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ARTÍCULO ORIGINAL

DMP-1 and Arterial Stiffness

The relationship between serum dentin matrix Acidic Phosphoprotein-1, Sortilin levels and arterial stiffness in hemodialysis patients

Relación entre la Fosfoproteína Ácida-1 de la matriz dentinaria sérica, los niveles deSortilina y la rigidez arterial en pacientes en hemodiálisis

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RESUMEN

Introducción: La principal causa de muerte en pacientes en hemodiálisis (HD) es la enfermedad cardiovascular. La fosfoproteína ácida de la matriz dentinaria-1 (DMP-1) y la sortilina son dos moléculas asociadas con eventos cardiovasculares; se desconoce su importancia en pacientes en HD. En este estudio, nuestro objetivo fue investigar la relación entre los niveles séricos de DMP-1 y sortilina y la rigidez arterial en pacientes en HD. **Materiales y métodos**: Se incluyeron en el estudio 80 individuos, 60 pacientes en HD y 20 controles sanos. La rigidez arterial se midió de forma no invasiva con el dispositivo Mobil-O-Graph. La DMP-1 sérica y la sortilina se midieron mediante ELISA en muestras de sangre tomadas antes de la diálisis. **Resultados**: La DMP-1 fue mayor en los pacientes en HD que en los controles sanos. Se consideró que los pacientes con un valor de VOP ≥10 presentaban una rigidez arterial aumentada. Los pacientes con mayor rigidez arterial eran mayores, presentaban un índice de masa corporal (IMC) y una presión arterial sistólica (PAS) más elevados, y niveles más bajos de creatinina y DMP-1. En el análisis de correlación, la Velocidad de la Onda del Pulso (VOP) se correlacionó positivamente con la edad, el IMC y la PAS, e inversamente con la creatinina y la DMP-1. La DMP-1 se correlacionó

negativamente con la edad y la proteína C reactiva (PCR). En el análisis de regresión, se observó que la PAS y la DMP-1 eran factores que afectaban a la VOP. **Conclusión**: Nuestro estudio es el primero en investigar la relación entre la DMP-1 sérica y la rigidez arterial en pacientes con HD. Como resultado de nuestro estudio, se observó que la DMP-1 sérica estaba inversamente relacionada con la rigidez arterial en pacientes con HD, mientras que la sortilina sérica no estaba relacionada.

Palabras clave: Rigidez arterial; Dmp-1; Sortilina

ABSTRACT

Introduction: The most important cause of death in hemodialysis (HD) patients is cardiovascular system disease. Dentin Matrix Acidic Phosphoprotein-1 (DMP-1) and sortilin are two molecules associated with cardiovascular events; their significance in HD patients is unknown. In this study, we aimed to investigate the relationship between serum DMP-1 and sortilin levels and arterial stiffness in HD patients. **Materials and Methods**: A total of 80 individuals, 60 HD patients, and 20 healthy controls were included in the study. Arterial stiffness measurements were performed non-invasively with the Mobil-O-Graph device. Serum DMP-1 and sortilin were measured using the ELISA method in blood samples taken before dialysis. **Results**: DMP-1 was higher in HD patients than in the healthy controls. Patients with a Pulse Wave Velocity (PWV) value ≥10 were considered to have increased arterial stiffness. Patients with increased arterial stiffness were older, had higher body mass index (BMI) and systolic blood pressure (SBP), and lower creatinine and DMP-1. In the correlation analysis, PWV was positively correlated with age, BMI, and SBP and inversely correlated with creatinine and DMP-1. DMP-1 was negatively correlated with age and C-reactive protein (CRP). In the regression analysis, SBP and DMP-1 were found to be factors affecting PWV. **Conclusion**: Our study is the first to investigate the relationship between serum DMP-1 and arterial stiffness in HD patients. As a result of our study, we found that serum DMP-1 was inversely related to arterial stiffness in HD patients, and serum sortilin was unrelated.

Keywords: Arterial stiffness; Dmp-1; Sortilin

INTRODUCTION

The most important cause of death in patients suffering from End Stage Kidney Disease (ESKD) is cardiovascular (CV) system disease (1). Arterial stiffness (AS) is an important indicator of atherosclerosis and CV events. Elevated AS leads to a heightened risk of CV disease through the induction of systolic hypertension (HT), left ventricular hypertrophy, and impairment in coronary perfusion (2). Arterial stiffness is known to be increased in ESKD patients compared to the normal population (3).

Significant changes in bone mineral metabolism are also observed in ESKD patients; loss of bone mass and increased bone fragility are the most important. The increase in Fibroblast Growth Factor (FGF-23) is held to be responsible for the pathophysiology of these conditions (4). FGF-23 is a phosphate and vitamin D regulatory hormone synthesized by osteocytes (5). Increased FGF-23 in ESKD patients has been associated with CV diseases and all causes of mortality (6). It is also thought to contribute to the development of left ventricular hypertrophy, which is an important precursor of heart failure in ESKD patients (7).

Dentin Matrix Acidic Phosphoprotein-1 (DMP-1) is an extracellular matrix propeptide produced by osteocytes (8). While it is mainly expressed in bones and teeth, DMP-1 is also expressed in lower amounts in soft tissues such as the heart, kidney, and salivary glands (9). DMP-1 is a regulator of bone mineralization in osteocytes, reducing FGF-23 expression from osteocytes and increasing bone mineralization. It does this by protecting osteocytes against apoptosis (10). Also, it regulates cell adhesion and differentiation and activates matrix metalloproteinase-9 (11). It is possible to say that DMP-1 acts as an inhibitor of vascular calcification. A study on 223 peritoneal dialysis patients showed that low DMP-1 was associated with vascular calcification and CV events (12). The situation in HD patients is unknown.

Sortilin, on the other hand, acts as a receptor for cytokines, lipids, and some enzymes. It is defined as a protein reported to play an active role in inflammation, atherosclerosis, and lipoprotein metabolism. It is thought to play a role in the development of AS by being produced from smooth muscle cells (13-15).

In this study, for the first time in the literature, we aimed to investigate the relationship between serum DMP-1 and sortilin and AS in HD patients.

MATERIALS AND METHODS

This cross-sectional study was conducted in the HD unit of Kahramanmaras Sutcu Imam University Faculty of Medicine Hospital. Approval for the study was received from the Ethics Committee of Kahramanmaras Sutcu Imam University Faculty of Medicine dated 11.10.2022 and numbered 2022/228-02. Before the study, patients were informed, and consent forms were signed. The study has been conducted following the Declaration of Helsinki.

Patients under 18 years of age and over 90 years of age, patients on HD treatment for less than 3 months, patients on peritoneal dialysis, patients with signs of active infection, patients on acute HD treatment due to acute kidney injury, electrolyte disturbance or uremic emergency were excluded.

Arterial stiffness measurement

A single cuff arteriograph device (I.E.M. GmbH brand Mobile-O-Graph PWA) was used. On the day of the patient's arrival for HD, in the meed-week dialysis session, after being allowed to rest for at least 30 minutes before HD, the device was attached to the patient's arm that does not have an arteriovenous fistula; data such as age, and gender were entered, three measurements were made at 30-second intervals, and their averages were taken. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate, pulse wave velocity (PWV), and augmentation index (AI) were recorded by this device.

DMP-1 and Sortilin measurement

Before HD and AS measurements, 6-8 ml venous blood samples were taken from the patients by phlebotomy method in a tube that did not contain anticoagulants. It was centrifuged at 4000 rpm and stored

at -80 0C, and then serum DMP-1 and Sortilin were measured using the ELISA method. Commercial ELISA kits (e3956Hu, e3966Hu; Biossay Technology Laboratory, Zhejiang, China) were used for testing serum DMP-1 and Sortilin.

Arterial stiffness

Since PWV 10 m/s is stated as the limit for target organ damage in the 2023 ESH Arterial Hypertension Management Guideline published by the International Society of Hypertension (ISH) and the European Renal Association (ERA) in December 2023, patients were diagnosed with AS according to the PWV value (PWV ≥10 m/s with AS and PWV <10 m/s without AS)(16).

Data collection

Patients' age, gender, HD duration, additional diseases such as diabetes mellitus (DM) and coronary artery disease (CAD), monthly biochemical laboratory tests, and calculations such as Kt/V and Urea reduction rate (URR), which are dialysis adequacy indicators, were obtained from patient files.

Statistical analysis

Continuous variables of the patients determined by measurement were given as mean±SD and categorical data determined by counting were given as the number of patients or percentages. Kolmogorov Smirnov and/or Shapiro-Wilk tests were used to analyze continuous data for normal distribution. Student-t or Mann-Whitney U tests were used to compare continuous variables, depending on whether the data followed a normal distribution. In correlation analysis, Pearson or Spearman correlation analysis was used depending on the distribution feature of the data. Multiple linear regression analysis was used to evaluate factors affecting PWV. The regression analysis first calculated the raw beta coefficients and confidence intervals with the "enter" method. Then, beta coefficients and confidence intervals were re-evaluated from the multiple regression model obtained by adjusting for age. A p-value of less than 0.05 was considered statistically significant. SPSS 26.0 (IBM Corp. 2019 IBM SPSS Statistics for Windows, version 26.0. Armonk, NY: IBM Corp) package program was used for analysis.

RESULTS

A total of 80 individuals, including 60 HD patients and 20 healthy controls, were included in our study. The average age of the patients was 51.1±15.4 years; 56.7% were male, and 43.3% were female. Considering the accompanying chronic disease history, 75% had HT, 31.6% had DM, and 20% had CAD. The patients ' demographic data and laboratory results are detailed in **Table 1**.

HD and control groups were similar in age. As expected, the HD group's blood urea nitrogen (BUN) and creatinine values were significantly higher than healthy controls. While the DMP-1 was higher in the HD group than in healthy controls, there was no difference between the two groups regarding Sortilin. The data of both groups are presented comparatively in **Table 2**.

Table 1: Demographic Data and Laboratory Results of the HD Group

Variables	**n=60** **Mean ± SD**	**min-max**
Age (years)	51,1 ± 15,4	20 – 82
Gender (male) (%)	56,7	
Duration of HD (months)	65,3 ± 50,9	7 – 201
BMI (kg/m²)	26,3 ± 5,3	15,7 – 40,0
SBP (mmHg)	138 ± 22	64 – 197
DBP (mmHg)	89 ± 18	44 – 138
DM (%)	31,6	
HT (%)	75	
CAD (%)	20	
BUN (mg/dL)	63 ± 21	26 – 132
Creatinin (mg/dL)	8,6 ± 2,2	3,3 – 13,0
Sodium (mmol/L)	135 ± 4	121 – 142
Potassium (mmol/L)	4,8 ± 0,8	3,0 – 7,3
Calcium (mg/dL)	7,9 ± 0,7	6,0 – 11,0
Phosphorus (mg/dL)	5,1 ± 1,8	1,0 – 11,0
iPTH (pg/mL)	438 ± 414	3 – 1699
Glucose (mg/dL)	130 ± 81	65 – 597
LDL cholesterol (mg/dL)	78 ± 25	13 – 157
Triglycerides (mg/dL)	148 ± 80	36 – 455
CRP (mg/L)	17,8 ± 19,3	1,9 – 84,0
Albumin (mg/dL)	38,6 ± 5,2	25 – 49,1
Uric acid (mg/dL)	5,8 ± 1,1	3,0 – 9,0
Kt/V	1,2 ± 0,3	1,0 – 2,0
URR (%)	73 ± 6	59 – 87
Mean PWV (m/s)	8,1 ± 1,8	4,5 – 12,3
Mean AI (%)	24,7 ± 10,3	5,0 – 43,3
DMP-1 (ng/mL)	18,7 ± 16,5	0,5 – 59,2

Sortilin (ng/mL)	5,2 ± 4,1	1,2 – 20,6

***HD**: hemodialysis, **BMI**: body mass index, **SBP**: systolic blood pressure, **DBP**: diastolic blood pressure, **DM**: diabetes mellitus, **HT**: hypertension, **CAD**: coronary artery disease, **BUN**: blood urea nitrogen, **iPTH**: intact parathormone, **LDL**: low-density lipoprotein **CRP**: C-reactive protein, **URR**: urea reduction rate, **PWV**: pulse wave velocity, **AI**: augmentation index, **DMP**: dentin matrix acidic phosphoprotein*

Table 2: Comparison of HD and Control Groups

Variables	**HD n=60 Mean ± SD**	**Control n=20 Mean ± SD**	**p**
Age (years)	51,1 ± 15,4	50,3 ± 7,6	0,60
BUN (mg/dL)	63 ± 21	14 ± 6	<0,001
Creatinin (mg/dL)	8,6 ± 2,2	0,7 ± 0,2	<0,001
DMP-1 (ng/mL)	18,7 ± 16,5	11,8 ± 10,6	0,008
Sortilin (ng/mL)	5,2 ± 4,1	4,3 ± 3,6	0,172

***HD**: hemodialysis, **BUN**: blood urea nitrogen, **DMP**: dentin matrix acidic phosphoprotein*

When the patients were divided into two groups as having AS (PWV ≥10) and not having AS (PWV <10) according to the PWV value, it was determined that 18.3% (n= 11) of the patients had AS. When these two groups were compared, the group with AS was observed to be older (69.5±5.2 vs. 47.0±13.8; p<0.001). Body mass index (BMI) (30.5±5.0 vs. 25.4±4.9; p=0.008) and SBP (149±18 vs. 136±23; p=0.048) were higher and creatinine (7.4±1.7 vs. 8.9±2.3; p=0.020) and DMP-1 (10.5±11.2 vs. 20.6±17.0; p =0.024) were lower in the AS group. Both groups ' demographic data and laboratory results are presented in detail in **Table 3**.

Table 3: Demographic Data and Laboratory Results of AS Subgroups of the HD Patients

Variables	**AS (+) n=11 Mean ± SD**	**AS (–) n=49 Mean ± SD**	**P**
Age (years)	69,5 ± 5,2	47,0 ± 13,8	**<0,001**
Gender (male) (%)	36,4	61,2	0,133
Duration of HD (months)	72,0 ± 63,8	63,8 ± 49,1	0,683
BMI (kg/m²)	30,5 ± 5,0	25,4 ± 4,9	**0,008**
SBP (mmHg)	149 ± 18	136 ± 23	**0,048**
DBP (mmHg)	87 ± 14	90 ± 19	0,486
DM (%)	45,5	28,6	0,277
HT (%)	81,8	72,2	0,738
CAD (%)	36,4	16,3	0,133
BUN (mg/dL)	61 ± 16	64 ± 22	0,657
Creatinin (mg/dL)	7,4 ± 1,7	8,9 ± 2,3	**0,020**
Sodium (mmol/L)	136 ± 5	136 ± 4	0,620
Potassium (mmol/L)	4,6 ± 0,6	4,9 ± 0,9	0,219
Calcium (mg/dL)	8,1 ± 0,7	7,9 ± 0,8	0,531
Phosphorus (mg/dL)	4,8 ± 1,1	5,2 ± 2,0	0,321
iPTH (pg/mL)	325 ± 239	464 ± 443	0,158
Glucose (mg/dL)	137 ± 48	129 ± 87	0,694
LDL cholesterol (mg/dL)	85 ± 17	77 ± 27	0,256
Triglycerides (mg/dL)	124 ± 48	155 ± 85	0,115
CRP (mg/L)	23,5 ± 16,3	18,5 ± 18,2	0,803
Albumin (mg/dL)	35,2 ± 11,5	33,4 ± 13,2	0,651
Uric acid (mg/dL)	5,7 ± 1,1	5,9 ± 1,2	0,628
Kt/V	1,2 ± 0,3	1,3 ± 0,3	0,382
URR (%)	75 ± 6	73 ± 7	0,410
Mean AI (%)	25,8 ± 14,2	24,4 ± 9,4	0,767

DMP-1 (ng/mL)	10,5 ± 11,2	20,6 ± 17,0	**0,024**
Sortilin (ng/mL)	4,2 ± 2,0	5,4 ± 4,4	0,811

***HD**: hemodialysis, **BMI**: body mass index, **SBP**: systolic blood pressure, **DBP**: diastolic blood pressure, **DM**: diabetes mellitus, **HT**: hypertension, **CAD**: coronary artery disease, **BUN**: blood urea nitrogen, iPTH: intact parathormone, **LDL**: low-density lipoprotein **CRP**: C-reactive protein, **URR**: urea reduction rate, **PWV**: pulse wave velocity, **AI**: augmentation index, **DMP**: dentin matrix acidic phosphoprotein*

In the correlation analysis, PWV was strongly correlated with age ($p<0.001$ and $r=0.87$). PWV was also positively correlated with BMI and SBP ($p=0.001$, $r=0.43$; $p=0.003$, $r=0.37$, respectively) and inversely correlated with creatinine and DMP-1 ($p=0.011$, $r=-033$; $p=0.008$, $r=-0.34$, respectively). AI was positively correlated with SBP ($p=0.027$ and $r=0.29$). DMP-1 was negatively correlated with age and C-reactive protein (CRP) ($p=0.008$, $r=-0.34$; $p=0.017$, $r=-0.31$, respectively). No significant correlation was detected between Sortilin and other variables. Correlation analyses are presented in detail in **Table 4**.

In the regression analysis, when SBP, calcium, phosphorus, uric acid, CRP, and DMP-1 were analyzed with the "enter" method, SBP (p=0.002, B=0.03; 95% CI=0.012 to 0.053) and DMP-1 (p=0.019, B=-0.03; 95% CI=-0.062 to -0.006) were found to be significantly associated with PWV. However, when the analysis was repeated after adjusting for age, the significance of DMP-1 disappeared. Parameters that independently predicted PWV in adjusted analysis were age (p<0.001 B=0.19; 95% CI:0.102 to 0.115) and SBP (p<0.001, B=0.03; 95% CI=0.030 to 0.039). Multiple linear regression analysis on factors affecting PWV is presented in detail in **Table 5**.

Table 4: Correlation analysis for PWV, AI, DMP-1, and Sortilin

Variables	**PWV**		**AI**		**DMP-1**		**Sortilin**	
	p	**R**	**p**	**r**	**p**	**r**	**p**	**r**
Age (years)	**<0,001**	0,87	0,770	-0,04	**0,008**	-0,34	0,311	-0,13
BMI (kg/m²)	**0,001**	0,43	0,410	0,19	0,164	-0,18	0,680	-0,05
SBP (mmHg)	**0,003**	0,37	**0,027**	0,29	0,480	-0,09	0,597	-0,07
Creatinin (mg/dL)	**0,011**	-0,33	0,720	-0,05	0,073	0,23	0,878	-0,02
Calcium (mg/dL)	0,816	-0,03	0,860	-0,02	0,817	0,03	0,410	0,11
Phosphorus (mg/dL)	0,495	0,09	0,241	0,15	0,427	-0,11	0,152	-0,19
iPTH (pg/mL)	0,725	0,05	0,515	0,09	0,316	0,13	0,547	-0,08
CRP (mg/L)	0,631	0,06	0,158	0,19	**0,017**	-0,31	0,189	-0,17
Albumin (mg/dL)	0,135	-0,20	0,831	0,03	0,160	0,19	0,888	0,02
Uric acid (mg/dL)	0,426	0,11	0,909	-0,02	0,954	0,01	0,319	-0,13
DMP-1 (ng/mL)	**0,008**	-0,34	0,724	-0,05	-	-	0,268	0,15
Sortilin (ng/mL)	0,274	-0,14	0,211	-0,16	0,268	0,15	-	-

***PWV**: pulse wave velocity, **AI**: augmentation index, **DMP**: dentin matrix acidic phosphoprotein, **BMI**: body mass index, **SBP**: systolic blood pressure, **iPTH**: intact parathormone, **CRP**: C-reactive protein*

Table 5: Multiple Linear Regression Analysis on Factors Associated with PWV

Variables	**Unadjusted**			**Adjusted**		
	B	**P**	**95% CI**	**B**	**p**	**95% CI**
Constant	4,34	0,122	-1,201 to 9,886	-2,25	0,001	-3,498 to -1,006

SBP (mmHg)	0,03	0,002	0,012 to 0,053	0,03	<0,001	0,030 to 0,039
Calcium (mg/dL)	-0,17	0,551	-0,748 to 0,403	0,02	0,747	-0,103 to 0,143
Phosphorus (mg/dL)	-0,12	0,359	-0,376 to 0,139	0,01	0,698	-0,045 to 0,066
Uric acid (mg/dL)	0,30	0,151	-0,112 to 0,708	-0,02	0,670	-0,108 to 0,070
CRP (mg/L)	<0,001	0,995	-0,024 to 0,024	-0,004	0,167	-0,009 to 0,002
DMP-1 (ng/mL)	-0,03	0,019	-0,062 to -0,006	-0,001	0,729	-0,007 to 0,005
Age (years)	-	-	-	0,19	<0,001	0,102 to 0,115

***SBP**: systolic blood pressure, **CRP**: C-reactive protein, **DMP**: dentin matrix acidic phosphoprotein*

DISCUSSION

No study in the literature has investigated the relationship between AS and serum DMP-1 in HD patients. Our study is the first study on this subject. In a study conducted only in peritoneal dialysis (PD) patients, serum DMP-1 was shown to be associated with vascular calcification. Although there are studies on the relationship between Sortilin and AS, there are few studies on the existence of this relationship in HD patients, and the results are contradictory. In this cross-sectional study, we found that serum DMP-1 was inversely correlated with AS in HD patients, and serum Sortilin was not associated with AS.

The limited information about DMP-1 has mainly been obtained from studies on hereditary hypophosphatemic rickets—inactivating mutations of DMP-1 result in autosomal recessive hypophosphatemic rickets (ARHR). In ARHR, DMP-1 deficiency and FGF-23 production in osteocytes increase FGF-23 circulation. Increased FGF-23 inhibits renal phosphate reabsorption, leading to hypophosphatemia's development, impaired bone mineralization, and growth defects resulting in osteomalacia and rickets (17-19). No disease has been described in the literature related to DMP-1 excess (20).

In the study conducted by Pereira et al., it was stated that detecting changes in DMP-1 and FGF-23 expression in bone biopsies may reflect very early changes in osteocyte metabolism, even in stage 2-4 chronic kidney disease patients (21). In the study by Zhu et al., it was stated that osteocyte markers DMP-1, E-11, and Sclerostin increased with in vitro vascular smooth muscle calcification. These data were also supported by studying an in vivo mouse model of vascular calcification (22). In a study conducted by Shi et al., it was stated that high DMP-1 in patients with hemorrhagic fever and renal syndrome due to Hantavirus were associated with the disease stage, severity, and degree of acute kidney injury. This relationship was supported by a correlation between the increase in vascular permeability due to Vascular Endothelial Growth Factor (VEGF) and DMP-1, which increases in the Hantavirus infection (23). Dussold et al. reported that DMP-1 expression decreased in ESKD patients (9). However, studies also report that elevated FGF-23 and DMP-1 may accompany each other, especially in ESKD patients with poor phosphorus control, to suppress FGF-23 levels due to phosphorus control disorder (21, 24). It has been reported that DMP-1 is abnormally degraded in ESKD patients undergoing HD (25). In our study, although DMP-1 was higher in the HD group than in the control group, it was lower in the HD group in patients with AS than in those without. In this respect, we obtained results that overlap and differ from the literature. While the fact that it is lower in the patient group with AS coincides with literature data, FGF-23 levels may be higher in HD patients than in healthy volunteers. Since we did not examine the FGF-23 level, this issue needs further examination with more comprehensive studies and evaluation regarding additional factors affecting the results.

In the study conducted by Yoon et al., 223 PD patients were examined, and it was determined that the level of vascular calcification was associated with DMP-1. It has been stated that this relationship continues after eliminating the effects of factors such as calcium, phosphorus, high-sensitivity CRP (hs-CRP), and FGF-23. It has been reported that an increase in AS is observed in PD patients with low DMP-1 (12). Although similar data were obtained with our study regarding results, lateral lumbar radiographs were used to measure vascular calcification in this study. Since AS measurements were measured with arteriographic devices in our study, the reliability of the measurement results is higher. In addition, this study is the only study in the literature on this subject conducted on dialysis patients. Since it only includes PD patients, it does not give sufficient insight into HD patients.

Dussold et al. reported that DMP-1 supplementation in Col4a3−/− mice prevented osteocyte apoptosis, preserved bone mass, partially reduced FGF-23 levels by reducing FGF-23 transcription, and increased serum phosphate. They also reported that, despite impaired renal function and worsening hyperphosphatemia in mice with ESKD, DMP-1 prevented the development of left ventricular hypertrophy and increased survival (9). The study conducted by Du et al. stated that DMP-1 could slow down the pathological process leading to diabetic nephropathy by reducing oxidative stress and inhibiting TGF-b signaling pathway activation in rats and could be used to prevent diabetic nephropathy (26). It has been stated that DMP-1 replication may be a potential new therapeutic strategy to improve bone quality, reduce FGF-23 levels, and prevent cardiac hypertrophy and early death in ESKD (20). Our study found that DMP-1 was negatively correlated with age and CRP. Since we could not detect a statistically significant relationship with other parameters, we think more comprehensive studies are needed to make inferences on this subject. Many studies show the relationship between AS and serum Sortilin or SORT1 gene mutations in different patient populations (27,28). In the only study conducted on HD patients on this subject, Xu et al. reported that serum Sortilin may be a marker of coronary artery calcification and cardiovascular and cerebrovascular events in HD patients (29). This effect of Sortilin is explained by its active role in inflammation, atherosclerosis, and lipoprotein metabolism, as well as its role in the development of AS by being produced from smooth muscle cells (13-15). However, in some studies, the view that this effect of Sortilin is unrelated to its effect on lipid metabolism comes to the fore (15). Sun et al. showed that Sortilin is effective in the early stages of vascular calcification (30). In the present study, unlike previous studies in the literature, Sortilin did not differ between the HD group and the control group. Likewise, it did not differ in patients with AS. We think that our small number of patients may have affected this result.

A relationship between AS and factors such as age, high blood pressure, history of renal failure, presence of chronic inflammation, presence of metabolic syndrome, and history of diabetes has been shown (31,32). In our study, PWV was associated with age, SBP, and DMP-1 level, similar to the literature.

One of the limitations of our study is that DMP-1 and Sortilin were measured from a single serum sample from the patients and the control group, and the average of three measurements made on the same day was taken for AS. More valuable results can be obtained if the changes in AS, serum DMP-1, and Sortilin over time and their relationship with this change are examined with multiple measurements. Apart from this, the fact that the FGF-23 was not measured can also be considered a limitation.

CONCLUSION

As a result, although the factors affecting AS in our study were age, SBP, and serum DMP-1, age is the most important factor determining AS. There is a negative relationship between DMP-1 and AS depending on the age factor. According to Sortilin, more comprehensive studies are needed to discuss these relationships.

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