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Abdominal aorta and pelvic artery calcifications on plain radiographs may predict mortality in chronic kidney disease, hemodialysis and renal transplantation

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Abstract

Purpose Vascular calcification is common in chronic kidney disease (CKD) and predicts poor patient outcomes. While computed tomography is the gold standard for evaluation of vascular calcification, plain radiograph offers a simpler and less costly alternative. The calcification of abdominal aorta, iliac and femoral arteries has been evaluated by plain radiograph, but the data on their outcome predictabilities are still limited. The present study investigated the role of abdominal aortic calcification (AAC) and pelvic arterial calcification (PAC) in predicting overall morality in non-dialysis CKD stages 2–5 (CKD 2–5), maintenance hemodialysis (HD) and long-term kidney transplant (KT) patients.

Methods Four hundred and nineteen patients were included. Lateral abdominal and pelvic radiographs were obtained. The degree of AAC and PAC was evaluated according to the methods described previously by Kaupplia et al. and Adragao et al. Patients were followed prospectively for 5 years.

Results AAC and PAC scores correlated well with the correlation coefficients of 0.442 for CKD 2–5, 0.438 for HD and 0.586 for KT ($p < 0.001$). Patients with AAC score > 6 or PAC score > 1 were older, showed higher prevalence of DM and had higher serum phosphate and PTH but lower serum albumin and eGFR. A more severe degree of AAC was associated with an increase in KT duration, whereas a more severe degree of PAC was associated with worsening kidney function and prolonged dialysis vintage. Kaplan–Meier survival curves revealed AAC score > 6 as a significant predictor of all-cause mortality in CKD 2–5 but not in HD or KT, whereas PAC score > 1 was a significant predictor of all-cause mortality in all three populations. After adjusting for age, the predictability of AAC was lost, whereas PAC remained an independent predictor of mortality in all three populations. Adjustments for cardiovascular and CKD risk factors including age, gender, BMI, DM, serum albumin, calcium and phosphate attenuated the predictability of PAC in HD but not in CKD 2–5 or KT patients.

Conclusion PAC was better than AAC in predicting mortality in CKD, HD and KT patients.

Keywords Medial · Intimal · Coronary · ESRD · Renal · Transplantation

Introduction

In chronic kidney disease (CKD) patients, vascular calcification (VC) is more common than the general population, occurs earlier in life and predicts poor patient outcomes [1–3]. VC can be differentiated into two types according the area within the arterial wall. Calcification within the intima is frequently observed in large arteries in association with atherosclerosis and lumen obliteration. Calcification within the media occurs predominantly in medium-sized and small-sized muscular arteries and is characterized by arterial media thickening and poor arterial compliance without lumen obliteration [4, 5]. Risk factors associated with VC

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include both traditional cardiovascular (CV)- and CKD-related risk factors such as aging, diabetes, hypertension, dyslipidemia, worsening kidney function, prolonged dialysis vintage and increased calcium and phosphate load [6]. Although computed tomography (CT) is the gold standard for evaluation of VC, plain radiograph offers a less costly alternative with less radiation exposure [7]. Kidney disease improving global outcome (KDIGO) guidelines suggests a use of lateral abdominal radiograph to detect the presence or absence of VC in CKD stages 3–5 patients, as a reasonable alternative to CT-based imaging [8]. In addition to lateral abdominal radiograph which detects abdominal aortic calcification (AAC), plain radiographs of chest, pelvis, both hands and feet can also be utilized to evaluate the calcification of aortic arch, iliac arteries, femoral arteries and small arteries of hands and feet [9–11]. Although both AAC score described by Kauppila et al. and pelvic arterial calcification (PAC) with bilateral hand calcification score described by Adragao et al. correlate well with coronary artery calcification (CAC) score obtained by CT, the data on their abilities to predict mortality especially in non-dialysis CKD patients and kidney transplant (KT) recipients are still lacking [10, 12–15]. The present study examined the abilities of AAC and PAC on lateral abdominal and pelvic radiographs in predicting mortality in three groups of CKD population: non-dialysis CKD stages 2–5 (CKD 2–5), maintenance hemodialysis (HD) and long-term KT (KT) patients.

Methods

Patients

This study was approved by the Ethical Committee on Human Rights Related to Researches Involving Human Subjects of the Faculty of Medicine, Ramathibodi Hospital, Mahidol University and was conducted according to the Declaration of Helsinki. Informed consent was obtained from all participants. Non-dialysis CKD stages 2–5 patients, maintenance HD patients who were on KT waiting list and long-term KT recipients were recruited consecutively during the routine follow-up visits to the outpatient nephrology clinic of Ramathibodi hospital. Only KT recipients who had been transplanted for at least 1 year were enrolled due to the stabilization of mineral metabolites and hormones could take up to 12 months [16]. Patients with acute illnesses including active malignancy, active infection and acute kidney injury (acute allograft dysfunction), and those who were scheduled to undergo high-risk operation were excluded. At the time of recruitment, none of the patients received non-calcium phosphate binders, calcimimetic, bisphosphonates, teriparatide or denosumab because these drugs were not widely available in Thailand at the time of enrollment. The prescribed active vitamin D was calcitriol or alfacalcidol. Fifty-three percent of the KT recipients were living-related, and 47% were deceased donor transplantation. The maintenance immunosuppressive regimens included corticosteroid in all patients.

Biochemical data, vascular calcification and outcome

Medical chart review was performed to collect the data on baseline demographics and characteristics. Blood samples and plain radiographs were obtained at the time of enrollment. Serum calcium was corrected based on the following equation: Corrected Ca = serum Ca + [(40 − serum albumin) ÷ (10 × 0.8)]. Estimated GFR (eGFR) was calculated using the modified MDRD formula [17]. AAC

Table 1 Baseline demographics of all patients

Parameters	CKD 2–5 (n = 160)	HD (n = 125)	KT (n = 134)
Age (years)	62.7 ± 12.3	49.5 ± 13.2	48.7 ± 11.6
Male gender (n/%)	92 (57.5)	63 (50.5)	81 (60.4)
BMI (kg/m^2)	25.8 ± 4.5	22.4 ± 3.9	23.7 ± 4.3
Hypertension (n/%)	140 (87.5)	93 (74.4)	103 (76.9)
Dyslipidemia (n/%)	128 (80)	59 (47.2)	86 (64.2)
DM (n/%)	85 (53.1)	36 (28.8)	31 (23.1)
CVD (n/%)	29 (18.1)	22 (17.6)	8 (6)
Dialysis vintage (months)	–	44.4 (28.3–72.9)	23.5 (8–48)
KT duration (months)	–	–	88 (43–138)
Causes of CKD or ESRD (n/%)			
DM	52 (32.3)	34 (27.2)	16 (11.9)
HTN/renovascular disease	60 (37.9)	16 (12.8)	10 (7.5)
Chronic glomerulonephritis	35 (21.7)	59 (47.2)	98 (73.1)
Others	8 (5)	5 (4)	7 (5.2)
Unknown	5 (3.1)	11 (8.8)	3 (2.2)

was determined in a lateral lumbar spine radiograph, and the amount of VC was scored according to the method described previously by Kauppila et al. (total score 0–24) [12]. The presence of linear calcification in each iliac or femoral artery seen in a pelvic radiograph was scored as one (total score 0–4) according to the method described previously by Adragao et al. [10]. All X-rays were reviewed by two physicians who had the expertise with reading VC on plain radiograph and were blinded to clinical data. The correlation of VC scores from two physicians was 0.938. The data obtained from one physician were used in analyses. The study commenced in June 2010, and patients were followed prospectively until death or until February 2016.

Statistical analysis

Data are presented as mean ± SD unless specified otherwise. The correlation between two continuous variables was analyzed by the Pearson's correlation. The Chi-square test was applied to test the difference among the two or more groups of categorical data. The trend of multiple groups was analyzed by linear-by-linear association. Two continuous variables were compared using the Student's t test or non-parametric test. Patient survival was analyzed by Kaplan–Meier survival curve and Cox regression analysis. AAC score > 6 and PAC score > 1 were selected as cutoffs because previous studies have shown their associations with decreased patient survival [10, 18]. Variables with the p value < 0.05 in univariate Cox regression analysis were selected as covariates in the multivariate models. p value < 0.05 is considered statistically significant. All computations were performed using the SPSS 17.0 software (SPSS, Chicago, IL).

Table 2 Baseline characteristics according to abdominal aortic calcification scores

Parameters	CKD 2–5		HD		KT	
	AAC ≤ 6 (N = 115)	AAC > 6 (N = 45)	AAC ≤ 6 (N = 95)	AAC > 6 (N = 30)	AAC ≤ 6 (N = 106)	AAC > 6 (N = 28)
Age	60 ± 12.7	69.5 ± 7.6**	40.1 ± 12.5	60.4 ± 8.7**	45.5 ± 10.2	60.6 ± 8.7**
Male gender (%)	62.6	44.4*	50.5	50	58.5	67.9
BMI (kg/m^2)	25.6 ± 4.7	26.4 ± 4.1	22.4 ± 3.9	22.5 ± 4.1	23.5 ± 4.4	24.4 ± 4.1
Hypertension (%)	89.6	82.2	74.2	82.8	75.5	85.7
Dyslipidemia (%)	79.1	82.2	43.6	62.1	61.3	75
DM (%)	46.1	71.1**	25.5	41.1	17.9	42.9**
Dialysis vintage (months)	–	–	43.7 (26.4–70)	50.9 (31.4–102)	22 (7–48)	36 (10–60)
KT duration (months)	–	–	–	–	80 (39–128)	103.5 (63.5–159)*
Calcium binder (g/week)	0.98 ± 1.77	1.93 ± 3.11*	4.53 ± 6.11	4.86 ± 6.11	1.15 ± 2.11	0.63 ± 1.29
Active vitamin D (μg/week)	0.06 ± 0.3	0.17 ± 0.44	2.34 ± 3.99	2.04 ± 4.16	0.08 ± 0.29	0.29 ± 1.33
Calcium (mg/dL)[a]	9.3 ± 0.5	9.4 ± 0.5	9.7 ± 0.8	9.7 ± 0.9	9.4 ± 0.6	9.5 ± 0.7
Phosphate (mg/dL)	3.8 ± 0.6	4. ± 0.9*	5.2 ± 1.9	4.7 ± 1.7	3.5 ± 0.6	3.8 ± 1.3
Albumin (g/L)	39.1 ± 4.7	37.2 ± 4.6*	37 ± 4.3	34.8 ± 5*	40.1 ± 4.7	38.6 ± 4
Cholesterol (mg/dL)	193 ± 51	189 ± 44	179 ± 45	177 ± 47	196 ± 35	183 ± 41
ALP[b] (U/L)	72.5 (51–88.8)	74 (58–94.5)	93 (72.5–139)	101 (78.3–201)	69 (55–93)	55 (44–93)
PTH (pg/mL)	64 (46–107)	68.3 (48.6–119)*	281 (112–667)	368 (195–935)	76.3 (60–111)	80.8 (52.4–110)
25-OH-D[c] (ng/mL)	20.2 ± 7.6	19.5 ± 13	25.7 ± 10	24.2 ± 13	19.5 ± 6.7	20.2 ± 11
eGFR (mL/min/1.73 m^2)	35.4 ± 16.1	29.5 ± 13.3*	–	–	55 ± 19.9	55.9 ± 18.7

* p < 0.05; ** p < 0.01 versus AAC ≤ 6

[a]Corrected calcium

[b]Alkaline phosphatase

[c]25-Hydroxyvitamin D

Results

Relationships between baseline characteristics and VC

AAC scores correlated well with PAC scores with the correlation coefficients (r) of 0.442, 0.438 and 0.586 for CKD 2–5, HD and KT, respectively ($p < 0.001$ in all groups). Demographic data of all patients are shown in Table 1. Baseline characteristics and laboratory data according to AAC and PAC scores are shown in Tables 2 and 3. Patients with AAC score > 6 or PAC score > 1 were older, showed heightened prevalence of diabetes and had higher serum phosphate and PTH but lower serum albumin and eGFR. Increased KT vintage was associated with a more degree of AAC, whereas prolonged dialysis vintage was associated with a more severe degree of PAC. Relationships between AAC and PAC scores with kidney function and dialysis vintage are shown in Figs. 1 and 2. The proportion of patients with PAC score > 1 increased with advancing CKD stages (Fig. 1) and prolonged dialysis vintage (Fig. 2) in CKD 2–5, KT and HD. The proportion of patients with AAC score > 6 increased with advancing CKD stages only in CKD 2–5 but not in KT (Fig. 1). There was no relationship between AAC score > 6 with prolonged dialysis vintage in any group of the patients (Fig. 2). AAC and PAC scores did not show correlations with BMI, hypertension, doses of calcium and active vitamin D, serum calcium, alkaline phosphatase and 25-OH-D levels (Tables 2 and 3).

Mortality prediction of AAC and PAC

The median follow-up period was 62.7, 52 and 62.5 months, and death occurs in 15, 18 and 9% in CKD 2–5, HD and KT, respectively. Kaplan–Meier survival curves revealed AAC score > 6 as a significant predictor of all-cause mortality in CKD 2–5 but not in HD or KT, whereas PAC score > 1 was a significant predictor of all-cause mortality in all three populations (Fig. 3). Similarly, in univariate Cox regression analyses, AAC score > 6 predicted mortality only in CKD 2–5 patients, whereas PAC score > 1 predicted mortality in

Table 3 Baseline characteristics according to pelvic arterial calcification scores

Parameters	CKD 2–5		HD		KT	
	PAC ≤ 1 (N = 131)	PAC > 1 (N = 29)	PAC ≤ 1 (N = 87)	PAC > 1 (N = 37)	PAC ≤1 (N = 107)	PAC > 1 (N = 27)
Age	61.6 ± 12.2	67.6 ± 11.4*	46.6 ± 12.9	55.8 ± 11.4**	46.4 ± 11.3	57.8 ± 8.2**
Male gender (%)	61.1	41.4	51.7	45.9	58.9	66.7
BMI (kg/m^2)	25.8 ± 4.7	25.6 ± 4	22.3 ± 3.8	22.8 ± 4.2	23.5 ± 3.7	24.5 ± 6.1
Hypertension (%)	86.3	93.1	75.3	77.8	74.8	85.2
Dyslipidemia (%)	80.2	79.3	39.5	66.7**	64.5	63
DM (%)	49.6	69	16.3	61.1**	15.9	51.9**
Dialysis vintage (months)	–	–	41.9 (26–66.3)	58.2 (39.8–102)*	22 (7–40)	36 (14–84)*
KT duration (months)	–	–	–	–	89 (40.5–139)	83 (48–137)
Calcium binder (g/week)	1.11 ± 1.96	1.9 ± 3.3	4.89 ± 6.2	4 ± 5.9	1 ± 1.7	1.1 ± 2.8
Active vitamin D (μg/week)	0.07 ± 0.31	0.18 ± 0.47	2.36 ± 4.18	2.12 ± 3.74	0.07 ± 0.27	0.35 ± 1.37
Calcium (mg/dL)[a]	9.3 ± 0.4	9.4 ± 0.6	9.7 ± 0.9	9.6 ± 0.8	9.4 ± 0.5	9.5 ± 0.8
Phosphate (mg/dL)	3.8 ± 0.7	4.1 ± 0.7*	5.3 ± 1.9	4.6 ± 1.6	3.5 ± 0.6	3.8 ± 1.4
Albumin (g/L)	39.1 ± 4.7	36.3 ± 4.3**	37.2 ± 4.5	34.8 ± 4.3**	40.6 ± 4.1	36.9 ± 5.3**
Cholesterol (mg/dL)	194 ± 50	187 ± 46	183 ± 46	169 ± 44	194 ± 34	187 ± 47
ALP[b] (U/L)	71.5 (53–91.3)	75 (48–87)	92.5 (67–140)	103 (82.8–163)	67.5 (53–93.3)	69 (48.3–95)
PTH (pg/mL)	60.4 (45.2–106)	79.3 (54.2–158)*	334 (148–646)	208 (98.5–737)	76.3 (60–107)	83.5 (51.1–121)
25-OH-D[c] (ng/mL)	20.2 ± 8.5	19 ± 12.7	26.2 ± 10.3	23.1 ± 11.5	19.5 ± 6.7	20.3 ± 11.2
eGFR (mL/min/1.73 m^2)	35.4 ± 15.5	26.3 ± 14**	–	–	57 ± 18.9	48.1 ± 21.1*

* $p < 0.05$; ** $p < 0.01$ versus PAC ≤ 1

[a]Corrected calcium

[b]Alkaline phosphatase

[c]25-Hydroxyvitamin D

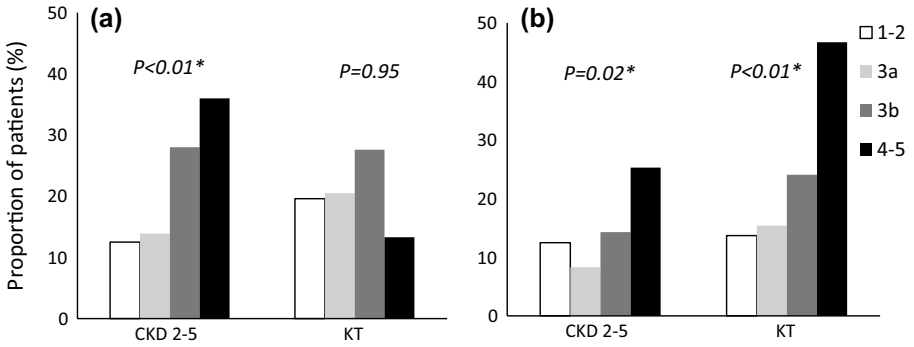

Fig. 1 Proportion of patients with AAC score > 6 (**a**) and PAC score > 1 (**b**) according to CKD stages (1–2, 3a, 3b, 4–5) in non-dialysis CKD patients (CKD 2–5) and long-term KT recipients (KT)

all three groups of patients (Table 4). After adjusting for age (Model 1), the predictability of AAC was lost, whereas PAC score > 1 remained an independent predictor of mortality in all three populations (Table 5). After adjusting for CV risks (Model 2), PAC score > 1 remained an independent predictor of mortality in CKD 2–5 patients and KT recipients. The adjustment for both CV and CKD risks (Model 3) did not alter the results. Only after further adjusting for eGFR in Model 4, the predictability of PAC was attenuated in KT recipients but not in CKD 2–5 patients.

Discussion

The present study investigated the predictive ability of AAC and PAC on plain radiograph in non-dialysis CKD, maintenance HD and long-term KT patients. PAC appeared to perform better than AAC in predicting overall mortality in all groups of CKD patients.

VC is particularly common in CKD due to the high prevalence of CV risks as well as the presence of CKD-specific risk factors. VC naturally progresses rapidly with advancing CKD stages [19]. After successful transplantation, the progression slows down but can still be observed in most patients [20, 21]. Multi-slice CT is the gold standard for detection and quantitation of VC, but plain radiograph offers a more convenient and less costly alternative with the benefit of low radiation exposure. The degree of AAC obtained from lateral abdominal radiograph and PAC obtained from pelvic radiograph correlates well with CAC score obtained from CT [13]. While the association between increased CAC score and mortality is well documented, the predictive values of VC score from plain radiograph and outcomes are less clear.

In the present study, AAC score correlated well with PAC score and a more severe degree of AAC and PAC was associated with aging, DM, increased serum phosphate and PTH, lower serum albumin and eGFR indicating that both CV- and CKD-related risk factors participated in the development and progression of VC. These findings are in line with the previous reports [6, 22–26]. As for outcome prediction, AAC score > 6 was able to predict future death in non-dialysis CKD patients. The same trends were observed in HD and KT patients, but the magnitude did not reach statistical significance. After the adjustment for age, the predictive value of AAC was lost. These data suggest that the predictive ability of AAC was weak, and the degree of AAC was largely related to aging. Although previous studies have reported an independent association between the severity of AAC and mortality in HD patients, such data in non-dialysis CKD patients and KT recipients are still limited and less clear [18, 27–29]. The two studies in non-dialysis CKD patients that analyzed AAC from both plain radiograph and CT were not able to establish an independent relationship with mortality after adjusting for age or other comorbidities [25, 30]. These findings are similar to the present study. In another cohort of 742 non-dialysis CKD patients, the association with mortality after adjusting for CV risk

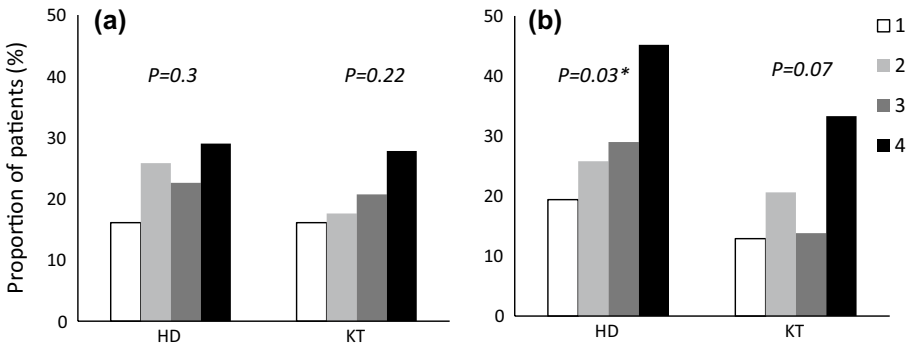

Fig. 2 Proportion of patients with AAC score > 6 (**a**) and PAC score > 1 (**b**) according to the quartiles of dialysis vintage in maintenance HD patients (HD) and long-term KT recipients (KT). Quartiles 1–4 for KT are 0–8, 8–23.5, 23.5–48 and > 48 months. Quartiles 1–4 for HD are 1–28, 28–44, 44–73 and > 73 months

factors could only be established when AAC was obtained from CT but not from plain radiograph [14]. Analyses of AAC prior to or shortly after transplantation revealed an independent association with mortality only in the study that used CT but not lateral abdominal radiograph [31, 32]. In the present study, the low sensitivity of plain radiograph likely contributed to the lack of association between AAC and mortality in HD patients. Nevertheless, the predictive ability of AAC in non-dialysis CKD patients was also hampered substantially by aging. The present study was the first to

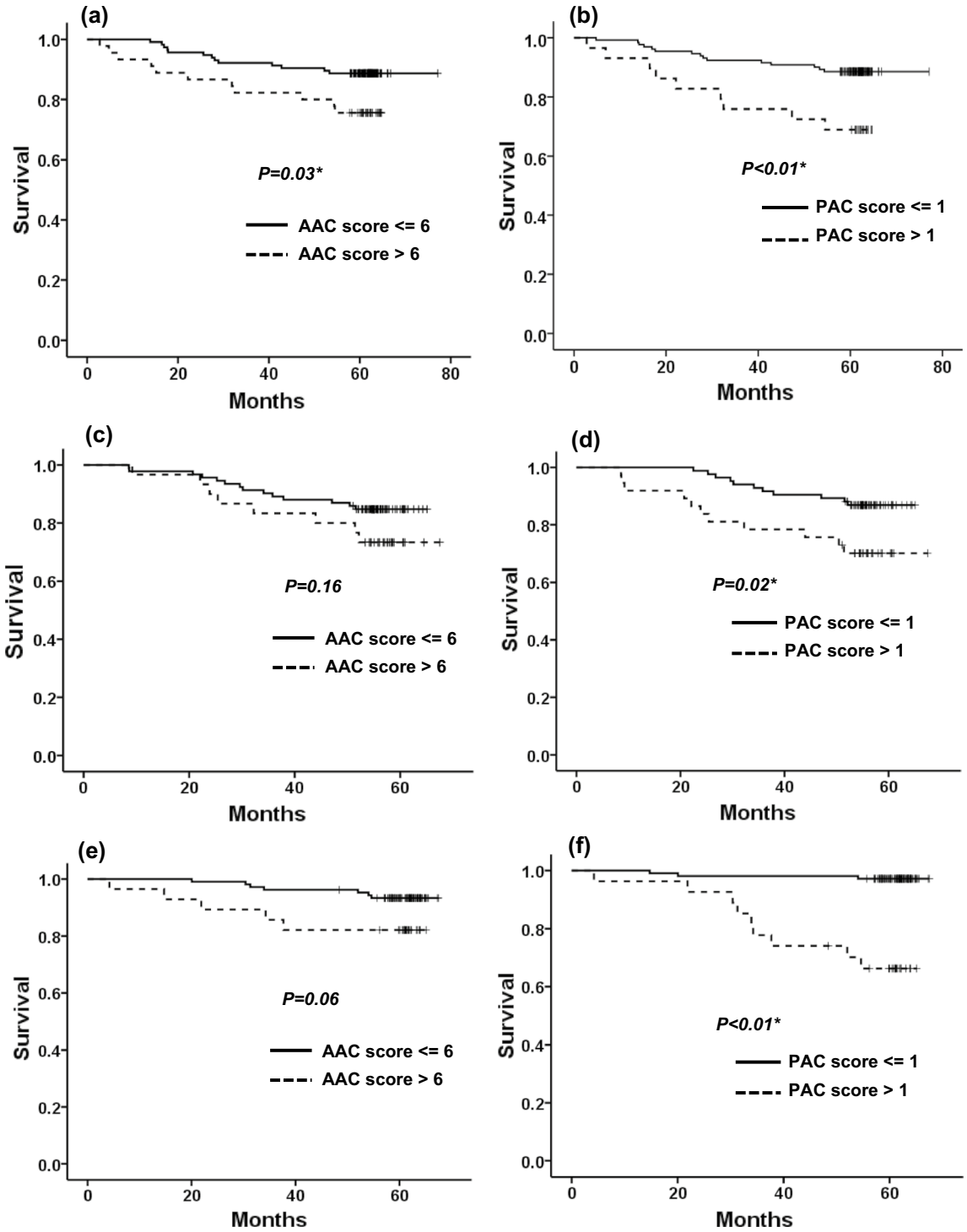

Fig. 3 Kaplan–Meier survival curves of AAC and PAC scores in CKD stages 2–5 (**a**, **b**), maintenance HD (**c**, **d**) and KT patients (**e**, **f**)

examine the association between AAC and patient outcome in long-term KT recipients. The predictive ability of AAC in this population was weak at best. The degree of AAC appeared to increase with increasing KT duration but not with worsening allograft function suggesting that the development and progression of AAC associated more closely to atherosclerosis than uremic milieu [33]. More evidence to support this assumption is in Figs. 1 and 2, which showed poor correlations between the degree of AAC with kidney function and dialysis vintage.

As for PAC, there have been only few published studies related to its outcome predictability. Studies by Adragao et al. reported an association between the combined calcification score of medial-type calcification of iliac and femoral arteries and small arteries of both hands with mortality in ESRD and non-dialysis CKD patients [10, 25, 34]. The analysis of only PAC in ESRD patients also revealed an independent association with mortality [6, 29]. There has never been any report on the relationship between PAC and mortality in non-dialysis CKD patients or long-term KT patients. In the present study, PAC score > 1 predicted mortality in all three groups of CKD patients and this relationship was independent of aging. Further adjustment for other CV risk factors attenuated the predictive ability of PAC in HD patients but not in non-dialysis CKD patients or long-term KT recipients. Addition of CKD risk factors including serum albumin, calcium and phosphate to the model did not alter the result. After adjusting for eGFR, the predictive value of PAC still remained in non-dialysis CKD patients but was lost in long-term KT recipients. These data suggest that PAC was more robust than AAC in predicting mortality and was less interfered by other confounders. The explanation for this observation may be related to the type of calcification and its relationship to CKD. The degree of calcification in iliac and femoral arteries was graded according to Adragao et al. method, and therefore, only linear-type medial calcification was analyzed. As mentioned earlier, calcification in the intima is more common in the aorta, whereas calcification in the media increased in medium-sized and smaller muscular arteries. Due to these reasons, AAC likely comprised mostly of intimal calcification and PAC consisted mainly of medial calcification. A large body of evidence documented the role of uremic milieu in the development and progression of medial calcification [5, 35]. The data from the present study also confirmed such evidence. With advancing CKD stages and prolonged dialysis vintage, the number of patients with PAC score > 1 substantially increased. The better ability of PAC to predict mortality could be related to its representation of medial calcification, which links more closely to CKD. In long-term KT recipients, the degree of PAC correlated strongly with the decline in allograft function but less so with previous dialysis experience. A successful return of kidney function allows vascular remodeling to occur in most patients, and a regression of VC has been reported in up to 20% of long-term KT recipients [36, 37]. Due to these reasons, the degree of VC observed in KT patients did not entirely reflect the previous damage from uremic environment but also represented an ongoing repair.

Table 4 Univariate Cox regression analysis for factors associated with mortality

Parameters	CKD 2–5 HR (95% CI)	HD HR (95% CI)	KT HR (95% CI)
Age (years)	1.07 (1.04–1.11)**	1.05 (1.01–1.09)*	1.09 (1.03–1.15)**
Male gender	2.35 (0.93–5.91)	1.14 (0.49–2.65)	1.36 (0.41–4.52)
BMI (kg/m^2)	1.01 (0.92–1.1)	1.07 (0.97–1.19)	0.87 (0.74–1.03)
Dyslipidemia (Y/N)	2.84 (0.67–12.1)	1.39 (0.58–3.29)	0.77 (0.24–2.42)
DM (Y/N)	2.22 (0.92–5.35)	4.79 (1.98–11.56)**	2.48 (0.79–7.82)
Ln dialysis vintage	–	1 (0.99–1.01)	1.1 (0.67–1.81)
Ln KT vintage	–	–	1.6 (0.65–3.97)
Laboratory data			
Calcium (mg/dL)[a]	2.42 (1–5.84)*	0.79 (0.48–1.29)	0.73 (0.27–1.95)
Phosphate (mg/dL)	0.55 (0.27–1.15)	0.83 (0.64–1.07)	2.42 (1.39–4.2)*
Albumin (g/L)	0.96 (0.86–1.03)	0.88 (0.8–0.97)*	0.82 (0.75–0.9)**
Ln PTH (pg/mL)	0.98 (0.54–1.78)	0.74 (0.53–1.03)	1.57 (0.68–3.62)
25-OH-D (ng/mL)	0.97 (0.92–1.03)	0.97 (0.93–1.01)	1.01 (0.94–1.09)
eGFR (ml/min/1.73 m^2)	1 (0.98–1.03)	–	0.94 (0.91–0.98)**
Vascular calcification			
AAC > 6	2.35 (1.05–5.25)*	1.84 (0.77–4.39)	2.93 (0.9–9.22)
PAC > 1	3.04 (1.33–6.96)**	2.64 (1.14–6.08)*	13.9 (3.74–51.3)**

* $p < 0.05$; ** $p < 0.01$

[a]Corrected calcium

Table 5 Multivariate Cox regression models for factors associated with mortality

Parameters	AAC > 6	PAC > 1		
	CKD 2–5	CKD 2–5	HD	KT
Model 0: unadjusted				
HR (95% CI)[a]	2.35 (1.05–5.25)*	3.04 (1.33–6.96)**	2.64 (1.14–6.08)*	13.9 (3.74–51.3)**
Model 1: age				
HR (95% CI)	1.52 (0.68–3.4)	2.41 (1.05–5.52)*	2.59 (1.15–5.84)*	8.4 (2.03–34.8)**
Model 2: CV[b] risks (age, gender, BMI, DM)				
HR (95% CI)	–	2.37 (1–5.53)*	1.1 (0.4–3.01)	7.8 (1.8–33.8)**
Model 3: CV and CKD risks (age, gender, BMI, DM, albumin, serum calcium, serum phosphate)				
HR (95% CI)	–	2.62 (1.1–6.28)*	–	4.68 (1.03–21.3)*
Model 4: CV, CKD risks and eGFR (age, gender, BMI, DM, albumin, serum calcium, serum phosphate, eGFR)				
HR (95% CI)	–	2.64 (1.1–6.4)*	–	3.67 (0.85–15.8)

* $p < 0.05$; ** $p < 0.01$

[a]Hazard ratio (95% confidence interval)

[b]Cardiovascular, variables with p value < 0.05 in univariate analyses were selected as covariates in multivariate models

The present study was limited by the small number of patients in each group. Only all-cause mortality was analyzed due to the lack of accurate data on cardiovascular mortality.

In conclusion, the predictive ability of AAC for mortality was weak and largely dependent on aging. PAC was a better predictor of mortality in all three populations of CKD.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethics approval This study was approved by the Ethical Committee on Human Rights Related to Researches Involving Human Subjects of the Faculty of Medicine, Ramathibodi Hospital, Mahidol University and was conducted according to the Declaration of Helsinki.

Informed consent Informed consent was obtained from all participants.

Availability of data and materials Data supporting this study are available upon request.

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