

*Original Article*

## A plain X-ray vascular calcification score is associated with arterial stiffness and mortality in dialysis patients

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### Abstract

**Background.** Vascular calcifications are highly prevalent in dialysis patients and are associated with arterial stiffness and mortality. The use of simple and inexpensive methods to evaluate arterial stiffness and vascular calcifications is desired. The objective of this study was to evaluate the relationship of a simple vascular calcification score (SVCS) with pulse wave velocity (PWV) and pulse pressure (PP) and to evaluate their association with all-cause mortality.

**Methods.** 101 haemodialysis patients (71 men; 19% diabetic) were evaluated. At baseline, arterial stiffness was measured by PP and by PWV with Complior. SVCS was evaluated in plain X-ray of pelvis and hands.

**Results.** During a 43-month observational period, 31 patients died. By Kaplan–Meier analysis, SVCS >3 ( $P = 0.001$ ), PP > 70 mmHg ( $P = 0.001$ ) and PWV > 10.5 m/s ( $P < 0.001$ ) were found to be associated with lower cumulative survival. Adjusting for multiple variables, association with mortality was maintained for SVCS >3 (HR = 3.308,  $P = 0.032$ ) and PP > 70 mmHg (HR = 3.227,  $P = 0.031$ ) in all patients and for PWV > 10.5 m/s (HR = 2.981,  $P = 0.047$ ) in non-diabetic patients. Age ( $P < 0.001$ ), systolic pressure ( $P = 0.004$ ) and SVCS > 3 ( $P = 0.032$ ) were associated with PWV. Diabetes ( $P = 0.031$ ), calcium carbonate dose ( $P = 0.009$ ) and SVCS > 3 ( $P = 0.012$ ) were associated with PP.

**Conclusion.** Higher SVCS, PWV and PP were associated with higher mortality in this population. SVCS was associated with arterial stiffness. Simple and inexpensive methods such as PP or SVCS may be used to detect mortality risk and to provide important information that may be relevant for guiding therapeutic intervention in dialysis patients.

**Keywords:** arterial stiffness; haemodialysis; mortality; vascular calcification

### Introduction

It is clearly demonstrated that dialysis patients have a much higher cardiovascular mortality when compared with the general population [1]. This high cardiovascular risk in chronic kidney disease (CKD) patients is only partly explained by traditional risk factors [2]. Vascular calcifications evaluated by ultrasonography [3], plain X-ray [4], electron beam computed tomography [5] or multislice computed tomography [6] have been associated with mortality in dialysis patients. KDIGO has recommended a new classification for mineral and bone disorder of chronic kidney disease patients (CKD-MBD) that includes the evaluation of vascular calcifications [7]. Arterial stiffness is an alteration of the arterial wall properties with multiple causes, some of which are old age, diabetes, hypertension and medial calcification. All these features are highly prevalent in dialysis patients, and arterial stiffness is a common finding in this population. In dialysis patients, arterial stiffness has been associated with all-cause and cardiovascular mortality [8], but this finding is not universal [9]. One of the KDIGO Imaging Work Group research questions is the evaluation of the relationship between the radiological vascular calcification assessment and the measurement of vascular stiffness by pulse wave velocity (PWV) and pulse pressure (PP) [7]. Vascular calcifications evaluated by ultrasonography [10] and by plain X-ray [11] have already been associated with arterial stiffness in dialysis patients. We developed a simple vascular calcification score (SVCS) evaluated in plain X-ray of pelvis and hands that was a predictor of cardiovascular mortality and was associated with higher risk of coronary disease, peripheral artery disease and cardiovascular hospitalizations [12]. The objective of this study was to evaluate the relationship of this SVCS with PWV and PP and to evaluate the association of vascular calcification and arterial stiffness with all-cause mortality in our patients.

### Study design

This study was a cross-sectional analysis performed in a group of prevalent haemodialysis (HD) patients to evaluate the relationship between a SVCS evaluated in plain X-ray

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with PWV and PP. This group of patients was followed prospectively during a period of 43 months for evaluation of the impact of vascular calcifications and arterial stiffness in all-cause mortality.

### Population

One hundred and one patients (71 men and 30 women), treated with HD for at least 6 months, with a mean age of  $58.8 \pm 15.5$  (26–89) years and mean HD duration of  $55.8 \pm 54.8$  (6–289) months, from a single HD unit, accepted to participate in this study that was approved by the institutional scientific board; 19 patients (18.8%) were diabetic. In the 6 months before PWV evaluation, 89 and 41 patients were treated with calcium carbonate and calcitriol, respectively. The mean calcium carbonate and calcitriol prescribed doses in these patients were  $2.5 \pm 1.3$  [1–8] g/day and  $1.1 \pm 0.6$  [0.25–3]  $\mu$ g/week, respectively. Oral or intravenous calcitriol was administered in 25 and 16 patients, respectively. No patients received sevelamer or cinacalcet as they were not available at the time of the study; 71 patients received anti-hypertensive treatment (one single medication in 25 patients and two different medications in 46 patients). At baseline, diagnosis of vascular disease was based on a query answered by the attending physicians, concerning previous clinical manifestations and test results, according to the usual standard of care. Coronary artery disease was diagnosed if the patient had a positive stress test, had suffered a myocardial infarction or had been submitted to a percutaneous coronary intervention or coronary bypass surgery. Diagnosis of cerebral vascular disease was based on the occurrence of stroke or transient ischaemic attack or the detection of an old cerebral infarction in computed tomography. Peripheral arterial disease was diagnosed if there was claudication, ischaemic ulcers, lower limb amputation, revascularization or diagnosis of obstruction by Doppler or angiography. Coronary artery disease was diagnosed in 20 patients (19.8%), peripheral artery disease was present in 16 patients (15.8%) and cerebral vascular disease was identified in 4 patients (4%). During a period of 43 months, 31 patients died and 8 patients received a kidney transplant. No patient was lost for follow-up.

### Vascular calcifications and arterial stiffness

Vascular calcifications were evaluated at baseline by a single observer blind to clinical data, in plain X-ray of pelvis and hands by a method previously described in detail [12]. Pelvis films were divided into four sections by two imaginary lines: a horizontal line over the upper limit of both femoral heads and a median vertical line over the vertebral column. Hands films were divided for each hand by a horizontal line over the upper limit of the metacarpal bones. Pelvis films evaluated iliac and femoral arteries (ileo-femoral score) and hands films evaluated radial and digital arteries (hands score). Any vascular calcification lining the vessel walls, either in an irregular pattern or in a linear pattern, was considered. The presence of vascular calcifications in each section was rated as 1 and its absence as 0. The total vascular calcification score was the sum of

all sections and ranged from 0 to 8. Arterial stiffness was evaluated by PWV and by PP. PWV was evaluated twice, at baseline, 24 h after a HD session, using a non-invasive automated device, Complior. Complior measures the propagation of the same individual pulse wave between two arterial points. The proximal and distal sensors were located in the carotid and femoral arteries, respectively. The velocity of the pulse wave is calculated with the formula distance/time, where the distance corresponds to the distance between the suprasternal notch and the femoral artery pulse at the groin, and the time corresponds to the time that takes a pulse wave that originates in the heart to reach the femoral artery. The Complior software calculates the velocity of conduction. PP was evaluated by the formula (systolic blood pressure – diastolic blood pressure). The mean values of PP were time averaged for the 6-month period preceding PWV evaluation, corresponding to the mid-week HD session in the day of the monthly blood sample collection. PP was calculated from the predialysis evaluation of blood pressure.

### Biochemical analysis

Mid-week Kt/V and predialysis serum levels of the following biochemical parameters were evaluated and time averaged for the 6 months preceding the evaluation of PWV. Kt/V, Ca, P, Ca  $\times$  P product, alkaline phosphatase, albumin and C-reactive protein (CRP) were evaluated every month. Ca levels were adjusted to albumin levels. Total intact iPTH (iPTH) was evaluated every 3 months by immunochemiluminescence (three evaluations per patient) using a second generation assay, Elecsys 2010 from Roche Diagnostics, Basel, Switzerland. CRP was evaluated with an immunoturbidimetric assay. Total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides were evaluated twice.

### Statistical analysis

Data are presented as frequencies for categorical variables and mean values with SD for continuous variables. Comparison between groups was performed by the independent samples *t*-test, chi-square and Fisher exact test when appropriate. Correlation was performed using the Pearson correlation coefficient. Survival curves were estimated by Kaplan–Meier analysis and compared by the log-rank test. A Cox regression model was used to identify predictors of mortality. Variables in this model, besides the vascular calcification score, PWV and PP, were age, HD duration, diabetes, presence of previous vascular disease, body mass index (BMI), systolic pressure and calcitriol and calcium carbonate doses. Separate Cox regression models using the enter method were applied to evaluate the adjusted hazard ratio mortality of vascular calcification score, PWV and PP. Independent association of vascular calcification with PWV and with PP was evaluated in linear regression models adjusting for age, HD duration, diabetes, cholesterol levels, systolic pressure, BMI, and calcitriol and calcium carbonate doses. The absence of collinearity among explanatory factors was checked in all models based on standard procedures. The receiver operating characteristic (ROC) curve

**Table 1.** Demographic, biochemical and clinical factors

	All patients	Pulse wave velocity (m/s)		Pulse pressure (mmHg)		Plain X-ray score	
		≤10.5	>10.5	≤70	>70	≤3	>3
<i>N</i> (%)	101	61 (60%)	40 (40%)	68 (67%)	33 (33%)	42 (42%)	58 (58%)
Age (years)	58.9 ± 15.5	53.1 ± 15.2	<b>67.6 ± 11.3**</b>	56.2 ± 15.8	<b>64.3 ± 13.6*</b>	51.1 ± 15.9	<b>64.4 ± 12.7**</b>
Male gender ( <i>N</i> , %)	71 (70%)	45(74%)	26 (65%)	47 (69%)	24 (73%)	27 (64%)	44 (75%)
Diabetes ( <i>N</i> , %)	19 (19%)	6 (10%)	<b>13 (33%)*</b>	8 (12%)	<b>11 (33%)*</b>	3 (7%)	<b>16 (27%)*</b>
HD duration (months)	55.8 ± 54.8	56.7 ± 59.0	57.4 ± 45.6	54.2 ± 51.8	62.7 ± 58.3	47.8 ± 48.6	63.5 ± 56.8
Systolic pressure (mmHg)	145.1 ± 25.7	141.3 ± 24.4	151.0 ± 26.8	133.3 ± 19.8	<b>169.4 ± 18.5**</b>	136.5 ± 21.4	<b>151.3 ± 26.9**</b>
Diastolic pressure (mmHg)	82.7 ± 13.7	84.2 ± 14.9	80.6 ± 11.5	81.0 ± 14.0	86.3 ± 12.5	82.2 ± 13.7	83.1 ± 13.8
Mean arterial pressure (mmHg)	103.5 ± 16.3	103.2 ± 17.1	104.0 ± 15.1	98.5 ± 15.3	<b>114.0 ± 13.1**</b>	100.3 ± 15.5	105.8 ± 16.6
Ca (mg/dL)	9.3 ± 0.9	9.3 ± 0.9	9.4 ± 0.8	9.2 ± 0.9	9.5 ± 0.8	9.2 ± 1.0	9.4 ± 0.7
P (mg/dL)	5.2 ± 1.4	5.4 ± 1.3	4.9 ± 1.5	5.4 ± 1.4	4.9 ± 1.4	5.4 ± 1.2	5.1 ± 1.5
iPTH (pg/mL)	476.4 ± 442	526.2 ± 483.7	400.3 ± 362.2	495.7 ± 441.9	436.4 ± 446.5	452.5 ± 394.3	493.3 ± 475.7
Total cholesterol (mg/dL)	203.4 ± 49.3	201.6 ± 49.8	206.4 ± 49.1	208.4 ± 50.0	192.0 ± 46.7	207.4 ± 49.5	200.6 ± 49.4
Albumin (g/dL)	4.4 ± 0.6	4.4 ± 0.7	4.3 ± 0.4	4.4 ± 0.6	4.4 ± 0.4	4.4 ± 0.7	4.4 ± 0.4
CRP (mg/dL)	1.28 ± 0.6	1.23 ± 0.3	1.35 ± 0.8	1.25 ± 0.2	1.33 ± 0.9	1.25 ± 0.36	1.31 ± 0.7
Kt/V	1.41 ± 0.2	1.43 ± 0.2	1.38 ± 0.2	1.40 ± 0.2	1.41 ± 0.1	1.43 ± 0.2	1.38 ± 0.2
Body mass index (Kg/cm <sup>2</sup> )	24.2 ± 4.8	24.1 ± 5.2	22.9 ± 3.9	24.8 ± 5.1	23.1 ± 4.0	24.9 ± 5.7	23.7 ± 4.1
Ca dose (g/day)	2.45 ± 1.31	2.47 ± 1.22	2.41 ± 1.49	2.33 ± 1.16	2.72 ± 1.61	2.52 ± 1.55	2.39 ± 1.13
Calcitriol dose (µg/week)	1.14 ± 0.6	1.13 ± 0.66	1.15 ± 0.52	1.14 ± 0.65	1.13 ± 0.53	1.17 ± 0.74	1.12 ± 0.53
Anti-HTA drugs (≥2) ( <i>N</i> , %)	46 (46%)	26 (43%)	20 (50%)	20 (29%)	<b>26 (79%)**</b>	12 (29%)	<b>34 (74%)**</b>
CAD ( <i>N</i> , %)	20 (20%)	7 (12%)	<b>13 (33%)*</b>	12 (18%)	8 (24%)	7 (17%)	13 (22%)
PAD ( <i>N</i> , %)	16 (16%)	4 (7%)	<b>12 (30%)*</b>	4 (6%)	<b>12 (36%)**</b>	2 (5%)	<b>14 (24%)*</b>
Vascular disease ( <i>N</i> , %)	32 (32%)	11 (18%)	<b>21 (53%)**</b>	16 (24%)	<b>16 (49%)*</b>	8 (19%)	<b>24 (41%)*</b>
All-cause death ( <i>N</i> , %)	31 (31%)	10 (16%)	<b>21 (53%)**</b>	14 (20%)	<b>17 (52%)**</b>	5 (12%)	<b>26 (44%)**</b>

CRP = C-reactive protein; CAD = coronary artery disease; PAD = peripheral artery disease.

\* $P < 0.05$ ; \*\* $P < 0.01$ .

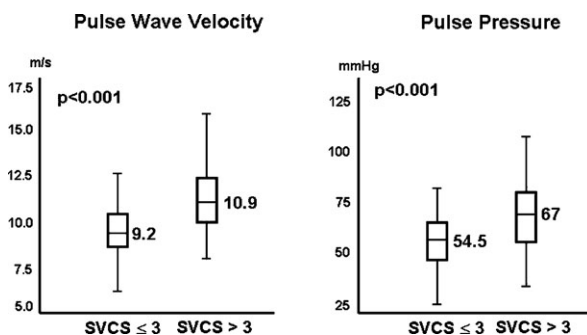
analysis allowed the identification of the best cut-off values in relation with all-cause mortality for plain X-ray score (SVCS >3), PWV (>10.5 m/s) and PP (>70 mmHg). These cut-off values were used to compare groups in univariate analysis and to compare survival.

Statistical analyses were performed with the SPSS system 15.0 (SPSS Inc., Chicago, IL, USA) and with the Medcalc program version 6.0 (Medcalc software, Mariakerke, Belgium). For all comparisons and statistical tests, a  $P$ -value < 0.05 implied the rejection of the null hypothesis and the result was considered statistically significant.

## Results

### Descriptive and univariate analysis

In this group of 101 patients, vascular calcifications were present in 77 patients. A SVCS > 3, a PWV > 10.5 m/s and a PP > 70 mmHg were observed in 59, 42 and 33 patients, respectively. In univariate analysis (Table 1), higher PWV, higher PP and higher vascular calcification score were associated with older age and with higher prevalence



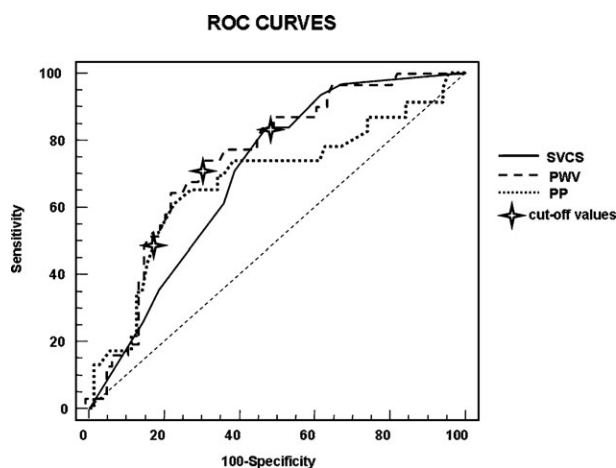
**Fig. 1.** A simple vascular calcification score >3 was associated with higher pulse wave velocity and with higher pulse pressure.

of diabetes, vascular disease and all-cause mortality. The calcium carbonate dose was correlated with systolic pressure ( $r = 0.277$ ;  $P = 0.005$ ) and with PP ( $r = 0.226$ ;  $P = 0.023$ ). Patients with SVCS > 3, when compared with patients with SVCS ≤ 3, had a higher PWV (11.2 ± 1.9 versus 9.3 ± 1.5 m/s;  $P < 0.001$ ) and a higher PP (68.2 ± 20.4 versus 54.3 ± 13 mmHg,  $P < 0.001$ ) (Figure 1).

**Table 2.** Vascular calcification and arterial stiffness (linear regression)

Dependent variable	Independent variables	B	CI	Significance	R <sup>2</sup>
Pulse wave velocity (all patients)	Age	0.055	0.032–0.079	<0.001	0.424
	Systolic pressure	0.021	0.007–0.035	0.004	
	SVCS >3	0.845	0.074–1.615	0.032	
Pulse pressure (all patients)	Diabetes	10.102	0.926–19.278	0.031	0.268
	Calcium carbonate (g/day)	3.281	0.844–5.719	0.009	
	SVCS >3	10.103	2.315–17.890	0.012	

SVCS = simple vascular calcification score; PP = pulse pressure; PWV = pulse wave velocity.



**Fig. 2.** ROC curves of simple vascular calcification score, pulse wave velocity and pulse pressure in relation with all-cause mortality.

#### Factors independently associated with PWV and with PP

In all patients, using linear regression with the enter method and adjusting for multiple factors (Table 2), a higher vascular calcification score was directly associated with PWV ( $P = 0.032$ ) and with PP ( $P = 0.012$ ). Other factors explaining PWV were age ( $P < 0.001$ ) and systolic pressure ( $P = 0.004$ ). Diabetes ( $P = 0.031$ ) and calcium carbonate dose ( $P = 0.009$ ) were directly associated with PP.

#### ROC curve analysis of mortality

During a 43-month observational period, 31 (30.7%) patients died. All-cause mortality was associated with a SVCS >3 (AUC = 0.701; 95% CI [0.602–0.788]; 84% sensitivity, 53% specificity, 88% negative predictive value and 1.78 positive likelihood ratio), with a PWV >10.5 m/s (AUC = 0.738; 95% CI [0.641–0.820]; 71% sensitivity, 69% specificity, 85% negative predictive value and 2.26 positive likelihood ratio) and with a PP >70 mmHg (AUC = 0.640; 95% CI [0.539–0.733]; 48% sensitivity, 81% specificity, 78% negative predictive value and 2.61 positive likelihood ratio) (Figure 2). There was no difference in the AUC between ROC curves.

#### Cumulative survival and all-cause mortality risk

Lower cumulative survival (Figure 3) was observed in patients with a SVCS >3 (32.7 versus 40.8 months; log

rank = 10.8;  $P = 0.001$ ), with a PP >70 mmHg (30.9 versus 38.8 months; log rank = 10.8;  $P = 0.001$ ) and with a PWV >10.5 m/s (31.3 versus 39.3; log rank = 13.3;  $P < 0.001$ ). In diabetic patients, higher PWV was not associated with higher mortality: 4 deaths in 6 patients with PWV ≤10.5 m/s (67%) versus 8 deaths in 13 patients with PWV >10.5 m/s (62%). In Cox regression analysis, using the enter method (Table 3), the mortality-adjusted hazard ratio was 3.308 ( $P = 0.032$ ) for SVCS >3, 3.227 ( $P = 0.031$ ) for PP > 70 mmHg in all patients and was 2.981 ( $P = 0.047$ ) for PWV >10.5 m/s in non-diabetic patients. Entering vascular calcification score, PWV and PP in the same model and using the enter method, SVCS > 3 (HR = 4.247,  $P = 0.015$ ), PP > 70 mmHg (HR = 3.795,  $P = 0.031$ ), lower BMI (HR = 0.856,  $P = 0.017$ ) and vascular disease at baseline (HR = 2.551,  $P = 0.047$ ) were associated with mortality (Table 4).

## Discussion

In general population, it was demonstrated that, in patients older than 60 years of age, higher PP was associated with higher cardiovascular risk [13]. In dialysis patients it was demonstrated that a higher PP evaluated before or after HD was associated with higher mortality in non-diabetic patients [14] or in all patients [15] and that higher aortic PWV was associated with mortality [8]. Vascular calcifications, evaluated by different methodologies [3–6,12], have been associated with mortality in dialysis patients. In this study, we tried to answer one of the research questions suggested by the KDIGO Imaging Work Group: the evaluation of the relationship between the radiological vascular calcification assessment and the measurement of vascular stiffness by PWV and by PP [7]. Vascular calcifications evaluated by ultrasonography have already been associated with increased stiffness of large elastic-type arteries [10]. The Kauppila score, [16] evaluating calcifications in the abdominal aorta, which is an elastic artery, was the first plain X-ray calcification score to be correlated with arterial stiffness, evaluated by carotid-femoral PWV [11]. In this study, we used a SVCS evaluated in plain X-ray of pelvis and hands that has been previously associated with higher cardiovascular mortality, cardiovascular disease and cardiovascular hospitalizations [12]. We verified that this score, although evaluating only muscular arteries, was associated both with carotid-femoral PWV and with PP. In the same dialysis population,

**Table 3.** Adjusted hazard ratio of all-cause mortality (Cox regression)

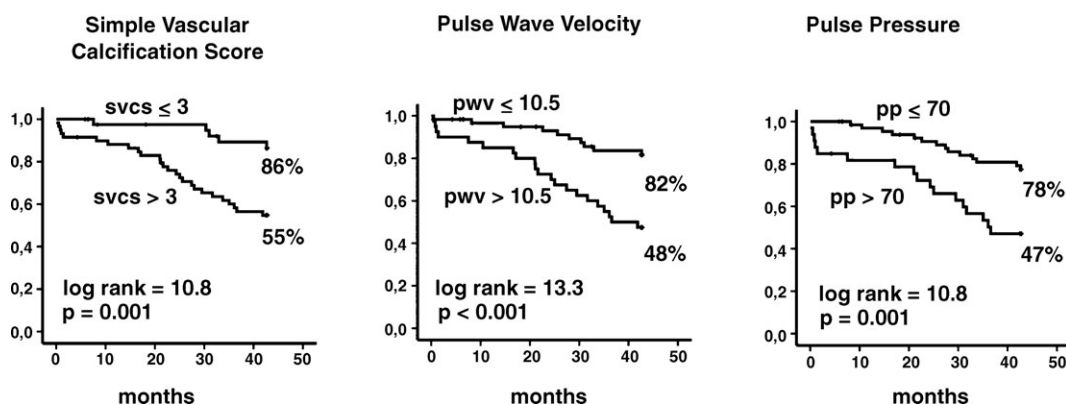
	Independent variables	B	HR	CI	Significance
All patients	SVCS >3	1.196	3.308	1.109–9.863	0.032
All patients	PP >70 mmHg	1.171	3.227	1.114–9.347	0.031
Non-diabetic patients	PWV >10.5 m/s	1.092	2.981	1.013–8.775	0.047

SVCS = simple vascular calcification score; PP = pulse pressure; PWV = pulse wave velocity; HR = adjusted hazard ratio.

**Table 4.** Predictors of all-cause mortality (Cox regression)

Dependent variable	Independent variables	B	HR	CI	Significance
All-cause mortality (all patients)	Age	0.004	1.004	0.966–1.044	0.824
	HD duration (months)	0.000	0.999	0.992–1.006	0.805
	Diabetes	0.348	1.416	0.508–3.948	0.506
	Vascular disease at baseline	0.936	<b>2.551</b>	1.014–6.419	<b>0.047</b>
	Systolic pressure (mmHg)	−0.022	0.978	0.955–1.002	0.077
	Body mass index (kg/cm <sup>2</sup> )	−0.156	<b>0.856</b>	0.753–0.972	<b>0.017</b>
	Calcium carbonate (g/day)	−0.100	0.905	0.651–1.259	0.554
	Calcitriol (µg/week)	−0.161	0.851	0.455–1.594	0.615
	SVCS >3	1.446	<b>4.247</b>	1.319–13.673	<b>0.015</b>
	PP >70 mmHg	1.334	<b>3.795</b>	1.132–12.722	<b>0.031</b>
	PWV >10.5 m/s	−0.026	0.974	0.367–2.589	0.958

SVCS = simple vascular calcification score; PP = pulse pressure; PWV = pulse wave velocity; HR = adjusted hazard ratio.

**Fig. 3.** A simple vascular calcification score >3, a pulse wave velocity >10.5 m/s and a pulse pressure >70 mmHg were associated with lower survival.

higher vascular calcification score, higher PWV and higher PP were associated with mortality with comparable hazard ratios and with similar AUC in ROC curve analysis. In our study, PWV was an independent predictor of mortality only in non-diabetic patients, probably because, in diabetic patients, mortality was equally high with higher or lower PWV. In a study evaluating a large cohort of HD patients, Tozawa *et al.* [14] observed that PP was also a predictor of mortality only in non-diabetic patients. Covic *et al.* [9] verified an opposite situation: in a group of young HD patients with a low prevalence of cardiovascular disease, arterial stiffness evaluated by the augmentation index was not a predictor of mortality. PWV evaluation requires a specific device and is not widely available. In our study, simple and inexpensive methods such as the evaluation of PP or the assessment of the SVCS with plain X-ray were enough to detect higher cardiovascular risk. Diagnosis of arterial stiffness and vascular calcification has the advantage of also providing important information that can be used for

guiding therapeutic intervention in dialysis patients. Identification of patients with higher PP may orientate the choice of anti-hypertensive treatment with special indication for inhibition of the renin–angiotensin axis and avoidance of inappropriate reduction of diastolic blood pressure that may threaten coronary reserve [17]. At the present time, it also seems possible to interfere in some factors associated with the development of vascular calcifications. Some studies in dialysis patients have already demonstrated that vascular calcifications may progress or remain stable depending on the control of mineral metabolism alterations [5, 18] and that phosphate binder choice may have an impact on mortality [5]. London *et al.* showed an association between vascular calcifications and low bone turnover [19] and found a significant interaction between calcium-containing phosphate binders and aortic calcification and stiffness in the presence of adynamic bone disease [20]. The presence or extension of vascular calcifications may be an indication for an intensive hyperphosphataemia control, for an adequate choice of

phosphate binder and for avoidance of PTH oversuppression. In several studies, association of a calcium carbonate dose with vascular calcifications [3–5,18,20,21] and with PWV [8,20] has already been described and in our patients we have also verified a correlation between the calcium carbonate dose and PP. We have not verified any association between calcium carbonate and calcitriol treatment with survival.

Different methods can be used to evaluate vascular calcifications in dialysis patients. Electron beam computed tomography and multislice computed tomography are considered to be the gold standard for the evaluation of coronary calcifications. They perform a quantitative assessment of coronary calcification that permits the evaluation of calcification progression but are very expensive. Screening vascular calcifications in dialysis patients may be performed by different and inexpensive plain X-ray methods [4,11,12,22] that have the advantage of being easily interpreted by the attending physician. The SVCS and Kauppila score are semi-quantitative scores with cut-off values associated with higher cardiovascular risk. A cardiovascular calcification index using the Kauppila score and valvular calcification evaluated by echocardiography has been demonstrated to be associated with coronary calcification in HD patients [23]. Simpler methods to evaluate vascular calcifications seem to be an attractive option but the final choice would depend on the available tests and on the preference of the nephrologist.

In summary, a SVCS evaluated in plain X-ray and PP were associated with higher mortality in dialysis patients. PWV was associated with higher mortality in non-diabetic patients. In this study, we demonstrate that a SVCS evaluated in plain X-ray of pelvis and hands is associated with the arterial stiffness evaluated by PWV and PP. Identification of vascular calcifications in dialysis patients is included in the classification of CKD-MBD, and simple and inexpensive plain X-ray methods are available for that purpose. Arterial stiffness or the presence of vascular calcifications are an alert sign for an increased mortality risk, and this information may be relevant for guiding therapeutic intervention in dialysis patients, such as selecting the most adequate anti-hypertensive regimen or achieving an effective mineral metabolism management.

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## References

- Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. *Am J Kidney Dis* 1998; 32(5 Suppl 3): S112–S119
- Cheung AK, Sarnak MJ, Yan G *et al.* Atherosclerotic cardiovascular disease risks in chronic hemodialysis patients. *Kidney Int* 2000; 58: 353–362
- Blacher J, Guerin AP, Pannier B *et al.* Arterial calcifications, arterial stiffness, and cardiovascular risk in end-stage renal disease. *Hypertension* 2001; 38: 938–942
- London GM, Guérin AP, Marchais SJ *et al.* Arterial media calcification in end-stage renal disease: impact on all-cause and cardiovascular mortality. *Nephrol Dial Transplant* 2003; 18: 1731–1740
- Block GA, Raggi P, Bellasi A *et al.* Mortality effect of coronary calcification and phosphate binder choice in incident hemodialysis patients. *Kidney Int* 2007; 71: 438–441
- Matsuoka M, Iseki K, Tamashiro M *et al.* Impact of high coronary artery calcification score (CACS) on survival in patients on chronic hemodialysis. *Clin Exp Nephrol* 2004; 8: 54–58
- Moe S, Drüeke T, Cunningham J *et al.* Kidney disease: improving global outcomes (KDIGO). Definition, evaluation, and classification of renal osteodystrophy: a position statement from kidney disease: improving global outcomes (KDIGO). *Kidney Int* 2006; 69: 1945–1953
- Guérin AP, Blacher J, Pannier B *et al.* Impact of aortic stiffness on survival in end-stage renal disease. *Circulation* 1999; 99: 2434–2439
- Covic A, Mardare N, Gusbeth-Tatomir P *et al.* Arterial wave reflections and mortality in haemodialysis patients—only relevant in elderly, cardiovascularly compromised? *Nephrol Dial Transplant* 2006; 21: 2859–2866
- Guérin AP, London GM, Marchais SJ *et al.* Arterial stiffening and vascular calcifications in end-stage renal disease. *Nephrol Dial Transplant* 2000; 15: 1014–1021
- Raggi P, Bellasi A, Ferramosca E *et al.* Association of pulse wave velocity with vascular and valvular calcification in hemodialysis patients. *Kidney Int* 2007; 71: 802–807
- Adragao T, Pires A, Lucas C *et al.* A simple vascular calcification score predicts cardiovascular risk in haemodialysis patients. *Nephrol Dial Transplant* 2004; 19: 1480–1488
- Franklin SS, Larson MG, Khan SA *et al.* Does the relation of blood pressure to coronary heart disease risk change with aging? The Framingham Heart Study. *Circulation* 2001; 103: 1245–1249
- Tozawa M, Iseki K, Iseki C *et al.* Pulse pressure and risk of total mortality and cardiovascular events in patients on chronic hemodialysis. *Kidney Int* 2002; 61: 717–726
- Klassen PS, Lowrie EG, Reddan DN *et al.* Association between pulse pressure and mortality in patients undergoing maintenance hemodialysis. *JAMA* 2002; 287: 1548–1555
- Kauppila LI, Polak JF, Cupples LA *et al.* New indices to classify location, severity and progression of calcific lesions in the abdominal aorta: a 25-year follow-up study. *Atherosclerosis* 1997; 132: 245–250
- Covic A, Gusbeth-Tatomir P, Goldsmith DJ. Arterial stiffness in renal patients: an update. *Am J Kidney Dis* 2005; 45: 965–977
- Chertow GM, Burke SK, Raggi P. Treat to Goal Working Group. Sevelamer attenuates the progression of coronary and aortic calcification in hemodialysis patients. *Kidney Int* 2002; 62: 245G–252G
- London GM, Marty C, Marchais SJ *et al.* Arterial calcifications and bone histomorphometry in end-stage renal disease. *J Am Soc Nephrol* 2004; 15: 1943–1951
- London GM, Marchais SJ, Guérin AP *et al.* Association of bone activity, calcium load, aortic stiffness, and calcifications in ESRD. *J Am Soc Nephrol* 2008; 19(9): 1827–1835
- Goodman WG, Goldin J, Kuizon BD *et al.* Coronary-artery calcification in young adults with end-stage renal disease who are undergoing dialysis. *N Engl J Med* 2000; 342: 1478–1483
- Okuno S, Maeno Y, Maekawa K *et al.* Presence of abdominal aortic calcification is significantly associated with all-cause and cardiovascular mortality in maintenance hemodialysis patients. *Am J Kidney Dis* 2007; 49: 417–425
- Muntner P, Ferramosca E, Bellasi A *et al.* Development of a cardiovascular calcification index using simple imaging tools in haemodialysis patients. *Nephrol Dial Transplant* 2007; 22: 508–514

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