenance Peritoneal Dialysis Patients

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Keywords

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Abstract

Objective: To investigate the occurrence of vascular calcification (VC) in different types of arteries in patients with maintenance peritoneal dialysis (PD) patients and its influencing factors. **Methods:** This study enrolled PD patients with stable status who has received PD treatment for more than 6 months in Peking University People's Hospital. We used plain X-ray films of abdomen, pelvis, and hands to quantitatively evaluate VC of large artery (abdominal aorta, iliac artery), medium artery (femoral artery, radial artery), and small artery (finger arteries). Two radiologists read and scored radiographs blindly. Demographic data, clinical characteristics, Charlson comorbidity index (CCI), baseline and time-average laboratory indices including parameters of calcium phosphorus metabolism, serum albumin, PD adequacy were collected. A logistic regression model was used to estimate the influencing factors of different sites of VC. **Results:** (1) 154 PD patients were enrolled in this study: seventy-eight males, mean age was 60.4 ± 13.9 years, and median PD duration was 24 (16.39) months. The major primary disease was

diabetic nephropathy (39%). (2) Among the 154 PD patients, the proportion of calcification of large artery was the highest (found in 100 patients, accounting for 64.9%); then the medium artery (66, 42.9%); and 15 of small artery, accounting for 9.7%. (3) Logistic regression showed that older age, longer dialysis duration, lower baseline serum intact parathyroid hormone (iPTH), and higher CCI scores were independent risk factors of large artery calcification ($p < 0.05$), and higher CCI scores, higher baseline serum triglycerides (TG), lower baseline serum iPTH, and time-average iPTH were independent risk factors of medium and small arteries. **Conclusions:** In PD patients, the occurrence of large artery calcification was higher than others. Among different sites of VC, the abdominal aortic calcification was most likely to occur, and the proportion of small artery calcification was low. Calcification of medium and small arteries can exist alone without calcification of large artery. Large artery calcification was more likely to occur in patients with older age, longer dialysis duration, lower baseline serum iPTH levels and higher CCI scores. Patients with higher CCI scores, higher baseline TG and lower baseline iPTH, and time-average iPTH were more likely to develop small and medium artery calcification.

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Introduction

The incidence of cardiovascular disease (CVD) in patients with end-stage renal disease (ESRD) is 20–30 times higher than that of the general population [1]. Peritoneal dialysis (PD) is one of the main renal replacement treatments in ESRD patients. Registration data from different countries showed that CVD is the primary cause of mortality in PD patients, accounting for more than 50% of the causes of death [1–4]. Vascular calcification (VC) is a common complication of ESRD patients, an important cause of CVD, and an independent predictor of all-cause death and cardiovascular (CV) death in dialysis patients [5, 6]. VC is an important component of chronic kidney disease-mineral and bone disorder (CKD-MBD), which is a pathologic process that occurs in response to dysregulated or inappropriate environmental stimuli [7]. There are 2 main forms of arterial calcification in ESRD patients: intimal calcification, associated with atherosclerosis with irregular patchy calcification, and medial calcification, associated with aging, diabetes, and ESRD, commonly occurring in the peripheral muscular arteries with linear or orbital calcification [8].

The clinical practice guideline for CKD-MBD of Kidney Disease: Improving Global Outcomes (KDIGO) suggested that if patients with CKD stages 3–5 have vascular or valvular calcification, they should be seen as having the highest CV risk, and use this information to guide the management of CKD-MBD [9, 10]. Therefore, it is important to estimate the occurrence of VC in PD patients and find out its influencing factors.

Regarding methods of assessing VC, electron beam computed tomography or multi-slice computed tomography are highly sensitive and specific for assessing the calcification score of coronary artery, and are the gold standard for diagnosing VC. However, due to the high demand for equipment and the high cost of inspection, they have been restricted as routine screening methods.

Although the prevalence of VC is higher in patients with CKD, arteries in some sites are not sensitive to calcification compared to large arteries, such as finger arteries [11]. The speed, mechanism, pathophysiological manifestations, risk factors, and prognosis of different grades of arterial calcification may be different. Most studies only described VC at specific sites: studies by Okuno et al. [5], Honkanen et al. [12], and Wong et al. [13] have reported significant associations between abdominal aortic calcification (AAC) and CV mortality and all-cause mortality in patients; Hong et al. [6] reported that calcification of iliac artery and femoral artery were associated with patients' all-cause mortality in a retrospective cohort

study of 214 hemodialysis (HD) patients by using pelvic plain film. The vascular smooth muscle cells with different embryonic origin may have different calcification susceptibilities, and this may lead to different prevalence of VC in different sites of arteries [14]. O'Neill et al. [15] estimated breast artery calcification in CKD patients. Their study was based on histological analysis of small arteries and arterioles in breast tissue with diameter of 10–1,500 μ m. They concluded that the pathogenesis of medial calcification differs among different types and sizes of arteries. Furthermore, the expression and activity of calcification inhibitors such as matrix Gla protein and pyrophosphate in different blood vessels may vary and contribute to different susceptibility of VC. Adragao et al. [16] found that a simple VC score evaluated by plain radiographic films of pelvis and hands was strongly associated with CV mortality of HD patients.

Till now, most studies only described VC at specific sites, and rarely described VC in different sites of arteries in patients with dialysis [6]. There was no report on the occurrence of VC in different arteries of PD patients. The incidence of arterial calcification varied from site to site and the influencing factors may vary. Therefore, this study aimed to investigate the occurrence of VC in different sites of arteries (including abdominal aorta, iliac artery, femoral artery, radial artery, and finger artery) in PD patients by X-ray films. Meanwhile, we investigate the influencing factors of VC in different arteries to guide the treatment of complications and improve patients' prognosis.

Materials and Methods

Study Design and Subjects

This single-center cross-sectional observational study enrolled maintenance PD patients with ESRD in Peking University People's Hospital from April 2014 to August 2015. Inclusion criteria for participants were age >18 years old, PD duration $\geq$ 6 months and stable clinical condition. Exclusion criteria were patients with acute complications such as heart failure, severe infection, and malignant tumors. The study was approved by the Ethics Committee of Peking University People's Hospital (ethical approval number: 2018PHB073).

All the subjects used conventional glucose-based, lactate-buffered PD solutions (Ultrabag; Baxter Healthcare, Guangzhou, China; Mg^{2+} 0.25 mmol/L, Ca^{2+} 1.25 mmol/L or 1.75 mmol/L, Na^+ 132 mmol/L, and Cl^- 96 mmol/L). The daily dialysate exchange dose was more than 6 L, received either by continuous ambulatory PD or intermittent PD.

Methods

Demographic Data

Demographic information and clinical characteristics were collected for all enrolled patients. Data included age, gender,

PD duration, primary renal disease, the presence or absence of diabetes, body mass index, and Charlson comorbidity index (CCI).

Evaluation of VC

We used lateral abdominal radiograph, frontal pelvic radiograph, and both hands radiographs to evaluate the calcification of abdominal aorta, iliac artery, femoral artery, radial artery, and finger arteries. According to the definition of anatomy and histology, the arteries were divided into large, medium, and small arteries according to the size of the luminal diameter and the components of the media [17, 18]. The abdominal aorta and the iliac artery belong to the large artery, the femoral artery and the iliac artery belong to medium artery, and the finger arteries belong to the small artery.

The method used to evaluate calcification was described previously [19]: the lateral abdominal radiographs were divided into 2 sections by a horizontal line over the intervertebral space between L2 and L3; radiographs of the pelvis were divided by 2 lines: a horizontal line just above the femoral heads and a median vertical line; and radiographs of each hand were divided by a horizontal line over the proximal end of the metacarpals. The presence of calcification in any section was given 1 point and scores from all sectors summed up to a total score. The highest total score is 10 points. The radiographs were reviewed by 2 radiologists who were blinded to the real situation.

Baseline and Time-Average Laboratory Indices

The baseline clinical data were the values of laboratory indices within 3 months after starting PD treatment, including serum corrected total calcium (Ca), phosphate (P), serum intact parathyroid hormone (iPTH), alkaline phosphatase, albumin, triglycerides (TG), total cholesterol, serum creatinine, low-density lipoprotein cholesterol (LDL-C), carbon dioxide combining power, hemoglobin, total urea clearance, and total creatinine clearance rate.

The time average indices: laboratory indices were collected every 3 months from the start of PD to time of X-ray examination. After calculation, the arithmetic mean values were obtained as time-average indices. At the same time, the time-average systolic blood pressure, diastolic blood pressure, pulse pressure, PD ultrafiltration, and urine output were collected.

Statistical Methods

Measurement data are expressed as mean $\pm$ SD, or median with IQR appropriately, and categorical data are expressed as percentages or ratios. Differences in mean and median values between groups with and without AAC were evaluated by using the independent sample *t* test or Wilcoxon rank-sum test respectively. Categorical data between groups were compared by using the chi-square test. The independent influencing factors of VC were analyzed by logistic regression analysis. The SPSS (version 22.0) statistical software was used for statistical analyses and *p* value < 0.05 was considered to be statistically significant.

Results

Demographic Data and Clinical Characteristics

A total of 154 PD patients were included in the present study, including 78 males (50.6%), with an average age of

60.4 $\pm$ 13.9 years (21–75) and a median dialysis duration of 24 (16, 39) months. Primary renal disease was predominantly diabetic nephropathy (*n* = 60, 39.0%), followed by chronic glomerulonephritis (*n* = 58, 37.7%), chronic tubulointerstitial nephropathy (*n* = 17, 11.0%), hypertensive renal disease (*n* = 17, 11.0%), and others (*n* = 2, 1.3%). There were 65 patients (42.2%) with diabetes. The clinical and laboratory data of the patients are shown in Table 1.

VC in Different Sites of Arteries in PD Patients

Among the 154 patients, the proportion of large artery calcification (abdominal aorta and/or iliac artery) was the highest (*n* = 100, 64.9%); followed by the medium artery calcification (femoral artery and/or radial artery; *n* = 66, 42.9%) and small artery calcification (finger arteries; *n* = 15, 9.7%). The prevalence and distribution of VC in different sites are shown in Tables 2 and 3.

Influencing Factors of VC in Different Sites of Arteries The Occurrence and Influencing Factors of Large Artery Calcification in PD Patients

Patients were divided into 2 groups according to the presence or absence of large artery calcification. Compared with the non-large artery calcification group, patients in the large artery calcification group exhibited older age, longer PD duration, higher proportion of diabetes and diabetic nephropathy, higher CCI scores, higher baseline TG, lower baseline iPTH, and lower baseline albumin (*p* < 0.05; Tables 4, 5). Logistic regression analysis showed that older age, longer dialysis duration, lower baseline serum iPTH, and higher CCI scores were independent risk factors of large artery calcification (*p* < 0.05; Table 6).

The Occurrence and Influencing Factors of Medium and Small Arteries Calcification in PD Patients

Patients were divided into 2 groups according to the presence or absence of medium and small arteries calcification. Compared with the non-calcification group, patients in the medium and small arteries calcification group manifested an older age, higher proportion of male, higher proportion of diabetes and diabetic nephropathy, higher CCI scores, higher time-average creatinine clearance rate, higher baseline TG level, lower DBP, lower baseline and time-average iPTH level, and lower time-average TG level (*p* < 0.05; Tables 7, 8). Logistic regression analysis showed higher CCI scores and higher baseline TG levels, and lower baseline and time-average iPTH were independent risk factors of medium and small arteries calcification (*p* < 0.05; Table 9).

Table 1. Demographic and clinical characteristics of all patients

Variables	All patients (n = 154)
Age, years	60.41±13.88
Gender, male, n (%)	78 (50.6)
PD duration, months	24 (16–39)
Primary renal disease, n (%)	
DN	60 (39.0)
CGN	58 (37.7)
CTIN	17 (11.0)
Hypertensive renal disease	17 (11.0)
Others	2 (1.3)
Baseline laboratory indices	
Serum corrected Ca, mmol/L	2.31±0.24
Serum P, mmol/L	1.49±0.36
Serum iPTH, pg/ml	166.67±160.22
Serum ALP, mmol/L	83.56±42.45
HB, g/L	114.66±10.33
Serum ALB, g/L	38.40±3.88
Serum TG, mmol/L	1.89±0.84
Serum Tcho, mmol/L	4.97±1.04
Serum CO ₂ CP, mmol/L	27.89±9.11
Diabetes, n (%)	65 (42.2)
SBP, mm Hg	130.96±13.45
DBP, mm Hg	76.75±9.86
Urinary output, mL/24 h	410 (113–766.75)
Total daily fluid removal, mL	592 (526.8–689.5)
BMI, kg/m ²	23.02±3.71
CCI	3 (2–4)
Time-average laboratory indices	
Serum corrected Ca, mmol/L	2.34±0.12
Serum P, mmol/L	1.49±0.23
Serum iPTH, mmol/L	197.09±131.56
Serum ALP, mmol/L	80.44±24.13
Kt/V, /week	1.68 (1.63–1.72)
Ccr, L/week/1.73 m ²	50.34 (48.66–52.79)
HB, g/L	113 (109.8–116)
Serum ALB, g/L	38.42±2.89
Serum Scr, umol/L	790.56±228.74
Serum TG, mmol/L	1.99±0.65
Serum Tcho, mmol/L	5.07±0.71
CO ₂ CP, mmol/L	26.9 (25.7–27.7)

DN, diabetic nephropathy; CGN, chronic glomerulonephritis; CTIN, chronic tubulointerstitial nephropathy; Ca, calcium; P, phosphate; iPTH, intact parathyroid hormone; ALP, alkaline phosphatase; HB, hemoglobin; ALB, albumin; TG, triglycerides; CO₂CP, carbon dioxide combining power; BMI, body mass index; CCI, Charlson comorbidity index; Kt/V, total urea clearance; Ccr, creatinine clearance rate.

Discussion

According to the study of Gan et al. [19], the sensitivity and specificity of plain radiography in the diagnosis of abdominal aortic calcification is 60.2 and 100%, respec-

Table 2. Vascular calcification in different sites of PD patients (n = 154)

	Presence, n (%)	Absence, n (%)
Abdominal aortic calcification	93 (60.4)	61 (39.6)
Iliac artery calcification	39 (25.3)	115 (74.7)
Femoral artery calcification	57 (37.0)	97 (63.0)
Radial artery calcification	38 (24.7)	116 (75.3)
Digital artery calcification	15 (9.7)	139 (90.3)

PD, peritoneal dialysis.

Table 3. The distribution of vascular calcification in different sites of arteries (n = 111)

Large artery calcification	Medium artery calcification	Small artery calcification	n (%)
+	–	–	45 (40.5)
+	+	–	41 (36.9)
+	–	+	0 (0)
–	+	–	10 (9.0)
–	–	+	0 (0)
–	+	+	1 (0.9)
+	+	+	14 (12.6)

tively. And the sensitivity and specificity of plain radiography in the diagnosis of iliac and femoral arteries calcification is 24.8 and 100%, respectively [19]. Therefore, our study used X-ray plain films to estimated VC of different sites. We found that the large artery (abdominal aorta, iliac artery) had the highest calcification rate (64.9%), and the calcification rate of the medium and small arteries (femoral artery, radial artery, and digital artery) was 42.9%. The median calcification score was 3 (2.6) in patients with large artery calcification, and the median calcification score was 5 (3.7) in patients with calcification of the medium and small arteries, suggesting that the calcification was more severe in patients with medium and small arteries calcification; 83.3% of medium and small arteries calcification was accompanied by large artery calcification and 16.7% was not, indicating that calcification of medium and small arteries can also exist alone without large artery calcification. The incidence of calcification in different arteries is different and may be related to the structure of different size of arterial walls. Atherosclerosis often involves large arteries and promotes the formation of patchy calcification in the arterial intima. Calcification of

Table 4. Comparisons of demographic and clinical data between patients with and without large artery calcification

Variables	Large artery calcification (<i>n</i> = 100)	Non-large artery calcification (<i>n</i> = 54)	<i>t</i> or <i>Z</i>	<i>p</i> value
Calcification score	3.00 (2.00–6.00)	0 (0–0)	–9.395	0.000*
Age, years	65.36±11.50	51.24±13.30	–5.51	0.000*
Gender, male, <i>n</i> (%)	52 (52.0)	26 (48.2)	0.208	0.736
PD duration, months	29.5 (18.0–42.0)	20.0 (15.0–32.3)	–2.244	0.025*
DN, <i>n</i> (%)	52 (52.0)	10 (18.5)	16.343	0.000*
DM, <i>n</i> (%)	56 (56.0)	9 (16.7)	22.24	0.000*
SBP, mm Hg	132.37±13.39	130.08±16.04	–0.944	0.347
DBP, mm Hg	76.88±10.53	76.69±9.45	–0.111	0.912
PP, mm Hg	55.49±13.91	53.39±14.09	0.889	0.375
Total daily fluid removal, mL	600.00 (522.32–650.00)	604.55 (497.50–718.75)	–0.477	0.633
BMI, kg/m ²	23.24±3.74	22.55±3.64	–1.095	0.275
CCI	4 (3–4)	2 (2–3)	–4.711	0.000*

* *p* < 0.05.

PD, peritoneal dialysis; CCI, Charlson comorbidity index; PP, pulse pressure; BMI, body mass index.

Table 5. Comparisons of biochemical data between patients with and without large artery calcification

Variables	Large artery calcification (<i>n</i> = 100)	Without large artery calcification (<i>n</i> = 54)	<i>t</i> or <i>Z</i>	<i>p</i> value
Time-averaged				
Serum Ca, mmol/L	2.32±0.13	2.31±0.15	–0.623	0.533
Serum P, mmol/L	1.51±0.26	1.46±0.26	–1.254	0.213
Serum alkaline phosphatase, U/L	79.80±24.93	780.04±25.46	–1.912	0.976
Serum iPTH, pg/mL	139.37 (69.09–242.75)	190.93 (105.27–254.50)	–1.980	0.056
Kt/V, /week	1.69 (1.66–1.74)	1.62 (1.66–1.79)	–1.579	0.114
Ccr, L/week/1.73 m ²	51.26 (48.89–54.00)	50.12 (47.91–53.76)	–1.187	0.235
Hb, g/L	112.14 (107.18–115.95)	111.79 (108.33–115.89)	–0.170	0.865
Serum albumin, g/L	38.25±3.09	38.70±3.09	0.865	0.388
Serum creatinine, μmol/L	791.07±243.67	775.07±234.04	–0.331	0.740
Serum TG, mmol/L	1.97±0.92	2.05±0.61	–1.375	0.169
Serum Tcho, mmol/L	4.95±0.74	5.17±0.80	1.686	0.094
Serum carbon dioxide combining power, mmol/L	26.87 (25.82–27.97)	26.81 (25.86–27.75)	–0.318	0.750
Baseline serum corrected Ca, mmol/L	2.34±0.24	2.27±0.21	–1.683	0.094
Baseline serum P, mmol/L	1.47±0.34	1.53±0.38	–1.000	0.317
Baseline serum iPTH, pg/mL	101.75 (32.18–216.60)	163.05 (76.15–268.38)	–2.575	0.010*
Baseline serum alkaline phosphatase, mmol/L	74.00 (59.00–98.00)	69.50 (56.75–87.00)	–0.869	0.385
Baseline hemoglobin, g/L	114.49±10.44	114.96±10.22	0.270	0.787
Baseline serum albumin, g/L	37.79±3.87	39.54±3.67	–2.388	0.017*
Baseline serum TG, mmol/L	2.01±0.90	1.69±0.67	–2.183	0.029*
Baseline serum Tcho, mmol/L	4.99±1.04	4.92±1.04	–0.078	0.938
Baseline serum carbon dioxide combining power, mmol/L	27.06±2.60	29.43±14.95	–1.494	0.135

* *p* < 0.05.

Table 6. Influencing factors independently associated with large artery calcification in PD patients in the logistic regression model

Variables	B	OR	95% CI	<i>p</i> value
Age, years	0.081	1.084	1.045–1.124	0.000*
PD duration, months	0.036	1.036	1.007–1.066	0.013*
CCI score	0.504	1.656	1.123–2.440	0.011*
Baseline serum iPTH, pg/mL	−0.004	0.996	0.993–0.999	0.016*

* $p < 0.05$.

PD, peritoneal dialysis; CCI, Charlson comorbidity index; iPTH, intact parathyroid hormone.

Table 7. Comparisons of demographics and clinical data between patients with and without medium and small arteries calcification

Variables	Medium and small artery calcification (<i>n</i> = 66)	Without medium and small artery calcification (<i>n</i> = 88)	<i>t</i> or <i>Z</i>	<i>p</i> value
Calcification score	5.00 (3.00–7.00)	0 (0–0)	−9.321	0.000*
Age, years	63.85±12.43	57.83±14.41	−2.778	0.005*
Gender, male, <i>n</i> (%)	40 (60.6)	38 (43.2)	4.581	0.036*
PD duration, months	24.0 (15.0–35.0)	24.0 (16.0–42.8)	−0.698	0.485
DN, <i>n</i> (%)	43 (65.2)	19 (21.6)	29.755	0.000*
DM, <i>n</i> (%)	44 (66.7)	21 (23.9)	28.327	0.000*
SBP, mm Hg	132.26±14.49	131.06±14.33	−0.512	0.609
DBP, mm Hg	79.32±9.82	74.94±10.01	−2.708	0.008*
PP, mm Hg	52.94±14.88	56.12±13.16	1.401	0.163
Total daily fluid removal, mL	602.28 (432.50–634.37)	602.28 (536.65–700.00)	−1.524	0.127
BMI, kg/m ²	23.55±3.86	22.58±3.55	−1.501	0.133
CCI	4.0 (4.0–5.0)	2.0 (2.0–3.3)	−6.411	0.000*

* $p < 0.05$.

PD, peritoneal dialysis; BMI, body mass index; CCI, Charlson comorbidity index.

large arteries observed in plain films includes both intimal calcification associated with atherosclerosis and medial calcification. Meanwhile, medium and small arteries are less susceptible to atherosclerosis, so the calcification observed in the X-ray films is mainly the medial calcification. A study showed that in the linear calcification mechanism of small arteries, passive deposition of calcium salts is more effective than active ossification, which may be one of the reasons for the different rates of calcification in different sizes of arteries [6].

The results of Logistic regression analysis showed that older age, longer dialysis duration, higher CCI scores, and lower baseline serum iPTH were independent risk factors of large artery calcification. Aging is a traditional risk factor for VC. As the age increases, lipid deposition, increased connective tissue components, decreased smooth muscle and elastin, and calcification are observed in the intima of the vessel wall. However, long dialysis duration may cause

the imbalance of positive regulators (such as inflammatory cytokines, reactive oxygen species, advanced glycation end products, Ca, P, iPTH) and negative regulators (such as klotho, matrix-gla protein, fetuin-A, osteoprotegerin, and osteopontin) in uremia environment [20], and promote the occurrence of VC, which are consistent with studies reported [21, 22]. Compared with large artery calcification, aging and dialysis duration have less effect on the medium and small arteries calcification. It may be that the body aging, tissue degradation, and atherosclerosis have less effect on the medium and small arteries calcification.

Considering that VC is a complication of slow onset and progression, time-average laboratory indices may better evaluate the control of patients with comorbidities and investigate the influencing factors of VC. Therefore, our study included time-average laboratory indices and baseline indices of PD patients. Previous studies have shown that high levels of serum P, Ca, and iPTH were risk factors

Table 8. Comparisons of biochemical data between patients with and without medium and small artery calcification

Variables	Medium and small artery calcification (n = 66)	Without medium and small artery calcification (n = 88)	t or Z	p value
Time-averaged				
Serum corrected Ca, mmol/L	2.31±0.13	2.32±0.14	-0.473	0.636
Serum P, mmol/L	1.48±0.23	1.50±0.28	0.636	0.526
Serum alkaline phosphatase, U/L	72.25 (60.48–85.23)	77.55 (63.81–92.19)	-1.376	0.169
Serum iPTH, pg/mL	137.54 (67.51–208.16)	192.59 (102.27–304.85)	-2.380	0.017*
Kt/V, /week	1.69 (1.65–1.79)	1.68 (1.63–1.74)	-1.514	0.130
Ccr, L/week/1.73 m ²	51.46 (49.25–56.02)	50.12 (48.05–52.30)	-2.035	0.042*
Hb, g/L	111.31 (104.80–115.85)	112.52 (109.24–115.91)	-1.101	0.271
Serum albumin, g/L	38.40±3.47	38.41±2.79	0.002	0.998
Serum serum creatinine, umol/L	785.36±254.96	785.53±229.06	0.004	0.997
Serum TG, mmol/L	1.84±0.59	2.12±0.94	-1.986	0.047*
Serum Tcho, mmol/L	5.07±0.76	5.00±0.78	-0.530	0.597
Serum carbon dioxide combining power, mmol/L	27.33 (25.83–28.27)	26.61 (25.85–27.62)	-1.526	0.127
Baseline serum corrected Ca, mmol/L	2.33±0.28	2.30±0.20	-0.557	0.578
Baseline serum P, mmol/L	1.49±0.37	1.50±0.35	-0.827	0.408
Baseline serum iPTH, pg/mL	90.45 (28.10–158.33)	151.95 (54.10–314.28)	-3.224	0.001*
Baseline serum alkaline phosphatase, mmol/L	76.50 (59.00–98.75)	69.00 (56.25–89.50)	-1.293	0.196
Baseline hemoglobin, g/L	114.55±11.33	114.74±9.58	0.114	0.909
Baseline serum albumin, g/L	37.80±3.93	38.85±3.80	1.672	0.097
Baseline serum TG, mmol/L	2.07±0.97	1.76±0.70	-2.300	0.030*
Baseline serum Tcho, mmol/L	4.85±1.05	5.06±1.03	-1.548	0.122
Baseline serum carbon dioxide combining power, mmol/L	26.80±2.42	28.70±11.84	-1.656	0.098

* $p < 0.05$.**Table 9.** Influencing factors independently associated with medium and small artery calcification in PD patients in the logistic regression model

Variables	B	OR	95% CI	p value
CCI score	0.942	2.564	1.722–3.817	0.000*
Baseline serum iPTH, pg/mL	-0.005	0.995	0.991–0.999	0.008*
Time-average serum iPTH, pg/mL	-0.004	0.996	0.992–0.999	0.026*
Baseline serum TG, mmol/L	0.726	2.068	1.136–3.764	0.017*

* $p < 0.05$.

PD, peritoneal dialysis; CCI, Charlson comorbidity index; iPTH, intact parathyroid hormone; TG, triglycerides.

for VC in dialysis patients. IPTH can increase the expression of cartilage matrix and increase the intracellular calcium content, thereby promoting the formation of VC [21, 22]. The results of our study showed that there was no significant difference in serum Ca and P levels between patients with and without large artery calcification. There was no correlation between baseline and time-average serum Ca, P level, and VC, while lower serum iPTH was an independent influencing factor of larger, medium, and small arteries calcification. The possible reasons are as fol-

lows: (1) our center has consistently adhered to continuous quality improvement for Ca and P metabolic disorders, so the laboratory indices of most patients are within the target range. The average serum Ca of the enrolled patients is 2.32 mmol/L, P 1.49 mmol/L, which minimized the influence of Ca and P metabolic disorders on patients. The 2009 and 2017 KDIGO guidelines suggested that the target range of iPTH for patients with CKD stage 5D is approximately 2 to 9 times the upper normal limit for the assay [9, 10], for us, is 150–600 pg/ml. The mean time-average iPTH of the

enrolled patients in this study was 197.09 pg/mL, of which 52 (33.8%) were at 150–300 pg/mL, 34 (22.1%) were at 300–600 pg/mL, and 67 (43.5%) were less than 150 pg/mL. There were 58 (37.7%) patients with baseline iPTH levels of 150–600 pg/mL, 91 (59.1%) with <150 pg/mL, and few patients with high iPTH (>600 pg/mL), only 5 (3.2%). Therefore, the relationship between high iPTH and VC cannot be confirmed, but it indicates that lower iPTH is also prone to VC. This result is consistent with recent studies: both high iPTH and low iPTH levels may cause VC [23, 24]. A study by London et al. [25] showed that HD patients with VC had lower iPTH levels than patients without VC. Elder et al. [26] reported that an HD patient with low bone turnover was treated by recombinant human PTH and bone biopsy demonstrated the mineral apposition rate increased, and serum and urine markers were consistent with improved bone turnover. These influences may have contributed to the resolution of calciphylaxis. Animal studies of Shao et al. [27] suggested that an action of intermittent injection of recombinant human PTH-(1–34) is a direct inhibition of VC and proliferation through actions on vascular PTH receptors. This reminds us not only to pay attention to the iPTH level when patients already starting PD treatment, but also to follow-up the CKD patients who have not started dialysis. Pay attention to the regular monitoring of iPTH before dialysis and rationally apply the active vitamin D to maintain the balance of Ca and P to avoid low iPTH and even low bone turnover in CKD patients. After starting dialysis treatment, it is necessary to maintain regular monitoring of iPTH level to avoid the occurrence and progress of VC. (3) The occurrence of VC is a complex process involving multiple factors. The Ca load (including drugs and dialysate), malnutrition, immune status, and aging are all influencing factors, which may affect the onset and progression of VC.

The present study showed that high CCI score was a common risk factor for large, medium, and small arteries calcification. Patients with complications at the beginning of PD were more likely to develop VC, indicating that VC was associated with comorbidities, especially CKD and diabetes. Therefore, patients who have various comorbidities at the beginning of dialysis should be actively treated for each comorbidity, and regular monitoring serum Ca and P levels and the progression of VC [25].

In addition to higher CCI scores and lower baseline and time-average iPTH levels, higher baseline TG was also an independent risk factor for medium and small arteries calcification. In CKD patients, the phenomenon of lipid metabolism disorder is quite common. Elevated TG levels accelerate lipid exchange and can cause elevated

LDL levels and decreased HDL levels. Chronic oxidative stress situation converts LDL into oxidized LDL. Oxidized LDL can induce vascular smooth muscle cells trans-differentiate into osteoblasts and accelerate the progression of VC. HDL plays a key role in maintaining vascular reactivity and anti-oxidative stress in endothelial cells, which can slow the progression of atherosclerosis.

There were also some limitations in this study. First, the number of study participants was relatively small. Second, the evaluation of the progression of VC in patients has not been considered; thus, the impact of progress rate of VC on prognosis may be ignored. Third, this study did not include the patient's medication, such as the use of calcium-containing P binders, calcitriol, and other drugs. These drugs may have impacts on the patient's Ca and P metabolism and VC.

Conclusion

In summary, in PD patients, the occurrence and influencing factors of different sites of arterial calcification were different. The proportion of large artery calcification was highest, and the proportion of small artery calcification was the lowest. Calcification of small and medium arteries can exist alone without calcification of large artery. Large artery calcification was more likely to occur in patients with older age, longer PD duration, lower baseline iPTH level, and higher CCI scores. Patients with higher CCI scores, higher baseline iPTH level, and higher baseline TG level were more likely to develop small and medium arteries calcification. Regular assessment of VC is beneficial to guide the clinical management and treatment of CKD-MBD.

Ethics Statement

The study was approved by the Ethics Committee of Peking University People's Hospital. As this was a retrospective study using medical records without any intervention, informed consent was exempted by the Ethics Committee.

Disclosure Statement

No conflict of interest is declared by any of the authors.

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