



## ARAŞTIRMA / RESEARCH

# Effect of vitamin D deficiency on osteoarthritis and bone mineral density in elderly patients

D vitamini eksikliğinin yaşlı hastalarda osteoartrit ve kemik mineral dansitesi üzerine etkisi

Kenan Özler

Konya Beyşehir Devlet Hastanesi, Ortopedi ve Travmatoloji Kliniği, Konya, Turkey

*Cukurova Medical Journal 2019;44(Suppl 1):375-382.*

### Abstract

**Purpose:** We aimed to determine the effect of inadequate vitamin D level on osteoarthritis (OA) and bone mineral density (BMD) in female and male elderly patients with early and late stage OA with different BMD, and also the relationship between vitamin D and knee function scores in female and male OA patients.

**Materials and Methods:** One hundred and fortytwo female and one hundred thirty-five male knee OA patients were enrolled in the study. The knee OA was classified as early and late stage. WOMAC score, KOOS score, BMD and Vitamin D levels were measured.

**Results:** Vitamin D levels patients were statistically significantly lower in female OA than male OA group. Calcium and phosphorus levels were significantly higher in female OA patients than male OA group. There was no difference between vitamin D, vitamin B12, calcium, phosphorus, WOMAC score and KOOS scores in early and late stage OA patients with osteoporosis, osteopenia and normal BMD. WOMAC score was significantly higher in male patients with osteoporosis early stage and late stage OA than patients with osteopenia and normal BMD. The age odds ratio (OR) was 1,047 (95% CI = 1,009-1,086) in female OA patients, and OR was 1.090 (95% CI = 1,021-1,163) in male OA patients.

**Conclusion:** Vitamin D supplementation may be said increase BMD, slow down the progression of osteoporosis, reduce pain, but have no effect on OA progression and knee function scores.

**Keywords:** Vitamine D deficiency, osteoarthritis, bone mineral density, WOMAC score, KOOS score

### Öz

**Amaç:** Farklı kemik mineral yoğunluğu (KMY) olan kadın ve erkek erken ve geç evre osteoartritli (OA) yaşlılarda, vitamin D düzeyinin OA ve KMY üzerine etkisini ve ayrıca D vitamini ve diz fonksiyon skorları arasındaki ilişkiyi belirlemeyi amaçladık.

**Gereç ve Yöntem:** Çalışmaya diz OA olan yüz kırk iki kadın ve yüz otuz beş erkek hasta alındı. Diz OA erken ve geç evre olarak sınıflandırıldı. Western Ontario ve McMaster Universities Osteoarthritis indexi (WOMAC) indeksi, Knee Injury ve Osteoarthritis Outcome Skoru (KOOS) hesaplandı ayrıca KMY ve D vitamini düzeyleri ölçüldü.

**Bulgular:** Kadın OA de D vitamini düzeyleri erkek OA grubuna göre istatistiksel olarak anlamlı derecede düşüktü. Kadın OA hastalarında kalsiyum ve fosfor düzeyleri erkek OA grubuna göre anlamlı olarak daha yüksekti. Osteoporoz, osteopeni ve normal KMY olan erken ve geç dönem OA hastalarında vitamin D, vitamin B12, kalsiyum, fosfor, WOMAC indeksi ve KOOS skorları arasında fark yoktu. Osteoporozlu erken evre ve geç evre OA olan erkek hastalarda osteopenisi ve normal KMY olanlara göre WOMAC indexi anlamlı olarak daha yüksekti. Kadın OA olan hastalarda yaş odds oranı (OR) 1,047 (% 95 CI = 1,009-1,086), erkek OA olan hastalarda OR = 1.090 (% 95 CI = 1,021-1,163) idi.

**Sonuç:** D vitamini takviyesinin, osteoporozun ilerlemesini yavaşlattığı, ağrıyı azalttığı, KMY arttırdığı söylenebilir, ancak OA progresyonu ve diz fonksiyon skorları üzerinde hiçbir etkisi yoktur.

**Anahtar kelimeler:** Vitamin D eksikliği, osteoartrit, kemik mineral yoğunluğu, WOMAC indeksi, KOOS skoru

Yazışma Adresi/Address for Correspondence: Dr. Kenan Özler, Konya Beyşehir Devlet Hastanesi, Ortopedi ve Travmatoloji Kliniği, Konya, Turkey E-mail: kenozler@hotmail.com  
Geliş tarihi/Received: 21.05.2019 Kabul tarihi/Accepted: 04.08.2019 Çevrimiçi yayın/Published online: 27.09.2019

## INTRODUCTION

Knee degenerative arthritis (Osteoarthritis) is the most common disabling illness among elderly people. Prevalence of knee OA is higher in women compared to men of age  $\geq 60$ <sup>1</sup>. Another important topic of elderly individuals, particularly postmenopausal women, is that the decrease in bone mineral density (BMD). Vitamin D could be a plays a role in some events associated with bone metabolisms such as calcium metabolism, osteoblastic efficiency, bone ossification, and cartilage turnover<sup>2</sup>. It is accepted that degenerative knee arthritis and osteoporosis are positively related to aging which diseases are due to bone metabolism. Although deficiency of vitamin D is associated with osteoporosis and fractures in elderly peoples, the role of D vitamin deficiency is unclear inside the pathological process of OA<sup>3</sup>. Polymorphisms of vitamin D gene associated with studies showed that osteoporosis and OA could also be related to this illness<sup>4</sup>. Insufficient vitamin D has been demonstrated in osteoporosis<sup>5</sup>. Bergink et al. according to that the intake of low vitamin D supplementation would possibly improve the progression of OA and notably the improvement of the vitamin D status in the old peoples could protect against the development and worsening of degenerative arthritis in those with low BMD<sup>6</sup>. McAlindon et al. reported that clinic knee OA patients gave vitamin D and were followed for two years, and also, they showed that OA patients who were receiving cholecalciferol no reduction in knee function<sup>7</sup>.

The effect of vitamin D on bone metabolism should be discussed in terms of the role of OA and BMD. In our study, we aimed to identify the influence of inadequate vitamin D level on knee OA and BMD in female and elderly male people with early and late-stage OA with different BMD, and additionally to work out the connection among D vitamin and knee function scores in female and male OA individuals.

## MATERIALS AND METHODS

One hundred and two female and one hundred thirty-five male knee OA patients were collected from the Orthopedics Department of Beyşehir State Hospital Between 2016-2017 years. The diagnosing of knee OA determined by radiographic characteristic, the Kellgren, and Lawrence (K&L) scale was chosen. The K&L scale is used in the

staging of OA according to the radiographic features. The identification of OA has accomplished the K&L scale accordingly and required the presence of all five radiological criteria: osteophytes on the joint side, periarticular ossicles, joint area narrowing (JSN), small pseudocysts regions within the subchondral bone and changed the formation of the bone ends<sup>8</sup>. OA patients were divided into five stages: stage 0 (no changes in x-ray), stage 1 (osteophyte and no JSN), stage 2 (osteophyte and JSN), stage 3 (medium multiple osteophytes, JSN, minimal sclerosis and deformity of bone ends) and stage 4 (giant osteophytes, evident JSN, severe sclerosis and deformity of bone ends). Stage-1 and -2 were thought of as early-stage OA (EOA) and stage-3, -4 were considered of late-stage OA (LOA)<sup>9</sup>.

A dual-energy X-ray absorptiometry (DXA, Stratos dR 2D Fan Beam DEXA) technique was used to evaluate BMD measurement of male and female OA patients over the past year, and a T-score was decided. Specifically, bone density (BMD; g/cm<sup>2</sup>) was determined at the hip (neck of femoral, intertrochanter space, and trochanter major) and posterior-anterior lumbar spine. Osteoporosis and osteopenia were determined as place T-scores  $\leq -2.5$  and among  $-2.5$  and  $-1.9$ . The patients were homogenized for body mass index (BMI). BMI was calculated in kilograms / square meter (kg / m<sup>2</sup>)<sup>10</sup>. Patients with a BMI of  $\geq 30$  kg / m<sup>2</sup> were considered obese. Patients with BMI  $<30$  kg / m<sup>2</sup> were considered non-obese. We did not include patients with a BMI of  $\geq 30$  kg / m<sup>2</sup><sup>11</sup>. Clinical examination and anthropometric measurements were recorded for all participants in this study.

Overall, OA patients provided an informed consent form, and the study ethics committee approval was obtained from the local Ethical Committee of Necmettin Erbakan University (approval date/number:11.04.2019/648).

Exclusion criteria included using steroids and intraarticular hyaluronic acid injections treatment, using vitamin D supplement, infectious diseases, diabetes or Addison's disease knee, surgical process or other, septic arthritis, rheumatoid arthritis, obesity, neurological or neuromuscular disorders, bone tumor, chemo- or radiation therapy, and patients using any bisphosphonate or selective estrogen receptor modulator over the past year. Patients whose D vitamin levels were above the values in the max reference range were not included within the study as a result of they did not have vitamin D

insufficiency.

## Measures

### The Western Ontario and McMaster Universities Osteoarthritis (WOMAC) Score

This scale was accustomed to assess the knee functions of knee degenerative joint disease. The WOMAC score consisted of three groups of questions: pain, stiffness, and functional disorder, and a total of twenty-four queries were asked to the groups. One of five answers for every question was accepted: none, slight, middle, severe, and massive. WOMAC pain score was minimum 0, and maximum 20, WOMAC stiffness range was minimum 0, and maximum 8 and WOMAC, functional impairment range, was minimum 0 and maximum 68 12. If the WOMAC score is 70 percent or more, the knee function score is considered to be impaired in the Turkish population <sup>13</sup>.

### Knee Injury and Osteoarthritis Outcome Score (KOOS)

It was developed in 1995 to assess the symptoms and functional status of knee injuries and knee osteoarthritis. The KOOS score has five subgroups: Pain, other symptoms, functional status related to daily living activities, a functional condition in sports and leisure activities, and knee-related quality of life. Each subscale is scored between 0-100. (0 indicates a severe problem, 100 indicates no problem). Changes of 10 points or more are clinically significant <sup>14</sup>. The reliability coefficients of the COOS score are between 0.85-0.89 in the Turkish population <sup>15</sup>.

## Laboratory methods

All participants blood samples were obtained with venipuncture and processed within 1 hour after withdrawal by centrifugation at 5000 revolutions/minute for 15 min. Serum Vitamin D, calcium, vitamin B12, and phosphorus levels were analyzed with the utilization of an ADVIA Centaur immunochemical assay System (SIEMENS), and the results are presented as ng / mL, mg / dl, pg / mL and mg / dL respectively. The subsequent reference ranges were used for blood serum vitamin D (9,5-39,6 ng / mL), calcium (8,2-10,2 mg / dl), vitamin B12 (210-915 pg / mL) and phosphorus (2,5-5 mg / dL) levels. In our study, the reference range of vitamin D level was 9.5-39.6 ng / mL. In our study, we did not include patients with a vitamin D level >

39.6 ng/ml. Serum 25 (OH) D level less than 20 ng / mL is considered to be vitamin D insufficiency if vitamin D level between 21 and 29 ng / mL is considered to be vitamin D deficiency and vitamin D sufficient level 40-60 ng / mL <sup>16</sup>.

## Statistical analysis

Data statistical analysis was made using SPSS-22 due to Windows (SPSS Inc., Chicago). Variables were shown as mean where applicable. OA, in line with the K&L scale, was divided into EOA and LOA. The mean variations among groups were compared with Sample t-test. Nominal data were statistical analyzed by the chi-square test. Knee OA was divided into three groups (osteoporosis, osteopenia, and normally) according to BMD. Variables between male and female EOA and LOA were assessed by The Analysis of Covariance (ANOVA). Univariate and multivariate regression analyses were provided for determined odds ratios (OR) and 95% confidence intervals for the association between age, laboratory parameters with WOMAC score in female and male OA individually. A p-value >.05 was noted as statistically significant.

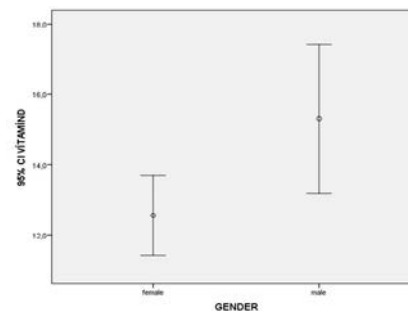


Figure 1- Vitamin D levels in female and male OA patients

## RESULTS

Two hundred seventy-seven patients with OA were included in this study. One hundred forty-two were women, and 135 were men. The baseline anthropometric and biochemical characteristics, given in Table 1 in female and male OA patients. Male and female OA groups were homogenized with age and BMI. WOMAC score and KOOS score were not different in female and male OA patients. The distribution ratios of OA stages were homogeneous in the groups. Rates of osteoporosis and osteopenia

were not different among men and women OA groups. Vitamin D levels were  $12.57 \pm 0.57$  ng/ml in female OA patients and  $15.18 \pm 7.34$  ng/ml in male OA patients. Patients levels of Vitamin D were statistically significantly lower in female OA than male OA group ( $p = .025$ ) (Figure 1). Calcium and

phosphorus levels were  $8.811 \pm 0.05$  mg / dl,  $8,52 \pm 0,18$  mg / dl in female OA and  $3,49 \pm 0,09$  mg / dl,  $2,90 \pm 0,81$  mg/dl in male OA, respectively. Calcium and phosphorus levels were significantly higher in female OA than male OA group ( $p = .045$  and  $p = .001$ ) (Table 1).

**Table 1. Clinical, anthropometric and laboratory features in female and male OA patients.**

	Female N=142	Male N=50	P -Value
Age (year)	58.82 ±10.14	61.50 ± 11.34	0.122
BMI (kg/m <sup>2</sup> )	29.17 ± 0.46	27.78 ± 0.62	0.111
	Stage 1	36 (25.4%)	0.559
	Stage 2	38 (26.8%)	
	Stage 3	34 (23.9%)	
	Stage 4	34 (23.9%)	
WOMAC Score	53.63 ± 1.50	54.52 ± 2.65	0.767
KOOS score	84.01 ± 3.32	82.08 ± 5.41	0.765
Calcium (mg/dl)	8.811 ± 0.05	8.52 ± 0.18	0.045
Phosphorus (mg/dl)	3.49 ± 0.09	2.90 ± 0.81	0.001
Vitamin B12 (pg/ml)	336.91 ± 20.50	334.42 ± 22.26	0.946
Vitamin D ( ng/mL)	12.57 ± 0.57	15.18 ± 7.34	0.025
BMD	< 1.5	33 (32%)	0.821
	1.5- 2.49	27 (26.2%)	
	≥ 2.5	43 (41.7%)	

BMI; body mass index, WOMAC Score; The Western Ontario and McMaster Universities Osteoarthritis score KOOS score; The Knee Injury and Osteoarthritis Outcome Score, BMD; bone mineral density, p-value; statistical significance < 0,05.

**Table 2. Anthropological, clinical and laboratory features of early-stage and advanced-stage OA patients with osteoporosis, osteopenia and normal BMD.**

	Early Stage Female OA					Late Stage Female OA				
	osteoporosis (a)	osteopenia (b)	Normal BMD (c)	P -value **	P -value *	osteoporosis (a)	osteopenia (b)	Normal BMD (c)	P- value **	P -value *
Age (year)	57.50 ± 2.42	52.40 ± 0.95	49.60 ± 0.89	P(ab)=0.03 P(ac)<0.01 P(bc)=ns	<0.01	69.83 ± 1.30	63.60 ± 1.43	63.36 ± 2.26	P(ab)=0.003 P(ac)=0.009 P(bc)=ns	0.004
Vitamin D ( ng/mL)	14.78 ± 2.12	12.25 ± 1.14	12.12 ± 1.15	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	12.98 ± 1.56	12.39 ± 1.24	11.57 ± 1.56	P(ab)=ns P(ac)=ns P(bc)=ns	ns
Vitamin B12 (pg/ml)	254.56 ± 48.66	288.36 ± 19.23	339.80 ± 44.80	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	451.38 ± 68.73	331 ± 38.3	272. 21 ± 19.25	P(ab)=ns P(ac)=0.047 P(bc)=ns	ns
Calcium (mg/dl)	9.09 ± 0.18	8.85 ± 0.13	8.92 ± 0.12	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	8.56 ± 0.10	8.81 ± 0.13	8.82 ± 0.11	P(ab)=ns P(ac)=ns P(bc)=ns	Ns
Phosphorus (mg/dl)	3.38 ± 0.10	3.39 ± 0.94	3.66 ± 0.31	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	3.59 ± 0.14	3.47 ± 0.98	3.22 ± 0.16	P(ab)=ns P(ac)=ns P(bc)=ns	Ns
Womac Score	42.79 ± 3.95	45.76 ± 2.92	44.17 ± 2.14	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	58.10 ± 2.94	67.60 ± 3.36	68 ± 4.24	P(ab)=0.036 P(ac)=ns P(bc)=ns	Ns
Koos skoru	54 ± 4.84	59 ± 3.72	48.06 ± 2.71	P(ab)=ns P(ac)=ns P(bc)=0.09	Ns	116.66 ± 5.79	121.64 ± 4.51	113. 79 ± 6.67	P(ab)=ns P(ac)=ns P(bc)=ns	Ns

BMI; body mass index, WOMAC Score; The Western Ontario and McMaster Universities Osteoarthritis score, KOOS score; The Knee Injury and Osteoarthritis Outcome Score, BMD; bone mineral density, p-value; statistical significance < 0.05. p-value \*, with in group, p-value\*\*, between groups,

We looked at anthropometric and laboratory characteristics between EOA and LOA patients with osteoporosis, osteopenia, and normal BMD. The age was significantly higher of osteoporosis EOA and LOA women patients than normal BMD and osteopenia ( $p < .001$  and  $p = .004$ , respectively) (Table 2). There was no difference between vitamin D, vitamin B12, calcium, phosphorus, WOMAC score and KOOS scores in early and late-stage OA

patients with normal BMD and reduced BMD (osteoporosis and osteopenia) (Table 2).

WOMAC score was higher in male with osteoporosis EOA and LOA than patients with osteopenia and normal BMD ( $p = .011$  and  $p = .039$ , respectively) (Table 3). Age, vitamin D, B12 vitamin, calcium, phosphorus, and KOOS scores were not different in EOA and LOA patients with osteoporosis, osteopenia, and BMD normal (Table 3).

**Table 3. Anthropological, clinical and laboratory features of early stage and advanced stage OA male patients with osteoporosis, osteopenia and normal BMD.**

	Early -Stage Male OA					Late- Stage Male OA				
	Osteoporosis (a)	Osteopenia (b)	Normal BMD (c)	P-value**	P-value*	Osteoporosis (a)	Osteopenia (b)	Normal BMD (c)	P-value**	P-value*
Age (year)	59 ± 2.64	52.42 ± 2.07	53.10 ± 2.83	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	69 ± 3.73	69 ± 1.72	68.75 ± 5.97	P(ab)=ns P(ac)=ns P(bc)=ns	Ns
Vitamin D (ng/mL)	12.36 ± 2.85	15.25 ± 2.22	15.61 ± 2.41	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	14.22 ± 2.34	18.10 ± 2.32	9.67 ± 1.91	P(ab)=ns P(ac)=ns P(bc)=ns	ns
Vitamin B12 (pg/ml)	268.33 ± 34.03	363.4 ± 42.33	260.7 ± 14.39	P(ab)=ns P(ac)=ns P(bc)=0.039	Ns	362.14 ± 51.87	368.69 ± 66.3	342.25 ± 57.89	P(ab)=ns P(ac)=ns P(bc)=ns	ns
Calcium (mg/dl)	8.70 ± 0.30	8.90 ± 0.16	9.28 ± 0.25	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	8.40 ± 0.17	8.48 ± 0.16	8.86 ± 0.12	P(ab)=ns P(ac)=ns P(bc)=ns	ns
Phosphorus (mg/dl)	2.63 ± 0.73	3.21 ± 0.16	2.76 ± 0.18	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	2.94 ± 0.18	2.88 ± 0.16	2.60 ± 0.15	P(ab)=ns P(ac)=ns P(bc)=ns	ns
Womac Score	55.67 ± 11.9	49.83 ± 3.96	35 ± 1.68	P(ab)=ns P(ac)=0.016 P(bc)=0.009	0.011	78.43 ± 3.86	59.62 ± 4.89	57 ± 8.39	P(ab)=0.019 P(ac)=0.042 P(bc)=ns	0.039
Koos skoru	55 ± 18.24	49.75 ± 4.41	51.50 ± 7.39	P(ab)=ns P(ac)=ns P(bc)=ns	Ns	114 ± 12.38	112.23 ± 6.42	100 ± 13.62	P(ab)=ns P(ac)=ns P(bc)=ns	ns

BMI; body mass index, WOMAC Score; The Western Ontario and McMaster Universities Osteoarthritis score, KOOS score; The Knee Injury and Osteoarthritis Outcome Score, BMD; bone mineral density, p-value; statistical significance < 0.05. p-value \*, with in group, p-value\*\*, between groups,

**Table 4. Multivariate regression analysis to determine the factors associated with WOMAC Score in male and female OA patients.**

	Female		Male	
	AUC (95%CI)	p-value	AUC (95%CI)	p-value
Age (year)	1.047 (1.009-1.086)	0.014	1.090 (1.021-1.163)	0.009
Vitamin D (ng/ml)	1.023 (0.973-1.077)	0.375	1.032 (0.951-1.119)	0.455
Vitamin B12 (pg/ml)	1.001 (1.000-1.002)	0.195	1.003 (0.999-1.006)	0.173
Calcium (mg/dl)	0.860 (0.454-1.627)	0.642	0.977 (0.550-1.736)	0.938
Phosphorus (mg/dl)	1.065 (0.754-1.505)	0.719	0.526 (0.143-1.940)	0.335
Osteoporosis	1.182 (0.499-2.799)	0.703	0.625 (0.155-2.523)	0.509
Osteopenia	0.724 (0.305-1.715)	0.463	0.212 (0.037-1.211)	0.081

WOMAC Score; The Western Ontario and McMaster Universities Osteoarthritis score.

Multiple regression analysis was made to evaluate the associated with between knee function score

(WOMAC score) and variables in male and female OA patients. The age odds ratio (OR) was 1,047

(95% CI = 1,009-1,086) in old female OA, and OR was 1.090 (95% CI = 1,021-1,163) in male OA patients. The older age was statistically associated with the WOMAC score in the male and female OA groups. ( $p=.014$  and  $p=.009$ , respectively) (Table 4). D vitamin, B12 vitamins, calcium, phosphorus, osteoporosis, and osteopenia were not associated with WOMAC score in female and male OA patients (Table 4).

## DISCUSSION

Knee degenerative arthritis disease is especially widespread in old individuals, and there nowadays is no therapy that may slow or stop its progression. At constant time, osteoporosis, which leads to decreased BMD, degraded architecture and fragile of bones, affects both sexes, however, the main burden of the disease is widespread in postmenopausal women<sup>17</sup>.

OA and osteoporosis diseases are a major reason for morbidity in the aged population. The relationship between OA and BMD is complex, conflicting, and bone metabolism plays a role within the pathophysiology of each. Studies have shown that OA risk is reduced in patients with high BMD<sup>18,19</sup>. The Dong-gu Study demonstrated that knee joint narrowing (JSN) and subchondral cysts in OA patients are negatively associated with BMD of the lumbar spine and femoral neck<sup>20</sup>. G1 et al. have shown that the risk for osteoporotic fracture does not seem to decrease despite a high BMD in patients with OA, probably due to postural instability and muscle strength. Low BMD at the lumbar spine is associated with a lower incidence of knee OA, although it does not arrest the progression of knee OA<sup>21</sup>.

D vitamin is essential factors for osseous remodeling and turnover<sup>22</sup>. Breijawi and et al. detected a higher rate of vitamin D deficiency, independent of the BMD in aged<sup>23</sup>. D Vitamin has been shown to induce synthesis of proteoglycans in invitro environment mature articular cartilage<sup>24</sup>, and this mentioned that vitamin D might affect cartilage turnover. In our study, we found that vitamin D levels were significantly lower females than males in older OA patients with low serum vitamin D levels. Also, there wasn't a difference between D vitamin and calcium levels in osteoporosis and osteopenia groups of women with EOA and LOA. Only LOA patients were older than the EOA. Karina et al. reported that vitamin D levels in OA patients who underwent knee arthroplasty were not associated with degenerative

osteoarthritis progression. At the same time, they have shown that there is no relationship between T scores and OA stages<sup>25</sup>. Başkan et al. investigated the relationship between OA stage and functional status and serum vitamin D levels in patients with knee OA, reported that there was no correlation between serum vitamin D level and OA stage and KOOS score<sup>26</sup>. Heidari et al. Found that those with a serum level > 20 ng / ml as vitamin D deficiency showed that vitamin D levels were insufficient in the knee OA patients under 60 years of age compared to the control group<sup>3</sup>. Çakar et al. Showed that 90% of patients with knee OA had vitamin D deficiency, and there was no difference according to vitamin D level, according to VAS, WOMAC score, and BMI<sup>27</sup>. Arden et al. have stated that vitamin D supplementation hasn't functioned in knee OA clinical follow-up<sup>28</sup>. Bergink et al. have said that vitamin D levels are not associated with changes in joint space or risk of cartilage loss in knee OA, hip and hand OA<sup>29</sup>. Ding et al. reported that exposure to sunlight and serum 25 (OH) D levels were associated with decreased knee cartilage loss<sup>30</sup>. In our study, we determined WOMAC score was higher the osteoporosis group than with the osteopenia group in both early-stage and late-stage male OA patients, but we could not find any difference between vitamin D levels. When we look at the results of the studies, it is shown that low D vitamin level is associated with OA progression and osteoporosis development, but the relationship between OA and vitamin D deficiency is not clear<sup>31</sup>. Divya et al. gave vitamin D supplementation the patients with 107 knee OA with vitamin D level  $\leq 50$  nmol / L and after 12 months showed a decrease in knee pain and improved knee function compared to the placebo group<sup>32</sup>. Muraki et al. have stated that D vitamin may be associated with pain, not with radiographic imaging changes in knee OA<sup>33</sup>. It is known that advanced age, female gender, and physical demand were related to the pain of knee<sup>34,35</sup>, and radiographic knee OA<sup>36</sup>. When we evaluated the effective factors for the knee function score in our study, we found that only the age factor was related to the male and female.

After all; the high WOMAC score of late OA patients may cause restraint in movements and decrease in systemic BMD, and D-vitamin supplementation may be said increase BMD, slow down the progression of osteoporosis, reduce pain, but have no effect on OA progression and knee function scores. The limitation of our current study is that the sample size, also further studies with larger cohorts and with different

techniques are needed to validate the findings of the present study.

**Yazar Katkıları:** Çalışma konsepti/Tasarımı: KÖ; Veri toplama: KÖ; Veri analizi ve yorumlama: KÖ; Yazı taslağı: KÖ; İçerigin eleştirel incelenmesi: KÖ; Son onay ve sorumluluk: KÖ; Teknik ve malzeme desteği: KÖ; Süpervizyon: KÖ; Fon sağlama (mevcut ise): yok.

**Bilgilendirilmiş Onam:** Katılımcılardan yazılı onam alınmıştır.

**Hakem Değerlendirmesi:** Dış bağımsız.

**Çıkar Çatışması:** Yazarlar çıkar çatışması beyan etmemişlerdir.

**Finansal Destek:** Yazarlar finansal destek beyan etmemişlerdir.

**Destekleyen Kurum:** Konya Beyşehir Devlet Hastanesi

**Proje Numarası:** local ethics committee: approval date/number:05.04.2019/86

**Teşekkür:** Konya Beyşehir Devlet Hastanesi, Konya Sağlık İl Müdürlüğü

**Author Contributions:** Concept/Design : KÖ; Data acquisition: KÖ; Data analysis and interpretation: KÖ; Drafting manuscript: KÖ; Critical revision of manuscript: KÖ; Final approval and accountability: KÖ; Technical or material support: KÖ; Supervision: KÖ; Securing funding (if available): n/a.

**Informed Consent:** Written consent was obtained from the participants.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** Authors declared no conflict of interest.

**Financial Disclosure:** Authors declared no financial support

## REFERENCES

- Zhang Y, Jordan JM. Epidemiology of osteoarthritis. *Clin Geriatr Med*. 2010;26:355–69.
- Lane NE, Gore LR, Cummings SR, Hochberg MC, Scott JC, Williams EN et al. Serum vitamin D levels and incident changes of radiographic hip osteoarthritis: a longitudinal study. *Arthritis Rheum*. 1999;42:854-60.
- Heidari B, Heidari P, Hajian-Tilaki K. Association between serum vitamin D deficiency and knee osteoarthritis. *Int Orthop*. 2011;35:1627–31.
- Dequeker J. Inverse relationship of the interface between osteoporosis and osteoarthritis. *J Rheumatol*. 1997;24:795e8.
- Lips P, Hosking D, Lippuner K, Norquist JM, Wehren L, Maalouf G et al. The prevalence of vitamin D inadequacy amongst women with osteoporosis: an international epidemiological investigation. *J Intern Med*. 2006;260:245–54.
- Bergink AP, Uitterlinden AG, Van Leeuwen JP, Buurman CJ, Hofman A, Verhaar JA et al. Vitamin D status, bone mineral density, and the development of radiographic osteoarthritis of the knee: The Rotterdam Study. *J Clin Rheumatol*. 2009;15:230–7.
- McAlindon T, LaValley M, Schneider E, Nuite M, Lee JY, Price LL, et al. Effect of vitamin D supplementation on the progression of knee pain and cartilage volume loss in patients with symptomatic osteoarthritis: a randomized controlled trial. *JAMA*. 2013;309:155–62.
- Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. *Ann Rheum Dis*. 1957;16:494e502
- Schiphof D, Boers M, Bierma-Zeinstra S. Differences in descriptions of Kellgren and Lawrence grades of knee osteoarthritis. *Ann Rheum*. 2008;67:1034–6.
- Keys A, Fidanza F, Karvonen MJ, Kimura N, Taylor HL. Indices of relative weight and obesity. *J Chron Dis*. 1972;25:329–43.
- Adams KF, Schatzkin A, Harris TB, Kipnis V, Mouw T, Ballard-Barbash R et al. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. *N Engl J Med*. 2006;355:763–78.
- Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol*. 1988;15:1833–40.
- Tüzün EH, Eker L, Aytar A, Daşkapan A, Bayramoğlu M. Acceptability, reliability, validity and responsiveness of the Turkish version of WOMAC osteoarthritis index. *Osteoarthritis Cartilage*. 2005;13:28-33.
- Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)-- the development of a self-administered outcome measure. *J Orthop Sports Phys Ther*. 1998;28:88–96.
- Paker N, Buğdaycı D, Sabırlı F, Özel S, Ersoy S. Knee Injury, and Osteoarthritis Outcome Score: Reliability and Validation of the Turkish Version. *Türkiye Klinikleri Journal of Medical Science*. 2007;27:350-6.
- Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon MC, Hanley DA, Heaney RP et al. Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2011;96:1911-30.
- Weinstein SL. 2000–2010: the bone and joint decade (editorial). *J Bone Joint Surg Am*. 2000;82:1-3.
- Crema MD, Nevitt MC, Guermazi A, Felson DT, Wang K, Lynch JA et al. Progression of cartilage damage and meniscal pathology over 30 months is associated with an increase in radiographic tibiofemoral joint space narrowing in persons with knee OA--the MOST study. *Osteoarthritis Cartilage*. 2014;22:1743-7.
- Zhang Y, Hannan MT, Chaisson CE, McAlindon TE, Evans SR, Aliabadi P et al. Bone mineral density and risk of incident and progressive radiographic knee osteoarthritis in women: the Framingham study. *J Rheumatol*. 2000;27:1032-7.
- Wen L, Shin MH, Kang JH, Yim YR, Kim JE, Lee JW et al. The relationships between bone mineral density and radiographic features of hand or knee osteoarthritis in older adults: data from the Dong-gu Study. *Rheumatology (Oxford)*. 2016;55:495-503.
- Im GI, Kim MK. The relationship between osteoarthritis and osteoporosis. *J Bone Miner Metab*. 2014;32:101-9.
- Goula T, Kouskoukis A, Drosos G, Tselepis AS, Ververidis A, Valkanis C et al. Vitamin D status in patients with knee or hip osteoarthritis in a

- Mediterranean country. *J Orthop Traumatol J Orthop Traumatol*. 2015;16:35-9.
23. Breijawi N, Eckardt A, Pitton MB, Hoelzl AJ, Giesa M, von Stechow D et al. Bone mineral density and vitamin d status in female and male patients with osteoarthritis of the knee or hip. *Eur Surg Res*. 2009;42:1-10.
  24. Rai V, Dietz NE, Dilisio MF, Radwan MM, Agrawal DK. Vitamin D attenuates inflammation, fatty infiltration, and cartilage loss in the knee of hyperlipidemic micro swing. *Arthritis Res Ther*. 2016;18:203.
  25. Linde KN, Puhakka KB, Langdahl BL, Søballe K, Krog-Mikkelsen I, Madsen F et al. Bone mineral density is lower in patients with severe knee osteoarthritis and attrition. *Calcif Tissue Int*. 2017;101:593-601.
  26. Başkan MB, Yurdakul GF, Aydın E, Sivas F, Bodur H. Effect of vitamin D levels on radiographic knee osteoarthritis and functional status. *Turk J Phys Med Rehab*. 2018;64:1-7.
  27. Cakar M, Ayanoglu S, Cabuk H, Seyran M, Dedeoglu SS, Gurbuz H. Association between vitamin D concentrations and knee pain in patients with osteoarthritis. *Peer J*. 2018;6:e4670.
  28. Arden NK, Cro S, Sheard S, Doré CJ, Bara A, Tebbs SA et al. The effect of vitamin D supplementation on knee osteoarthritis, the VIDEO study: a randomized controlled trial. *Osteoarthritis Cartilage*. 2016;24:1858-66.
  29. Bergink AP, Zillikens MC, Van Leeuwen JP, Hofman A, Uitterlinden AG, van Meurs JB. 25-Hydroxyvitamin D and osteoarthritis: A meta-analysis including new data. *Semin Arthritis Rheum*. 2016;45:539-46.
  30. Ding C, Cicuttini F, Parameswaran V, Burgess J, Quinn S, Jones G. Serum levels of vitamin D, sunlight exposure, and knee cartilage loss in older adults. *Arthritis Rheum*. 2009; 60:1381e9.
  31. Mabey T, Honsawek S. Role of Vitamin D in osteoarthritis: molecular, Cellular, and Clinical Perspectives. *Int J Endocrinol*. 2015;2015:383918.
  32. Divya S, Abhishek M, Amar Chandra S, Ajai S, Natu SM, Sarita Agarwal et al. Does Vitamin D Improve Osteoarthritis of the Knee: A Randomized Controlled Pilot Trial. *Clin Orthop Relat Res*. 2013;471:3556-62.
  33. Muraki S, Dennison E, Jameson K, Boucher BJ, Akune T, Yoshimura N et al. Association of vitamin D status with knee pain and radiographic knee osteoarthritis. *Osteoarthritis Cartilage*. 2011;19:1301-6.
  34. Ho-Pham LT, Lai TQ, Mai LD, Doan MC, Pham HN, Nguyen TV. Prevalence of radiographic osteoarthritis of the knee and its relationship to self-reported pain. *PLoS One*. 2014;9(4):e94563.
  35. Rice DA, Kluger MT, McNair PJ, Lewis GN, Somogyi AA, Borotkanics R et al. Persistent postoperative pain after total knee arthroplasty: a prospective cohort study of potential risk factors. *Br J Anaesth*. 2018;121:804-812.
  36. Muraki S, Akune T, Oka H, Mabuchi A, En-yo Y, Yoshida M et al. Association of occupational activity with radiographic knee osteoarthritis and lumbar spondylosis in elderly patients of population-based cohorts: a large-scale population-based study. *Arthritis Rheum*. 2009;61:779e86.