Comparison of Fetuin-A, Vitamin D, Monounsaturated Fatty Acid, and Vascular Calcification on Plain Radiography Between Dialysis Modalities

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Introduction. Low fetuin-A and vitamin D and high monounsaturated fatty acid (MUFA) contents are associated with vascular calcification (VC) in dialysis patients. We aimed to demonstrate the difference in fetuin-A, vitamin D, MUFA, and VC on plain radiography between patients on hemodialysis and peritoneal dialysis (PD).
Materials and Methods. We recruited 31 hemodialysis and 30 PD patients. We examined plain radiography of the feet, hands, pelvis, and lateral lumbar spine and defined significant VC as abdominal aortic calcifications scores of 5 and higher, VC scores of the hands and pelvis of 3 and higher, or arterial media calcifications of the feet on plain radiography.
Results. The mean age, dialysis duration, and prevalence of VC on plain radiography were not significantly different in PD patients compared to hemodialysis patients. However, fetuin-A ($P < .001$) and MUFA ($P = .001$) were significantly higher, whereas serum albumin and 25-hydroxyvitamin D ($P < .001$) were significantly lower in PD patients compared to hemodialysis patients. Hemodialysis patients who demonstrated significant VC on plain radiography had longer dialysis vintage, higher prevalence of coronary artery disease, and higher MUFA than patients without significant VC. Peritoneal dialysis patients who demonstrated significant VC on plain radiography had lower fetuin-A levels and higher C-reactive protein than patients without significant VC. Fetuin-A was an independent risk factor related with VC on plain radiography in PD patients.
Conclusions. Fetuin-A, 25-hydroxyvitamin D, and MUFA were significantly different, although the prevalence of VC on plain radiography was not different according to dialysis modality.

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INTRODUCTION

Cardiovascular disease is the most frequent cause of morbidity and mortality in dialysis patients. Vascular calcification (VC) is highly correlated with cardiovascular disease and commonly detected in dialysis patients.[1] Vascular calcification and VC scores on plain radiography images have been shown to be predictors of cardiovascular disease and cardiovascular mortality in patients with end-stage renal disease.[1-4] Vascular calcification scores of 3 and higher on plain radiographic films of the pelvis and hands are associated with coronary artery disease (CAD) in hemodialysis patients.[1] It has been reported that abdominal

aortic calcification (AAC) score higher than 5 is linked with the risk of cardiovascular disease in dialysis patients.[5] A recent report showed that the prevalence of CAD is associated with the presence of medial artery calcification on plain radiography of the feet in hemodialysis patients.[6] Therefore, significant VC on plain radiography can be a vital clue for cardiovascular disease and cardiovascular mortality in dialysis patients.

The erythrocyte membrane monounsaturated fatty acid (MUFA) content, including oleic acid, is significantly higher in patients with acute coronary syndrome than healthy groups.[7] Peritoneal dialysis (PD) patients have higher erythrocyte membrane MUFA compared to hemodialysis patients.[8] Higher erythrocyte membrane MUFA content was associated with VC on plain radiography in hemodialysis patients.[9] However, it is not clear whether this association is also found in PD patients. Meanwhile, low concentrations of 25-hydroxyvitamin D are associated with increased risks for mortality and arterial calcification in hemodialysis patients.[10,11] Peritoneal dialysis patients have lower 25-hydroxyvitamin D compared to hemodialysis patients,[12] but there is no evidence that lower 25-hydroxyvitamin D of PD patients may accelerate VC observed on plain radiography.

Fetuin-A, which is one of the important factors and acts as VC inhibitor, is significantly higher in PD patients compared to hemodialysis patients.[13,14] However, there is no report comparing VC prevalence and fetuin-A according to dialysis modality. Furthermore, it is uncertain whether the prevalence of VC on plain radiography is different according to the dialysis modality although hemodialysis and PD patients have different levels of VC-related factors. Therefore, this study was aimed at demonstrating any difference between patients on PD and hemodialysis in terms of fetuin-A, 25-hydroxyvitamin D, and erythrocyte membrane MUFA content and the prevalence of VC on plain radiography. In addition, we sought for more important factors associated with VC on plain radiography according to dialysis modality.

MATERIALS AND METHODS

Study Population

We recruited 31 hemodialysis patients and 30 PD patients from the Dong-A University dialysis center for this cross-sectional study. Informed consent was obtained from all enrolled patients. This study was approved by the Dong-A University Hospital Institutional Review Board. All patients aged 20 to 80 years were considered eligible for study inclusion if they had been receiving dialysis treatment for at least 6 months. Patients with a history of hospital admission within the past 3 months, patients with a history of dialysis modality change and patients with a history of active infection within 3 months were excluded. The enrolled hemodialysis patients received regular hemodialysis 3 times weekly. Bicarbonate-based dialysis solutions and polysulfone dialysis filters (Fresenius, Bad Homburg, Germany) were used. The enrolled PD patients received 4 exchanges per day using a standard regimen (8 L/d). Systolic blood pressure and diastolic blood pressure were measured in the sitting position before hemodialysis, and casual blood pressure was taken as the average of 2 consecutive measurements taken in PD patients.

Laboratory Measurements

Routine laboratory tests, including blood hemoglobin, serum glucose level, blood urea nitrogen concentration, and serum levels of creatinine, albumin, calcium, phosphorus, intact parathyroid hormone, C-reactive protein, total cholesterol, triglycerides, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol were obtained using fasting blood samples. The body mass index was also determined. Fetuin-A (Bio Vendor Laboratory Medicine Inc, Brno, Czech Republic) was measured by enzyme-linked immunosorbent assay. Serum 25-vitamin D (DiaSorin, Stillwater, MN, USA) was measured using a radioimmunoassay kit. Blood samples were obtained by venipuncture from PD patients and prior to dialysis from hemodialysis patients, and immediately placed on ice.

Plasma and erythrocytes were promptly separated by centrifugation and stored at -70°C until assayed. Isolated erythrocytes were methylated by the addition of boron trifluoride methanol-benzene for 10 minutes at 100°C. Fatty acid methyl esters were analyzed by gas chromatography (Shimadzu 2010AF, Shimadzu Scientific Instrument, Japan) with a 100-m SP2560 capillary column (Supelco, Bellefonte, PA, USA). Fatty acids were identified by comparison with known standards (GLC-727; Nu-Chek Prep, Elysian, MN, USA). Oleic acid and

MUFA contents are expressed as weight percentages.

We defined CAD patients as those with previous a diagnosis by coronary angiography, echocardiography, electrocardiography changes, elevated troponin-I, or myocardial single photon emission computed tomography scan.

Vascular Calcification

We observed patients' plain radiography images of the feet, hands, pelvis, and lateral lumbar spine and estimated the VC scores with previously reported methods. The abdominal aortic calcification (AAC) was graded using a previously reported system, in which the location and severity of calcification deposits at each lumbar vertebral segment (L1 to L4) were evaluated.[15,16] An AAC score of 5 or higher is associated with the risk of cardiovascular disease.[5] The radiographic films of the pelvis and hands were divided into 4 sections by two imaginary lines: a horizontal line over the upper limit of both the femoral heads and a median vertical line over the vertebral column. The films of the hands were divided, for each hand, by a horizontal line over the upper limit of the metacarpal bones. The presence of linear calcifications in each section of the pelvis and the hand was counted as 1 and its absence as zero. The final score was the sum of all sections, ranging from zero to 8. In a previous study, receiver operating characteristic curve analysis identified a VC score of 3 as the best cut-off value associated with cardiovascular mortality and cardiovascular events.[1] On radiographs of the feet, the score was zero when medial artery calcification is absent and the score was 1 when VC is present. We defined significant VC as any of the following on plain radiography: AAC score $\geq$ 5; VC score of the hands and pelvis $\geq$ 3; or medial artery calcification of the feet. The AXIOM Aristors MX/VX (SIEMENS, Erlangen, Germany) radiographic equipment with a digital imaging system was used (exposure conditions, 45 kVp to 50 kVp [4mAs]). Two nephrologists individually decided VC scores on plain radiography without information from patients. Initial interpretation correlation coefficient was 0.99 ($P < .001$). Finally, consensus was reached on the interpretation of all radiography images.

Statistical Analyses

We initially decided on a minimum sample size of 80 because the minimum correlation coefficient was 0.22 between VC on plain radiography and CAD, based on our previous study. However, we stopped enrollments of patients because permitted investigation period was closed.

Data are presented as mean ± standard deviation. The nonparametric Mann-Whitney U test was used to compare the data and the Pearson chi-square analysis was used to compare the categorical data between the two groups. Linear regression analysis using the backward elimination method was applied to determine the risk factors independently associated with significant vascular calcification. The variables included age, dialysis duration, CAD, pulse pressure, MUFA, and fetuin-A. *P* values of less than .05 were considered significant. All statistical calculations were performed with the SPSS software (Statistical Package for the Social Sciences, version 18.0, SPSS Inc, Chicago, Ill, USA).

RESULTS

Characteristics of Study Populations

Clinical and biochemical characteristics of patients by dialysis modality are shown in Table 1. The mean age, sex distribution, dialysis duration, prevalence of diabetes mellitus, and prevalence of significant VC on plain radiography (60.0% versus 61.3 %) were not significantly different between the PD patients and the hemodialysis patients. However, fetuin-A levels (408.1 ± 79.0 mg/dL versus 297.8 ± 71.1 mg/dL), body mass index, total cholesterol, low-density lipoprotein cholesterol, MUFA, and oleic acid levels were significantly higher in the PD patients compared to the hemodialysis patients. Systolic blood pressure, pulse pressure, blood urea nitrogen, serum albumin, and 25-hydroxyvitamin D (11.7 ± 8.0 ng/mL versus 22.6 ± 5.8 ng/mL) were significantly lower in the PD patients compared to the hemodialysis patients. The percentage of active vitamin D medication was significantly lower in the PD patients compared to the hemodialysis patients (33.3% versus 64.5%).

Characteristics of Patients by Vascular Calcification

Patients who showed significant VC on plain radiography had longer dialysis vintage, higher prevalence of CAD, and higher erythrocyte membrane MUFA contents (18.1 ± 2.2 weight % versus 16.8 ± 1.8 weight %) than patients without

Table 1. Clinical and Biochemical Characteristics of Patients on Dialysis

Parameter	Hemodialysis (n = 31)	Peritoneal Dialysis (n = 30)	*P*
Age, y	56.2 ± 10.4	55.7 ± 10.5	.86
Dialysis duration, mo	51.2 ± 40.1	44.9 ± 21.5	.45
Sex			
Male	21	23	
Female	10	7	.07
Coronary artery disease, %	9 (29.0)	5 (16.7)	.36
Diabetes mellitus, %	19 (61.3)	16 (53.3)	.61
Significant vascular calcification, %	19 (61.3)	18 (60.0)	> .99
Systolic blood pressure, mm Hg	155.7 ± 22.5	136.8 ± 26.0	.004
Diastolic blood pressure, mm Hg	81.2 ± 14.4	78.3 ± 12.4	.41
Pulse pressure, mm Hg	74.5 ± 19.2	58.5 ± 20.9	.003
Body mass index, kg/m^2	21.1 ± 3.0	23.6 ± 3.2	.002
Fetuin-A, mg/dL	297.8 ± 71.1	408.1 ± 79.0	< .001
Blood urea nitrogen, mg/dL	78.8 ± 18.3	52.7 ± 18.0	< .001
Creatinine, mg/dL	10.9 ± 2.5	11.6 ± 8.6	.65
Calcium, mg/dL	8.6 ± 0.8	8.6 ± 0.7	.97
Phosphorus, mg/dL	4.9 ± 1.8	4.4 ± 1.0	.18
Intact parathyroid hormone, pg/mL	262.8 ± 216.3	268.2 ± 183.6	.92
25-hydroxyvitamin D, ng/mL	22.6 ± 5.8	11.7 ± 8.0	< .001
Albumin, g/dL	3.90 ± 0.18	3.80 ± 0.38	.04
Hemoglobin, g/dL	10.3 ± 1.1	10.1 ± 1.1	.47
Total cholesterol, mg/dL	150.4 ± 32.9	179.5 ± 39.2	.003
High-density lipoprotein, mg/dL	38.8 ± 8.9	42.0 ± 14.0	.29
Triglyceride, mg/dL	149.2 ± 113.1	166.9 ± 75.4	.48
Low-density lipoprotein, mg/dL	82.7 ± 29.8	101.3 ± 33.9	.03
C-reactive protein, mg/dL	0.6 ± 1.2	0.5 ± 1.1	.72
Monounsaturated fatty acid, %	17.6 ± 2.1	19.7 ± 2.4	.001
Oleic acid, %	16.1 ± 1.9	17.7 ± 2.1	.002

significant VC in hemodialysis patients (Table 2). The percentage of active vitamin D medication including calcitriol (63.2% versus 66.7%), fetuin-A levels, and 25-hydroxyvitamin D were similar in hemodialysis patients with significant VC on plain radiography compared to hemodialysis patients without significant VC.

Patients who showed significant VC on plain radiography had higher a percentage of diabetes mellitus, higher C-reactive protein level, and lower fetuin-A level than patients without significant VC in the PD group. The 25-hydroxyvitamin D levels were lower (9.8 ± 6.8 ng/mL versus 16.7 ± 9.6 ng/mL), and the percentage of active vitamin D medication including calcitriol was higher (38.9% versus 25.0%), but was not significant in PD patients with significant VC on plain radiography compared to the PD patients without significant VC. Erythrocyte membrane MUFA and oleic acid contents were similar in PD patients with significant VC on plain radiography compared to PD patients without significant VC.

Intact parathyroid hormone level, calcium phosphorus product (significant VC, 42.0 ± 17.6 versus no significant VC, 43.1 ± 14.8 in hemodialysis patients; 37.9 ± 10.8 versus 38.0 ± 8.4 in PD patients), phosphorus levels, and calcium load (significant VC, 2.50 ± 2.17 g/d versus no significant VC, 2.26 ± 1.32 g/d in hemodialysis patients; 2.07 ± 1.67 g/d versus 1.75 ± 1.36 g/d in PD patients) were not significantly different according to significant VC in hemodialysis and PD patients.

Clinical and Laboratory Findings by Vascular Calcification Method

Higher prevalence rates of diabetes mellitus and CAD and higher erythrocyte membrane MUFA contents were seen in patients who showed medial artery calcification of the feet or hands and pelvis VC score of 3 and higher on plain radiography than in the patients without medial artery calcification or hands and pelvis VC score less than 3 in the

Table 2. Clinical and Biochemical Characteristics of Patients on Dialysis With and Without Significant Vascular Calcification (VC)

Parameter	Hemodialysis		Peritoneal Dialysis	
	Significant VC (n = 19)	No Significant VC (n = 12)	Significant VC (n = 18)	No Significant VC (n = 12)
Age, y	58.1 ± 10.7	53.2 ± 9.7	56.5 ± 10.4	54.4 ± 11.0
Dialysis duration, mo	60.4 ± 38.1*	36.6 ± 40.5	43.6 ± 19.5	46.8 ± 25.1
Coronary artery disease, %	9 (47.4)*	0	5 (27.8)*	0
Diabetes mellitus, %	13 (68.4)	6 (50.0)	13 (72.2)*	3 (25.0)
Systolic blood pressure, mm Hg	152.5 ± 21.1	160.8 ± 24.6	137.7 ±28.8	135.4 ± 22.5
Diastolic blood pressure, mm Hg	78.7 ± 14.5	85.3 ± 13.8	76.9 ± 12.7	80.4 ± 12.1
Pulse pressure, mm Hg	73.8 ± 20.5	75.6 ± 17.7	60.8 ± 22.7	55.0 ± 17.9
Body mass index, kg/m^2	21.2 ± 3.0	20.9 ± 3.1	23.1 ± 3.4	24.2 ± 3.0
Fetuin-A, mg/dL	297.4 ± 63.0	298.5 ± 85.3	376.7 ± 71.0*	455.2 ± 68.0
Blood urea nitrogen, mg/dL	77.5 ± 15.5	80.7 ± 22.5	50.5 ± 13.6	56.0 ± 23.4
Creatinine, mg/dL	11.0 ± 2.5	10.8 ±2.8	9.9 ± 3.8	14.2 ± 12.7
Calcium, mg/dL	8.6 ± 0.8	8.7 ± 0.8	8.6 ± 0.6	8.6 ± 0.8
Phosphorus, mg/dL	4.8 ± 1.9	5.0 ± 1.8	4.3 ± 1.05	4.4 ± 1.0
Intact parathyroid hormone, pg/mL	254.7 ± 206.5	275.6 ± 239.0	272.6 ± 207.0	260.3 ± 143.0
25-hydroxyvitamin D, ng/mL	22.8 ± 6.6	22.3 ± 3.5	9.8 ± 6.8	16.7 ± 9.6
Albumin, g/dL	3.9 ± 0.1	4.0 ± 0.1	3.7 ± 0.3	3.8 ± 0.3
Hemoglobin, g/dL	10.3 ± 1.2	10.4 ± 0.8	10.1 ± 1.1	10.1 ± 1.1
Total cholesterol, mg/dL	144.8 ± 33.7	159.3 ± 30.8	172.5 ± 27.1	190.0 ± 52.1
High-density lipoprotein, mg/dL	36.8 ± 8.2	41.9 ± 9.4	40.3 ± 10.3	44.5 ± 18.4
Triglyceride, mg/dL	144.8 ± 33.7	159.3 ± 30.8	172.5 ± 27.1	190.0 ± 52.1
Low-density lipoprotein, mg/dL	79.1 ± 31.3	88.5 ± 27.4	95.8 ± 26.7	109.5 ± 42.5
C-reactive protein, mg/dL	0.8 ± 1.5	0.2 ± 0.3	0.7 ± 1.3*	0.1 ± 0.1
Monounsaturated fatty acid, %	18.1 ± 2.2*	16.8 ± 1.8	19.9 ± 2.5	19.5 ± 2.4
Oleic acid, %	16.5 ± 2.0	15.6 ± 1.6	17.7 ± 2.2	17.8 ± 2.0

*P < .05 compared to the subgroup with no VC

hemodialysis group (Tables 3 and 4). The prevalence of CAD was significantly higher in patients with an AAC score of 5 and higher than in patients with a lower score in the hemodialysis group. Fetuin-A levels were significantly lower (Table 3), and the percentage of patients with diabetes mellitus was significantly higher in patients with medial artery calcification of the feet compared to patients without medial artery calcification of the feet in the PD group. Patients who showed calcification of the hands and a pelvis VC score of 3 and higher on plain radiography had a higher prevalence rate of diabetes mellitus than patients with a lower score in the PD group. The prevalence rates of CAD and dialysis duration were significantly higher in the patients with an AAC score of 5 and higher than the patients with lower score in the PD group (Table 5).

Factors Associated with Significant Vascular Calcification

In univariable analysis, CAD history (β = 0.508, P = .004) was associated with significant VC in hemodialysis patients. The CAD history (β = 0.365,

Table 3. Clinical and Biochemical Characteristics of Patients on Dialysis by Vascular Calcification (VC) on Plain Radiography of Feet

Parameter	Hemodialysis		Peritoneal Dialysis	
	Feet VC (n = 14)	No Feet VC (n = 17)	Feet VC (n = 10)	No Feet VC (n = 20)
Age, y	58.0 ± 12.1	54.7 ± 9.0	55.0 ± 13.7	59.9 ± 11.7
Diabetes mellitus, %	12 (85.7)*	7 (41.2)	9 (90.0)*	7 (35.0)
Coronary artery disease, %	6 (42.9)*	2 (11.8)	2 (20.0)	3 (15.0)
Dialysis duration, mo	45.9 ± 27.8	55.6 ± 48.4	56.1 ± 13.7	57.1 ± 13.0
Fetuin-A, mg/dL	302.5 ± 72.5	294.0 ± 71.8	358.7 ± 43.3*	432.8 ± 82.0
25-hydroxyvitamin D, ng/mL	18.0 ± 7.1	17.9 ± 8.4	6.7 ± 3.9	14.3 ± 8.5
Monounsaturated fatty acid, %	18.5 ± 1.8*	17.0 ± 2.1	20.2 ± 2.3	19.5 ± 2.5

*P < .05 compared to the subgroup with no VC

Table 4. Clinical and Biochemical Characteristics of Patients on Dialysis by Vascular Calcification (VC) Score on Plain Radiography of Hands and Pelvis

Parameter	Hemodialysis		Peritoneal Dialysis	
	Hands and Pelvis Score ≥ 3 (n = 13)	Hands and Pelvis Score < 3 (n = 18)	Hands and Pelvis Score ≥ 3 (n = 9)	Hands and Pelvis Score < 3 (n = 21)
Age, y	58.3 ± 11.6	55.4 ± 9.3	56.8 ± 7.8	55.3 ± 12.0
Diabetes mellitus, %	11 (84.6)*	7 (41.2)	8 (88.9)*	7 (35.0)
Coronary artery disease, %	9 (46.2)*	12 (11.1)	3 (33.3)	2 (9.5)
Dialysis duration, mo	59.0 ± 42.9	46.8 ± 39.0	40.4 ± 16.7	45.6 ± 23.3
Fetuin-A, mg/dL	295.9 ± 49.3	290.2 ± 78.0	381.9 ± 81.8	425.6 ± 73.4
25-hydroxyvitamin D, ng/mL	17.6 ± 7.9	18.7 ± 7.5	9.5 ± 5.0	12.8 ± 9.2
Monounsaturated fatty acid, %	18.5 ± 2.4*	17.0 ± 1.7	19.1 ± 2.7	19.9 ± 2.3

*P < .05 compared to the subgroup with low VC score

Table 5. Clinical and Biochemical Characteristics of Patients on Dialysis by Abdominal and Aortic Calcification (AAC) Score on Plain Radiography

Parameter	Hemodialysis		Peritoneal Dialysis	
	AAC Score ≥ 5 (n = 10)	AAC Score < 5 (n = 21)	AAC Score ≥ 5 (n = 11)	AAC Score < 5 (n = 19)
Age, y	59.4 ± 8.6	55.3 ± 11.0	56.0 ± 7.6	55.5 ± 12.1
Diabetes mellitus, %	7 (70.0)	11 (55.0)	7 (63.6)	9 (47.4)
Coronary artery disease, %	5 (50.0)*	3 (14.3)	5 (45.5)*	0
Dialysis duration, mo	65.5 ± 38.8	45.4 ± 40.6	54.0 ± 15.6*	39.6 ± 23.1
Fetuin-A, mg/dL	280.3 ± 39.5	298.9 ± 76.2	396.0 ± 79.8	415.1 ± 79.9
25-hydroxyvitamin D, ng/mL	21.6 ± 6.8	16.4 ± 7.5	10.8 ± 6.8	12.5 ± 9.2
Monounsaturated fatty acid, %	18.1 ± 2.5	17.4 ± 2.0	19.3 ± 2.8	19.9 ± 2.2

*P < .05 compared to the subgroup with low AAC score

Table 6. Regression Analysis for Risk Factors Associated With Significant Vascular Calcification

Parameter	Hemodialysis		Peritoneal Dialysis	
	β	*P*	β	*P*
Age	-0.092	.626	0.034	.847
Dialysis duration	0.292	.098	-0.029	.867
Coronary artery disease	0.469	.013	0.348	.031
Pulse pressure	0.019	.912	0.039	.831
Monounsaturated fatty acid	0.327	.081	-0.096	.611
Fetuin-A	-0.157	.364	-0.495	.009

P = .047) and fetuin-A (β = -0.495, P = .005) were associated with significant VC in univariable analysis of PD patients. Multivariable analysis showed that the CAD history was an independent factor associated with significant VC in hemodialysis patients, and the CAD history and fetuin-A levels were independent factors associated with significant VC in PD patients (Table 6).

DISCUSSION

In this study, we observed that the prevalence of significant VC was not different between PD and hemodialysis patients although fetuin-A levels, erythrocyte membrane MUFA content, and 25-hydroxyvitamin D related with VC were significantly different according to dialysis modality. It is difficult to explain why the prevalence of significant VC was not different between PD and hemodialysis patients whose conditions associated with VC were different. This question can be partially explained by considering the strengths and weaknesses. Higher fetuin-A levels of PD patients may delay VC formation caused by relatively lower 25-hydroxyvitamin D level and higher erythrocyte membrane MUFA of PD patients. Conversely, higher 25-hydroxyvitamin D and lower erythrocyte membrane MUFA of hemodialysis patients compared to PD patients may overcome lower fetuin-A levels of hemodialysis patients in the aspect of VC formation. However, further prospective studies are necessary to elucidate this hypothesis.

Fetuin-A, a 59-kDa glycoprotein, is associated with fat accumulation, insulin resistance, and metabolic syndrome in human studies.[17-19] Peritoneal dialysis patients have a higher risk for metabolic syndrome compared to hemodialysis patients because of an

increased risk of metabolic disturbances, such as high serum glucose level, dyslipidemia, and weight gain.[20] Consistent with previous studies, higher fetuin-A levels of PD patients compared to hemodialysis patients was found in the present study. Higher fetuin-A levels in PD patients may be related with metabolic problems. However, Wang and associates showed that malnutrition was related with valvular calcification and low fetuin-A levels in PD patients.[21] Lower fetuin-A levels are associated with vascular stiffness and VC on plain radiography in PD patients.[22] In the present study, low fetuin-A levels were independent factor associated with significant VC on plain radiography in PD patients. Therefore, fetuin-A levels can be affected by metabolic components and nutritional status and higher fetuin-A may work for VC inhibition in PD patients. Meanwhile, the role of fetuin-A for preventing VC is not clear in hemodialysis patients. Our present data showed that fetuin-A levels were similar according to significant VC and each VC scoring method in hemodialysis patients. A recent report showed that time-averaged fetuin-A was associated with coronary artery calcification score on computed tomography in hemodialysis patients.[23] Further investigations are needed to prove the importance of fetuin-A levels results in VC inhibition especially in hemodialysis patients.

High erythrocyte membrane MUFA contents of hemodialysis patients were consistently related with medial artery calcification of the feet and hands and pelvis VC score ≥ 3 in the present study. Therefore, high erythrocyte membrane MUFA contents may reflect conditions that are prone to form medial artery calcification of the feet and hands and pelvis VC in hemodialysis patients. However, this finding was not prominent in the AAC score on plain radiography. It is of note that low fetuin-A levels were associated with medial artery calcification of the feet but was not prominent in the VC of other sites in our PD patients. Also, presence of diabetes was an important factor in PD and hemodialysis patients with medial artery calcification of the feet and hands and pelvis VC score ≥ 3 but not related with AAC score ≥ 5. Diabetes was not an independent factor related with the AAC score on lateral lumbar spine radiography in the CORD study.[5] Therefore, different factors may be related to the formation of VC according to the position and the size of arteries. Further studies regarding VC site specific pathogenesis are required.

The uremic state is characterized by a systemic inflammatory condition and oxidative stress. Osteoblastic differentiation of vascular smooth muscle cells caused by inflammatory cytokines and reactive oxygen species result in VC formation in dialysis patients.[24] Zittermann and colleagues demonstrated that vitamin D influences processes that are important for intimal and medial artery calcification such as pro-inflammatory cytokine release, adhesion molecule release, and proliferation and migration of vascular smooth muscle cells.[25] An independent and negative association was found between serum 25-hydroxyvitamin D and VC on plain radiography in patients with chronic kidney disease stages 4 and 5.[26] Thus, vitamin D deficiency, especially in PD patients, may be related with VC formation although a significant difference of 25-hydroxyvitamin D according to significant VC was not found in this study. Further prospective studies are necessary to confirm the effect of vitamin D on significant VC on plain radiography.

The interpretation of the current study was limited because of the small sample size and the cross-sectional nature of the study. In addition, there were so many factors we checked compared to the number of enrolled patients and number of enrolled patients was smaller than planned sample size. Despite these limitations, our study demonstrated that factors related with significant VC were different between dialysis modalities and much higher fetuin-A levels were associated with the low prevalence of significant VC and medial artery calcification of the feet in PD patients. Further prospective studies are warranted to find factors for preventing VC formation depending on dialysis modality.

CONCLUSIONS

Significantly different fetuin-A, 25-hydroxyvitamin D, and erythrocyte membrane MUFA contents were found between PD and hemodialysis patients, although the prevalence of VC on plain radiography was not different according to dialysis modality. Fetuin-A levels was an independent risk factor related with VC on plain radiography in PD patients, but fetuin-A levels of hemodialysis patients were not related with VC on plain radiography. Further prospective studies on a large scale are

necessary to explain cross-talk of several factors related with VC on plain radiography according to dialysis modality.

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CONFLICT OF INTEREST

None declared.

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