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Original Article

The levels of 25-hydroxy vitamin D, parathyroid hormone, calcitonin and lipid profiles in patients with calcaneal spur

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ABSTRACT

Objectives: The aim of this study was to investigate the 25-hydroxyvitamin D (25(OH)D), parathyroid hormone (PTH), and calcitonin levels and lipid profiles in patients with calcaneal spurs.

Patients and methods: Between March 2018 and June 2019, a total of 50 patients (30 males, 20 females; mean age: 39.8±8.1 years; range, 24 to 54 years) admitted to our clinic with heel pain and diagnosed with heel spurs based on radiographic images were included. The control group consisted of 50 age- and sex-matched healthy volunteers (32 males, 18 females; mean age: 35.7±9.6 years; range, 20 to 56 years). Blood samples were collected from all participants. Total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride, phosphate, and calcium levels were measured using the colorimetric method. The PTH and 25(OH)D levels were measured using the chemiluminescent microparticle immunoassay. Calcitonin levels were detected using the chemiluminescent immunometric assay.

Results: In the patients with calcaneal spurs, 25(OH)D and HDL-C levels were significantly lower ($p<0.001$), while LDL-C, triglyceride, and PTH levels were significantly higher ($p<0.05$, $p<0.002$ and $p<0.001$, respectively). There was no significant difference in the calcium, phosphate, body mass index, and calcitonin levels between the groups.

Conclusion: Our study results suggest that calcaneal spur formation is associated not only with weight-related pressure, but also with lipid levels and hormonal alterations involved in calcium metabolism. Based on these findings, hormonal alterations and lipids should be considered in patients with calcaneal spurs.

Keywords: 25-hydroxy vitamin D, calcaneal spur, calcium, heel spur, lipid profile, parathyroid hormone.

Bony spurs can form on any bone, joint, or where ligaments or tendons attach to bones. A calcaneus is the most commonly affected tarsal bone and the primary site for bony spurs.[1] Calcaneal spurs (i.e., heel spurs), characterized by a bony outgrowth of the heel bone, were first described by Plettner, a German physician, in 1900.[2] Calcaneal spurs are a common cause of heel pain and foot discomfort in most of patients admitted to the orthopedics clinic.[3] It affects about 10% of the overall population.[4] It may impair the quality of life of patients and lead to hip, waist, and back pain due to altered gait pattern. Despite its high prevalence and burden of calcaneal spurs, the underlying etiology has not been fully understood, yet. The most common theory is that repetitive traction of the plantar fascia insertion into the calcaneus results in reactive ossification of the enthesis and inflammation, leading to the formation of calcaneal spurs.[5] It recurrent microtrauma in the pathogenesis of calcaneal spurs plays a major role. In addition, obesity, aging, and some sports activities such as running, jumping, and ballet have been

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blamed.[6,7] Although there are several studies about the diagnosis and treatment of calcaneal spurs in the literature, studies investigating underlying metabolic mechanisms are scarce.

In bone growth and formation, growth hormone (GH), parathyroid hormone (PTH), estrogen, and 25-hydroxyvitamin D (25(OH)D) play a central role. The latter is responsible for intestinal absorption of calcium, magnesium, and phosphate which is essential to maintain skeletal calcium balance.[8] Previous studies have demonstrated a possible relationship between vitamin D deficiency, chronic pain, and tibial pain.[9,10] The PTH regulates serum calcium levels through its effect on the bone, kidney, and intestine. In addition, it enhances the release of calcium from the large reservoir within the bone.[11] Ionized calcium and phosphate are also the main regulators of serum calcium levels, involving in the bone formation and metabolism.[12] Although these hormones and components are closely related to the bone formation and bone diseases, they have not been studies patients with calcaneal spurs to date.

Many nutritional factors such as sugars (glucose) and fats (lipids) can also play an important role in bone metabolism and maintenance of bone health.[13] Cholesterol, low-density lipoprotein-cholesterol (LDL-C) and triglyceride levels increase in individuals who consume high-fat diets, and it has been well documented that impaired lipid profile is associated with metabolic syndrome and obesity. In addition, in many studies, consumption of high-fat diets causes low bone mineral density, decreased bone strength, negative microstructural alterations in the cancellous bone compartment, and low levels of inflammation.[14] Some authors have also reported that high cholesterol levels may be associated with abnormal tendon structure and tendon pain.[15] Therefore, lipid levels may be related to the calcaneal spur.

In the present study, we aimed to evaluate 25(OH)D, PTH, and calcitonin levels in patients with calcaneal spurs and to investigate the role of metabolic parameters in the formation of the disease.

PATIENTS AND METHODS

The current study was designed as a case-control study. Between March 2018 and June 2019, a total of 50 patients (30 males, 20 females; mean age: 39.8±8.1 years; range, 24 to 54 years) admitted to our clinic with heel pain and diagnosed with heel spurs based on radiographic images were included (Figure 1). The control group consisted of 50 age-, sex-, and body mass index (BMI)-matched healthy volunteers (32 males, 18 females; mean age: 35.7±9.6 years; range, 20 to 56 years). Due to the seasonal variations of serum 25(OH)D, the blood samples were collected simultaneously from both the patient and control group to minimize the effect of seasonal variability. Patients with chronic diseases such as malignancies and diabetes mellitus, receiving vitamin supplements such as vitamin D supplements, those who exercise regularly, and having hypothyroidism or hyperthyroidism were excluded from the study. In addition, those having osteopenia, spondyloarthropathy, osteoporosis, and kidney diseases were excluded. The control group consisted of healthy volunteers having no bone metabolism disorder, any history of chronic disease, receiving no calcium mineral supplements, and having no previous diagnosis of a heel spur or bone-related disease. Data including demographic and clinical characteristics of all participants were recorded. Height and weight of the participants were measured in light indoor clothing and without shoes. The BMI was calculated by dividing the body weight in kilogram divided by body height in meter square (kg/m^2). Obesity was defined as a BMI of ≥30 kg/m^2. A written informed consent was

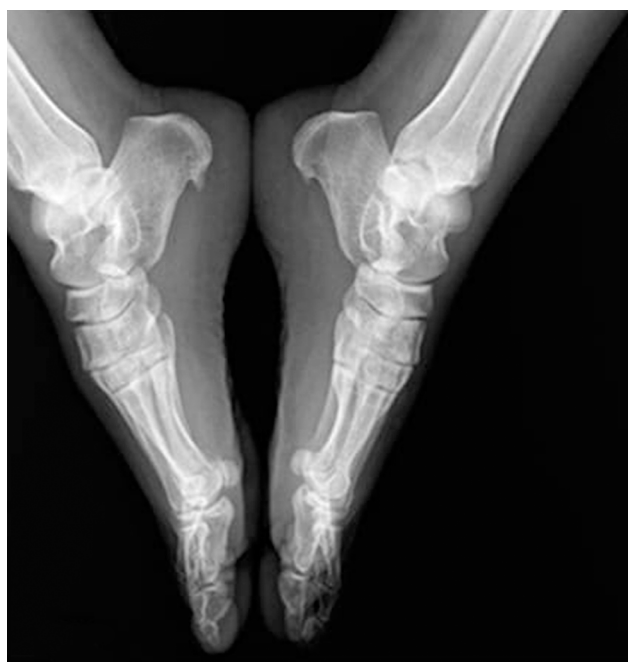

Figure 1. Bilateral foot radiograph showing calcaneal spurs.

obtained from each participant. The study protocol was approved by the Van Yüzüncü Yıl University, Ethics Committee (Date: 31/01/2018-No.10/2018). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Blood samples were collected from all participants. A total of 3-mL blood samples were drawn into dry tubes and centrifuged at 3,500 g for 10 min to obtain serum samples. The serum samples were divided into two aliquots and stored at -80°C until analysis. Phosphate, calcium, total cholesterol, high-density lipoprotein cholesterol (HDL-C), LDL-C, and triglyceride levels by the colorimetric method with the Abbott Architect C 16200 autoanalyzer using original reagents from the Abbott Diagnostics (Abbott Laboratories Inc., Abbott Park, IL, USA). The HDL-C levels were analyzed using the accelerator selective detergent method, while triglycerides using the triglyceride glycerol phosphate oxidase method and LDL using the Fried Ewald formula on an Abbott Architect autoanalyzer (Abbott Laboratories Inc., Abbott Park, IL, USA). The PTH and 25(OH)D levels were measured using the chemiluminescent microparticle immunoassay (Architect i2000sr; Abbott Laboratories Inc., Abbott Park, IL, USA). Calcitonin levels were detected using the chemiluminescent immunometric assay method (IMMULITE 2000 Siemens, Siemens Healthcare Diagnostics, Tarrytown, NY, USA).

Statistical analysis

The study power analysis was performed using the G*Power version 3.1.9.2 software (Heinrich-Heine-Universität, Düsseldorf, Düsseldorf, Germany). A total of 35 subjects were needed for each group with an effect size (alpha) of 0.8, an alpha error of 0.05 and 95% study power. Considering possible dropouts, each group consisted of 50 participants. Statistical analysis was performed using the SPPS version 20.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation (SD). The Shapiro-Wilk test was used to analyze normal distribution of variables. The independent samples t-test was used to analyze significant differences between the groups. The Student's t-test was performed to analyze significant differences between the patient and control groups. Pearson correlation analysis was performed using the Pearson correlation test. A p value of <0.05 was considered statistically significant.

RESULTS

In our study, there was no significant difference in the age and sex between the groups (p=0.225 and p=0.786, respectively). Demographic and clinical characteristics of both groups are summarized in Table 1. The participants were not obese, but they were overweight (BMI >25 kg/m^2). However, there was no statistically significant difference in the BMI levels between the patient and control groups (p=0.744).

In addition, we found no significant difference in the calcium and phosphate levels between the groups (p=0.216 and p=0.771, respectively). However, the PTH levels were significantly higher in the patients with calcaneal spurs than those of healthy controls (p=0.001), although the levels were within the reference range in both groups (reference range: 5 to 68.3 pg/mL). The level of 25(OH)D levels were significantly lower in the patients with calcaneal spurs than those of the healthy controls (p=0.001) (Figure 2). In addition, the HDL-C levels were significantly lower in the patients with calcaneal

TABLE 1
Demographic and clinical characteristics of patient and control groups

	Patient group (n=50)	Control group (n=50)		95% CI	
	Mean±SD	Mean±SD	p	Lower	Upper
Age (year)	39.8±8.1	35.7±9.6	0.200	-2.26	10.5
Height (cm)	172.4±8.6	168.4±9.4	0.145	-1.42	9.42
Weight (kg)	75.4±11.1	75.4±13.9	0.248	-3.14	11.8
BMI (kg/m^2)	26.8±2.9	26.4±5.4	0.744	-2.13	2.93

SD: Standard deviation; CI: Confidence interval; BMI: Body mass index.

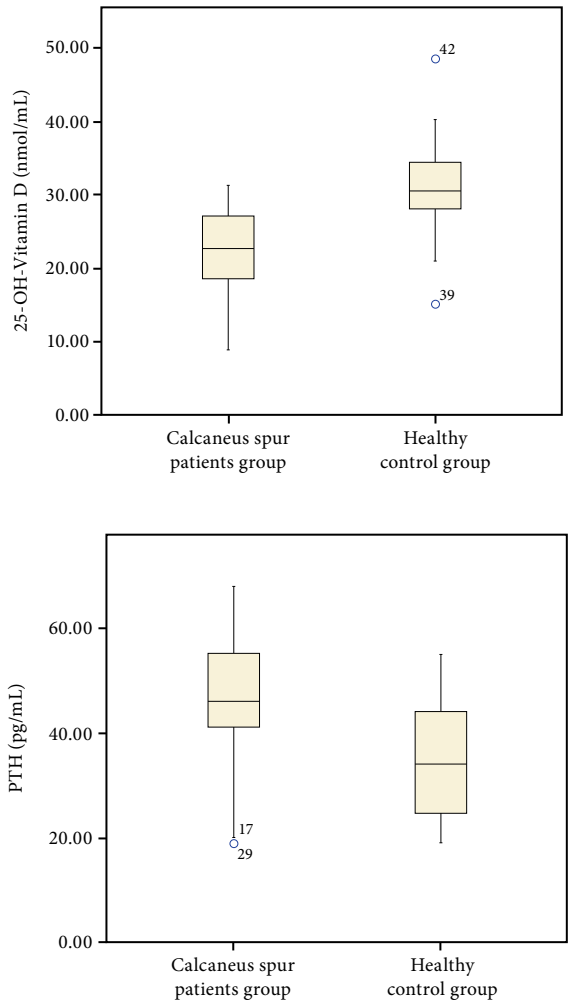

Figure 2. The distribution of 25(OH)D and PTH levels in patient and control groups.

PTH: Parathyroid hormone; 25(OH)D: 25-hydroxy vitamin D

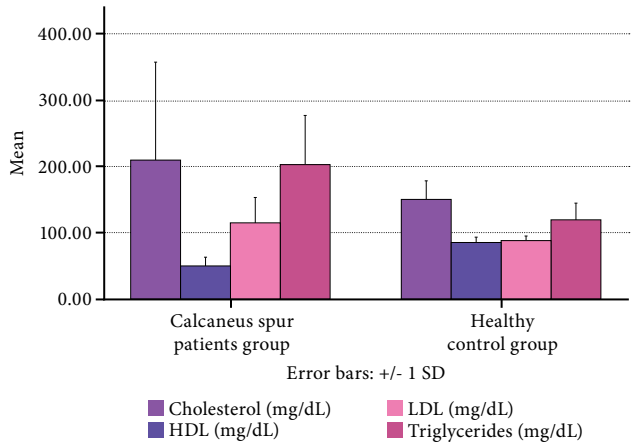

Figure 3. The distribution of total cholesterol, HDL-C, LDL-C, and triglyceride levels in patient and control groups.

HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol;

spurs than the healthy controls (p<0.001). However, the patient group had significantly higher LDL-C and triglyceride levels than the control group (p=0.001). Although not statistically significant, the total cholesterol levels were also higher in the patients with calcaneal spurs (p=0.074) (Figure 3). Laboratory results of both groups are presented in Table 2.

According to the correlation analysis, we found a positive correlation between the 25(OH)D and calcium levels in the patients with calcaneal spur, although not statistically significant (r=0.392, p=0.088). In addition, we found a negative correlation between the PTH and calcium levels in the patients with calcaneal spurs, although not

TABLE 2
Laboratory results of patient and control groups

	Patient group (n=50)	Control group (n=50)		95% CI	
	Mean±SD	Mean±SD	*p*	Lower	Upper
Total cholesterol (mg/dL)	209.5±95.7	148.2±28.9	0.074	-6.14	128.7
HDL-C (mg/dL)	49.5±13.3	55.4±8.5	<0.001	-42.5	-0.29
LDL-C (mg/dL)	113.8±39.7	87.2±8.2	0.001	8.31	44.6
Triglyceride (mg/dL)	202.1±75.2	118.5±25.8	<0.001	48.3	118.7
Phosphate (mg/dL)	3.3±0.7	3.3±0.3	0.771	-0.28	0.38
Calcium (mg/dL)	8.6±1.0	8.9±0.6	0.216	-0.83	0.19
Calcitonin (pg/mL)	4.8±2.3	5.2±3.3	0.858	-4.51	3.77
PTH (pg/mL)	45.9±13.1	34.1±10.6	0.0012	4.75	18.8
25(OH)D (ng/mL)	21.8±6.3	30.9±7.1	0.0011	-12.9	-0.52

SD: Standard deviation; CI: Confidence interval; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; PTH: Parathyroid hormone; 25(OH)D: 25-hydroxyvitamin D.

TABLE 3
Correlation analysis results of patients with calcaneal spurs

	Calcium (mg/dL)	Phosphate (mg/dL)	PTH (pg/mL)	25-(OH)D (nmol/mL)	Calcitonin (pg/mL)	Triglycerides (mg/dL)	HDL-C (mg/dL)	LDL-C (mg/dL)	Total cholesterol (mg/dL)
PTH (pg/mL)									
r	-0.328	0.589**	1	0.055	-0.213	-0.024	0.071	0.519*	-0.164
p	0.158	0.006		0.819	0.366	0.933	0.767	0.019	0.490
n	50	50	50	50	50	50	50	50	50
25(OH)D (nmol/mL)									
r	0.392	0.211	0.055	1	0.472*	-0.632*	0.547**	-0.345*	0.322
p	0.088	0.373	0.819		0.035	0.011	0.001	0.014	0.166
n	50	50	50	50	50	50	50	50	50
Calcitonin (pg/mL)									
r	0.013	-0.378	-0.024	-0.632*	0.033	1	-0.174	-0.351	-0.326
p	0.963	0.165	0.933	0.011	0.906		0.535	0.199	0,235
n	50	50	50	50	50	50	50	50	50

25(OH)D: 25-hydroxy vitamin D; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; PTH: Parathyroid hormone; * p<0.005; ** p<0.001.

statistically significant (r=-0.328, p=0.158). We also observed a statistically significant and positive correlation between the 25(OH)D and HDL-C levels (r=0.547, p=0.001) and a negative correlation between the 25(OH)D and LDL-C levels in the patients with calcaneal spur (r=-0.345, p=0.014). The correlation analysis results are summarized in Table 3.

DISCUSSION

In general, a calcaneal spur is defined as a bony outgrowth from the anterior medial aspect of the calcaneal tuberosity; however, there is no exact definition in the literature.[16] Although there are several proposals regarding the formation of calcaneal spurs, most of them are related to mechanical derangements.[17] Traditionally, it has been hypothesized that calcaneus spurs occur through repetitive stress/traction of the plantar fascia insertion into the calcaneus or through the intrinsic muscular system, resulting in inflammation and spur formation.[18-20] Some authors have also suggested that calcaneal spur formation may be associated with obesity.[21,22] However, many have proposed that not only mechanical causes play a role in the calcaneal spur formation, but also metabolic factors play a role, as the calcaneal spur formation does not occur in all obese individuals or those engaged in sports. Therefore, in our study, we investigated the role of hormone and lipid profiles which are effective on bone metabolism both in the patients with calcaneal spurs and healthy controls. To the best of our knowledge, this is the first study to examine metabolic parameters in patients with calcaneal spurs. In the present study, we found no significant difference in the levels of total cholesterol. However, the HDL-C levels were significantly lower, and the LDL-C and triglyceride levels were significantly higher in the patients with calcaneal spurs than healthy controls. On the other hand, the BMI measurements were similar between the groups. In previous studies, obesity was shown to be a risk factor for heel pain and calcaneal spur. Aydogdu et al.[23] reported that calcaneal spurs were more common among individuals with obesity, showing a higher incidence among patients with obesity accompanied by type 2 diabetes than non-diabetic patients with obesity. This finding indicates that not only obesity is a risk factor for calcaneal spur formation, but also metabolic factors may play a role. In our study, to equalize the effect of BMI on the calcaneal spur formation, the control group was comprised of BMI-matched healthy individuals. However, we found impaired lipid profile

in the patients with calcaneal spurs. Furthermore, the calcium levels were higher in the patients with calcaneal spurs than healthy controls; however, it did not reach statistical significance. On the other hand, both groups had similar phosphate levels. Calcium and phosphate are known to be important minerals for bone metabolism and body. Calcaneal spurs may be also caused by impaired calcification of the tendons.[24,25] To the best of our knowledge, this is also the first study to examine calcium and phosphate levels in patients with calcaneal spurs. Although calcium levels were found to be higher in the patient group, the difference was not statistically significant. However, further prospective studies would be helpful to establish a definite conclusion.

Furthermore, vitamin D, PTH, and calcitonin are responsible for maintaining extracellular calcium homeostasis. Vitamin D enhances intestinal calcium absorption, while PTH is secreted in response to low-circulating calcium concentrations.[26] Calcitonin is an important hormone for maintaining bone development and normal blood calcium levels in early life; however, elevated or decreased calcitonin levels do not cause problems in adults.[27] In our study, the levels of PTH were significantly higher in the patients with calcaneal spurs than healthy controls. This can be attributed to low 25(OH)D levels in patients with calcaneal spurs. Previous studies have shown that vitamin D is not only associated with bone metabolism, but also associated with many diseases including malignancies, cardiovascular diseases, autoimmune disorders, and diabetes mellitus.[28] In addition, the effects of vitamin D on muscle tissue and posture have been examined. Boersman et al.[29] reported that low 25(OH)D levels were associated with impaired postural balance. Similarly, Akdeniz et al.[30] found improved postural balance and reduced fall risk in the female patients with higher vitamin D concentrations. In our study, the levels of 25(OH)D were significantly lower in the patients with calcaneal spurs than healthy controls. This finding indicates that vitamin D deficiency may cause impaired postural balance and muscle tissue, increasing the risk for calcaneal spur formation. Vitamin D deficiency has been also shown to be associated with muscle and bone pain. In some studies, but not all, the use of vitamin D supplementation exerted positive effects on pain control.[31] Based on these findings, it may be reasonable to examine 25(OH)D levels in patients with calcaneal spurs and to prescribe vitamin D supplementation. However, further studies are needed to confirm these findings.

In the correlation analysis, we found that 25(OH)D was positively and statistically significantly correlated with the HDL-C levels and negatively correlated with the LDL-C levels. These results are consistent with previous studies.[32,33] These results indicate that a deterioration of both lipid metabolism and calcium homeostasis may occur due to 25(OH)D deficiency in patients with calcaneal spurs.

It has been shown that 25(OH)D concentrations can be affected by seasonal variations and, in particular, serum 25(OH)D concentrations increase in summer.[34] To minimize this effect in our study, the blood samples were collected simultaneously in the summer season from both the patient and control groups.

Nonetheless, there are some limitations to this study. The main limitation is that 25(OH)D, PTH, calcitonin, calcium, and phosphate were unable to be evaluated during follow-up in the patients with calcaneal spurs. In addition, alkaline phosphatase levels were unable to be measured. No posture analysis was able to be performed. Therefore, further, large-scale studies are needed to confirm these findings.

In conclusion, our study results suggest that obesity is not the only risk factor for calcaneal spur formation and hormonal alterations involved in calcium metabolism may play a role. Despite cross-sectional design of this study, the finding suggesting that the mean serum 25(OH)D levels were significantly lower in the patient group than the healthy controls and were below the reference threshold indicates that 25(OH)D levels can be measured in patients with calcaneal spur. In addition, the fact that LDL-C is high in patients with calcaneal spur and low HDL-C indicates that lipid profile is associated with the calcaneal spur. Based on these findings, it seems to be useful for clinicians to consider hormonal changes and lipid levels in this patient population.

Declaration of conflicting interests

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