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Vascular Calcification on Plain Radiographs Is Related with the Severity of Lesions Detected by Coronary Angiography in Dialysis Patients

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Coronary artery disease (CAD) is a primary cause of mortality and morbidity in dialysis patients. However, it is difficult to select the proper point for coronary angiographic procedure, because dialysis patients frequently do not display typical symptoms. Vascular calcification (VC) scores of artery or aorta on plain radiographs are associated with CAD events and may be predictive of CAD in dialysis patients. Therefore, we evaluated whether high or meaningful VC scores on plain radiographs are related with the severity of lesions detected by coronary angiography (CAG) in dialysis patients. We retrospectively enrolled dialysis patients who underwent CAG and checked several plain radiographs within one year before or after CAG. Significant VC is defined as high or meaningful VC scores, such as long abdominal aortic calcification and medial artery calcification on feet. Of all 55 patients, 41 patients (74.5%) exhibited significant VC on plain radiographs and 23 patients (41.8%) underwent stent insertion. Among the 23 patients, longer stents were used in 18 patients with significant VC (34.1 ± 19.5 mm vs. 16.6 ± 15.2 mm, P = 0.029). Patients with significant VC showed higher prevalence rate of severe coronary artery calcification (P = 0.007) and diffuse/tubular stenosis (P = 0.012), detected by CAG, than those without significant VC. Thus, high or meaningful VC scores on plain radiographs were associated with the degree of calcification or stenosis detected by CAG. In conclusion, VC scores on plain radiographs may be predictive of calcification or stenosis of coronary artery before CAG in dialysis patients.

Keywords: coronary angiography; coronary artery disease; hemodialysis; peritoneal dialysis; vascular calcification
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Introduction

Coronary artery disease (CAD) plays an important role in the morbidity and mortality of patients undergoing dialysis, and the incidence of CAD is increasing annually (Go et al. 2004; Tonelli et al. 2006). Patients undergoing dialysis infrequently display classical symptoms such as chest discomfort. These atypical courses make it difficult to decide whether diagnostic interventions such as coronary angiography (CAG) should be introduced. In addition, although CAG is the gold standard for evaluating CAD, it is an invasive, costly, and potentially harmful procedure.

Vascular calcification (VC) is common, and it is associated with cardiovascular morbidity and mortality in dialysis patients. VC on computed tomography (CT) has been suggested as a noninvasive screening method for evaluating CAD and predicting mortality in patients undergoing hemodialysis (HD), but this procedure requires expensive technical equipment (Kimura et al. 1999). Plain radiographs of several sites can be used for evaluating and scoring VC with cheap and easy methods. VC on plain radiographs shows linear railroad-track form like angiography indicating medial artery calcification or irregular patchy density reflecting intimal artery calcification. Previous studies illustrated that high or meaningful VC scores of artery or aorta on plain radiographs are associated with CAD events in dialysis patients. (Blacher et al. 2001; Adragao et al. 2004; An et al. 2009, 2010; Ogawa et al. 2009; Nitta and Ogawa 2011; An and Son 2013; Kwon et al. 2014).

Coronary artery calcification (CAC) on CT is associated with coronary plaque accumulation (Jug et al. 2013). Still, there are no reports comparing VC on plain radio-

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graphs to the degree of CAC or stenosis detected by CAG in patients undergoing dialysis. In this study, we evaluated whether high or meaningful VC scores on plain radiographs are really related with the severity of lesions detected by CAG and give a clue needing CAG in dialysis patients.

Materials and Methods

Patients

We performed a retrospective study of patients receiving dialysis. CAG was performed in 206 patients receiving dialysis between September 2004 and August 2013. Among them, 55 patients (24 undergoing peritoneal dialysis [PD] and 31 undergoing HD) who underwent plain radiography of the chest, hands and pelvis, feet, and lateral lumbar spine within 1 year before or after CAG were enrolled in this study, whereas patients who did not meet this criterion were excluded. The enrolled patients received regular HD three times weekly using bicarbonate-based dialysate and polysulfone dialyzers (Fresenius, Bad Homburg, Germany). The enrolled PD patients received four exchanges per day using a standard regimen (8 L/day). The patients were enrolled regardless of their cardiac function or C-reactive protein (CRP) levels.

Demographic factors such as age, gender, height, weight, and body mass index (BMI) at the time of CAG and clinical factors such as smoking status (never smoker and ex-smoker vs. current smoker), diabetes mellitus (DM), hypertension, CAD, cerebral vascular disease, and peripheral vascular disease were reviewed. BMI was calculated using weight and height (weight [kg]/height [m^2]). The Framingham risk score (FRS) was also evaluated.

This retrospective study was approved by the Dong-A University Hospital Institutional Review Board. Informed consent was waived because of the study's retrospective design the data were analyzed anonymously.

Vascular calcification

Plain anterior to posterior radiographs of the hands and pelvis, feet, chest radiograph for aortic arch calcification, and lateral lumbar spine view for abdominal aortic calcification (AAC) evaluated. VC scores were estimated using previously reported methods (Adragao et al. 2004; Honkanen et al. 2008; An et al. 2009, 2010; Ogawa et al. 2009; Nitta and Ogawa 2011; Verbeke et al. 2011).

In this study, we defined significant VC as any one finding among the following findings on plain radiographs which are high or meaningful VC score: AAC score ≥ 5 (Fig. 1); VC score of the hands and pelvis ≥ 3 (Fig. 2A, B); VC score of the aortic arch ≥ 25 (Fig. 3A); and the presence of medial artery calcification on the feet (Fig. 3B) (Blacher et al. 2001; Adragao et al. 2004; An et al. 2009, 2010;

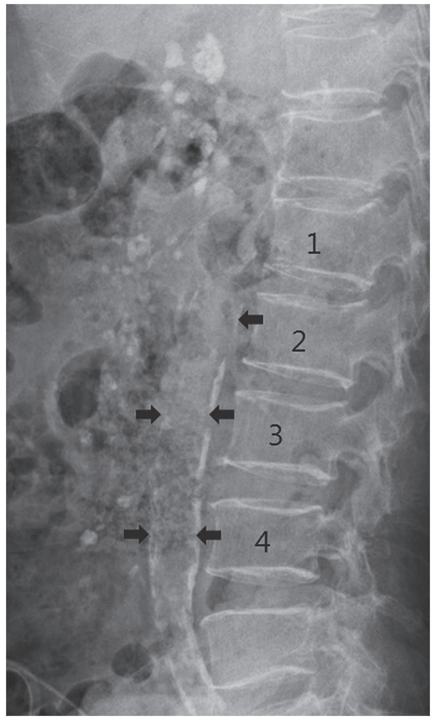

Fig. 1. Lateral lumbar spine view shows abdominal aortic calcification (AAC).
This patient has significant vascular calcification with AAC score ≥ 5. Arrows indicate calcification on the anterior and posterior wall of the abdominal aorta adjacent to vertebrae L1-L4.

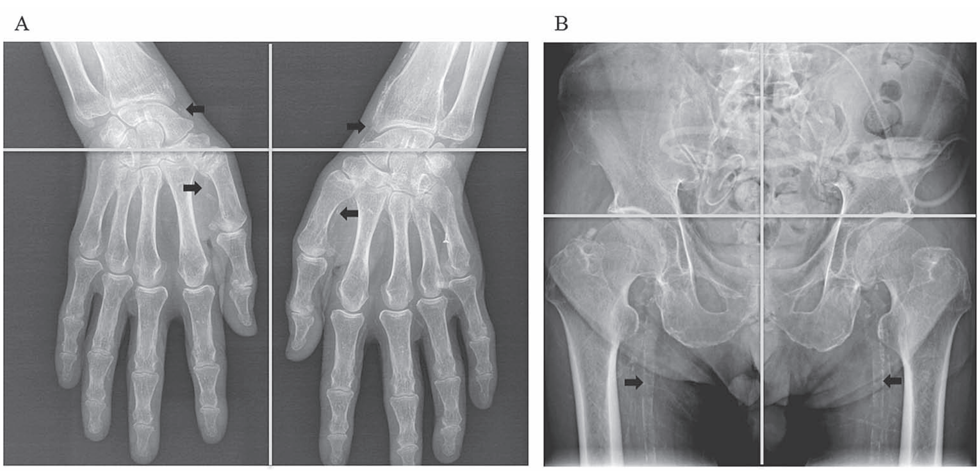

Fig. 2. Vascular calcification on plain radiographs of hands and pelvis.
Plain radiographs of hands (A) and pelvis (B) shows significant vascular calcification (VC) with VC score of the hands and pelvis ≥ 3. Arrows indicate VC like angiography.

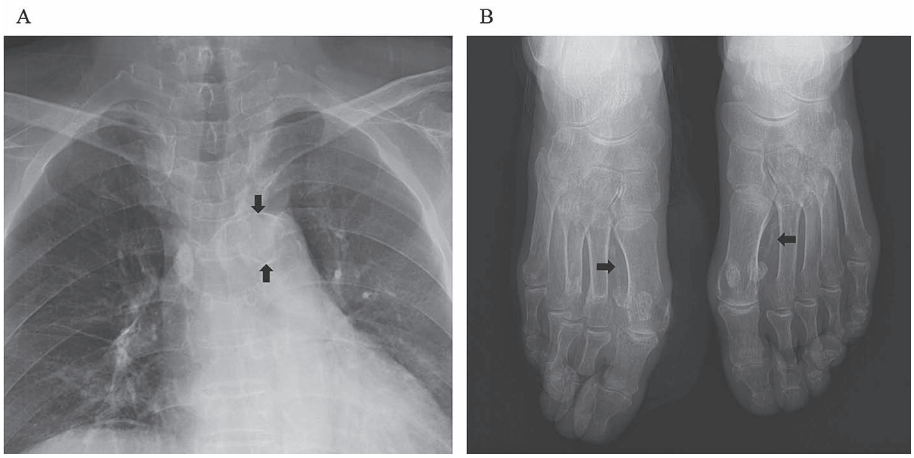

Fig. 3. Vascular calcification on plain radiographs of chest and feet.
(A) Arrows indicate calcification on aortic arch by plain chest radiograph. This patient has significant vascular calcification (VC) with VC score of the aortic arch ≥ 25. (B) Arrows indicate VC like angiography on plain radiograph of feet. This patient has significant VC with the presence of medial artery calcification on the feet.

Ogawa et al. 2009; Nitta and Ogawa 2011; An and Son 2013; Kwon et al. 2014). Two nephrologists individually determined VC scores on plain radiographs without information about patients. Consensus was reached on the interpretation of all radiographs.

CAG

We analyzed the following findings detected by CAG: number, length, or diameter of inserted stents; number of chronic total occlusion (CTO); number of luminal stenosis more than 70% in diameter; severity or type of calcification; and SYNTAX score.

The SYNTAX score was calculated using a previously described method (Serruys et al. 2009) as the sum of the points assigned to each individual lesion identified in the coronary artery with > 50% diameter narrowing in vessels > 1.5 mm in diameter. Therefore, high SYNTAX score on CAG means severe lesion of coronary artery. The degree of calcification detected by CAG was classified into four groups as follows (Ertelt et al. 2013): none, mild (Fig. 4A), moderate (Fig. 4B), and severe (Fig. 4C). The degree of stenosis detected by CAG was categorized as diffuse/tubular or discrete type (Gao et al. 1988). Analysis of CAG was performed by an experienced cardiologist who was blinded to the clinical and laboratory data.

Laboratory measurements

Serum levels of hemoglobin, creatinine, albumin, alkaline phosphatase, CRP, total cholesterol, glycosylated hemoglobin, troponin-I (Tn-I), and B-type natriuretic peptide (BNP) within 3 months of the time of CAG were examined. The highest values of Tn-I and BNP at the time of CAG were recorded.

Statistical analysis

The data are presented as the mean ± S.D. or frequency. The subjects' characteristics were analyzed using Student's *t*-test for continuous variables or the Chi-squared test for categorical variables. The Mann-Whitney *U* test was used to analyze non-parametric data. Pearson's correlation coefficient was applied to identify the correlation between the degree of calcification or stenosis detected by CAG and related parameters. To evaluate the factors independently associated with the degree of calcification or stenosis detected by CAG, multivariate logistic regression analysis was performed. All analyses were conducted using SPSS software (SPSS version 18.0, Chicago, IL). A P value < 0.05 was considered statistically significant.

Results

Clinical characteristics in accordance with significant VC

The baseline characteristics of the study participants are listed in Table 1. The mean age of the enrolled patients was 62.1 ± 9.9 years, and 31 patients undergoing HD were identified (56.4%). Of the 55 patients, 41 patients (74.5%) had significant VC on plain radiographs. Patients with significant VC were older, and they more commonly had a history of CAD. Stent insertion was performed in only 23 patients (41.8%) and longer stents were used in patients with significant VC among 23 patients inserted stent (34.1 ± 19.5 mm vs. 16.6 ± 15.2 mm, $P = 0.029$). A similar result was observed for the SYNTAX score (14.5 ± 15.6 vs. 5.1 ± 5.5, $P = 0.002$). Patients with significant VC had prevalence rate of severe CAC ($P = 0.007$) and diffuse/tubular stenosis ($P = 0.012$), detected by CAG, than those without significant VC.

Clinical characteristics in accordance with severity of CAC detected by CAG

We classified patients into two groups in accordance with the severe CAC detected by CAG (Table 2). The proportion of patients with AAC score ≥ 5 (68.0% vs. 40.0%, $P = 0.038$), hands and pelvis VC score ≥ 3 (64.0% vs. 30.0%, $P = 0.012$) and feet VC score ≥ 1 (72.0% vs. 33.3%, $P = 0.004$) was significantly higher for those with severe CAC than for those with none to moderate CAC. In patients with severe CAC detected by CAG, the proportion of patients with significant VC on plain radiographs was higher than that in patients with none to moderate CAC (92.0% vs. 60.0%, $P = 0.007$). Stent length (38.1 ± 19.4

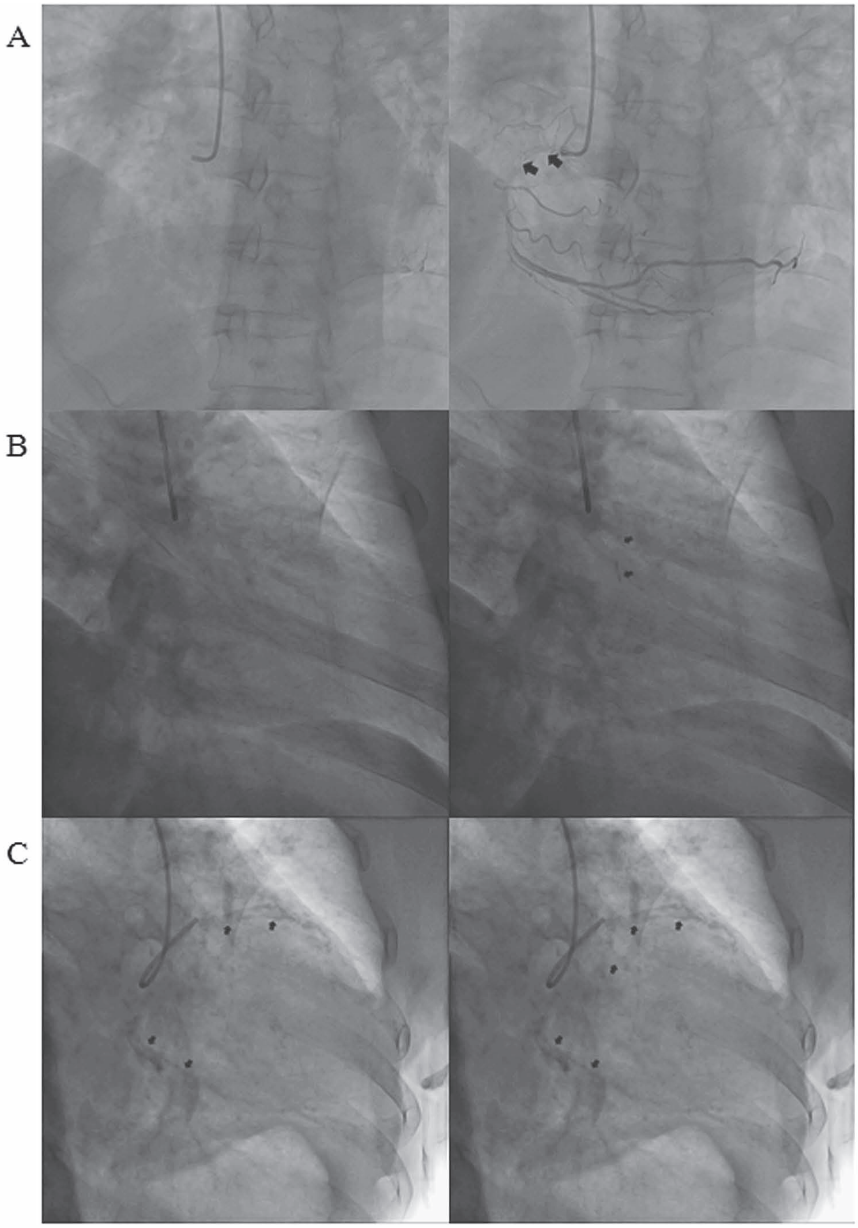

Fig. 4. Classification of coronary artery calcification on coronary angiography (CAG).
(A) Left and right panels are coronary angiographic images before and after the injection of a radio-contrast agent, respectively. Arrows indicate presence of radio-opaque lesions after the injection of a radio-contrast which is defined as mild calcification. (B) Both left and right panels are coronary angiographic images before the injection of a radio-contrast agent. There is no radio-opaque lesion during diastolic movement on left panel. Arrows indicate the presence of radio-opaque lesions during systolic movement which is defined as moderate calcification on right panel. (C) Arrows indicate the presence of radio-opaque lesions before the injection of a radio-contrast agent irrespective of heart movement (diastolic movement on left panel and systolic movement on right panel) which is defined as severe calcification.

mm vs. 21.7 ± 17.2 mm, $P = 0.019$), the prevalence of CTO and > 70% lesions (16.0% vs. 0%, $P = 0.023$ and 44.0% vs. 16.7%, $P = 0.026$, respectively), and SYNTAX score (18.6 ± 17.3 vs. 6.6 ± 7.9, $P = 0.003$) were also significantly higher in patients with severe CAC than in those without severe CAC detected by CAG. In patients with severe CAC detected by CAG, the prevalence rate of diffuse/tubular stenosis was significantly higher than that in the other group (88.0% vs. 43.3%, $P = 0.001$).

Clinical characteristics according to the character of stenosis detected by CAG

The patients were categorized according to the character of stenosis detected by CAG (discrete vs. diffuse/tubular; Table 3). Patients with diffuse/tubular stenosis were more likely to have AAC score ≥ 5 (68.6% vs. 25.0%, $P = 0.002$) and significant VC (85.7% vs. 55.0%, $P = 0.012$) than those with discrete stenosis. In patients with diffuse/tubular stenosis, the stent diameter (1.7 ± 1.4 mm vs. 0.9 ±

Table 1. Comparison of clinical characteristics between patients with significant vascular calcification (VC) and patients without significant VC among 55 patients.

Characteristics	Total (n = 55)	Significant VC		P value
		Negative (n = 14)	Positive (n = 41)	
Age (years)	62.1 ± 9.9	59.1 ± 11.6	63.1 ± 9.3	0.202
Male, n (%)	29 (52.7%)	6 (42.9%)	23 (56.1%)	0.392
DM, n (%)	39 (70.9%)	9 (64.3%)	30 (73.2%)	0.527
CAD history, n (%)	11 (20.0%)	0 (0%)	11 (26.8%)	0.030
HD, n (%)	31 (56.4%)	6 (42.9%)	25 (61.0%)	0.238
BMI (kg/m^2)	23.7 ± 3.5	23.4 ± 4.3	23.8 ± 3.3	0.765
SBP, mm Hg	132.1 ± 19.1	123.2 ± 16.6	135.1 ± 19.2	0.043
DBP, mm Hg	79.1 ± 10.9	75.0 ± 10.9	80.5 ± 10.7	0.105
Ejection fraction, %	49.9 ± 14.1	48.9 ± 17.0	50.2 ± 13.2	0.766
Framingham risk score	10.6 ± 5.1	10.5 ± 6.4	10.6 ± 4.6	0.957
Hemoglobin (g/dL)	10.2 ± 1.8	10.1 ± 1.4	10.2 ± 1.9	0.870
Creatinine (mg/dL)	8.8 ± 3.5	8.7 ± 2.7	8.9 ± 3.8	0.329
ALP (IU/L)	297.7 ± 99.0	281.4 ± 89.1	303.3 ± 102.6	0.479
CRP (mg/dL)	3.7 ± 7.6	4.7 ± 7.2	3.4 ± 7.8	0.585
Cholesterol (mg/dL)	172.1 ± 54.7	185.6 ± 51.6	167.5 ± 55.6	0.288
HbA1c (%)	7.0 ± 1.7	6.4 ± 1.6	7.2 ± 1.7	0.150
Troponin-I (ng/mL)	2.2 ± 4.0	2.1 ± 3.8	2.2 ± 4.2	0.991
BNP (pg/mL)	1,210.7 ± 1,136.4	912.5 ± 1,075.5	1,306.9 ± 1,157.8	0.346
Findings on CAG				
Stent diameter (mm)	1.4 ± 1.4	1.3 ± 1.6	1.4 ± 1.4	0.800
Stent length (mm)	29.6 ± 19.8	16.6 ± 15.2	34.1 ± 19.5	0.029
Inserted stent, n (%)	23 (41.8%)	5 (35.7%)	18 (43.9%)	0.592
CTO, n (%)	4 (7.3%)	1 (7.1%)	3 (7.3%)	0.983
> 70% lesion, n (%)	16 (29.1%)	2 (14.3%)	14 (34.1%)	0.158
SYNTAX score	12.1 ± 14.3	5.1 ± 5.5	14.5 ± 15.6	0.002
Severe CAC, n (%)	25 (45.5%)	2 (14.3%)	23 (56.1%)	0.007
D/T stenosis, n (%)	35 (63.6%)	5 (35.7%)	30 (73.2%)	0.012

VC, vascular calcification; DM, diabetes mellitus; CAD, coronary artery disease; HD, hemodialysis; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ALP, alkaline phosphatase; CRP, C-reactive protein; HbA1c, glycosylated hemoglobin; BNP, b-type natriuretic peptide; CAG, coronary angiography; CTO, chronic total occlusion; CAC, coronary artery calcification; D/T, diffuse/tubular.

1.4 mm, P = 0.050), stent length (35.8 ± 19.0 mm vs. 11.8 ± 7.9 mm, P < 0.001), and SYNTAX score (17.4 ± 15.2 vs. 2.7 ± 4.8, P < 0.001) were also significantly higher than those in patients with discrete stenosis. Additionally, patients with diffuse/tubular stenosis were more likely to have severe CAC than those with discrete stenosis (severe vs. none to moderate; 88.0% vs. 43.3%, P = 0.001).

Correlation between the degree of calcification or stenosis detected by CAG and related parameters

A significant correlation was observed between the degree of calcification or stenosis and related parameters (Table 4). Severe CAC detected by CAG was positively correlated with calcification on plain radiographs, such as significant VC (Pearson's correlation coefficient (r) = 0.366, P = 0.006), AAC score ≥ 5 (r = 0.279, P = 0.039), VC score of the hands and pelvis ≥ 3 (r = 0.340, P = 0.011), and medial artery calcification of at least one foot (r = 0.385, P = 0.004), but there was no correlation observed with VC score of the aortic arch. Severe CAC detected by CAG was positively correlated with stent length (r = 0.419, P = 0.019) and SYNTAX score (r = 0.424, P = 0.001).

Diffuse/tubular stenosis detected by CAG was positively correlated with calcification on plain radiographs, such as significant VC (r = 0.339, P = 0.011) and AAC score ≥ 5 (r =0.420, P = 0.001), but this finding was not related with VC score of the hands and pelvis ≥ 3, VC score of aortic arch ≥ 25, or medial artery calcification of at least one foot. Diffuse/tubular stenosis detected by CAG was positively correlated with stent diameter (r = 0.265, P = 0.050) and stent length (r = 0.540, P = 0.002; Table 4). Severe CAC was positively correlated with diffuse/tubular

Table 2. Comparison of clinical characteristics between patients with severe coronary artery calcification (CAC) and patients without severe CAC detected by CAG among 55 patients.

Characteristics	None to moderate calcification (n = 30)	Severe calcification (n = 25)	P value
Age (years)	62.5 ± 11.5	61.6 ± 7.9	0.762
Male, n (%)	14 (46.7%)	15 (60.0%)	0.324
DM, n (%)	20 (66.7%)	19 (76.0%)	0.448
CAD history, n (%)	6 (20.0%)	5 (20.0%)	1.000
HD, n (%)	18 (60.0%)	13 (52.0%)	0.551
BMI (kg/m^2)	23.4 ± 3.7	24.0 ± 3.3	0.531
SBP, mm Hg	131.0 ± 19.4	133.4 ± 19.1	0.647
DBP, mm Hg	78.3 ± 11.8	80.0 ± 10.0	0.578
Ejection fraction, %	49.3 ± 14.9	50.6 ± 13.3	0.743
Framingham risk score	10.5 ± 5.4	10.7 ± 4.8	0.878
Hemoglobin (g/dL)	10.3 ± 1.8	10.1 ± 1.8	0.655
Creatinine (mg/dL)	8.5 ± 3.2	9.2 ± 3.9	0.456
ALP (IU/L)	277.9 ± 89.9	321.5 ± 105.9	0.105
CRP (mg/dL)	2.7 ± 4.9	4.9 ± 9.9	0.282
Cholesterol (mg/dL)	180.9 ± 56.0	161.5 ± 52.2	0.192
HbA1c (%)	6.7 ± 1.6	7.4 ± 1.7	0.121
Troponin-I (ng/mL)	1.0 ± 1.4	3.7 ± 5.6	0.037
BNP (pg/mL)	1,170.2 ± 1,091.0	1,257.6 ± 1,215.3	0.810
Calcification scores on plain radiograph, n (%)			
Abdominal aorta ≥ 5	12 (40.0%)	17 (68.0%)	0.038
Hands and pelvis ≥ 3	9 (30.0%)	16 (64.0%)	0.012
Feet ≥ 1	10 (33.3%)	18 (72.0%)	0.004
Aortic arch ≥ 25	11 (36.7%)	15 (60.0%)	0.084
Significant vascular calcification	18 (60.0%)	23 (92.0%)	0.007
Findings on CAG			
Stent diameter (mm)	1.3 ± 1.5	1.4 ± 1.4	0.797
Stent length (mm)	21.7 ± 17.2	38.1 ± 19.4	0.019
Inserted stent, n (%)	11 (36.7%)	12 (48.0%)	0.396
CTO, n (%)	0 (0%)	4 (16.0%)	0.023
> 70% lesion, n (%)	5 (16.7%)	11 (44.0%)	0.026
SYNTAX score	6.6 ± 7.9	18.6 ± 17.3	0.003
Diffuse/tubular stenosis, n (%)	13 (43.3%)	22 (88.0%)	0.001

DM, diabetes mellitus; CAD, coronary artery disease; HD, hemodialysis; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ALP, alkaline phosphatase; CRP, C-reactive protein; HbA1c, glycosylated hemoglobin; BNP, b-type natriuretic peptide; CAG, coronary angiography; CTO, chronic total occlusion.

stenosis detected by CAG (r = 0.462, P < 0.001).

Independent factors associated with the degree of calcification or stenosis detected by CAG

To clarify the impact of the degree of calcification or stenosis detected by CAG, we performed multiple logistic regression analysis (Table 5). The presence of significant VC was independently associated with higher rates of severe CAC detected by CAG after adjustment for age, the FRS, and SYNTAX score (relative risk [RR] = 6.00; 95% confidence interval [CI] = 1.08-33.41; P = 0.041). In particular, medial artery calcification of the feet had an independent association with severe CAC detected by CAG (RR = 5.39; 95% CI = 1.39-20.87; P = 0.015).

An AAC score ≥ 5 was associated with diffuse/tubular stenosis detected by CAG (RR = 5.54; 95% CI = 0.99-31.14; P = 0.052). However, calcification at other sites on plain radiographs was not associated with the character of stenosis detected by CAG.

Discussion

In this study, we found that the presence of significant VC on plain radiographs was closely related with a longer stent length, a higher SYNTAX score, a higher prevalence rate of severe CAC and diffuse/tubular stenosis, detected by CAG, in patients undergoing dialysis. In particular, foot

Table 3. Comparison of clinical characteristics between patients with discrete lesion and patients with diffuse/tubular lesion detected by CAG among 55 patients.

Characteristics	Discrete lesion (n = 20)	Diffuse/Tubular lesion (n = 35)	P value
Age (years)	59.0 ± 11.2	63.9 ± 8.9	0.081
Male, n (%)	10 (50.0%)	19 (54.3%)	0.759
DM, n (%)	14 (70.0%)	25 (71.4%)	0.911
CAD history, n (%)	0 (0%)	11 (31.4%)	0.005
HD, n (%)	12 (60.0%)	19 (54.3%)	0.681
BMI (kg/m^2)	24.1 ± 4.3	23.4 ± 3.0	0.498
SBP, mm Hg	127.5 ± 18.4	134.7 ± 19.3	0.181
DBP, mm Hg	76.5 ± 12.3	80.6 ± 10.0	0.187
Ejection fraction, %	50.3 ± 14.8	49.7 ± 13.9	0.894
Framingham risk score	10.2 ± 6.0	10.8 ± 4.6	0.652
Hemoglobin (g/dL)	10.7 ± 1.8	9.9 ± 1.7	0.118
Creatinine (mg/dL)	9.3 ± 3.2	8.6 ± 3.7	0.514
ALP (IU/L)	305.5 ± 101.7	293.3 ± 98.6	0.663
CRP (mg/dL)	5.2 ± 10.9	2.9 ± 4.7	0.380
Cholesterol (mg/dL)	169.3 ± 71.4	173.7 ± 43.5	0.780
HbA1c (%)	6.8 ± 1.7	7.1 ± 1.7	0.631
Troponin-I (ng/mL)	1.3 ± 1.6	2.6 ± 4.8	0.150
BNP (pg/mL)	1,362.6 ± 1,194.9	1,140.2 ± 1,123.6	0.566
Calcification scores on plain radiograph, n (%)			
Abdominal aorta ≥ 5	5 (25.0%)	24 (68.6%)	0.002
Hands and pelvis ≥ 3	6 (30.0%)	19 (54.3%)	0.082
Feet ≥ 1	10 (50.0%)	18 (51.4%)	0.919
Aortic arch ≥ 25	8 (40.0%)	18 (51.4%)	0.414
Significant vascular calcification	11 (55.0%)	30 (85.7%)	0.012
Findings on CAG			
Stent diameter (mm)	0.9 ± 1.4	1.7 ± 1.4	0.050
Stent length (mm)	11.8 ± 7.9	35.8 ± 19.0	< 0.001
Inserted stent, n (%)	5 (25.0%)	18 (51.4%)	0.056
CTO, n (%)	0 (0%)	4 (11.4%)	0.285
> 70% lesion, n (%)	3 (15.0%)	13 (37.1%)	0.082
SYNTAX score	2.7 ± 4.8	17.4 ± 15.2	< 0.001
Severe CAC, n (%)	3 (15.0%)	22 (62.9%)	0.001

DM, diabetes mellitus; CAD, coronary artery disease; HD, hemodialysis; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ALP, alkaline phosphatase; CRP, C-reactive protein; HbA1c, glycosylated hemoglobin; BNP, b-type natriuretic peptide; CAG, coronary angiography; CTO, chronic total occlusion; CAC, coronary artery calcification.

calcification was more strongly associated with the degree of calcification detected by CAG, and AAC was more closely related with the character of stenosis detected by CAG. Therefore, physicians may consider the possibility of meaningful lesions on the coronary artery if patients undergoing dialysis have significant VC on plain radiographs. No study has evaluated the associations between VC on plain radiographs and findings detected by CAG, although previous studies identified a close relationship between VC and an increased risk of CAD (Moe and Chen 2008). This current study is the first to evaluate the relationship between VC on plain radiographs and coronary lesions detected by CAG.

The SYNTAX score is an angiographic grading tool used to determine the complexity of CAD, and it is the sum of the points assigned to each individual lesion identified in the coronary tree with > 50% diameter narrowing in vessels > 1.5 mm in diameter (Sianos et al. 2005; Serruys et al. 2009). High scores are associated with increasing cardiac mortality and major adverse cardiac events (He et al. 2011). In addition, the SYNTAX angiographic grading system was used alone to identify the potential risk for revascularization, and patients with high scores have a worse prognosis for revascularization with PCI compared to coronary artery bypass graft surgery (Serruys et al. 2009). In this study, we identified a significant association between the presence of

Table 4. Correlation between degree of calcification or stenosis detected by CAG and related parameters.

Characteristics	Severe calcification on CAG		Diffuse/Tubular stenosis on CAG	
	r	*P* value	*r*	*P* value
Age (years)	−0.042	0.762	0.237	0.081
DM, *n* (%)	0.102	0.457	0.015	0.913
Ejection fraction, %	0.045	0.743	−0.018	0.894
Framingham risk score	0.021	0.878	0.062	0.652
Calcification scores on plain radiograph, *n* (%)				
Abdominal aorta ≥ 5	0.279	0.039	0.420	0.001
Hands and pelvis ≥ 3	0.340	0.011	0.235	0.085
Feet ≥ 1	0.385	0.004	0.014	0.921
Aortic arch ≥ 25	0.233	0.087	0.110	0.424
Significant VC	0.366	0.006	0.339	0.011
Findings on CAG				
Stent diameter (mm)	0.036	0.797	0.265	0.050
Stent length (mm)	0.419	0.019	0.540	0.002
Inserted stent, *n* (%)	0.114	0.406	0.258	0.057
SYNTAX score	0.424	0.001	0.501	< 0.001
Severe CAC, *n* (%)			0.462	< 0.001
Diffuse/tubular stenosis, *n* (%)	0.462	< 0.001		

DM, diabetes mellitus; VC, vascular calcification; CAG, coronary angiography; CAC, coronary artery calcification.

Table 5. Independent factors associated with degree of calcification or stenosis detected by CAG.

Variables	Severe calcification on CAG		Diffuse/Tubular stenosis on CAG	
	RR[a] (95% CI)	*P* value	RR[a] (95% CI)	*P* value
Age (years)	0.95 (0.87 - 1.03)	0.180	1.05 (0.96 - 1.13)	0.285
Framingham risk score	1.07 (0.92 - 1.24)	0.403	0.97 (0.82 - 1.16)	0.754
SYNTAX score	1.07 (1.01 - 1.13)	0.020	1.25 (1.01 - 1.46)	0.004
Calcification scores on plain radiograph, *n* (%)				
Abdominal aorta ≥ 5	2.77 (0.71 - 10.73)[b]	0.142	5.54 (0.99 - 31.14)[b]	0.052
Hands and pelvis ≥ 3	3.36 (0.96 - 11.80)[b]	0.059	2.01 (0.45 - 9.02)[b]	0.361
Feet ≥ 1	5.39 (1.39 - 20.87)[b]	0.015	0.75 (0.17 - 3.39)[b]	0.710
Aortic arch ≥ 25	2.29 (0.67 - 7.84)[b]	0.187	1.66 (0.36 - 7.64)[b]	0.513
Significant VC	6.00 (1.08 - 33.41)[b]	0.041	2.97 (0.61 - 14.56)[b]	0.180

VC, vascular calcification.
[a]Clinical parameters (Age, Framingham risk score, SYNTAX score) were examined with significant vascular calcification.
[b]The effects of calcification scores were examined separately.

significant VC on plain radiographs and high SYNTAX score. Therefore, we suggest that the presence of significant VC on plain radiographs may predict higher SYNTAX score and a subsequently increased CAD risk in patients with dialysis.

Diffuse/tubular stenosis is the morphologic finding of diffuse concentric narrowing and narrowed irregular vessels with occluded branches (Gao et al. 1988). It was reported that diffuse/tubular stenosis was more likely to occur restenosis than discrete stenosis (Cassese et al. 2014). It has been also demonstrated that a longer stent length was independently associated with a higher likelihood of restenosis (Cassese et al. 2014). Our study demonstrated that a longer stent was needed in patients with diffuse/tubular stenosis than in those with discrete stenosis. In addition, stent length was significantly longer in patients with severe CAC detected by CAG than in those with no to mild/moderate calcification. Furthermore, severe CAC was positively correlated with diffuse/tubular stenosis detected by CAG. Patients with significant VC on plain radiographs had a higher prevalence rate of longer stent insertion, severe CAC, and diffuse/tubular stenosis detected by CAG in this study. Based on our data, physicians may prepare for the possibility of inserting longer stents if patients with dialysis have significant VC on plain radiographs.

The degree of calcification detected by CAG was correlated with both the presence of significant VC and the VC scores of several sites on plain radiographs. However, the character of stenosis detected by CAG was related with AAC but not with medial calcification of the feet, VC of the hands and pelvis, and VC of the chest on plain radiographs. These results partially support that different pathogenesis may be related to the formation of VC according to the positions of arteries. There are two main types of vascular calcifications, namely arterial intimal calcification and arterial media calcification (Amann 2008). Arterial intimal calcification is caused by intimal patchy calcifications of atherosclerotic plaques and occlusive lesions, and it is commonly identified in coronary arteries, carotid arteries, and the aorta (Shanahan et al. 1999). It is associated with aging and a clinical history of atherosclerosis. On the contrary, arterial medical calcification is a non-occlusive lesion observed in muscle-type conduit arteries, such as femoral, tibial, and uterine arteries. It is more closely associated with a clinical history of DM and end-stage renal disease (Lehto et al. 1996; Shanahan et al. 1999). Significant VC scores for several sites on plain radiographs are more reliable predictors of cardiovascular events than a high VC score at a single site of plain radiographs (London et al. 2003; Sigrist et al. 2007). In addition, an analysis of VC at a single site on plain radiographs can miss more than 30% of VC cases in patients receiving dialysis compared with an analysis of VC at five different sites (Kim et al. 2011). Because VC is related with various pathogeneses and clinical characteristics, taking plain radiographs of several areas will be helpful for evaluating significant VC and the degree of CAC or stenosis detected by CAG. In addition, the presence of medial artery calcification on the feet was only independent factor associated with degree of severe CAC among several sites on plain radiographs in this study. This result may be related with vessel size because the size of coronary artery is similar with dorsalis pedis artery of feet. Further prospective studies are necessary to elucidate the pathogenesis of VC formation according to vessel size or location.

The FRS is one of a number of scoring systems used to predict the risk of CAD. It includes traditional risk factors, such as age, gender, systolic blood pressure, hypertension treatment, total cholesterol and high-density lipoprotein cholesterol levels, and cigarette smoking (National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults 2002). In the general population, individuals with low, intermediate, and high FRS scores have a CAD risk of 10% or less, 10-20%, and 20% or more, respectively. Huang et al. (2013) suggested that an intermediate FRS could predict cardiovascular mortality, although a high FRS was not predictive. The FRS was not associated with VC on plain radiographs or the degree of CAC or stenosis detected by CAG in this study. These results suggest that the formation of VC on plain radiographs, CAC and stenosis detected by CAG are dominated by non-traditional risk factors. Further studies are needed.

This study had some limitations. First, because the number of participants was relatively small, and thus, the power of the study was limited. Second, the exclusion of many patients undergoing dialysis who also underwent CAG but not plain radiography resulted in selection bias. In addition, this study did not demonstrate that VC on plain radiographs was associated with stent insertion. Despite these limitations, this study demonstrated that significant VC on plain radiographs is a useful predictor of SYNTAX score, severe CAC, and diffuse/tubular stenosis detected by CAG in patients receiving dialysis. In addition, we found that the presence of foot calcification is the most reliable predictor for severe CAC detected by CAG, and an AAC score ≥ 5 is the most important indicator of diffuse/tubular stenosis detected by CAG among several VC scores.

In conclusion, VC scores on plain radiographs may be predictive of calcification or stenosis of coronary artery before CAG in dialysis patients. Further prospective studies are necessary to confirm the predictive role of significant VC scores on plain radiographs because identifying the patients receiving dialysis who are at high risk for CAD is important for preventing sudden cardiac death.

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Conflict of Interest

The authors declare no conflict of interest.

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