Serum Periostin Levels are Significantly Higher in Patients with Primary Hyperparathyroidism and Closely Related to Osteoporosis

Authors

Ismail Yigitdol[1], Erdinc Gulumsek[1], Huseyin Ali Ozturk[1], Fatih Necip Arici[1], Kubilay Akbal[1], Okan Pirinci[1], Mert Karacay[1], Tutku Naz Cihan[1], Zeynep Gizem Totik[1], Mustafa Aykut Akyildiz[1], Begum Seyda Avci[1], Akkan Avci[2], Hilmi Erdem Sumbul[1]

Affiliations

1 Department of Internal Medicine, University of Health Sciences – Adana Health Practice and Research Center, Adana, Turkey
2 Department of Emergency Medicine, University of Health Sciences – Adana Health Practice and Research Center, Adana, Turkey

Key words

primary hyperparathyroidism, periostin, osteoporosis, bone mineral density

received 09.12.2022
revised 28.02.2023
accepted 02.03.2023
published online 05.06.2023

Bibliography

Exp Clin Endocrinol Diabetes 2023; 131: 449–455
DOI 10.1055/a-2053-8090
ISSN 0947-7349

Georg Thieme Verlag, Rüdigerstraße 14,
70469 Stuttgart, Germany

Correspondence

Hilmi Erdem Sumbul
Department of Internal Medicine, University of Health Sciences – Adana Health Practice and Research Center,
Dr. Mithat Özsan Bulvarı Kışla Mah.
4522 Sok. No: 1 Yüreğir
Adana
Turkey
Fax: + (90) 506 6466586
erdemsumbul@gmail.com

ABSTRACT

Background Periostin is an emerging biomarker that plays a role in bone metabolism and may be associated with bone mineral density (BMD). This study is aimed to investigate serum periostin levels in patients with primary hyperparathyroidism (PHPT) and its correlation with BMD in these patients.

Methods Forty patients with newly diagnosed PHPT without co-morbidities and 30 healthy controls were included. Laboratory tests for the diagnosis of PHPT and serum levels of periostin were measured for all patients. BMD was measured on lumbar spines L1 and L4 by dual-energy X-ray absorptiometry (DEXA). Serum periostin levels were detected using an enzyme-linked immunosorbent assay (ELISA).

Results Serum periostin levels were significantly higher in patients with PHPT than in healthy controls ($p < 0.001$). Serum periostin levels were also significantly higher (mean 59.7 ± 11.0 ng/mL) in PHPT patients with osteoporosis than those without osteoporosis ($p = 0.004$). In logistic regression analysis, only serum periostin levels independently predicted the patients with osteoporosis. According to this analysis, every 1 ng/mL increase in serum periostin increased the risk of having osteoporosis by 20.6 %. When the cut-off for serum periostin level was 49.75 ng/mL, the patients with osteoporosis were predicted with 71.4 % sensitivity and 69.2 % specificity. Multivariate regression analysis revealed a negative correlation between serum periostin levels and L1-L4 T scores on DEXA.

Conclusion This is the first study to determine that serum periostin levels are higher in PHPT patients than those without PHPT and to demonstrate a significant association between serum periostin levels and T scores on DEXA in patients with PHPT. These findings will aid in detecting osteoporosis in patients with PHPT and making the decision for surgery in PHPT patients with no need for DEXA imaging that involves radiation.

Introduction

Parathyroid hormone (PTH) and vitamin D are the two main regulators of bone and mineral metabolism and have important critical roles in the regulation of calcium and phosphate metabolism and, therefore, in the maintenance and development of bone health [1]. Primary hyperparathyroidism (PHPT) is a common endocrine disorder, characterized by hypersecretion of PTH and hypercalcemia. Patients with PHPT may present with findings such as hypercalcemia, hypercalciuria, and osteoporosis, as well as with subclinical or overt nephrolithiasis or vertebral fractures [2]. Therefore, due to its catabolic effects, which lead to bone resorption and subsequent osteoporosis, PHPT is considered a cause of secondary osteoporosis [3]. Patients with hyperparathyroidism are at high risk for kidney stone formation, cortical bone loss, and fractures. In patients with PHPT,

surgery is recommended for patients younger than 50 years, patients with clinically significant hypercalcemia, osteoporosis or a fragility fracture, renal calculi, hypercalciuria, or impaired renal function [4].

Periostin, a 90 kDa extracellular matrix protein of 836 amino acids, was identified in 1999 and named after its expression in the periosteum of long bones [5]. It functions in the skeletal system both as a structural molecule of the bone matrix and as a signaling molecule through integrin receptors and the Wnt-beta-catenin pathways, thereby playing a role in osteoblastic activity and osteogenesis [6]. Periostin is mainly produced during ontogenesis and in adult connective tissues subjected to mechanical loads, such as heart valves, skin, periodontal ligaments, tendons, and bones [6]. In bone, the periosteum and osteocytes have the highest expression of periostin. Its production in these regions is controlled by mechanical stimuli, hormones (PTH), growth factors (TGF-b, BMP2), and cytokines (TNFα, IL-4, IL-13, and possibly PDGF). All these factors are known to have important roles in the regulation of bone remodeling [7]. Some studies suggest that serum periostin levels may be associated with serum parathormone levels [8]. As a result, many studies have been conducted to examine the relationship of this new molecule with bone metabolism and osteoporosis, and much information is now available regarding the role of periostin in bone fractures and osteoporosis [9].

Osteoporosis, one of the indications for surgery in patients with primary hyperparathyroidism, is diagnosed by measuring bone mineral density (BMD) using dual-energy X-ray absorptiometry (DEXA), an imaging method that includes radiation. Therefore, if a biochemical marker associated with osteoporosis can be identified in patients with PHPT, it may be important in the diagnosis and follow-up of osteoporosis in these patients. Our study aimed to investigate the relationship between osteoporosis and serum periostin levels in patients with primary hyperparathyroidism and to evaluate whether serum periostin levels can be used as a surrogate marker for predicting osteoporosis. In patients with PHPT, surrogate markers may play a role in reducing the need for a DEXA imaging procedure that includes radiation.

Materials and Method

Study population

This study was conducted prospectively, including 40 patients (mean age; 50.5 ± 14.0 years, male/female; 5/35) without co-morbidities and newly diagnosed with PHPT and 30 healthy controls (mean age; 47.2 ± 10.6 years, male/female; 19/21). The study participants were selected from the patients and volunteers who applied to XXXXXX Training and Research Hospital's Internal Medicine or Endocrinology and Metabolic Diseases Clinic between 01/01/2022 and 01/12/2022. PHPT was defined as elevated serum calcium level (adjusted for serum albumin level) along with elevated or inappropriately normal serum PTH level. The patients with musculoskeletal diseases, rheumatic diseases, inflammatory and hematological diseases, malignancy, pregnancy, cardiovascular disease, kidney disease, lung disease, and renal failure were excluded from the study. The study protocol was approved by the XXXXXX Training and Research Hospital's Local Ethics Committee, and written informed consent was obtained from all the participants.

Baseline characteristics of all groups were recorded after a detailed medical history and a complete physical examination. Body mass index (BMI) was calculated by measuring the weight and height of the patients. All subjects had laboratory tests and bone mineral density (BMD) scans of their lateral lumbar vertebrae (L1–L4) with DEXA (Lunar Prodigy; General Electric Medical Systems; WI, USA). Patients with T-score ≤ − 2.5 SD were diagnosed with osteoporosis. Each scan was manually analyzed by an experienced radiology specialist, for the lumbar spine for the consistent placing of the intervertebral spaces.

Biochemical measurements

In addition to routine blood tests for PHPT, periostin levels of the patients included in the study were analyzed, and blood samples were obtained from the patients in a bd vacutainer sst ii advance tube (BD Diagnostics – Preanalytical Systems, Dubai, United Arab Emirates), the serum part was separated by centrifugation at 2000 rpm for 10 min and stored at − 80 degrees in Eppendorf tubes. Serum periostin levels were measured using an enzyme-linked immunosorbent assay (ELISA) kit (eBioscience, Europe/International, Austria) following the manufacturer's instructions. Complete blood count analyses were performed with Sysmex XN 9000 brand device, and other biochemistry parameters were measured with Cobas C 701 brand biochemistry autoanalyzer (Roche, Germany).

Statistical analyses

All analyses were performed using the SPSS 22.0 (Chicago, IL, USA) statistical software package. Variables were divided into two groups as categorical and continuous variables. Whether the distribution of continuous variables is normal or not was evaluated with the Kolmogorov–Smirnov test. Continuous variables that showed normal distribution were compared using the Student t-test, whereas the Mann-Whitney U test was used for abnormally distributed samples. Continuous variables with normal distribution were expressed as mean ± SD, and abnormally distributed variables were expressed as median (interquartile range). The Chi-square test was used to compare categorical variables. Categorical variables were specified with numbers and percentages. The groups and their statistical comparisons are presented in tables. The variables found to be statistically significant in univariate analysis were included in the multivariate model, and multivariate logistic regression analysis was performed to determine the PHPT patients with a T score on DEXA ≤ − 2.5. A ROC curve analysis was performed to reassess markers that were independent variables in identifying PHPT patients as T score on DEXA ≤ − 2.5 and to determine the cut-off value of these markers. Parameters with the area under the curve (AUROC) > 0.70 were detected. For those parameters, the cut-off value was determined to ensure the best sensitivity and specificity in identifying the T score on DEXA ≤ − 2.5 PHPT patients. ROC curve was used to evaluate the diagnostic value of periostin for the T score on DEXA ≤ − 2.5. Univariate correlation analysis was performed using Pearson's and Spearman's correlation methods to determine parameters related to periostin level in patients with PHPT. Statistically significant parameters were included in a multivariate model and linear regression. Independent indicators affecting the periostin level were determined. Statistical significance was accepted as $p < 0.05$.

Results

Comparison of demographic and laboratory values of patients with primary hyperparathyroidism and healthy controls

Serum calcium, PTH, and serum periostin levels were significantly higher, while serum phosphorus level was significantly lower in the patients with PHPT compared to the healthy controls ($p < 0.001$, for each; ▶ **Table 1**). Other demographic and laboratory parameters were similar in both groups ($p > 0.05$ for each; ▶ **Table 1**).

In patients with PHPT, L1-L4 T scores on DEXA mean value was − 2.15 ± 0.76 (▶ **Table 1**). Of the 40 patients with PHPT, 14 (35.0 %) had osteoporosis (▶ **Table 2**). The PHPT patients' data were divided into two groups and evaluated according to the presence of osteoporosis (▶ **Table 2**).

Comparison of demographic and laboratory findings of patients with primary hyperparathyroidism according to the presence of osteoporosis

In PHPT patients with osteoporosis, L1-L4 T scores on DEXA mean value was − 2.94 ± 0.57; whereas in PHPT patients without osteoporosis, L1-L4 T scores on DEXA mean value was − 1.72 ± 0.44, and this difference was statistically significant ($p < 0.001$, ▶ **Table 2**). It was observed that serum periostin levels were significantly higher (mean value 59.7 ± 11.0 ng/ml) in PHPT patients with osteoporosis compared to PHPT patients without osteoporosis ($p = 0.004$, ▶ **Table 2**). Other demographic and laboratory parameters were similar in PHPT patients with and without osteoporosis ($p > 0.05$ for each; ▶ **Table 2**).

Multivariate logistic regression analysis for the detection of patients with primary hyperparathyroidism who had L1-L4 T score on dual-energy X-ray absorptiometry score ≤ − 2.5

The parameters found to be significantly different in patients with osteoporosis in the univariate analysis were further evaluated by multivariate analysis. The results revealed that only serum periostin levels independently predicted the patients with osteoporosis (▶ **Table 3**). According to this analysis, every 1 ng/mL increase in the serum periostin level increased the risk of having osteoporosis by 20.6 % (▶ **Table 3**).

Receiver operating characteristic curve (ROC) analysis for the detection of patients with L1-L4 T score in dual-energy X-ray absorptiometry score ≤ − 2.5

When the ROC analysis was performed to assess the importance of serum periostin level in determining patients with osteoporosis, the area under the curve (AUC) was found to be 0.826 (▶ **Figure 1**). According to our analysis, when a limit value of serum periostin level was taken as 49.75 ng/mL, serum periostin level predicted patients with osteoporosis with 71.4 % sensitivity and 69.2 % specificity (▶ **Figure 1**).

▶ **Table 1** Demographic and laboratory findings of patients with PHPT and healthy controls

Variable	PHPT n = 40	Healthy controls n:30	p-value
Age (year)*	50.5 ± 14.0	47.2 ± 10.6	0.292
Gender (female)	35 (87.5 %)	21 (70.0 %)	0.087
White blood cell (μL)*	6.85 ± 1.84	6.42 ± 1.52	0.302
Hemoglobin (g/dL)*	13.07 ± 1.46	12.7 ± 0.62	0.242
Platelet, IQR (K/mm3)	250.0 (194.75–315.5)	279.0 (261.5–326.0)	0.541
Glucose (mg/dL)*	90.8 ± 8.33	92.4 ± 9.43	0.455
Creatinine (mg/dL)*	0.81 ± 0.16	0.64 ± 0.13	0.219
Serum sodium (mmol/L)*	139.4 ± 2.13	140.1 ± 1.83	0.182
Serum potassium (mmol/L)*	4.51 ± 0.41	4.50 ± 0.39	0.908
Triglycerides, IQR (mg/dL)	101.0 (98.0–142.25)	111.0 (67.0–145.0)	0.418
LDL cholesterol, IQR (mg/dL)	137.5 (120.0–155.0)	117.0 (110.0–149.5)	0.114
Aspartate aminotransferase, IQR (U/L)	20.0 (15.25–26.75)	18.0 (16.0–23.0)	0.302
Alanine aminotransferase, IQR (U/L)	19.0 (13.0–24.75)	16.0 (11.75–32–75)	0.425
Alkaline phosphatase, IQR (U/L)	60.5 (56.0–65.0)	58.5 (55.75–66.75)	0.959
Serum albumin (gr/dL)*	4.19 ± 0.16	4.16 ± 0.49	0.778
Serum calcium (mg/dL)*	11.2 ± 1.20	9.8 ± 0.31	< 0.001
Serum phosphorus (mg/dL)*	2.80 ± 0.61	3.37 ± 0.52	< 0.001
Urine calcium, IQR (mg/day)	291.0 (196.0–450.0)	–	–
25(OH) Vit D, IQR (ng/mL)	18.0 (14.0–23.0)	13.45 (9.02–21.18)	0.495
Parathyroid hormone, IQR (pg/mL)	182.5 (120.0–325.25)	47.65 (30.0–57.60)	< 0.001
L1-L4 T scores on DEXA*	− 2.15 ± 0.76	–	–
Periostin (ng/mL)*	52.7 ± 9.96	33.9 ± 6.76	< 0.001

*: Mean ± standard deviation, IQR: interquartile range, LDL: low density lipoprotein, PHPT: primary hyperparathyroidism, 25(OH) Vit D: 25-hydroxyvitamine D, DEXA: dual-energy X-ray absorptiometry

▶ **Table 2** Demographic and laboratory findings of patients with PHPT according to the presence of osteoporosis

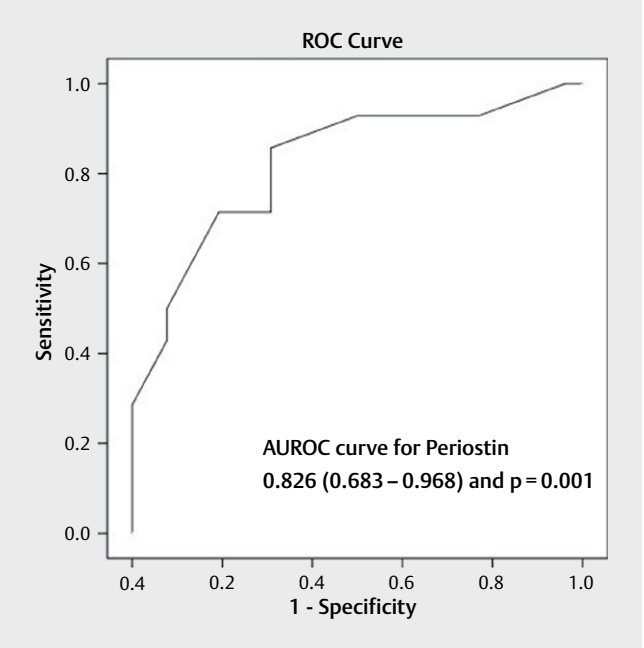
Variable	Osteoporosis present (+) n = 14 (35 %)	Osteoporosis absent (-) n:26 (65 %)	p-value
Age (year)*	55.5 ± 10.2	47.8 ± 15.2	0.101
White blood cell (μL)*	6.69 ± 2.50	6.94 ± 1.42	0.689
Hemoglobin (g/dL)*	13.3 ± 1.42	12.9 ± 1.49	0.479
Platelet, IQR (K/mm3)	218.5 (191.0–266.5)	289.5 (212.5–332.5)	0.463
Glucose (mg/dL)*	88.4 ± 9.35	92.0 ± 7.62	0.190
Creatinine (mg/dL)*	1.05 ± 0.40	0.65 ± 0.22	0.240
Serum sodium (mmol/L)*	138.6 ± 2.37	139.9 ± 1.89	0.69
Serum potassium (mmol/L)*	4.53 ± 0.42	4.50 ± 0.41	0.869
Triglycerides, IQR (mg/dL)	130.0 (100.0–149.25)	100.0 (95.5–124.0)	0.227
LDL cholesterol, IQR (mg/dL)	135.5 (119.75–150.25)	145.0 (131.25–154.5)	0.271
Aspartate aminotransferase, IQR (U/L)	19.0 (14.0–25.5)	20.0 (16.75–27.25)	0.320
Alanine aminotransferase, IQR (U/L)	17.0 (10.0–21.0)	19.0 (13.0–25.5)	0.184
Alkaline phosphatase, IQR (U/L)	56.0 (56.0–70.0)	64.0 (56.0–65.75)	0.887
Serum albumin (g/dL)*	4.20 ± 0.12	4.18 ± 0.18	0.711
Serum calcium (mg/dL)*	11.02 ± 1.15	11.38 ± 1.24	0.372
Serum phosphorus (mg/dL)*	2.95 ± 0.63	2.72 ± 0.59	0.256
Urine calcium, IQR (mg/day)	284.0 (134.0–400.0)	292.0 (195.5–490.0)	0.312
25(OH) Vit D, IQR (ng/mL)	17.0 (9,68–23.0)	18.03 (14.0–23.07)	0.441
Parathyroid hormone, IQR (pg/mL)	156.5 (100.77–442.25)	190.5 (125.25–302.0)	0.287
L1-L4 T scores on DEXA*	−2.94 ± 0.57	−1.72 ± 0.44	< 0.001
Periostin (ng/mL)*	59.7 ± 11.0	48.9 ± 6.92	0.004

*: Mean ± standard deviation, IQR: interquartile range, LDL: low density lipoprotein, 25(OH) Vit D: 25-hydroxyvitamine D, PHPT: primary hyperparathyroidism, DEXA: dual-energy X-ray absorptiometry

▶ **Table 3** Variable regression analysis for the detection of PHPT patients with osteoporosis.

Variable	Odds Ratio	95 % Confidence Interval	p-value
25(OH) Vit D (ng/mL)	0.900	0.752–1.078	0.254
Parathyroid hormone (pg/mL)	1.001	0.997–1.004	0.764
Serum calcium (mg/dL)	0.556	0.169–1.829	0.334
Urine calcium (mg/day)	1.000	0.994–1.005	0.915
Periostin (ng/mL)	1.206	1.060–1.373	0.004

25(OH) Vit D: 25-hydroxyvitamine D, PHPT: primary hyperparathyroidism



▶ **Figure 1** Receiver operating characteristic curve (ROC) analysis of serum periostin level for predicting the presence of osteoporosis in patients with primary hyperparathyroidism.

Parameters associated with serum periostin levels in patients with primary hyperparathyroidism

When univariate correlation analysis was performed to determine the parameters associated with serum periostin level, only L1-L4 T scores on DEXA were correlated with serum periostin level, and this correlation was negative. Furthermore, in multivariate regression analysis, L1-L4 T scores on DEXA were also independently correlated with serum periostin levels (▶ **Table 4**, ▶ **Figure. 2**).

Discussion

The most important finding of our study is that serum periostin level is increased in patients with PHPT and the level is higher in PHPT patients with osteoporosis compared to the PHPT patients

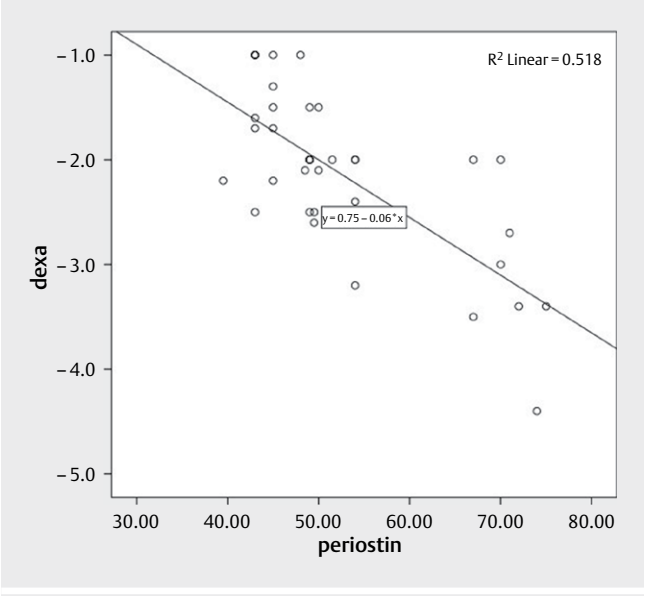
without osteoporosis. To the best of our knowledge, our study is the first to compare serum periostin levels in PHPT patients with healthy controls and demonstrate a close relationship between serum periostin level and T scores on DEXA in PHPT patients. The finding that serum periostin levels in patients with PHPT have a close and negative relationship with T-scores on DEXA suggests that periostin may be used in patients with PHPT to identify those with osteoporosis requiring surgery, without a need for DEXA imaging that involves radiation. Therefore, these data provided important information to the literature.

In patients with vitamin D insufficiency, vitamin D replacement was performed after blood samples were taken so that periostin results would not be affected, and secondary hyperparathyroidism was ruled out with appropriate test repetitions. Vitamin D insufficiency is common in the Turkish population [10, 11]. Therefore, most patients included in our study also had vitamin D deficiency. However, the statistically similar vitamin D levels in the study groups gave us the opportunity to compare the periostin levels. In addition, we did not observe any relationship between vitamin D levels and periostin in our study.

There are some differences in the estimates of the prevalence of osteoporosis in patients with PHPT, varying in the range of 39 % and 62.9 % according to different studies [2]. In our study, the rate of osteoporosis in patients with PHPT was 35 %. This may be due to the relatively lower mean age of the patients included in our study than other studies reported earlier. To the best of our knowledge, there is only one study examining serum periostin levels in patients with PHPT. According to this study conducted by Pepe et al. (2021), serum periostin level was significantly associated with a fracture in PHPT [12]. However, their study did not have a control group of patients without PHPT, and therefore, they could not compare serum periostin levels in PHPT patients compared to patients without PHPT. In addition, Pepe et al. (2021) also found that the mean serum periostin level of patients with fracture was significantly higher compared to the patients without fracture (46.2 ± 21.4 vs. 34.7 ± 13.5 ng/mL, p = 0.02) [12]. Furthermore, they did not indicate a correlation between periostin levels and BMD values, possibly because all patients included in that study were postmenopausal and most of them already had osteoporosis. On the other hand, in our study, serum periostin levels were significantly higher in the patients with PHPT compared to the healthy controls (mean value 52.7 ± 9.96 vs. 33.9 ± 6.76 ng/mL, p < 0.001). Furthermore, serum periostin levels were significantly higher in PHPT patients with osteoporosis compared to PHPT patients without osteoporosis (mean value 59.7 ± 11.0 vs. 48.9 ± 6.92 ng/mL, p = 0.004).

▶ **Table 4** The parameters associated with serum periostin level and linear regression analysis for parameters significantly correlated with serum periostin level in patients with PHPT

Variable	Univariate analyze		Multivariate analyze	
	p	r	p	β
L1-L4 T score on DEXA	< 0.001	− 0.671	< 0.001	− 9.414
DEXA: Dual X-ray Absorptiometry, * $R^2_{Adjusted}$ = 0.506, PHPT: primary hyperparathyroidism				



▶ **Figure 2** Scatter plot diagram for the relationship of T scores in dual-energy X-ray absorptiometry (DEXA) and serum periostin level.

Several clinical studies have examined the relationship of periostin with bone fracture and BMD. The first clinical study on the relationship between serum periostin levels and osteoporotic fracture risk was conducted by Rousseau et al. in 2014; they found that the risk of fracture increased in patients with high serum periostin levels [13]. In addition, Kim et al. (2015) concluded that serum periostin may be a potential biomarker to predict osteoporotic fracture risk, especially for nonvertebral regions, and there is an inverse relationship between periostin level and proximal femur BMD [14]. In a study highlighting the genetic polymorphism effect, Guo et al. (2022) found that serum periostin may be a predictor for the risk of vertebral fracture, and periostin is negatively correlated with trochanter and total hip BMD [15]. All these studies suggest that serum periostin levels can be altered by genetic differences or pathologies that directly affect bones, such as fractures, and therefore, periostin levels can be used as a predictor for bone fractures instead of BMD. In our study, the effect of PHPT on the bones may have caused higher periostin levels, especially in the osteoporotic group.

According to recent studies, periostin is closely related to cortical bone thickness, density, and porosity [16, 17]. Also, it has been suggested as an emerging potential biomarker for osteoporosis [18]. Thus, in our study, the existence of a relationship between periostin and bone architecture may have led to a significant relationship between serum periostin levels and BMD. In our study, periostin levels independently determined the presence of osteoporosis in patients with PHPT. The AUC for periostin was 82.6 % (95 % CI, 68.3–96.8 %; p = 0.001). In addition, when the cut-off value for serum periostin level was taken as 49.75 ng/ml, the sensitivity and specificity of serum periostin levels in predicting patients with osteoporosis were 71.4 % and 69.2 %, respectively.

In the management of patients with PHPT, making the surgical decision is one of the most important steps. Therefore, some studies have focused on biomarkers that may predict surgical needs in

this patient group. For example, in a study by Demirtas et al. (2020), CTRP3 levels decreased significantly decreased in patients with PHPT, and they were also related to osteoporosis, which is a surgical criterion in PHPT [19]. Also, in a study conducted by Gulumsek et al. (2022), native SH (thiol) values were lower in PHPT patients who were candidates for surgery. These findings suggest that native SH may be helpful in determining the indication for surgical treatment in asymptomatic PHPT patients [20]. Our study may also be helpful in detecting the presence of osteoporosis in PHPT patients and thus aiding the surgical decision in this patient group.

Limitations

The most important limitation of this study is that it is single-centered, cross-sectional, with a limited number of patients. In addition, periostin is expressed in many tissues other than bones. Although we tried to exclude the main confounding factors, this could have implications as we were not able to measure the bone-specific isoform. The other limitations of our study were that we did not study other bone biomarkers and genetic polymorphism, did not measure DEXA from other body regions such as obtaining densitometric values of the radius, did not consider additional factors such as smoking, exercise, and nutritional factors, did not include osteoporosis patients without PHPT and PHPT patients with fracture and did not evaluate the patients after the treatment.

Conclusion

In our study, serum periostin levels were significantly higher in patients with PHPT and negatively correlated with T scores on DEXA. To our knowledge, our study is the first to demonstrate an increase in periostin levels in patients with PHPT compared to patients without PHPT and also the first to demonstrate a correlation between serum periostin levels and osteoporosis in patients with PHPT. These findings might be helpful in determining the indication for surgical treatment in patients with PHPT without a need for an imaging method that involves radiation. Further studies with larger patient groups are required for better elucidation of the relationship between periostin levels and BMD in PHPT patients.

Acknowledgment

There is no person, institution, or company to be acknowledged.

Funding

This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Informed Consent

Written informed consent was obtained from all patients.

Ethical Approval

The ethics committee of the Adana City Training and Research Hospital approved the study.

Human Rights

This manuscript was carried out in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Conflicts of Interest

The authors have no conflict of interest to declare.

References

[1] Khundmiri SJ, Murray RD, Lederer E. PTH and vitamin D. Compr Physiol 2016; 6: 561–601. DOI:10.1002/cphy.c140071

[2] Walker MD, Silverberg SJ. Primary hyperparathyroidism. Nat Rev Endocrinol 2018; 14 (2): 115–125. DOI:10.1038/nrendo.2017.104

[3] Mazzuoli GF, D'Erasmo E, Pisani D. Primary hyperparathyroidism and osteoporosis. Aging (Milano) 1998; 10: 225–231. DOI:10.1007/BF03339656

[4] Insogna KL. Primary hyperparathyroidism. N Engl J Med 2018; 379: 1050–1059. DOI:10.1056/NEJMcp1714213

[5] Horiuchi K, Amizuka N, Takeshita S et al. Identification and characterization of a novel protein, periostin, with restricted expression to periosteum and periodontal ligament and increased expression by transforming growth factor beta. J Bone Miner Res 1999; 14: 1239–1249. DOI:10.1359/jbmr.1999.14.7.1239

[6] Bonnet N, Garnero P, Ferrari S. Periostin action in bone. Mol Cell Endocrinol 2016; 432: 75–82. DOI:10.1016/j.mce.2015.12.014

[7] Idolazzi L, Ridolo E, Fassio A et al. Periostin: The bone and beyond. Eur J Intern Med 2017; 38: 12–16. DOI:10.1016/j.ejim.2016.11.015

[8] Fortunati D, Reppe S, Fjeldheim AK et al. Periostin is a collagen associated bone matrix protein regulated by parathyroid hormone. Matrix Biol 2010; 29: 594–601. DOI:10.1016/j.matbio.2010.07.001

[9] Rachner TD, Khosla S, Hofbauer LC. Osteoporosis: Now and the future. Lancet 2011; 377: 1276–1287. DOI:10.1016/S0140-6736(10)62349-5

[10] Hekimsoy Z, Dinç G, Kafesçiler S et al. Vitamin D status among adults in the Aegean region of Turkey. BMC Public Health 2010; 10: 782. Published 2010 Dec 23. DOI:10.1186/1471-2458-10-782

[11] Cigerli O, Parildar H, Unal AD et al. Vitamin D deficiency is a problem for adult out-patients? A university hospital sample in Istanbul, Turkey. Public Health Nutr 2013; 16: 1306–1313. DOI:10.1017/S1368980012003588

[12] Pepe J, Bonnet N, Cipriani C et al. Higher serum levels of a cathepsin K-generated periostin fragment are associated with fractures in postmenopausal women with primary hyperparathyroidism: A pilot study. Osteoporos Int 2021; 32: 2365–2369. DOI:10.1007/s00198-021-06018-x

[13] Rousseau JC, Sornay-Rendu E, Bertholon C et al. Serum periostin is associated with fracture risk in postmenopausal women: A 7-year prospective analysis of the OFELY study. J Clin Endocrinol Metab 2014; 99: 2533–2539. DOI:10.1210/jc.2013-3893

[14] Kim BJ, Rhee Y, Kim CH et al. Plasma periostin associates significantly with non-vertebral but not vertebral fractures in postmenopausal women: Clinical evidence for the different effects of periostin depending on the skeletal site. Bone 2015; 81: 435–441. DOI:10.1016/j.bone.2015.08.014

[15] Guo YM, Cheng JH, Zhang H et al. Serum periostin level and genetic polymorphisms are associated with vertebral fracture in Chinese postmenopausal women. Genes (Basel) 2022; 13: 439. DOI:10.3390/genes13030439

[16] Walsh JS, Gossiel F, Scott JR et al. Effect of age and gender on serum periostin: Relationship to cortical measures, bone turnover and hormones. Bone 2017; 99: 8–13. DOI:10.1016/j.bone.2017.03.041

[17] Gerbaix M, Vico L, Ferrari SL et al. Periostin expression contributes to cortical bone loss during unloading. Bone 2015; 71: 94–100. DOI:10.1016/j.bone.2014.10.011

[18] Garnero P. The utility of biomarkers in osteoporosis management. Mol Diagn Ther 2017; 21: 401–418. DOI:10.1007/s40291-017-0272-1

[19] Demirtas D, Acıbucu F, Baylan FA et al. CTRP3 is significantly decreased in patients with primary hyperparathyroidism and closely related with osteoporosis. Exp Clin Endocrinol Diabetes 2020; 128: 152–157. DOI:10.1055/a-0899-5210

[20] Gulumsek E, Yesildal F, Koca H et al. Native thiol decreases in patients with asymptomatic primary hyperparathyroidism, especially in the presence of surgery indication. Minerva Endocrinol (Torino) 2022. DOI:10.23736/S2724-6507.22.03604-1 10.23736/S2724-6507.22.03604-1