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Original Paper

A Prospective Cohort Study Showing No Association Between Serum Sclerostin Level and Mortality in Maintenance Hemodialysis Patients

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Key Words
Sclerostin • CKD-MBD • Hemodialysis • Mortality • Aortic calcification

Abstract
Background/Aims: Potential relationships between serum sclerostin levels and the levels of bone metabolic markers in maintenance hemodialysis (MHD) patients have yet to be evaluated. This study sought to determine whether serum sclerostin levels are associated with mortality in MHD patients. ***Methods:*** We measured serum sclerostin levels in a Japanese MHD cohort, classified the patients into tertiles according to these levels, and followed their course for a 42-month period. ***Results:*** The cohort consisted of 389 MHD patients and there were 75 deaths. Kaplan-Meier analyses showed that the tertile of serum sclerostin was not associated with mortality risk. Cox analyses showed that there were no significant associations between serum sclerostin level and mortality. ***Conclusion:*** Serum sclerostin level was not an independent predictor of mortality in MHD patients after adjustment for several confounders. However, whether clinical interventions to modulate serum sclerostin levels in MHD patients would improve their survival remains to be determined.

Introduction

Chronic kidney disease-mineral and bone disorder (CKD-MBD) is a major complication of CKD [1] and has been found to predict outcomes in observational studies [2, 3]. However, the mechanisms that might explain the link between CKD-MBD and higher mortality risk

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remain unclear. Molecules synthesized by osteocytes, such as fibroblast growth factor 23 (FGF23), have been shown to be powerful predictors of mortality and cardiovascular events in CKD [4]. Consequently, osteocytes are now recognized as major cells that orchestrate bone remodeling through several molecular mechanisms [5], and the role of osteocytes in the pathophysiology of CKD-MBD has been investigated in recent studies [6].

The glycoprotein sclerostin is synthetized by osteocytes and inhibits the bone anabolic Wnt pathway, which promotes bone formation [7]. Serum sclerostin levels in hemodialysis (HD) patients are elevated, and inversely correlate with both serum parathyroid hormone (PTH) levels and bone formation rates [8]. Moreover, Sabbagh et al. reported that increased bone expression of sclerostin is a common and early event in HD patients [9] and that it plays a role in the pathophysiology of the CKD-MBD, possibly by increasing bone resistance to PTH. Although higher serum sclerostin levels would be expected to be associated with poorer outcomes, in HD patients they have been shown to be associated with improved survival instead [10]. As a result, there is still debate as to whether the circulating sclerostin level can serve as a new marker of CKD-MBD outcome. Moreover, the potential relationships between serum sclerostin levels and the levels of other CKD-MBD markers, such as FGF23, and of sclerostin modulators, such as inflammatory cytokines [11], have yet to be evaluated.

This study assessed whether serum sclerostin levels are associated with mortality in a Japanese MHD cohort that was followed up over 42 months.

Materials and Methods

Study design and subjects

This was a prospective, observational cohort study conducted at a single center in Japan. The subjects were recruited from among patients who had been routinely dialyzed via an arteriovenous fistula in the dialysis unit of Jyoban Hospital in Fukushima, Japan. In this study, an MHD patient was defined as a patient who had been receiving stable HD therapy for at least 6 months. The institutional review board of Jyoban Hospital approved the study protocol (no. 26-1), and the protocol was carried out in accordance with the Declaration of Helsinki guidelines regarding ethical principles for medical research involving human subjects. Written informed consent was obtained from every subject.

HD patients with a malignancy, active inflammation, liver cirrhosis, gastrointestinal bleeding, or severe illness were excluded from participation and were transferred to another dialysis unit for intensive care. The patients enrolled as subjects (n = 403) had undergone stable regular HD with a bicarbonate dialysate. Throughout the follow-up period, all patients received high-flux, high efficiency HD therapy, with a blood flow rate of 250-300 mL/min and dialysate flow rate of 500 mL/min, that was performed with bicarbonate buffer and a polysulfone dialyzer. The schedule was 3.5-4.0 h three times a week. Clinical and biochemical data were collected at baseline and serum samples were stored for further analysis in July 2012. Blood pressure (BP) was measured in the supine position after a 10-15-min rest, and the mean values for the 1- month period preceding enrollment were used in the statistical analysis. Dry weight was targeted to achieve a normotensive edema-free state. Information on history of previous cardiovascular disease (CVD) was collected from the medical records. Diabetes was recorded as present when there was a history of diabetes and/or an HbA1c concentration > 6.5% or prescription of a glucose-lowering agent.

Assessment of aortic arch calcification (AoAC)

Chest X-rays were assessed for the presence of AoAC by using a specific scale as previously described [12]. The scale, which was divided into 16 circumferences, was superimposed over the aortic arch on a chest radiograph and the number of sectors with calcification was divided by 16. The aortic arch calcification score (AoACS) was calculated after multiplication by 100 to express the results as a percentage. This value was used as the indicator of AoAC. Our previous study confirmed that AoACS correlated well with AoAC volume evaluated on a multi-slice CT scan ($r = 0.635$, $p < 0.001$).

Demographic, clinical, and laboratory data

Data on age, sex, diabetes mellitus, history of CVD, and dialysis vintage were collected at enrollment. Body mass index (BMI) was expressed in kg/m^2. Body weight was calculated as dry weight, defined as the post-dialysis weight of normotensive patients with no signs of overhydration. Urea kinetics were assessed by measuring the blood-based dialysis parameter, Kt/V [13], and the mean value of 3 measurements during each of the 3 months before the start of the study was used in the analysis. The normalized protein catabolism rate (nPCR) was used as an indirect indicator of protein intake and was calculated using a formula described previously [14].

Laboratory values for hemoglobin, creatinine, albumin, ferritin, calcium, phosphorus, alkaline phosphatase (ALP), and intact PTH were measured in July 2012. Baseline blood samples were collected before the dialysis session (2 days after the previous dialysis session) at the time of enrollment, and serum samples were frozen and stored for further analyses. Serum calcium values were corrected for the serum albumin concentration by the formula: corrected calcium (mg/dL) = total calcium + (4 – albumin). Serum FGF23 was measured using a sandwich-type enzyme-linked immunosorbent assay (ELISA) for human FGF23 (Kainos Laboratories Inc., Tokyo, Japan) that measures biologically active, full-length FGF23 by using two monoclonal antibodies for FGF23, as described previously [15, 16], and the intra-assay coefficient of variation (CV) of the measurements was <10%. Serum sclerostin was measured using a sandwich-type ELISA performed with commercial reagents (Biomedica Medizinprodukte, Vienna, Austria), as described previously [17], and the intra-assay CV of the measurements ranged from 5% to 7%.

Percentages of patients who were being treated with active vitamin D and phosphate binders were determined from the medical records.

Survival analyses

Overall mortality data were obtained from electronic and paper records. Patients were followed up for survival for 42 months. Patients were censored if they transferred to another dialysis clinic. CVD mortality was defined as death due to any of the following causes: myocardial infarction, arrhythmia, cardiac failure, stroke, ruptured aortic aneurysm. All other causes of death were designated as non-CVD mortality. The causes of death were collected from the medical records and classified as CVD or non-CVD mortalities.

Statistical analyses

Normally distributed continuous variables are reported as means ± standard deviation (SD), and non-normally distributed continuous variables are reported as median with 25th and 75th percentiles (IQRs). Categorical data are reported as percentages. Spearman correlation coefficients were calculated for potential predictor variables to identify confounders. To test for associations between serum sclerostin levels and clinical parameters, we examined serum sclerostin levels in tertiles according to the distribution of values in MHD patients.

Differences between groups were determined using the Kruskal-Wallis test followed by the Steel method, based on variable distributions for continuous variables and by the chi-square test for categorical variables. Fisher's exact test was used to compare proportions. Males and females and diabetics and non-diabetics were compared. In an attempt to determine the clinical factors associated with AoACS, we performed logistic regression analysis and determined odds ratios (ORs). We performed Cox proportional hazards analyses and calculated hazard ratios (HRs) with 95% confidence intervals (95% CIs) for the subsequent follow-up period (42 months), according to the serum sclerostin levels at baseline. Data were censored whenever a patient was transferred to another dialysis center or was lost to follow-up. The Kaplan-Meier method was used to estimate survival probabilities by means of the log-rank test. All analyses were performed by using the JMP for Windows software program (version 11, SAS Institute, Cary, NC, USA). A p value less than 0.05 was considered statistically significant.

Ethics approval and consent to participate

The Institutional Review Board of the Jyoban Hospital approved the study protocol (No. 26-1), and the protocols were carried out in accordance with the Declaration of Helsinki guidelines regarding ethical principles for medical research involving human subjects.

Written informed consent was obtained from all subjects.

Results

A total of 403 MHD patients were enrolled in this study. After excluding 14 patients because of missing data or transfer to another hospital, the remaining 389 patients whose stored serum volume was sufficient to measure sclerostin were included in the study (Fig. 1). The underlying diseases of end-stage renal disease (ESRD) were: diabetic nephropathy (n = 170), chronic glomerulonephritis (n = 126), hypertensive nephrosclerosis (n = 98), polycystic kidney disease (n = 8), chronic pyelonephritis (n = 3), and unknown (n = 6). As shown in Table 1, the median (IQR) age of the study population was 67 (58 – 76) years. Among the 389 patients, 65.3% were male and 45.8% had diabetes.

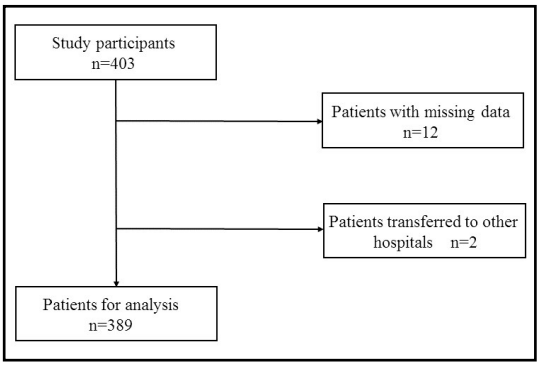


Fig. 1. Selection of the study subjects.

The median (IQR) baseline serum sclerostin level was 211 (143 – 288) pg/mL and the distribution of these levels in the study population is shown in Fig. 2. Because there is no recommended clinical threshold serum sclerostin value, the patients were classified into tertiles according to their sclerostin levels (Table 1).

The baseline clinical and demographic characteristics of the study population in each of the tertiles are shown in Table 1. In comparison with the 1st tertile (serum sclerostin: <161 pg/mL), the 3rd tertile (>260 pg/mL) contained a significantly lower percentage of females (59.2% vs. 21.2%, P < 0.0001) and had higher BMI values (21 vs. 23 kg/m^2, P < 0.0001), lower Kt/V values (1.47 vs. 1.29, P < 0.0001), higher serum FGF23 levels (2.12 vs. 5.31 ng/mL, P = 0.0002), lower serum intact PTH levels (131 vs. 87 pg/mL, P = 0.0013), lower serum ALP levels (257 vs. 217 U/L, P = 0.0001), and lower serum total cholesterol levels (161 vs. 149 mg/dL, P = 0.0079).

Males (265.7 ± 139.7 pg/mL) had significantly higher serum sclerostin levels than females (174.9 ± 93.7 pg/mL). The diabetic and non-diabetic groups had comparable serum sclerostin levels (241.6 ± 123.7 vs. 227.9 ± 139.8 pg/mL). Spearman's correlation analyses showed that the serum sclerostin levels correlated positively with BMI values (r = 0.206, P = 0.0001) and serum phosphorus levels (r = 0.115, P = 0.0324) but correlated negatively with the serum log PTH levels (r = -0.22287, P < 0.0001), ALP levels (r = -0.1895, P = 0.0004), total cholesterol levels (r = -0.1468, P = 0.0062), and Kt/V values (r = -0.2263, P < 0.0001).

There were 75 deaths during the 42-month follow-up period. The main cause of death was CVD (32 patients: congestive heart failure in 16, stroke in 8, myocardial infarction in 5, and arrhythmia in 3), followed by infection (30 patients: pneumonia in 17, sepsis in 13), malignancy in 7, gastrointestinal bleeding in 4, and unknown in 2.

We investigated 42-month mortality according to baseline serum sclerostin concentrations. Kaplan-Meier survival analysis indicated no significant differences among the patient groups defined by serum sclerostin tertiles in all-cause mortality (Fig. 3, P = 0.3492) or CVD mortality (Fig. 4, P = 0.3843). Because of the U-shaped association between the sclerostin levels and mortality, the 2nd tertile was used as the reference group for the Cox proportional hazards analysis. The Cox analyses showed no associations between serum sclerostin levels and mortality after adjustment for various confounders (Table 2). In addition, AoACS was not a significant predictor for all-cause and CVD-related mortality.

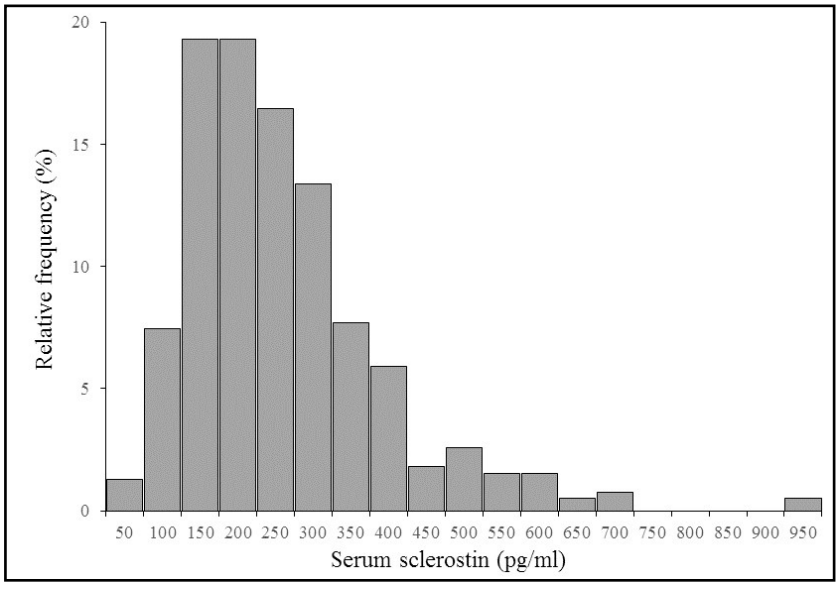
Patients in the 1st tertile had a higher AoACS than those in the 2nd tertile (P = 0.0453, Fig. 5). To examine the clinical factors associated with AoACS, we performed logistic regression analysis. As shown in Table 3, there were significant associations between AoACS and age (OR 1.08, 95% CI 1.05 – 1.11, P < 0.0001), female sex (OR 2.92, 95% CI 1.48 – 5.93, P = 0.0019). dialysis vintage (OR 1.01, 95% CI 1.00 – 1.01, P = 0.0007), presence of diabetes

(OR 3.29, 95% CI 1.89 – 5.83, P < 0.0001), and log FGF23 (OR 1.77, 95% CI 1.10 – 2.88, P = 0.0193).

Table 1. Baseline characteristics according to tertiles of serum sclerostin. CVD, cardiovascular disease; BMI, body mass index; BP, blood pressure; nPCR, normalized protein catabolic rate; FGF23, fibroblast growth factor 23; PTH, parathyroid hormone; ALP, alkaline phosphatase; CRP, C-reactive protein; AoACS, aortic arch calcification score. Corrected calcium was calculated as total calcium + (4.0 – albumin)

Characteristics	All	1st tertile (<161) n = 130	2nd tertile (≥161, <260) n = 127	3rd tertile (≥260) n =132	P-value
Age, years	67 (58–76)	70 (61–77)	66 (54–73)	65 (58 - 77)	0.0521
Female, %	34.7	59.2	23.6	21.2	<0.0001
Dialysis vintage, months	37 (14–88)	36 (15–94)	30 (8–74)	42 (22 - 93)	0.1023
History of CVD, %	10.0	13.1	7.1	9.6	0.2777
Diabetes, %	45.8	40.8	44.1	52.3	0.1571
BMI, kg/m^2	22 (20–24)	21 (19–23)	22 (19–24)	23 (21 - 25)	<0.0001
Systolic BP, mmHg	152.0±21.6	150.3 ± 20.2	153.5 ± 22.2	152.4 ± 22.4	0.5003
Diastolic BP, mmH	78.4±13.6	76.2 ± 13.1	79.8 ± 14.1	79.2 ± 13.5	0.0781
Creatinine, mg/dl	5.91 (4.52–7.61)	6.26 (4.32–8.12)	5.94 (4.76–7.42)	5.70 (4.5275 - 7.5675)	0.6692
Kt/V	1.34 (1.17–1.55)	1.47 (1.26–1.68)	1.31 (1.15–1.48)	1.29 (1.1625 - 1.4975)	<0.0001
nPCR, g/kg/day	0.86 (0.74–0.99)	0.82 (0.71–0.98)	0.87 (0.77–0.99)	0.87 (0.7425 - 0.9975)	0.2939
Sclerostin, pg/ml	211 (143–288)	120 (93–144)	209 (183–236)	337 (285 - 425)	<0.0001
FGF23, ng/ml	4.38 (1.06–12.60)	2.12 (0.59–7.51)	6.27 (1.34–19.17)	5.31 (1.69 – 12.59)	0.0002
Calcium,mg/dl,corrected	8.6 (8.3–9.1)	8.5 (8.2–9.0)	8.6 (8.2–9.1)	8.7 (8.3 - 9.2)	0.1635
Phosphorus, mg/dl	5.2 (4.3–6.0)	4.9 (4.2–5.8)	5.2 (4.5–6.0)	5.2 (4.3 - 6.3)	0.1934
Intact-PTH, pg/ml	109 (60–197)	131 (71–233)	110 (62–200)	87 (42 - 165)	0.0013
ALP, U/l	224 (179–281)	257 (197–318)	212 (173–267)	217 (174 - 267)	0.0001
CRP, mg/dl	0.12 (0.05–0.35)	0.11 (0.04–0.29)	0.15 (0.06–0.46)	0.12 (0.05 - 0.31)	0.2901
Albumin, g/dl	3.8 (3.6–4.0)	3.7 (3.5–3.9)	3.8 (3.6–4.0)	3.8 (3.6 – 4.0)	0.0299
Hemoglobin, g/dl	10.8 (10.2–11.7)	10.8 (10.1–11.8)	10.8 (10.2–11.6)	10.8 (10.2 - 11.7)	0.9116
Ferritin, ng/ml	40 (18–94)	44 (19–105)	38 (21–103)	34 (14 - 78)	0.1230
Total Cholesterol, mg/dl	156 (136–175)	161 (143–189)	156 (134–173)	149 (134 - 168)	0.0079
AoACS, %	12.5 (0–25.0)	12.5 (0–25.0)	0 (0–18.8)	12.5 (0 - 25.0)	0.0453
Vitamin D, %	4.9	7.7	2.4	4.6	0.1368
Calcium carbonate (%)	68.1	54.6	69.3	80.3	<0.0001
Sevelamer hydrochloride (%)	12.6	10.0	15.0	12.9	0.4842
Lanthanum carbonate (%)	33.7	32.3	30.7	37.9	0.4375
Other phosphate binder (%)	17.0	12.3	18.1	20.5	0.1959

Fig. 2. Distribution of serum sclerostin concentrations.



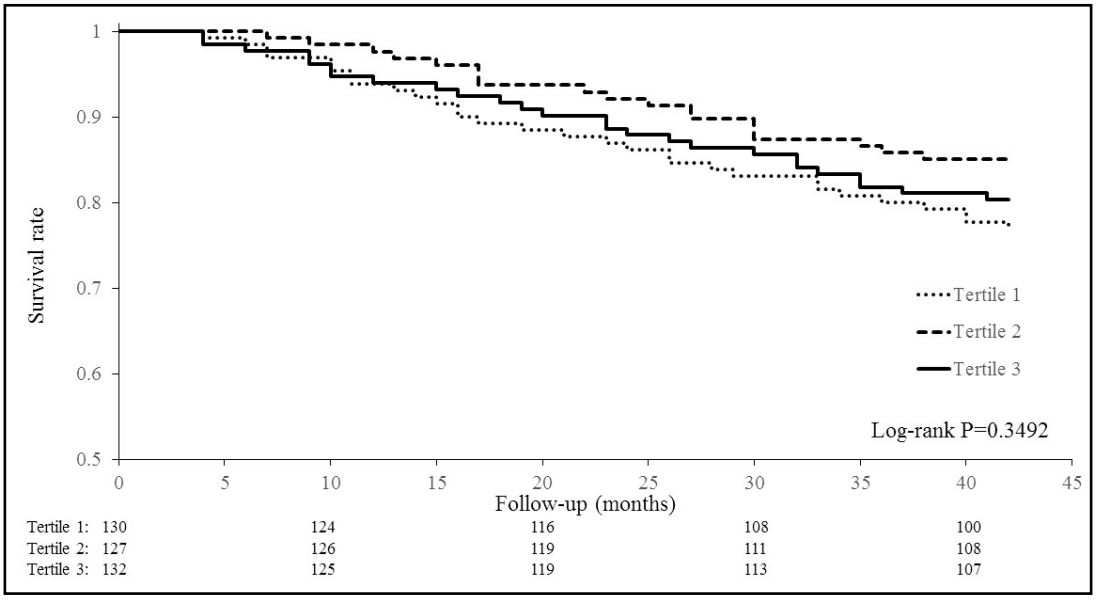


Fig. 3. Kaplan-Meier survival analysis for all-cause mortality at 42 months according to baseline serum sclerostin level tertiles.

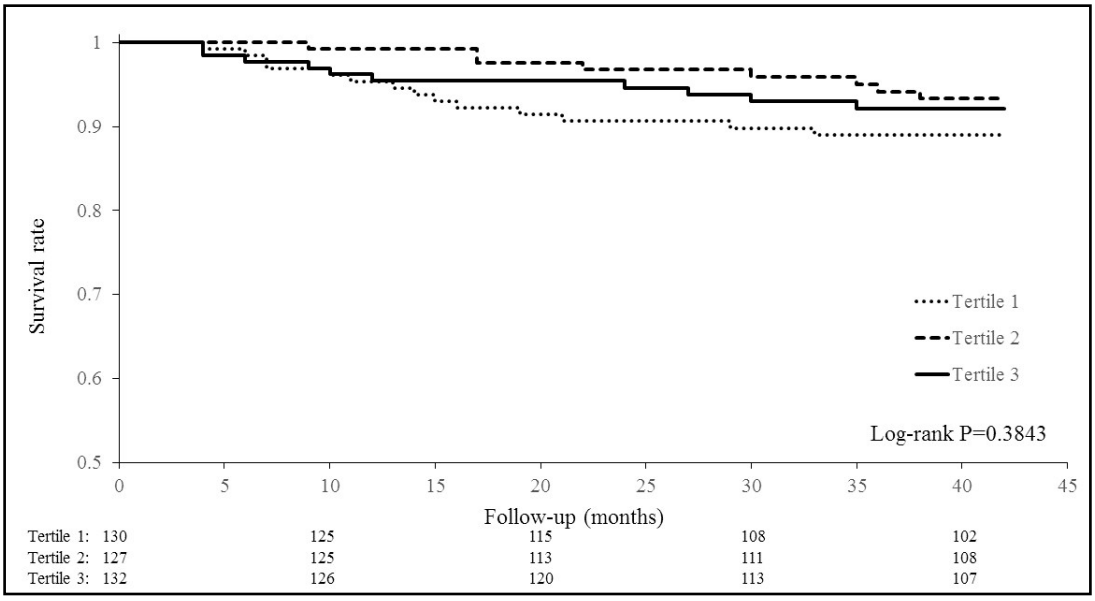


Fig. 4. Kaplan-Meier survival analysis for cardiovascular disease (CVD) mortality at 42 months according to baseline serum sclerostin level tertiles.

Table 2. Independent factors associated with all-cause and CVD-related mortality. Adjusted 1: adjustments for age and sex. Adjusted 2: additional adjustments for BMI, Kt/V, diastolic BP, total cholesterol, phosphorus, ALP, Log-iPTH, Dialysis vintage, Diabetes, Albumin

Parameter	Odds ratio (95% CI)	P-value
All-cause mortality		
Adjusted 1		
First tertile	1.60 (0.89–2.96)	0.1196
Second tertile	1 (ref)	-
Third tertile	1.23 (0.68–2.26)	0.4925
AoACS	1.07 (0.98–1.64)	0.1287
Adjusted 2		
First tertile	1.39 (0.0.73–2.69)	0.3215
Second tertile	1 (ref)	-
Third tertile	1.09 (0.56–2.14)	0.7980
AoACS	1.06 (0.95–1.17)	0.3129
CVD mortality		
Adjusted 1		
First tertile	1.72 (0.71–4.49)	0.2318
Second tertile	1 (ref)	-
Third tertile	1.16 (0.46–3.06)	0.7483
AoACS	1.10 (0.96–1.25)	0.1390
Adjusted 2		
First tertile	1.76 (0.67–4.93)	0.2495
Second tertile	1 (ref)	-
Third tertile	1.16 (0.42–3.34)	0.7774
AoACS	1.11 (0.95–1.28)	0.1644

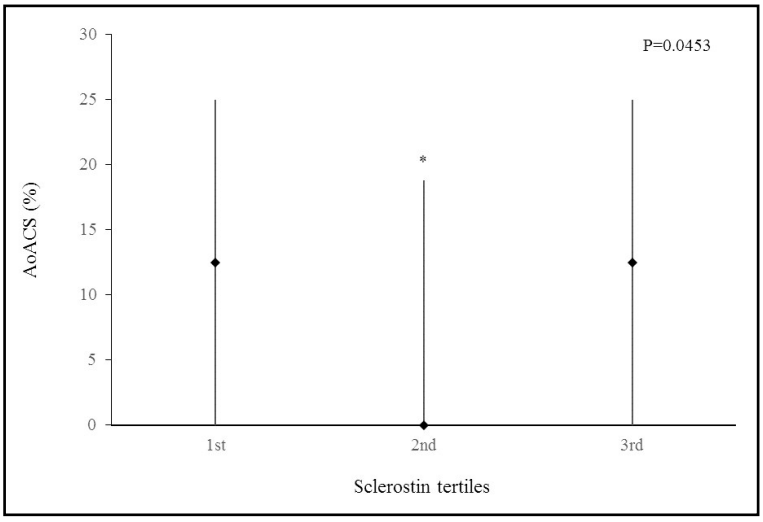


Fig. 5. Aortic arch calcification scores (AoACSs) according to the serum sclerostin tertile. Diamond: median. Asterisk: P<0.05 vs. 1st tertiles.

Discussion

This study found no significant differences between baseline serum sclerostin tertiles and mortality in MHD patients during a follow-up period of 42 months. However, we could not rule out the possibility that the serum sclerostin levels in MHD patients may be changeable by clinical factors associated with long-term mortality.

Various studies have found conflicting results for a correlation between serum sclerostin levels and all-cause mortality [18-20]. Some showed that serum sclerostin levels had no association with all-cause mortality [21-23], and two showed a significant negative association with all-cause mortality [24, 25]. A recent quantitative meta-analysis concluded that no significant association existed between sclerostin levels and either all-cause mortality or CVD mortality [26].

The discrepancies among these previous studies may be partly attributable to the heterogeneity of the study cohorts and the duration of observation periods. The patient populations varied among studies in terms of age, comorbid conditions, and dialysis vintage or even whether they were on dialysis therapy. Furthermore, since Moyses et al. [27] showed a significant difference between the measurements of serum sclerostin levels of HD patients

Table 3. Univariate and multivariate logistic regression of factors associated with AoACS

Characteristics	odds ratio	95% CI	Pvalue	odds ratio	95% CI	P-value
Age	1.07	1.05–1.09	<0.0001	1.08	1.05–1.11	<0.0001
Female	2.61	1.68–4.10	<0.0001	2.92	1.48–5.93	0.0019
Dialysis vintage	1.00	1.00–1.00	0.0442	1.01	1.00–1.01	0.0007
History of CVD	1.32	0.67–2.65	0.4234			
Diabetes	1.60	1.07–2.41	0.0220	3.29	1.89–5.83	<0.0001
BMI	0.93	0.88–0.99	0.0158	1.00	1.00–1.00	0.1810
Systolic BP	0.99	0.99–1.00	0.2738			
Diastolic BP	0.97	0.95–0.98	<0.0001	0.99	0.97–1.01	0.5703
Creatinine	1.00	0.91–1.11	0.9581			
Kt/V	2.46	1.18–5.25	0.0165	0.55	0.15–1.90	0.3411
nPCR	1.15	0.40–3.38	0.7945			
Sclerostin	1.00	1.00–1.00	0.4262			
Sclerostin 1st tertile	1.00			1.00		
Sclerostin 2nd tertile	0.58	0.35–0.95	0.0293	0.82	0.43–1.54	0.5517
Sclerostin 3rd tertile	0.82	0.50–1.35	0.4369	1.02	0.53 – 1.97	0.8524
FGF23	1.00	1.00–1.00	0.0423			
LogFGF23	0.80	0.60–1.07	0.1306	1.77	1.10 - 2.88	0.0193
Calcium, corrected	1.04	0.78–1.39	0.7986	0.88	0.56 - 1.40	0.5898
Phosphorus	0.87	0.76–1.00	0.0468	0.95	0.78 - 1.17	0.6470
Intact-PTH	1.00	1.00–1.00	0.0155			
LogPTH	0.58	0.34–0.99	0.0456	0.85	0.39 - 1.88	0.6967
ALP	1.00	1.00–1.00	0.7793			
CRP	0.99	0.82–1.21	0.9362			
Albumin	0.41	0.21–0.77	0.0053	1.40	0.58 - 3.39	0.4532
Hemoglobin	0.81	0.68–0.97	0.0206	0.84	0.67 - 1.04	0.1182
Ferritin	1.00	1.00–1.00	0.1817			
Total Cholesterol	1.00	0.99–1.00	0.9436			
Vitamin D	1.39	0.55–3.82	0.4893			
Calcium carbonate	0.95	0.61–1.45	0.8017			
Sevelamer hydrochloride	0.98	0.54–1.80	0.9490			
Lanthanum carbonate	1.06	0.69–1.62	0.7856			
Other phosphate binder	0.57	0.33–0.97	0.0382	0.72	0.36 - 1.41	0.3419

provided by two assays (TECO and Biomedica), such a difference could also factor into discrepancies among studies.

Higher serum sclerostin levels in HD patients than in the population with normal renal function may be attributable to two mechanisms. First, sclerostin, as an antagonist of bone formation, may inhibit vascular calcification by a mechanism similar to that in bone. This possible mechanism is supported by studies that have shown associations between high serum sclerostin levels and a lower prevalence and severity of vascular calcification [21, 28-30]. A second possible explanation for the positive association between sclerostin levels and increased prevalence and severity of vascular calcification may be that the former is lowered as a compensatory mechanism to counterbalance calcification caused by other mechanisms. This may be paradoxically supported by clinical studies that showed a positive association between sclerostin levels and vascular calcification [31, 32]. In our study, we observed a U-shaped association between serum sclerostin levels and aortic AoAC, suggesting that 2nd tertiles of serum sclerostin levels (161 – 260 pg/mL) may be associated with the inhibition of vascular calcification.

After its discovery as an important player in the physiology of bone formation, sclerostin became the focus of attention as a potential agent in the cross talk between bone and vascular walls. Previous studies have revealed a negative association between serum sclerostin levels and serum intact PTH levels. Patients with adynamic bone disease, which is characterized by low serum intact PTH levels, usually have severer vascular calcification than adynamic bone disease patients with normal or high intact PTH levels [33]. This association could be explained by increased sclerostin levels functioning as the missing link in adynamic bone disease patients. The serum sclerostin levels tend to decrease as their serum intact PTH

levels increase, and the low sclerostin levels of CKD patients may lead to greater vascular calcification.

In our study, serum sclerostin levels were higher in males than in females. Several clinical factors associated with sclerostin production and serum sclerostin levels have been identified other than renal dysfunction in non-CKD subjects, including age, BMI, diabetes, estrogen, and PTH [34, 35]. Relevant to our result is the previous finding that estrogen was associated with serum sclerostin levels [36]. Since most of our MHD patients were postmenopausal and estrogen levels in postmenopausal women are lower than in men of a similar age, serum sclerostin levels may be lower in females than males.

The present study had some limitations. First, it was based on a relatively small sample of MHD patients at a single center, which limits the ability to generalize the findings. Second, this study used only an observational approach and did not consider unknown confounding factors. Randomized, controlled trials will be needed to explore the role of sclerostin in the mortality risk of MHD patients.

Conclusion

This study showed that the serum sclerostin level in MHD patients is not an independent predictor of CVD mortality. However, whether clinical interventions to modulate sclerostin would improve the survival of MHD patients needs to be determined. Further studies are clearly needed to understand the impact of sclerostin on long-term mortality in MHD patients.

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Disclosure Statement

The authors have no conflicts of interest to declare.

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