



# What are the Determining Factors of Vascular Calcification and Is There any Relationship between Vascular Calcification, Arterial Stiffness, Fibroblast Growth Factor-23 and Fetuin-A in End Stage Kidney Disease Patients on Regular Hemodialysis?



Ozturk Y.<sup>1</sup>, Erdogmus S.<sup>2</sup>, Duman N.<sup>2</sup>

<sup>1</sup> Ankara University School of Medicine, Department of Internal Medicine, Ankara, Turkey

<sup>2</sup> Ankara University School of Medicine, Department of Nephrology, Ankara, Turkey

**INTRODUCTION AND OBJECTIVES:** More than half of deaths in end stage kidney disease (ESKD) patients are due to cardiovascular disease. The prevalence of vascular calcification; currently considered as a cardiovascular risk marker; increases in ESKD. The aim of the present study was to evaluate the determining factors of vascular calcification and elucidate the relationship between vascular calcification, arterial stiffness, fibroblast growth factor 23 (FGF-23) and Fetuin-A in ESKD patients on regular hemodialysis (HD).

**METHODS:** This is a cross-sectional study performed after the approval by Ankara University School of Medicine Ethics Committee for Clinical Studies in accordance with Helsinki Declaration guidelines and written informed consent were obtained from all participants (22 February 2014 No: 03-111-15). The foundation of Ankara University School of Medicine funded cost of the study.

74 patients on maintenance HD for at least three months at the Hemodialysis Unit of the Nephrology Department of Ankara University School of Medicine were enrolled to the study. Fasting blood samples were collected prior to hemodialysis upon the mid-week dialysis day in april 2015. Their previous 12 months data of demographic features, biochemical parameters and blood pressures (BP) were collected and averaged. Abdominal aortic calcification (AAK) scores were calculated from their lateral lumbar radiographies using Kauppila method by two separate people. Fetuin-A levels were measured with Human Fetuin-A ELISA kit (BioVendor Brno, Czech Republic). FGF-23 levels were measured with Human FGF-23 ELISA kit (Millipore Corp, ABD). Pulse Wave Velocities (PWV) calculated using SphygmoCor branded tonometry device (AtCor Medical Instruments, Illinois, USA).

**Table 1: Clinical characteristics and biochemical data of hemodialysis patients with and without vascular calcification**

	NVC (n: 35)	VC (n:39)	P
<b>Age</b>	<b>45,5 ± 14,09</b>	<b>62,1 ± 11,2</b>	<b>0,000</b>
Gender (male) (%)	48,6	56,4	0,5
Mean (range) duration of dialysis (monhs)	69,2 (8-240)	80,03 (8-276)	0,478
Tobacco use (%)	22,9	41	0,203
<b>Diabetes mellitus (%)</b>	<b>11,4</b>	<b>41</b>	<b>0,004</b>
Hypertension (%)	80	94,6	0,075
History of cardiovascular disease (%)	20	41	0,051
<b>Antihypertensive use</b>	<b>54,3</b>	<b>84,2</b>	<b>0,038</b>
Fetuin-A (ng/ml)	40,2 ± 15,7	36,6 ± 11,7	0,555
FGF-23 (pg/ml)	790,53 ± 1033	491,52 ± 809	0,208
<b>PWV</b>	<b>8,12 ± 2,17</b>	<b>10,25 ± 2,95</b>	<b>0,001</b>
<b>Body mass index (kg/m<sup>2</sup>)</b>	<b>25,17 ± 6,61</b>	<b>27,08 ± 4,71</b>	<b>0,021</b>
Systolic BP-before HD (mmHg)	120,6 ± 14,66	127,35 ± 14,9	0,055
Diastolic BP-before HD (mmHg)	73,03 ± 7,9	73,06 ± 7,97	0,985
<b>Systolic BP-after HD (mmHg)</b>	<b>108,65 ± 14,9</b>	<b>117,04 ± 14,15</b>	<b>0,015</b>
Diastolic BP-after HD (mmHg)	67,37 ± 8,78	69,8 ± 12,07	0,383
CaxP (mg <sup>2</sup> /dL <sup>2</sup> )	47,03 ± 9,79	45,5 ± 9,1	0,51
Serum calcium (mg/dL)	8,76 ± 0,53	8,80 ± 0,534	0,983
Serum phosphate (mg/dL)	5,38 ± 1,06	5,19 ± 0,945	0,256
Serum albumin (g/dL)	4,01 ± 0,505	4,01 ± 0,295	0,516
<b>Glukoz (mg/dL)</b>	<b>93,66 ± 35</b>	<b>113,36 ± 37,38</b>	<b>0,001</b>
<b>WBC (x10<sup>9</sup>/L)</b>	<b>6,91 ± 1,73</b>	<b>7,60 ± 1,40</b>	<b>0,030</b>
<b>CRP (mg/L)</b>	<b>8,8 ± 10,6</b>	<b>15,64 ± 16,18</b>	<b>0,009</b>
iPTH (pg/mL)	492 ± 423	459 ± 375	0,858
Ferritin (ng/mL)	412 ± 228	465 ± 236	0,337
Low density lipoprotein (mg/dL)	78,86 ± 22,7	89,11 ± 30,1	0,162
High density lipoprotein (mg/dL)	39,6 ± 12,84	36,78 ± 8,44	0,356

**RESULTS:** A total of 74 patients ( 35 women and 39 men) with a mean age of 55 (±15) were studied. Whereas 39 (52,7%) patients had vascular calcification (VC), 35 (47,3%) had not (NVC). Age (p:0,000), diabetes mellitus (p:0,004), antihypertensive use (p:0,038), PWV (p:0,001), body mass index (p:0,021), systolic BP after HD (p:0,015), glucose (p:0,001), white blood cell (WBC) (p:0,030), c-reactive protein (p:0,009) were significantly differed between groups (Table 1). Fetuin-A (p:0,555) and FGF-23 (p:0,208) levels were not significantly differed between groups. As shown in Table 2, multivariate regression analysis revealed age (β:0.209, p:0.001) was strongly related to vascular calcification (MODEL 1). When we exclude age; diabetes mellitus (β:5,23, p:0.008), antihypertensive use (β:1,84, p:0.018), and c-reactive protein (β:0,127, p:0,053) were independent variables of vascular calcification (MODEL 2).

**Table 2: Logistic regression analysis of vascular calcification**

	Odds ratio	C.I. (95%)	P	β
<b>MODEL 1</b>				
Age	1,105	1,051-1,162	0,000	0,1
<b>MODEL 2</b>				
Diabetes mellitus	6,4	1,49-27,8	0,012	1,86
CRP (mg/L)	1,051	1,003-1,101	0,036	0,050
Systolic blood pressure-after HD (mmHg)	1,046	1,007-1,087	0,021	0,045

**CONCLUSIONS:** Age, diabetes mellitus, use of antihypertensive and c-reactive protein were found to be independent variables of vascular calcification. There are conflicting results about the relationship between vascular calcification, arterial stiffness, FGF-23 and Fetuin-A in ESKD patients on regular HD. In our study; FGF-23 and Fetuin-A showed no correlation with AAK scores. While PWV had positive correlation in single variable correlation analysis, it had no correlation in multivariate regression analysis. It is important to follow up c-reactive protein levels and regulate blood pressure and glucose levels. Also we wants to emphasize that lateral lumbar radiography is still most available, cheap and reliable method to assess presence or absence of vascular calcification for patiens on regular hemodialysis.

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