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Original Article

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Peripheral vascular calcification in long-haemodialysis patients: associated factors and survival consequences

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Abstract

Background. Vascular calcifications (VCs) are frequently observed in chronic kidney disease (CKD) and haemodialysis (HD) patients. They have been associated with numerous factors, particularly hyperphosphataemia, excess calcium load, hypertension and increased mortality rate. The purpose of this study is to measure VCs in long-HD patients with good blood pressure and phosphate control, with the occasional use of sevelamer, using a plain radiological score to identify the associated factors and effects on the 1-year survival rate.

Methods. We studied HD patients from one centre using a semi-quantitative score ranging from 0 to 3 according to the severity and extent of VCs. The following patients' characteristics were compared according to their VC scores: medical history, treatments, blood pressure, standard biological data, fibroblast growth factor (FGF) 23, osteoprotegerin (OPG), whole PTH, β-crosslaps, bone alkaline phosphatases and bone mineral density scores. One-year survival analyses were also performed.

Results. Among the 250 HD patients of the centre, 161 were studied; the mean age was 67.2 ± 13 years, 45% of the subjects were females, 35% were diabetics, and they had been on dialysis for between 1–486 months (median: 45 months) with a 3 × 5–3 × 8 h dialysis schedule using 1.5 mmol/l dialysate calcium and providing a mean 2.25 ± 0.5 Kt/V. Only 17% of the patients were free from VCs and 11% had severe VCs. The factors associated with VCs were classified into 'classic' (age, diabetes, male gender, tobacco use, inflammation, more frequent warfarin treatment and peripheral vascular and cardiac diseases) and 'non-traditional' (higher FGF-23 and OPG serum levels, low albumin serum levels and low alfacalcidol and $CaCO_3$ use). In logistic regression, only age, diabetes and FGF-23 serum levels were associated with VC scores of 2 and 3. The patients with a score of 3 had a higher 1-year mortality rate (RR 2.1; $P = 0.01$) as compared to patients with a 0 score.

Conclusion. A plain radiological score showed the high prevalence (83%) of VCs in HD patients in spite of a long and intensive dialysis strategy and adherence to guidelines. The main associated factors were classic factors such as ageing and diabetes. No relationship was found with blood pressure and phosphataemia that remained well controlled in long dialysis; the association with FGF-23 serum levels may aggregate some non-traditional risk factors. The harmful effects of VCs on survival require their systematic assessment and optimization of the potentially modifiable associated factors in CKD and HD patients.

Keywords: bone mineral density; fibroblast growth factor (FGF)-23; long haemodialysis; mineral metabolism; vascular calcification

Introduction

Chronic kidney disease (CKD) patients display a higher cardiovascular mortality rate as compared to the general population [1]. Vascular calcifications (VCs) reflect the severity of vascular diseases and have been associated with morbidity and mortality in CKD and end-stage renal disease (ESRD) patients. VCs may promote arterial stiffness [2], left ventricular hypertrophy (LVH) [3], cardiovascular events [4] and mortality [2] depending upon the two distinct types of VCs: intimal and medial wall calcification. Moreover, VCs have been highly prevalent in CKD and haemodialysis (HD) patients [5–7]. Numerous risk factors have been reported for VCs. Some of these are 'classic', such as ageing [8], hypertension, diabetes [9] and dyslipidaemia; certain others are more specific to CKD and are 'non-traditional', such as mineral metabolism abnormalities, particularly hyperphosphataemia and extreme PTH serum levels [10–12], dialysis vintage [13] and excess administration of calcium salts [14–16].

VC is a pathological process occurring in response to an inappropriate environmental milieu [17]. Local and circulating inhibitors of soft-tissue mineralization are down-regulated in CKD patients leading to a phenotype

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transformation of vascular smooth muscle cells into osteocyte-like cells capable of undergoing the mineralization process [18].

Long dialysis allows for a better control of hyperphosphataemia with less phosphate binder administration [19] even with a large protein intake and better blood pressure control without anti-hypertensive therapy [20]. These two conditions may be associated with fewer VCs in long-HD patients.

Cardiac calcifications are measured with electron beam computed tomography (EBCT), which remains the optimal standard for assessing VCs. However, a plain radiological score of VC has also been used [2,21], which is sometimes associated with Doppler ultrasound, in good correlation with the reference technique [22].

The aim of the present study is to assess peripheral VCs from a semi-quantitative plain radiological score in patients treated with long intensive HD and sevelamer as a phosphate binder, in order to determine the associated factors and the effect of the VC score on the 1-year survival rate.

Methods

All the HD patients of our centre who had accepted to undergo the radiological study and the bone mineral density (BMD) test were studied between January 2006 and January 2007. BMD (QDR 4500 C; HOLOGIC Inc., Bedford, MA, USA) was undertaken on the day of the radiological study. The wrist *Z*-score and lumbar and hip *T*-scores were recorded for the analyses. The radiological semi-quantitative score ranged from 0 to 3 according to the severity and extent of the VC from eight fine-detail plain radiographic films (front pelvis, profile lumbar and knee, right hand and arm, chest, skull, and orthopantomogram). The VC scores were as follows: score 0, absence of VC; score 1, light aortic or iliac VC; score 2, major aortic + iliac + femoral VCs; score 3, severe diffuse VCs with aortic, iliac, femoral, popliteal and arm artery VCs. Patients were classified and compared according to their VC scores into four groups by the same radiologist who assessed the radiographic films.

We recorded the standard laboratory values, medical history, cardiovascular events and risk factors, treatments [statins, angiotensin conversion enzyme (ACE) inhibitors, warfarin, vitamin D, cinacalcet and phosphate binders] and some special markers: osteoprotegerin (OPG, ELISA; BioVendor Inc., Brno, Czech Republic), fibroblast growth factor (FGF)-23 (FGF-23, ELISA c-Term; Immutopics Inc., San Clemente, CA, USA), bone alkaline phosphatases (BALP, chemiluminescence; Beckmann Inc., Urbana, IL, USA), β-crosslaps (CTX, chemiluminescence; Roche®, Basel, Switzerland) and whole PTH (RIA; Scantibodies Inc., Santee, CA, USA). iPTH was measured using a second-generation assay (Roche®). All the samples were taken before a midweek session in the same week of the radiological study. Kt/V was calculated monthly by applying the eKt/V formula. For routine biology tests, the mean of the last 3 months' values was recorded. Furthermore, we recorded the mean of the pre-dialysis blood pressure values from the last month before the study.

Patients were haemodialyzed three times per week with a 5- to 8-h schedule using a polysulphone low-flux (FX8 and FX10, Helixone®; Fresenius S. E., Bad-Hombourg, Germany) or high-flux (FX80 and FX100) filter with a dialysate calcium concentration of 1.5 mmol/l in >90% of the cases.

Statistical analysis

According to the variable distribution, Student's *t*-test or the Mann–Whitney test was used to compare the groups. Fisher's exact test was applied for proportion comparison. One-way analysis of variance complementing Duncan's post-test was applied to compare the variables among the VC score groups. Logistic regression was applied to determine the factors significantly associated with a VC score of 2 or 3. Multiple regression analysis was applied between FGF-23 serum levels and the potentially associated factors. The 1-year survival rate, according to the VC score, was calculated using the Cox proportional hazard model adjusted for age, sex and diabetes. The results are reported as mean ± standard deviation. Differences with *P*-values ≤ 0.05 were considered statistically significant. Statistical analyses were performed by using MedCalc© software 9.3.1.0 (MedCalc Software, Mariakerke, Belgium).

Results

Among the 250 eligible HD patients, 161 were studied: 45% of these were females, 35% were diabetics and the mean age was 67.2 ± 13 years. They had been on dialysis for between 1–486 months (median: 45 months) with a 3 × 5 h (50%), 3 × 6 h (7%), 3 × 7 h (18%) or 3 × 8 h (25%) schedule (mean session time = 6 h 45 min). Most of the patients had remained on the same dialysis schedule since their first dialysis. The mean Kt/V was 2.25 ± 0.5. The administered treatments included alfacalcidol (48%), calcifediol (94%), cinacalcet (10%), sevelamer (39%), $CaCO_3$ (9%), ACE inhibitors (14%), statins (36%), warfarin (20%) and erythropoiesis-stimulating agent (ESA, 75%). Systematic supplementation with 25(OH)-vitamin D was initiated in vitamin D-deficient patients only 1 year prior to the study.

Among the 89 patients not included in the study, 54 refused to participate in the study, 8 had cancer with bone metastasis, 14 had severe dementia, 10 were hospitalized, 1 had spina-bifida and 2 underwent rapid kidney transplantation before the radiological study took place. Their characteristics did not differ from the subjects included in the study group.

Among the 161 patients, only 17% were free from VCs and 11% had severe VCs. Table 1 shows the comparison between the four groups divided according to the VC score. As compared to the patients with no VCs (score = 0), calcified patients were older, more often diabetics, of the male gender, smokers, more frequently had peripheral vascular disease with a history of stroke and cardiopathy, more frequent warfarin users, and with higher CRP and lower albumin serum levels. Blood pressure control was achieved in >90% of cases, primarily without anti-hypertensive medication. Hypertension, session time and Kt/V values were not associated with the VC score.

Table 1. Data comparison according to VC score

	Score = 0 ($n = 27$)	Score = 1 ($n = 55$)	Score = 2 ($n = 62$)	Score = 3 ($n = 17$)
Age (years)	$54.2 \pm 12^{b-d}$	64.7 ± 14^{a}	70.7 ± 13^{a}	72.8 ± 15^{a}
Dialysis vintage (months)	58 ± 67	73 ± 75	72 ± 70	68 ± 72
Female gender (%)	55^{d}	45	46	23^{a}
Diabetes (%)	$11^{c,d}$	$22^{c,d}$	$45^{a,b,d}$	76^{a-c}
Session time (min)	387 ± 72	381 ± 78	382 ± 102	342 ± 72
Kt/V	2.43 ± 0.6	2.45 ± 0.5	2.46 ± 0.6	2.16 ± 0.44
SBP (mmHg)	121.1 ± 20	122.3 ± 21	124.2 ± 22	130.3 ± 25
DBP (mmHg)	71.9 ± 10	71.2 ± 11	72.5 ± 12	69.9 ± 9
BMI (kg/m^2)	23.7 ± 5	25.5 ± 5	25.1 ± 5	26.1 ± 5
Smokers (%)	9^{d}	25	27	55^{a}
Peripheral vascular disease (%)	$0^{c,d}$	$11.5^{c,d}$	$23.3^{a,b,d}$	70^{a-d}
Stroke (%)	8^{d}	13^{d}	20^{d}	52^{a-c}
Ischaemic cardiac disease (%)	4^{d}	11.5	24.5	35^{a}
Chronic liver disease (%)	8	17	16	29
Parathyroidectomy (%)	3.7	11.8	4.5	17
Transplantation (%)	12	2	5	6
NPCR (g/kg/day)	1.37 ± 0.3	1.22 ± 0.3	1.3 ± 0.3	1.18 ± 0.3
EPO use (%)	76	71	72	87
Statin use (%)	23	39	35	52
ACE inhibitor use (%)	12	7	17	25
$CaCO_3$ % (dose g/day)	22^{c} (1.6 ± 2.1)	9 (1.5 ± 2)	4.8^{a} (1.7 ± 2.2)	5.8 (1.7 ± 2.6)
Sevelamer % (dose g/day)	44 (3.8 ± 4.2)	29 (3.4 ± 3.8)	43 (3.7 ± 4.2)	52 (3 ± 4)
Alfacalcidol % (dose μg/week)	63^{d} (3.5 ± 3)	49 (2.6 ± 2.2)	46 (3.2 ± 2.9)	29^{a} (2.6 ± 2.5)
Cinacalcet % (dose mg/day)	15 (53 ± 32)	5 (60 ± 45)	11 (54 ± 39)	18 (45 ± 29)
25(OH)D_3 % (dose g/day)	87 (13 ± 8)	92 (15 ± 8)	96 (17 ± 9)	96 (17 ± 9)
Warfarin use (%)	4^{d}	17^{d}	23^{d}	47^{a-c}
Hip *T*-score	-1.8 ± 1.5	-2.2 ± 1.4	-2.4 ± 1.5	-2.8 ± 1.6
Wrist *Z*-score	-1.3 ± 1	-1.6 ± 1	-1 ± 1	-1.1 ± 1
Lumbar *T*-score	-1.3 ± 1	-1.4 ± 1	-1 ± 1	-0.9 ± 1
Total calcaemia (mmol/l)	2.22 ± 0.16	2.19 ± 0.16	2.21 ± 0.16	2.15 ± 0.16
Phosphataemia (mmol/l)	1.42 ± 0.3	1.27 ± 0.3	1.47 ± 0.3	1.5 ± 0.3
iPTH (pg/ml)	254 ± 167	187 ± 152	271 ± 170	185 ± 200
Whole PTH (pg/ml)	113 ± 98	83 ± 66	91 ± 80	79 ± 67
BALP (μg/l)	20.2 ± 14	20.6 ± 14	17.7 ± 10	17.2 ± 12
CTX (μg/l)	2.5 ± 1.4	2.15 ± 1	1.9 ± 0.8	1.96 ± 1
OPG (pmol/l)	$11.8 \pm 14^{b-d}$	21.2 ± 18^{a}	22.3 ± 16^{a}	22.6 ± 18^{a}
FGF-23 (RU/ml)	$1781 \pm 1960^{c,d}$	$1844 \pm 2209^{c,d}$	$3589 \pm 4980^{a,b}$	$5186 \pm 6789^{a,b}$
Albumin (g/l)	38.7 ± 4^{d}	36.8 ± 4	35.9 ± 4^{a}	35.4 ± 4^{a}
CRP (mg/l)	7.5^{d}	11.1^{d}	13^{d}	$27.1^{a,b,c}$
25-OH vitamin D (nmol/l)	110 ± 52	108 ± 51	124 ± 52	113 ± 55

ANOVA: $^{a}P < 0.05$ with score = 0, $^{b}P < 0.05$ with score = 1, $^{c}P < 0.05$ with score = 2, $^{d}P < 0.05$ with score = 3.

Calcified patients were less frequently users of $CaCO_3$ and alfacalcidol; moreover, the use of sevelamer, statins and ACE inhibitors had no effects on the VC score. Hyperphosphataemia was uncommon with <8% of the patients having a phosphate serum level >1.8 mmol/l. It is noteworthy that the serum level of bone markers, calcium, phosphate and intact and whole PTH were independent of the calcification score, which was also true for dialysis vintage (Figure 1). HD patients with <6 months of dialysis vintage showed VCs in 77% of cases.

BMD *Z*- or *T*-scores were not associated with the VC score even if there was only a tendency to a lower hip *T*-score in severely calcified patients (Figure 2). Calcified patients had higher FGF-23 (Figure 3) and OPG serum levels. Multiple regression analysis between serum FGF-23 and potentially influential factors showed an independent association with calcaemia ($r = 0.17$, $P = 0.04$), phosphataemia ($r = 0.18$, $P = 0.02$) and alkaline phosphatase ($r = 0.12$, $P = 0.03$) but not with PTH or alfacalcidol dosage. The OPG serum levels were mainly related to age ($r = 0.38$, $P < 0.001$) and dialysis vintage ($r = 0.54$, $P < 0.001$).

Table 2. Logistic regression of factors associated with VC score of 2 and 3

Variable	Odds ratio	95% CI	*P*
Age	1.04	1–1.07	0.04
FGF-23	1.001	1–1.002	0.01
Diabetes	4.74	2–11.3	0.0003
Tobacco use	0.94	0.38–2.3	0.9
Female gender	0.79	0.3–1.8	0.5
Peripheral vascular disease	2.5	0.7–8.3	0.14
Coronaropathy	2.1	0.6–6	0.19
Albumin	0.98	0.89–1.1	0.8
OPG	1.01	0.98–1.03	0.28
CRP	0.99	0.97–1.02	0.9
Warfarin use	1.49	0.54	0.4

In logistic regression, only age, serum levels of FGF-23 and diabetes were associated with severe VCs (Table 2).

The overall survival rate was lower for calcified patients (Figure 4, score = 3 versus score = 0, $P = 0.006$) in the Cox model after adjustment for age, gender and diabetes.

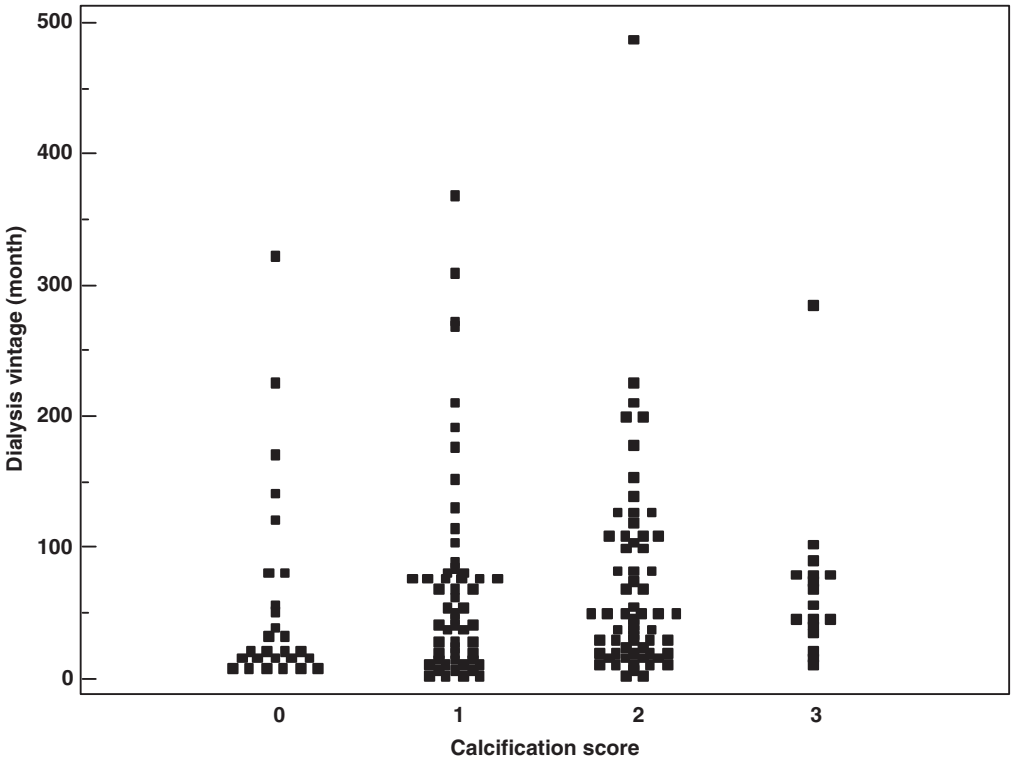

Fig. 1. Relationship between dialysis vintage and VC score.

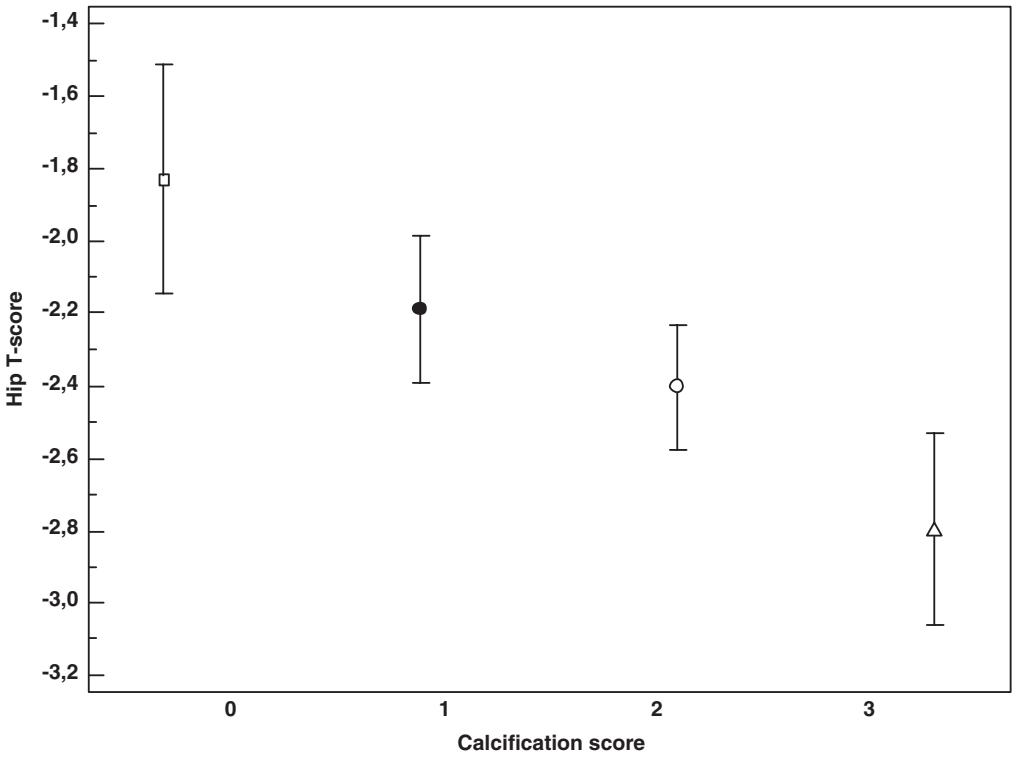

Fig. 2. Frequency distribution of BMD hip *T*-score according to VC score (mean ± SEM).

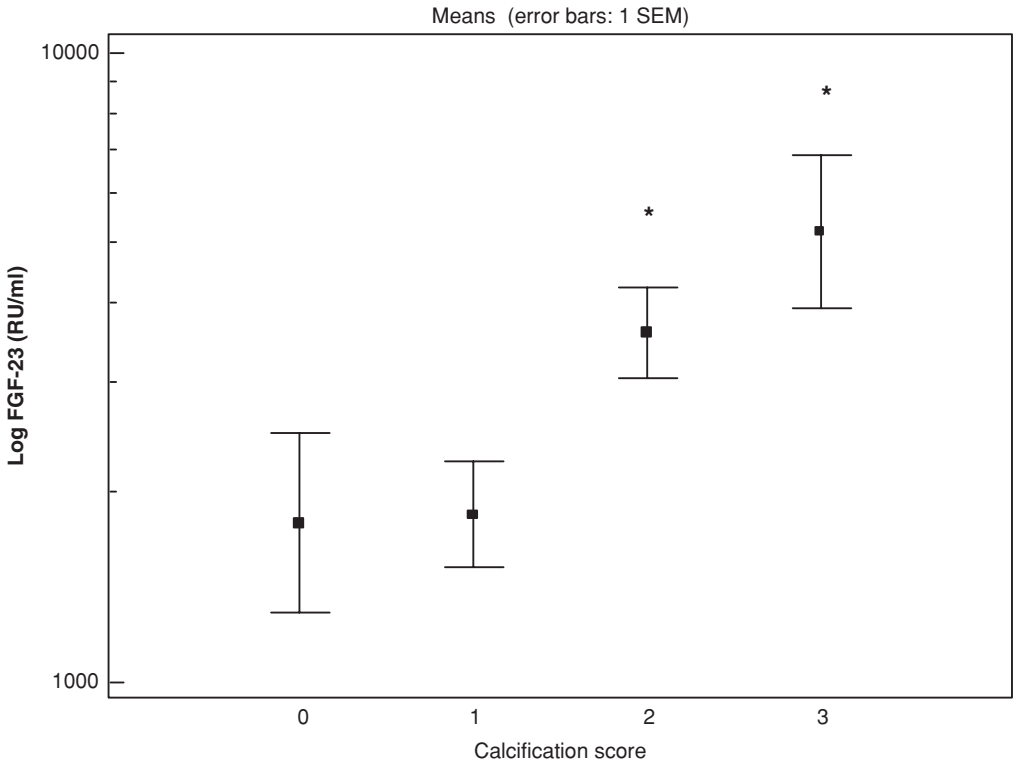

Fig. 3. Frequency distribution of FGF-23 serum level (expressed in log) according to VC score. $^{*}P < 0.05$ versus score = 0.

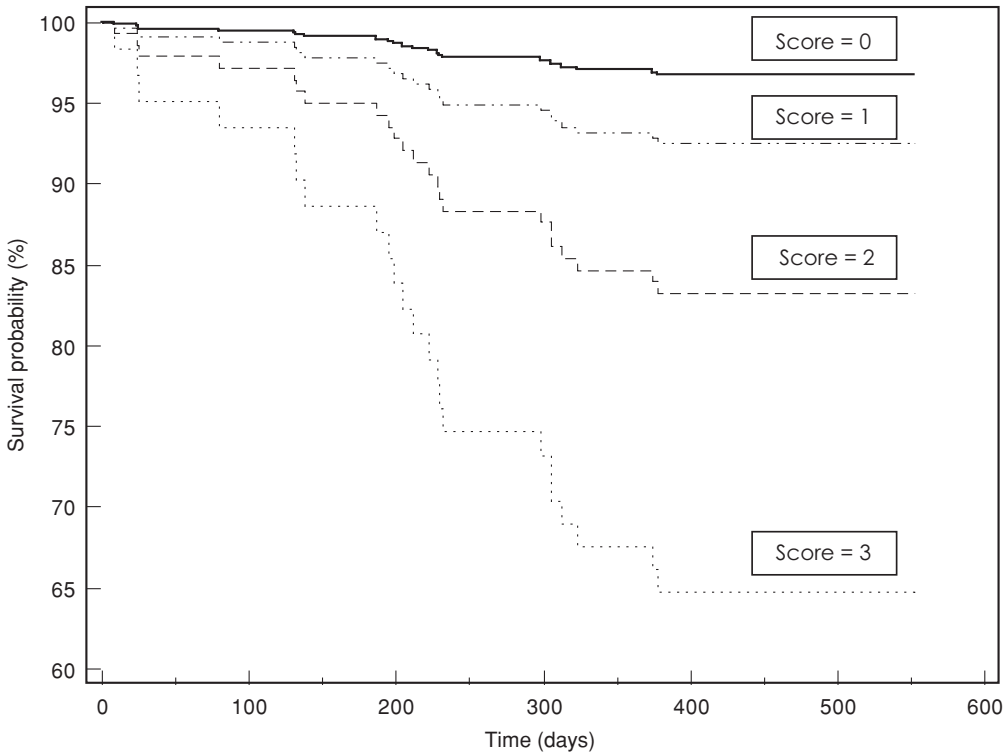

Fig. 4. Survival analysis comparison according to the calcification score. Proportional hazard Cox model adjusted for gender, diabetes and age. $P = 0.006$ between score 0 and score 3.

The relative risk for mortality was 2.1 (1.2–3.7, $P = 0.01$) for more calcified HD patients.

Discussion

Our study showed a high prevalence (83%) of radiological VCs in HD patients, even in those treated in long and intensive dialysis sessions with good control of hyperphosphataemia and hypertension with adherence to most recent guidelines. The association of VCs with the mortality rate, previous cardiovascular events and classic risk factors has been confirmed by our study. The impact of non-traditional factors appears to be more confusing.

A number of non-invasive imaging techniques are available for screening the presence of VCs [22]. We employed a plain radiological VC score that has been reported previously [23]. Even if the EBCT using the Agatston score remains the conventional standard for its greater reproducibility rate and direct association with coronary artery calcification (CAC) [24], this radiological score can be applied everywhere at a lower cost. Besides, an aortic VC score has been reported to be highly correlated with CAC [25].

VCs are frequently observed in CKD patients. In 2004, Russo *et al.* reported that 40% of all CKD patients had VCs as compared to 13% in a matched control population [5]. More recently, up to 90% of CKD patients were found to have abdominal aortic VCs using computed tomography [26]. HD patients have been reported to have VCs even more frequently; for example, 77.9% of HD patients had abdominal aortic calcifications and 57.4% had diffuse severe VCs versus 37.5% and 17% in the general population, respectively [6]. VCs in the femoral artery have been reported in 73% of HD patients [6], which is similar to the value of 83% of patients with at least one radiographic VC observed in our study.

The VC risk factors in CKD have been listed by Goodman *et al.* according to intimal and medial calcifications [27]. Medial wall calcifications are thought to be involved in the high frequency and the rate of progression of VCs in HD. Our VC score represented the aggregate of both intimal atherosclerotic and medial wall calcifications.

CKD patients are exposed precociously to classic cardiovascular risk factors, sometimes long before renal disease occurs. Among the classic factors, diabetes was the main factor associated with VCs in our study, similar to previous reports concerning the general population and CKD patients [28,29]. Diabetes-related VCs are known to occur long before the initiation of dialysis; further, diabetes is involved in both types of VCs but mainly in medial VCs. Hypertension is known to be involved mainly in intimal VCs that are less rapidly progressive. Besides, elevated blood pressure may also be a result of medial VCs. As reported previously in a population with less adequate blood pressure control [10], blood pressure values were not associated with VCs in our study with $<10\%$ of HD patients who remained hypertensive. Inflammation is an integral component of atherosclerosis that may worsen in severity by reducing fetuin-A synthesis and other circulating calcification-inhibiting factors [30]. Our data confirm the association between higher CRP serum levels and severe VCs.

The physiopathology of VCs is now better understood with new insights in the effect of non-traditional factors involved in CKD [18]. In contrast to what was believed previously, VCs are not the result of only passive phosphate and calcium accumulation in the vessel wall; in fact, they are caused primarily by an active process involving numerous regulating factors. VC formation involves the transformation of vascular smooth muscle cells into osteoblast-like cells and macrophage cells into osteoclasts. These transformations are regulated by some calcification inhibitors such as fetuin-A, matrix Gla protein (MGP), vitamin K, OPG, the klotho gene and by some calcification promoters such as Ca $\times$ P product, RANK ligand (RANKL) and bone morphogenic protein (BMP)-2 [31]. In CKD patients, an unfavourable uraemic milieu disturbs this regulation with frequent hyperphosphataemia, excess calcium load and loss of local calcification inhibitors. Among them, MGP is a vitamin K-dependant protein system that regulates both bone and vascular mineralization [32]. Warfarin, an MGP inhibitor, remains a potential risk factor for calciphylaxis in ESRD [33] and was associated with VCs in our study. OPG is an osteoclast-inhibiting factor produced by different tissues. [16,34]. In HD patients, its serum levels increase with age and dialysis vintage and have been associated with mortality and VC progression [35]. Our study confirms these data but it is not clear whether OPG is a deleterious protein. FGF-23 is a multifunctional protein that regulates mineral metabolism, ageing and probably VCs in combination with the klotho gene. FGF-23 is produced by osteocytes in cases of hyperphosphataemia; it inhibits calcitriol synthesis in the kidney. It has been associated with the calcification of brachial arteries in HD patients [23] but not with aortic calcification. In our study, FGF-23 serum levels were increased in all patients but particularly in the case of severe VCs. Even if the direct action of FGF-23 on VCs was not demonstrated, FGF-23 may reflect the presence of an unfavourable mineral metabolism environment in HD patients, i.e. chronic hyperphosphataemia, high BALP serum levels, hypercalcaemia and the use of excessive vitamin D derivatives.

In contrast with other studies, few associations were observed in our study between VCs, mineral metabolism and related treatments. Indeed, VCs have been associated with secondary hyperparathyroidism (SHPT) [36] or adynamic bone diseases [10,37], hyperphosphataemia [38,39], high Ca $\times$ P product [40], excessive calcium salt intake [10,14–16] and high dialysate calcium concentration [41]. Even if the Kidney Disease Outcomes Quality Initiative (KDOQI) recommended the level of dialysate calcium as 1.25 mmol/l [42], especially in the case of calcium-based phosphate binders and i.v. active vitamin D administration, this opinion is not supported by any evidence. In our centre, the dialysate calcium concentration was set to 1.75 and 1.6 mmol/l in the 1980s and 1990s, respectively. After the year 2000, it was generally set to 1.5 mmol/l, which is currently the most common prescription in French dialysis centres. The rationale for this standard dialysate calcium concentration is few oral calcium prescriptions and low intake of calcium through food (mean 600 mg/day) generally

observed in our centre. We did not administer $CaCO_3$ in the case of low iPTH serum levels, except after surgical parathyroidectomy with hypocalcaemia, but did so in some cases of SHPT. The deleterious role of calcium salts previously reported in some retrospective studies [14,15] or prospectively compared to sevelamer [43] may be related to adynamic bone diseases [37].

iPTH, whole PTH and bone marker serum levels were not associated with VCs in our patients. It is hypothesized that some of these risk factors display a J-curve with an increased risk of VCs for both higher and lower values. We failed to find any relationship between the VC scores and the time or the intensity of the dialysis sessions. Due to the efficient dialysis, the mean phosphate serum levels in our study were lower than those reported by London *et al.* [10] (mean phosphate level, 1.4 mmol/l versus 1.9 mmol/l, respectively), which may explain the lack of a relationship between the phosphate levels and VCs in our study. Yen *et al*. have reported a non-significant increase in CACs in younger HD patients 1 year after conversion to nocturnal daily HD [44]. Serum phosphate levels decreased significantly leading to cessation of the administration of calcium-based phosphate binders in most cases. These two conditions have failed to reverse VCs; however, they have probably slowed down their evolution.

Serum levels of 25(OH)D were not related with the VC score, as reported by London *et al.* [45] because we had been administering $25(OH)D_3$ to all the vitamin D-deficient HD patients since 1 year. Nevertheless, 90% of HD patients had been previously vitamin D deficient. Alfacalcidol, largely administered in the case of SHPT in our study, was less frequently prescribed in more severely calcified patients in the recent years. The same is true for calcium salts, which was mainly due to the nephrologists' awareness of the KDOQI recommendation in the case of calcified HD patients. Even if the role of vitamin D in the genesis of VCs has not been clearly demonstrated in large clinical human studies, nephrologists fear the potential increase in the risk of VCs in calcified patients. As for calcium salts, the potential toxicity of vitamin D may be related to adynamic bone diseases and higher Ca $\times$ P product [46].

It is hypothesized that our previous strategy, i.e. including higher dialysate calcium and more calcium salts in prescriptions, may have had an impact on the VC score observed in vintage patients.

The relatively small size of our sample did not allow us to separate cardiovascular causes from the overall mortality. However, in our study, the effect of VCs on the overall mortality is obvious for patients with severe calcification scores with a relative risk of 2 for patients with a VC score of 3 as compared to those with a score of 0.

Our study has some limitations. The semi-quantitative radiological score used was original and has not been validated elsewhere. The small number of patients in each group may influence the statistical significances. No bone histomorphometry was systematically performed and the information provided by bone markers on the bone turnover has not been completely validated, mostly for β-crosslaps. Comparison with a standard 3 $\times$ 4 h dialysis population using the same strategy was not possible; however, we did not observe any influence of the dialysis schedule on the VC score. The cross-sectional nature of our study did not allow the identification of all the factors associated with VC progression; in fact, we do not positively know whether our intensive dialysis strategy associated with the decreased calcium load is effective in preventing the worsening of vascular damage.

Conclusion

Using a plain radiological VC score, our study has shown the high prevalence of VCs in HD patients treated with a long and intensive dialysis schedule with good control of hypertension and hyperphosphataemia using mainly sevelamer. The high incidence of VCs in new HD patients and the previous excess calcium prescriptions may explain the apparent weak effect of such intensive dialysis. Besides, the VC score was associated with many factors, particularly older age and diabetes, that are non-modifiable. FGF-23 appears to be the only mineral metabolism-related factor independently associated with VCs. It is not clear whether it is an actor or a witness of an unfavourable uraemic milieu. With our study, we confirm the relationship between VC and mortality. These results may lead nephrologists to assess the peripheral VC scores of CKD and ESRD patients by a method that is widely available and relatively inexpensive and to precociously optimize the treatment of all potentially modifiable cardiovascular risk factors.

Conflict of interest statement. None declared.

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