



# Evaluation of the relationship between lateral epicondylitis and vitamin D

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Lateral epicondylitis (LE) is the most common cause of lateral elbow pain.<sup>[1]</sup> Lateral epicondylitis is common in the general population with a prevalence of 1 to 3%, and the highest incidence is between 40 and 50 years of age.<sup>[2,3]</sup>

The etiology of LE is not fully understood and appears to be independent of sex or ethnicity.<sup>[1,4]</sup> It is assumed that the main factors in the etiology are tenocyte proliferation caused by repetitive overuse and structurally abnormal collagen production. Several studies have shown that it is not a classical inflammatory process, but several cytokines may play a role in the etiology.<sup>[5]</sup>

In LE, the extensor carpi radialis brevis (ECRB) tendon is involved in more than 95% of all cases.<sup>[6]</sup> Nimura et al.,<sup>[7]</sup> in their study on 23 cadavers, showed that the ECRB tendon was in direct contact with the joint capsule above the humeroradial joint level and,

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## ABSTRACT

**Objectives:** This study aims to examine the relationship between low vitamin D levels and lateral epicondylitis (LE).

**Patients and methods:** Between January 2016 and January 2018, a total of 40 patients (17 males, 23 females; mean age: 38.6±10.7 years; range, 18 to 59 years) diagnosed with LE were included as the study group, while 66 patients (33 males, 33 females; mean age: 33.6±12.5 years; range, 18 to 58 years) who did not have any elbow complaints and met the study criteria were included as the control group. Both groups were compared in terms of vitamin D levels, of which levels of >30 ng/mL were considered normal, levels between 20-30 ng/mL were accepted as vitamin D insufficiency, and levels <20 ng/mL were categorized as vitamin D deficiency.

**Results:** Vitamin D levels of the LE group were significantly lower than the control group (p<0.001). The mean vitamin D level was 16.47±8.22 (range, 8.32 to 39.55) ng/mL in the LE group, and 23.64±8.4 (range, 11.6 to 49) ng/mL in the control group. While 31 of the patients (77.5%) diagnosed with LE had vitamin D deficiency, four (10%) had vitamin D insufficiency, and five (12.5%) had normal vitamin D levels. In the control group, 29 (43.9%) patients had vitamin D deficiency, 20 (30.3%) had vitamin D insufficiency, and 17 (25.8%) had normal vitamin D levels.

**Conclusion:** Although the etiology of LE has not been fully understood yet, vitamin D levels were significantly lower in LE patients in our study. This finding supports that low vitamin D may be one of the factors in the etiology of LE.

**Keywords:** Elbow, extensor carpi radialis brevis, lateral epicondylitis, pain, vitamin D.

therefore, the joint loads were transferred to the ECRB tendon. In their study, Ando et al.<sup>[8]</sup> suggested that the attachment area of the ECRB tendon on the lateral humeral epicondyle was 13 times smaller than the attachment area of the extensor carpi radialis longus (ECRL) tendon and, therefore, the ECRB tendon was more fragile. Bunata et al.,<sup>[9]</sup> on the other

hand, associated LE with friction between the ECRB tendon and the capitellum during elbow flexion and extension.

It is well known that vitamin D is vital for maintaining a balanced bone turnover and a healthy bone microenvironment. Previous studies have shown that untreated vitamin D deficiency results in well-known diseases such as osteoporosis, rickets, and osteomalacia and has a series of other effects on bones. Low levels of vitamin D in particular have been associated with metabolic diseases, cardiovascular diseases, certain types of cancer and infectious diseases, and exacerbation of many orthopedic disease patterns.<sup>[10-12]</sup>

Min et al.<sup>[13]</sup> performed an experimental study on tenocytes, assuming that vitamin D might have a protective effect on tendons, as well as on bones and muscles. Their study demonstrated that there was a vitamin D receptor on tenocytes and that when tenocytes suppressed by dexamethasone were exposed to vitamin D, type I collagen gene expression in tenocytes returned to normal.

Many studies on the etiology of LE focus on ECRB and elbow anatomy, while studies on low vitamin D levels mostly focus on bone pathologies and calcium metabolism.<sup>[6,7,10,11]</sup> Studies investigating the relationship between vitamin D and tendinopathy are not only limited in number, but also inconsistent.<sup>[13-15]</sup> To the best of our knowledge, there is no study showing the relationship between LE and low vitamin D levels. In the present study, we hypothesized that there might be a relationship between LE and low vitamin D levels. We, therefore, aimed to examine the relationship between vitamin D levels and LE.

## PATIENTS AND METHODS

This single-center, retrospective study was conducted at Necmettin Erbakan University Meram Medicine Faculty, Department of Orthopedics and Traumatology between January 2016 and January 2018. Among 147 patients with elbow pain who applied to our clinic, 40 (17 males, 23 females; mean age: 38.6±10.7 years; range, 18 to 59 years) who met the inclusion criteria and were diagnosed with LE were screened. Exclusion criteria were trauma history, previous upper extremity surgery, elbow arthrosis, metabolic bone diseases, endocrinological diseases affecting calcium-parathormone metabolism, infectious conditions, presence of neoplasia, rheumatological diseases, and kidney diseases. In addition, among 287 patients who

were admitted to our clinic for minor soft tissue traumas during the same period and checked for vitamin D levels, 66 (33 males, 33 females; mean age: 33.6±12.5 years; range, 18 to 58 years) with no upper extremity musculoskeletal complaints, no history of fractures or dislocations, and no muscle or tendon damage were included as the control group. Patients with acute minor lower extremity trauma were included to compose the control group from patients without chronic inflammatory conditions, non-inflammatory and degenerative orthopedic diseases, bone, tendon, or ligament injuries, long-term immobilizations, complaints about tendinitis in the region, continuous drug use due to other systematic chronic diseases, and using vitamin D replacement therapy for any reason.

Lateral epicondylitis was diagnosed based on medical history and physical examination. With lateral elbow pain, imaging studies are rarely needed at the initial examination. Thus, the diagnosis of LE was based on symptoms and physical examination alone. However, imaging techniques can rule out other abnormalities in the lateral elbow compartment, particularly if symptoms persist despite optimal conservative treatment.<sup>[1]</sup> On examination, the point of maximum tenderness is usually above the lateral epicondyle, sometimes 1 to 2 cm distal to the lateral epicondyle. Pain and tension in the tendon may occur on palpation of the ECRB tendon. With strong wrist extension, particularly when the elbow is extended and the forearm pronated, the pain would increase or recur. Resistive extension of the middle finger with the elbow extended is particularly painful due to the increased stress applied to the tendon, further supporting this diagnosis. Furthermore, there should be no numbness or tingling.<sup>[16]</sup>

There is no universal classification of vitamin D deficiency or insufficiency. In our study, vitamin D levels >30 ng/mL were considered normal, 20-30 ng/mL levels were accepted as vitamin D insufficiency, and <20 ng/mL as vitamin D deficiency. These levels are commonly used threshold levels.<sup>[17]</sup>

### Statistical analysis

The post-hoc power calculations were performed using the G\*Power version 3.1.9.4 software (Heinrich Heine University, Düsseldorf, Düsseldorf, Germany).

Statistical analysis was performed using the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were presented in mean ± standard deviation (SD), median (min-max)

TABLE I Demographic characteristics of the patients						
	LE group (n=40)			Control group (n=16)		
	n	Mean±SD	Range	n	Mean±SD	Range
Age (year)		38.6±10.7	18-59		33.6±12.5	18-58
Sex						
Male	17			33		
Female	23			33		
Side						
Right	24					
Left	16					

LE: Lateral epicondylitis; SD: Standard deviation.

TABLE II Comparison of vitamin D categories between the lateral epicondylitis and the control group				
	LE group		Control group	
	n	%	n	%
Vitamin D deficiency (0-19.9 ng/mL)	31	77.5	29	43.9
Vitamin D insufficiency (20-29.9 ng/mL)	4	10	20	30.3
Normal (>30 ng/mL)	5	12.5	17	25.8
P value				0.003

LE: Lateral epicondylitis.

or number and frequency. The Mann-Whitney U and chi-square tests were used to compare independent variables. A *p* value of <0.05 was considered statistically significant.

## RESULTS

Demographic data of the patients are summarized in Table I. When the two groups were compared in terms of age and sex, there was no significant difference (*p*=0.35 and *p*=0.51, respectively).

When the LE and control group were compared in vitamin D, patients with LE had significantly lower levels than the control group (*p*<0.001). The mean vitamin D level was 16.47±8.22 (range, 8.32 to 39.55) ng/mL in the vitamin D deficiency group and 23.64±8.4 (range, 11.6 to 49) ng/mL in the control group. While 31 of the patients (77.5%) diagnosed with LE had vitamin D deficiency, four (10%) had vitamin D insufficiency, and five (12.5%) had normal vitamin D levels. In the control group, 29 (43.9%) patients had vitamin D deficiency, 20 (30.3%) had vitamin D insufficiency, while 17 patients (25.8%) had normal vitamin D levels (Table II).

## DISCUSSION

The most important finding of this study is that patients with LE had significantly lower vitamin D levels. To the best of our knowledge, this is the first study in the literature from this aspect.<sup>[18]</sup>

While normal tendon tissue consists of 70% water, more than 85% of dry weight consists of type I collagen.<sup>[19,20]</sup> Since type I collagen is the main component of the tendon extracellular matrix (ECM), tendon tissue's structural and mechanical properties are largely dependent on the amount and quality of type I collagen.<sup>[19]</sup> Tenoblasts are fibroblasts of the tendon tissue that actively synthesize ECM components, particularly type I collagen,<sup>[21]</sup> while tenocytes are cells that maintain the integrity of ECM and ECM-related proteins by regulating type I collagen.<sup>[19]</sup> Min et al.<sup>[13]</sup> investigated the effects of vitamin D on tenocytes in their experimental histological study on human tenocytes. In their study, they administered dexamethasone to damage human tenocytes and examined the levels of tendon markers tenomodulin, tenascin, type I collagen, and type III collagen. Then, the tenocytes were exposed to vitamin D and 1-alpha hydroxylase to

investigate vitamin D receptors. They showed that tenomodulin, tenascin, and type I and type III collagen gene expression decreased in tenocytes suppressed by dexamethasone, and the expression of tenomodulin and type I collagen returned to normal when exposed to vitamin D. Furthermore, they showed that reactive oxygen species produced by dexamethasone decreased with vitamin D and that tenocytes had 1-alpha hydroxylase and vitamin D receptors and they interacted with vitamin D. In conclusion, Min et al.<sup>[13]</sup> in their experimental study on tenocyte cell cultures, reported that vitamin D had beneficial effects on tendons in addition to bones and muscles. In this context, significantly low levels of vitamin D in patients with LE may suggest that there may be a relationship between LE and decreased tendon protective effects of vitamin D.

Chen et al.<sup>[22]</sup> showed that the collagen-1 gene was downregulated in a mechanically stretched tendon through tumor necrosis factor-alpha (TNF- $\alpha$ ) and nuclear factor-kappa B (NF- $\kappa$ B) activation. In addition, Thankam et al.<sup>[19]</sup> showed an increased synthesis of metalloproteinase (MMP)-1, MMP-8, MMP-13, and gelatinases in damaged rotator cuff tendons and suggested that MMP-9 in particular caused rotator cuff tendinopathy by reducing the type I collagen/type III collagen ratio. In line with these studies, the importance of type I collagen reduction in the tendon in the development of tendinitis is clear. The effect of vitamin D on the production and amount of type I collagen in the tendon has been previously shown.<sup>[13]</sup> However, the etiology of LE cannot be fully explained by biomechanical factors such as the ECRB tendon being longer than other tendons in the lateral compartment of the elbow, the smaller footprint on the lateral humeral epicondyle than the ECRL, and the friction between the ECRB tendon and the capitellum during flexion and extension. Therefore, we believe that vitamin D deficiency alone cannot explain the etiology of LE. In addition to the biomechanical disadvantages of ECRB, we consider that vitamin D deficiency may also be a predictive factor for tendinitis. The relationship between vitamin D deficiency and tendinitis has been shown. We believe that this relationship is not specific to LE we examined in our study but may be related to tendinitis in other parts of the musculoskeletal system. In addition, the extent of the contribution of anatomic variations of the ECRB tendon and low levels of vitamin D to LE is unknown, and we consider that this situation would be also valid in other musculoskeletal system regions. Therefore,

tendinitis of other musculoskeletal regions should be evaluated together with their biomechanical properties. The presence of patients with LE and normal vitamin D levels in our study supports that low levels of vitamin D are not the only or the biggest factor in the etiology of tendinitis, and that many factors such as biomechanical, anatomical, and occupational components are involved in the etiology. We believe that future studies with patients with tendinitis in other parts of the musculoskeletal system or patients with more than one tendinitis would be helpful to further clarify the relationship between vitamin D and tendinitis.

Nonetheless, this study has some limitations. First, the study has a retrospective design, although the data were collected prospectively. Second, although the exclusion criteria were kept broad, the duration of the symptoms before the diagnosis of LE, and the duration of the symptoms that regressed after conservative treatment were unknown. The lack of long-term follow-up of patients with normal vitamin D levels and LE and the lack of information about the course of LE can be mentioned as further limitations. Anatomic factors contribute significantly to the etiology of LE, which has a complex pathophysiology. Although we did not include patients with a history of previous surgery and trauma, it is possible that patients cannot remember traumas. Therefore, this may be considered as another limitation. In the future, the place and role of vitamin D in the management of LE can be investigated by studying whether vitamin D replacement therapy given in addition to conservative treatment is superior to conservative treatment alone.

In conclusion, although the etiology of LE has not yet been fully understood, in our study, vitamin D levels were significantly lower in patients with LE. This study supports that low vitamin D may be one of the factors in the etiology of lateral epicondylitis.

**Ethics Committee Approval:** Ethical approval was obtained from Necmettin Erbakan University Ethical Committee (2022/3688). The study was conducted in accordance with the principles of the Declaration of Helsinki.

**Patient Consent for Publication:** Informed consent was obtained from all patients that their radiological images would be used for scientific purposes in accordance with the decision of the university ethics committee.

**Data Sharing Statement:** The data that support the findings of this study are available from the corresponding author upon reasonable request.

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