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Levels of osteocalcin and *N*-terminal telopeptide of type I collagen in men with ankylosing spondylitis: associations with disease course and structural-functional status of bone tissue

Sergii Shevchuk, Oksana Pavliuk ✉, Olena Shevchuk

Department of Internal Medicine No. 2, National Pirogov Memorial Medical University, Vinnytsya, Ukraine

Abstract

Introduction: The aim was to assess osteocalcin (OC) and *N*-terminal telopeptide of type I collagen (NTx) levels in men with ankylosing spondylitis (AS) and evaluate their relationship with the course of the disease and the structural and functional state of bone tissue.

Material and methods: The study was conducted on 83 male patients with AS and 29 healthy individuals constituting the control group. Disease activity and functional limitations were assessed using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondyloarthritis Disease Activity Score with C-reactive protein (ASDAS-CRP), and Bath Ankylosing Spondylitis Functional Index (BASFI) functional indices. Laboratory testing included CRP and markers of bone synthesis and resorption. Bone mineral density (BMD) of the lumbar spine and femoral neck was determined using dual-energy X-ray absorptiometry.

Results: The mean OC levels did not differ significantly between AS patients and the control group and showed no significant correlation with ASDAS, BASDAI, BASFI and CRP indices. On the other hand, NTx values were significantly higher in AS patients than in the control group (105.8 ±3.4 ng/ml vs. 92.6 ±5.1 ng/ml) and were closely related to the activity of the inflammatory process and low functional capacity. The structural and functional state of the bone is impaired by increased bone resorption. Thus, the proportion of patients with low BMD and fractures (68.2% and 27.3%) in the group of patients with high NTx content was 4–12 times higher than with optimal levels of this marker (17.7% and 2.2%). On the other hand, osteoproliferative changes were not associated with NTx levels but were dependent on serum OC levels. In particular, in the group of patients with syndesmophytes, serum OC values were higher (by 12.4%) than in the group without syndesmophytes.

Conclusions: Elevated NTx levels are associated with high inflammatory activity and low BMD. On the other hand, OC concentration is not associated with disease progression but is increased in individuals with syndesmophytes.

Key words: osteocalcin, BMD, ankylosing spondylitis, markers of bone tissue.

Introduction

A disorder of bone mineral density (BMD) in ankylosing spondylitis (AS) is a rather complex phenomenon. Paradoxically, structural damage in the form of ectopic formation of bone tissue, characteristic of localization, is accompanied by systemic loss of bone mass leading to the development of osteoporosis [1]. It is known that a decrease in BMD increases the risk of low-energy fractures in patients with AS by almost 4 times compared to the general population [2–4]. The causes and mechanisms of osteoporosis and its complications are still not well understood, with an active inflammatory process playing an important role. Thus, according to modern data, systemic inflammation, on the one hand, contributes

Address for correspondence

Oksana Pavliuk, Department of Internal Medicine No. 2, National Pirogov Memorial Medical University, 56 Pyrogova St., 21018 Vinnytsya, Ukraine, e-mail: pavliukoksana@ukr.net

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to the resorption of bone tissue, through increased differentiation of osteoclasts, and on the other hand, to the local increase in the synthesis of bone tissue, mainly due to the hyperproduction of tumor necrosis factor α (TNF-α) and interleukin-17 (IL-17), which leads to excessive activation of osteoblasts and pathological new bone formation [5–7]. Due to this, the determination of specific markers of bone tissue synthesis and resorption would make it possible to assess the state of bone metabolism and the development of the osteoporotic process in patients suffering from AS. Data from the literature regarding the level of remodeling markers in AS are quite contradictory. In a number of studies, an increase in the concentration of bone metabolism markers and a decrease in BMD have been observed [8, 9]. On the other hand, there are studies where no correlation was found between changes in BMD and the metabolic state of bone tissue in patients with AS [10]. The relationship between the course of the disease and the development of metabolic disorders of bone tissue in patients with AS also remains poorly understood. Therefore, the purpose of the study was to assess the levels of osteocalcin (OC) and *N*-terminal telopeptide of type I collagen (NTx) in men with AS and to evaluate their relationship with the course of the disease and the structural and functional state of bone tissue.

Material and methods

The main group included 83 men with AS aged 40.7 ±0.8 years. The average duration of the disease was 8.7 ±0.5 years. The control group included 29 apparently healthy individuals representative in terms of age and gender. The study participants underwent examination at the Rheumatology Department of Vinnytsia Research Institute of Rehabilitation of Persons with Disabilities. At the time of the study, men with AS were not taking basic disease-modifying therapy, hormonal therapy, or calcium and vitamin D preparations. All patients were diagnosed with AS according to the modified New York 1984 criteria [11] and the Assessment of SpondyloArthritis International Society (ASAS) criteria [12]. All patients underwent a comprehensive clinical and laboratory examination. The determination of clinical activity of AS was based on the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondyloarthritis Disease Activity Score with C-reactive protein (ASDAS-CRP index: < 1.3 – inactive AS; 1.3–2.1 – moderate activity; 2.1–3.5 – high activity; > 3.5 – very high activity), and functional capacity was assessed using the Bath Ankylosing Spondylitis Functional Index (BASFI). The level of the inflammatory activity marker C-reactive protein (CRP) was analyzed using standard laboratory methods in a medical institution. The marker of bone tissue remodeling (OC) was assessed by the immunoenzymatic method using the N-MID Osteocalcin ELISA Kit (Immunodiagnostic Systems, UK). The marker of bone resorption (NTx) was determined by the immunoenzymatic method using the Human NTXI kit (Elabscience, USA, catalog no.: E-EL-H0836, Lot: 31DCADXW39) according to the manufacturer's instructions.

Bone mineral density of the lumbar spine and femoral neck was determined using dual-energy X-ray absorptiometry (DEXA) on a Hologic Discovery W device (S/N 87227). In patients aged above 50 years, osteoporosis was diagnosed when BMD showed a decrease in the *T*-score ≤ –2.5 SD, while osteopenia was defined by a *T*-score range of –1 to –2.5 SD. For men aged up to 50 years, the *Z*-score was used; its decrease below ≤ –2.0 SD or less indicated a significant loss of bone mass.

Lateral plain radiographs of the cervical, thoracic, and lumbar spine were used to detect syndesmophytes. Lateral radiographs were scored according to the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS). The score includes the anterior corners of vertebrae C2 to T1 and T12 to S1, which are graded with 0 to 3 points each (0 = normal, 1 = erosion, sclerosis or squaring, 2 = syndesmophyte, 3 = bridging syndesmophyte).

Statistical analysis

Statistical processing of the obtained results was carried out using Microsoft Office Excel for Windows 2007 and the universal statistical program Statistica SPSS 10.0 for Windows. The following statistical values were determined: number of observations (*n*), arithmetic mean (*M*), standard error of the average value (*m*), and relative values (abs., %). The normality of the distribution was checked by the Shapiro-Wilk test. The parametric Student's *t*-test was used to assess the difference between groups for a normal distribution, and the Mann-Whitney *U* test for a distribution deviating from the normal distribution. When comparing the frequency of changes, Fisher's exact method was used, and the correlation of characteristics between indicators was determined using Pearson's correlation analysis (*r*) (differences at $p < 0.05$ were considered significant).

Bioethical standards

The study adhered to the guidelines outlined in the 1975 Declaration of Helsinki (revised in 2000) and received approval from the Ethics Committee of Vinnytsia National Pirogov Memorial Medical University, Protocol No. 25 of September 30, 2024. Informed consent was obtained from all patients.

Results

The analysis of the bone tissue synthesis marker level showed that individuals of the control group and patients with AS do not differ significantly. According to the results of the percentile analysis, it was established that in 95% of the control group, the level of OC was in the range of 8.11–21.5 ng/ml (P5–P95), and in patients with AS, the level of the marker was in the range of 3.4–20.6 ng/ml (P5–P95) (Table I). In contrast, the level of NTx was significantly different between controls and patients suffering from AS. Specifically, the average level of NTx in the control group was 92.6 ±5.1 ng/ml, while in patients suffering from AS it was significantly higher at 105.8 ±3.4 ng/ml. Since there are no clear criteria for gradation of OC and NTx levels in the literature, for further analysis we chose indicators that corresponded to P5, P5–P95 and P95 of the control group. The optimal OS level was 8.11–21.5 ng/ml (P5–P95), a low level was below 8.11 ng/ml (< P5), and a high level was above 21.5 ng/ml (> P95). The optimal NTx level was considered to be < 104.5 ng/ml (< P75), a high level was 104.5–131.8 ng/ml (P75–P95), and an extremely high level was ≥ 131.8 ng/ml (> P95).

The ranking of OC levels showed that 10.3% of the control group had low levels, and 89.7% had a relatively normal level, while among patients with AS, low levels were found in about 23%, while relatively normal and high indicators were observed in 71.9% and 4.9% of the patients, respectively. In the control group, the percentage of patients with a high level of NTx was 6.9%, an extremely high level was detected in 17.3% of patients, and in 75.8% it was within the normal range (Fig. 1). In patients with AS, the percentage of patients with a high level of NTx was 4 times higher than in the control group at 26.5%, an extremely high level was observed in 19.3% of patients, and a preserved level was observed in 54.2% of patients.

Table I. Percentile analysis of markers of bone tissue synthesis and resorption in the control group and in AS patients

Group	Average level (*M* ±*m*)	OC [ng/ml]					
		P_5	P_{10}	P_{25}	P_{75}	P_{90}	P_{95}
Control (*n* = 29)	12.9 ±0.9	8.1	8.3	10.1	14.5	20.3	21.5
Patients with AS (*n* = 82)	11.3 ±0.6	3.4	3.9	7.4	14.3	18.5	20.6
NTx [ng/ml]							
Control (*n* = 29)	92.6 ±5.1	58.9	64.0	71.4	104.5	121.2	131.8
Patients with AS (*n* = 83)	105.8 ±3.4*	66.7	68.1	84.5	133.3	147.5	155.3

** Significant difference between the patients suffering from AS and the control group.*
AS – ankylosing spondylitis, m – standard error of the average value, M – arithmetic mean, NTx – N-terminal telopeptide of type I collagen, OC – osteocalcin.

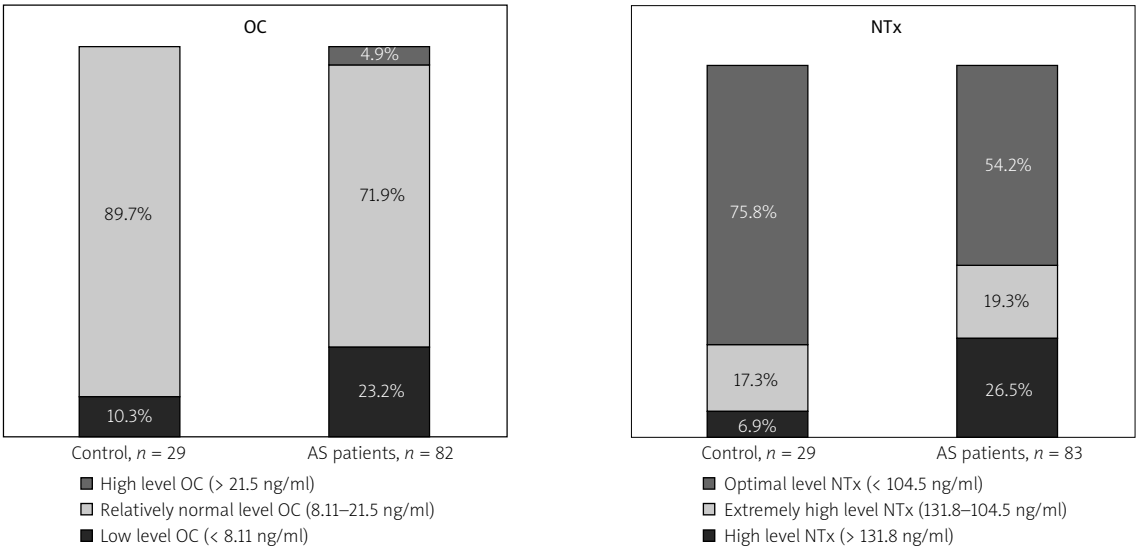

Fig. 1. Serum levels of osteocalcin and NTx in men with AS and controls.

**Sign indicated credible differences in relation to patients of the control.*
AS – ankylosing spondylitis, NTx – N-terminal telopeptide of type I collagen, OC – osteocalcin.

The study did not reveal a significant relationship between age and changes in the levels of bone tissue synthesis and resorption markers. Thus, the highest proportion of patients with a low level of OC was in the age group of 18–29 years and was 31.6%, in the age group of 30–44 years a low level of OC was registered in 30.8% of patients, and in the group of 45–59 years a low level of OC was registered in 27.3% of patients (Table II). Similar results were obtained when analyzing NTx levels, as the highest proportion of patients (36.4%) with high levels was also found in the 18–29 age group. The duration of the disease also did not affect the level of OC and NTx in blood serum.

The level of the bone tissue synthesis marker had no clear relationship with the activity of the inflammatory process. Thus, in patients with very high activity (ASDAS > 3.5), the proportion of patients with a low level of OC was 10% lower than in the group of patients with moderate activity (ASDAS < 3.5). According to the BASDAI, the average levels of the marker were comparable. The proportion of patients with a low content of OC probably did not differ in the groups depending on the functional capacity determined by the BASFI (Table III). On the other hand, the intensity of destruction of bone tissue was closely associated with high activity of the disease. It was found that patients with high BASDAI values (≥ 4) had a significantly higher (by 16.8%) average NTx concentration and the proportion of patients with a high level of the resorption marker than in the group of patients with BASDAI ≤ 4. Similar patterns were also found according to the BASFI, where in the group with low functional status (BASFI > 4) the proportion of patients with a high level of NTx was 1.5 times higher than in the group with preserved functional capacity (BASFI < 4). The correlation between NTx and CRP level was even stronger. Thus, in the group of patients with an optimal level of CRP, the average value of the resorption marker was 88.8 ±6.8 ng/ml, and in the groups with a high and very high level of CRP, the values were 109.4 ±4.6 ng/ml and 116.8 ±6.7 ng/ml, respectively.

Research has established that BMD disorders are primarily caused by increased resorption of bone tissue. In the group of patients with a high content of NTx, significantly lower BMD indicator levels were noted. Thus, the average values of the *Z*- and *T*-score of the lumbar spine and femoral neck were 4.6–1.9 and 3.1–1.5 times lower than in the group with normal levels of the resorption marker (Table IV). In addition, the proportion of patients with low BMD and fractures (68.2% and 27.3%) in the group of patients with a high content of NTx was 4–12 times higher than in the group with preserved levels of this marker (17.7% and 2.2%). In contrast, OC concentration was not significantly associated with low BMD and osteoporotic fractures. Thus, the percentage of patients with reduced BMD at different levels of OC was almost the same (36.5% and 36.8%).

However, the synthesis of pathologically new bone tissue and the development of osteoproliferative processes was closely associated with the content of OC (Table V). In the group of patients with syndesmophytes, the serum level of OC (12.1 ±0.9 ng/ml) was significantly higher than in the group without syndesmophytes (10.6 ±0.7 ng/ml).

Table II. Concentration of OC and NTx depending on the age of the patients and the duration of the disease

Group	Synthesis marker – OC		Resorption marker – NTx	
	M ±*m*	Low level (< 8.11 ng/ml) [*n* (%)]	*M* ±*m*	High level (> 131.8 ng/ml) [*n* (%)]
Depending on age				
18–29 years old (*n* = 19/22)	11.0 ±1.0	6 (31.6)	106.3 ±7.4	8 (36.4)
30–44 years old (*n* = 52/50)	11.2 ±0.8	16 (30.8)	107.5 ±4.4	11 (22.0)
45–59 years old (*n* = 11/11)	11.5 ±1.4	3 (27.3)	104.6 ±9.1	3 (27.3)
Depending on the duration of the disease				
< 5 years (*n* = 13/13)	12.6 ±1.0	1 (7.7)	102.2 ±8.0	4 (30.8)
5–10 years (*n* = 42/45)	10.5 ±0.9	15 (35.7)	106.5 ±4.8	12 (26.7)
> 10 years (*n* = 27/25)	11.5 ±1.1	9 (33.3)	109.7 ±6.4	6 (24.0)

m – standard error of the average value, M – arithmetic mean, NTx – N-terminal telopeptide of type I collagen, OC – osteocalcin.

Table III. Relationship of OC and NTx levels with activity indicators according to ASDAS, BASDAI, BASFI functional index and pro-inflammatory mediator CRP

Indicator		Synthesis marker – OC		Resorption marker – NTx	
		M ±m	Low level (< 8.11 ng/ml) [*n* (%)]	M ±m	High level (> 131.8 ng/ml) [*n* (%)]
ASDAS	< 3.5 (*n* = 42/42)	10.3 ±0.9	15 (36.5)	100.7 ±4.6	9 (21.4)
	> 3.5 (*n* = 40/41)	12.1 ±0.7	10 (26.3)	113.0 ±5.0	13 (31.7)
R		–0.15		0.21	
BASDAI	≤ 4 (*n* = 24/23)	10.9 ±1.2	8 (33.3)	95.5 ±4.3	3 (13.1)
	> 4 (*n* = 58/60)	11.3 ±0.7	17 (30.3)	**111.1 ±4.5***	**19 (31.6)***
R		–0.12		**0.37#**	
BASFI	< 4 (*n* = 23/24)	11.5 ±1.2	7 (30.4)	97.7 ±6.2	4 (16.6)
	> 4 (*n* = 59/59)	11.1 ±0.7	18 (30.5)	110.5 ±4.1	18 (30.5)
R		–0.18		**0.25#**	
CRP	< 5.4 (*n* = 20/18)	10.3 ±1.4	8 (40.0)	88.8 ±6.8	2 (11.1)
	5.4–13.4 (*n* = 41/44)	11.4 ±0.8	12 (29.3)	**109.4 ±4.6***	13 (29.5)
	> 13.4 (*n* = 21/21)	11.5 ±1.1	5 (23.8)	116.8 ±6.7*	7 (33.4)
R		–0.13		0.30#	

** Significant differences in relation to patients with the lowest BASDAI and CRP indicators, p < 0.05.*
 # Significant correlation.
ASDAS – Ankylosing Spondyloarthritis Disease Activity Score, BASDAI – Bath Ankylosing Spondylitis Disease Activity Index, BASFI – Bath Ankylosing Spondylitis Functional Index, CRP – C-reactive protein, m – standard error of the average value, M – arithmetic mean, NTx – N-terminal telopeptide of type I collagen, OC – osteocalcin.

Table IV. Relationship of levels of OC and NTx with the structural state of bone tissue in men with AS

BMD indicators	Synthesis marker – OC		Resorption marker – NTx	
	Preserved level (*n* = 63)	Low level (*n* = 19)	Preserved level (*n* = 61)	High level (*n* = 22)
Lumbar spine				
Z-score	–0.9 ±0.2	–1.2 ±0.2	–0.45 ±0.2	**–2.1 ±0.2***
T-score	–1.0 ±0.2	–1.2 ±0.1	–0.70 ±0.2	**–2.17 ±0.2***
BMD [g/sm^2]	1.01 ±0.01	0.96 ±0.02	1.01 ±0.02	**0.86 ±0.03***
Femoral neck				
Z-score	–1.2 ±0.1	–1.5 ±0.2	–0.62 ±0.1	**–1.22 ±0.1***
T-score	–1.4±0.1	–1.7 ±0.2	–1.07 ±0.1	**–1.59 ±0.2***
BMD [g/sm^2]	0.76 ±0.01	0.66 ±0.02	0.78 ±0.01	**0.71 ±0.02***
Number of patients with reduced BMD [*n* (%)]	23 (36.5)	7 (36.8)	8 (17.7)	**15 (68.2)***
Number of patients with syndesmophytes [*n* (%)]	29 (46.1)	5 (26.3)	14 (31.1)	10 (45.5)
Number of patients with fractures [*n* (%)]	9 (14.3)	2 (10.5)	1 (2.2)	**6 (27.3)***

** Significant differences in relation to patients with a preserved NTx level, p < 0.05.*
BMD – bone mineral density, NTx – N-terminal telopeptide of type I collagen, OC – osteocalcin.

Table V. Serum levels of OC and NTx in patients with osteoproliferative changes in bone tissue

Indicators	Osteoproliferative changes	
	Patients without syndesmophytes (n = 48)	Patients with syndesmophytes (n = 34)
Synthesis marker		
OC [ng/ml], $M \pm m$	10.6 ±0.7	**12.1 ±0.9***
Resorption marker		
NTx [ng/ml], $M \pm m$	102.5 ±4.13	113.9 ±6.03

** Significant difference in relation to the group of patients without syndesmophytes.*
m – standard error of the average value, M – arithmetic mean, NTx – N-terminal telopeptide of type I collagen, OC – osteocalcin.

Discussion

Thus, research has established that in men with AS, resorptive processes in bone tissue prevail over biosynthetic ones. In particular, low levels of OC were found in 23% of patients with AS, while in the control group such levels were found in 9.1% of the patients. As for the average concentration of the marker, it was only 12% lower than in the control group. On the other hand, a high level of NTx, as a marker of resorption, was found in 26.5% of patients suffering from AS, while in the control group it was in 6.9%. The average content of NTx was also significantly higher in AS patients than in the control group (105.8 ±3.4 ng/ml vs. 92.6 ±5.1 ng/ml). Literary data on this issue in AS patients are quite contradictory. Thus, according to a previous study [13], the average level of OC was lower in patients with AS than in the control group, while in other studies [14, 15], the level of OC in patients with AS did not differ from that in the control group, or was even 50% higher [16, 17]. Our results are consistent with other researchers' data on NTx levels. In particular, it has been reported that there were significantly (relative to control) higher levels of markers of bone tissue resorption in patients [8, 18]. However, other research results [19, 20] showed that serum levels of markers of bone decay did not differ significantly between patients with AS and healthy controls.

We did not find any influence of age and duration of the disease on the concentration of bone tissue remodeling markers in blood serum. However, in the study of Huang et al. [18], a significant relationship was found between OC and the duration of the disease (r = 0.324; p = 0.034), and according to the data of Arends et al. [8], close associations were found between age, disease duration, and resorptive processes in AS patients.

One of the unfavorable pathogenetic factors of disturbances in the metabolic state of bone tissue is the systemic inflammatory process. Literature data clearly indicate that high disease activity stimulates osteoclastogenesis and leads to destructive processes in bone tissue [21, 22]. We observed that the increase in NTx levels in patients with AS was closely associated with the activity of the inflammatory process. Thus, the highest proportions of patients with a high level of the bone resorption marker are in the groups of patients with high and very high activity according to ASDAS and BASDAI. N-terminal telopeptide of type I collagen levels were also associated with increased serum levels of the pro-inflammatory mediator C-reactive protein. On the other hand, the concentration of OC did not depend on the inflammatory process. In particular, with very high activity and low functional capacity (ASDAS > 3.5; BASDAI > 4; BASFI > 4), the content of the marker in blood serum was comparable to that found in patients with moderate activity and preserved functional capacity (ASDAS < 3.5; BASDAI < 4; BASFI < 4). Our data are consistent with the results of other studies [16, 19, 23] in which it was found that the levels of OC in blood serum were not correlated with any of the clinical (ASDAS, BASDAI) and laboratory (CRP, ESR) markers of the inflammatory process, and the level of urinary N-telopeptide was significantly higher in patients with high disease activity [20]. However, there is also research in which no relationship was found between disease activity and markers of bone resorption in AS patients [19].

The intensity of destructive processes in the bone was closely associated with changes in BMD identified by dual-energy X-ray absorptiometry, as well as with the presence of fractures. In particular, in patients with a high level of NTx, the Z-score at the level of the lumbar spine was 4.6 times lower (femurs – 1.9 times) compared to that at the optimal level of NTx, at –2.1 ±0.2 (–1.22 ±0.10) vs. –0.45 ±0.2 (–0.62 ±0.10). In parallel with the increase in serum NTx, the proportion of individuals with a decrease in BMD and fractures significantly increased. Thus, in men with a destruction marker level of > 131.8 ng/ml, a decrease in densitometric indicators was found in 68.2% of patients, and the proportion of patients with fractures was 12 times higher than at the optimal level of this marker. A number of scientific studies have reported that the generalized loss of bone

mass in patients with AS is associated with a high content of markers of bone destruction [16, 24].

The study found that OC concentration was not significantly associated with low BMD and osteoporotic fractures. Instead, the synthesis of pathological new bone tissue and the development of osteoproliferative changes were closely associated with the content of OC in blood serum. Thus, in the group of patients with syndesmophytes, the serum values of OC were significantly higher (by 12.4%) than in the group without syndesmophytes. The data of other scientists are quite contradictory. In particular, Arends et al. [8] reported that increased levels of OC in AS patients were associated with reduced BMD. On the other hand, several studies [17, 25] have demonstrated that patients with pronounced syndesmophytes and ankylosis of the spine have significantly higher levels of markers of bone tissue synthesis.

Summarizing our data, we can state that in studied group of men with AS, OC levels did not differ from those of the control group, whereas the concentration of the resorption marker (NTx) was significantly elevated. Levels of NTx were associated with high disease activity and low BMD. These data support the theory that patients with AS have imbalanced bone metabolism and that inflammatory activity may affect bone metabolism and lead to osteoporosis.

Study limitations

This study had some limitations. First, it was a single-center study and the sample size was relatively small. Second, the measurement of serum bone remodeling markers was performed only once and mainly in patients with high inflammatory activity and the study group with AS consisted only of men. Third, the treatment given to the patients was not taken into account, and there was no follow-up period.

Conclusions

An increase in the levels of the bone resorption marker (NTx) is associated with a decrease in BMD (*Z*-, *T*-score, BMD) and occurrence of fractures and is not related to the presence of syndesmophytes; in contrast, OC levels are not associated with decreased BMD and fractures, but are increased in individuals with syndesmophytes.

The NTx levels are closely associated with BASDAI inflammatory process activity ($r = 0.37$, $p < 0.05$), CRP levels ($r = 0.30$, $p < 0.05$), and functional capacity according to BASFI ($r = 0.25$, $p < 0.05$) and are not related to the age of the patients and the duration of the disease. Osteocalcin levels do not correlate with the course of the disease.

Disclosures

Conflict of interest: The authors declare no conflict of interest.
Funding: No external funding.
Ethics approval: The study was approved by the Institutional Bioethics Committee of the National Pirogov Memorial Medical University, Vinnytsya, Ukraine (approval number 25 dated September 30, 2024).
Data availability: The data that support the findings of this study are available on request from the corresponding author (O.P.)

References

1. Tan S, Bagheri H, Lee D, et al. Vertebral Bone Mineral Density, Vertebral Strength, and Syndesmophyte Growth in Ankylosing Spondylitis: The Importance of Bridging. Arthritis Rheumatol 2022; 74: 1352–1362, DOI: 10.1002/art.42120.
2. Hu ZB, Wei B, Wu SK, et al. Changes in bone mineral density and bone metabolic indexes in ankylosing spondylitis mouse model complicated with osteoporosis. Exp Ther Med 2018; 16: 811–815, DOI: 10.3892/etm.2018.6220.
3. Kim JW, Park S, Jung JY, et al. Prevalence and Factors of Osteoporosis and High Risk of Osteoporotic Fracture in Patients with Ankylosing Spondylitis: A Multicenter Comparative Study of Bone Mineral Density and the Fracture Risk Assessment Tool. J Clin Med 2022; 11: 2830, DOI: 10.3390/jcm11102830.
4. Malochet-Guinamand S, Pereira B, Tatar Z, et al. Prevalence and risk factors of low bone mineral density in spondyloarthritis and prevalence of vertebral fractures. BMC Musculoskelet Disord 2017; 18: 357, DOI: 10.1186/s12891-017-1718-7.
5. Briot K, Roux C. Inflammation, bone loss and fracture risk in spondyloarthritis. RMD Open 2015; 1: e000052, DOI: 10.1136/rmdopen-2015-000052.
6. Coury F, Peyruchaud O, Machuca-Gayet I. Osteoimmunology of Bone Loss in Inflammatory Rheumatic Diseases. Front Immunol 2019; 10: 679, DOI: 10.3389/fimmu.2019.00679.
7. Goldring SR. Osteoimmunology and bone homeostasis: relevance to spondyloarthritis. Curr Rheumatol Rep 2013; 15: 342, DOI: 10.1007/s11926-013-0342-2.
8. Arends S, Spoorenberg A, Bruyn GA, et al. The relation between bone mineral density, bone turnover markers, and vitamin D status in ankylosing spondylitis patients with active disease: a cross-sectional analysis. Osteoporos Int 2011; 22: 1431–1439, DOI: 10.1007/s00198-010-1338-7.
9. Kwon SR, Lim MJ, Suh CH, et al. Dickkopf-1 level is lower in patients with ankylosing spondylitis than in healthy people and is not influenced by anti-tumor necrosis factor therapy. Rheumatol Int 2012; 32: 2523–2527, DOI: 10.1007/s00296-011-1981-0.
10. Visvanathan S, van der Heijde D, Deodhar A, et al. Effects of infliximab on markers of inflammation and bone turnover and associations with bone mineral density in patients with ankylosing spondylitis. Ann Rheum Dis 2009; 68: 175–182, DOI: 10.1136/ard.2007.084426.

11. van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984; 27: 361–368, DOI: 10.1002/art.1780270401.
12. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. Ann Rheum Dis 2011; 70: 896–904, DOI: 10.1136/ard.2011.151027.
13. Altindag Ö, Karakoç M, Soran N, et al. Bone Mineral Density in Patients with Ankylosing Spondylitis. Rheumatism 2008; 23: 42–45.
14. Prietl B, Treiber G, Pieber TR, Amrein K. Vitamin D and immune function. Nutrients 2013; 5: 2502–2521, DOI: 10.3390/nu5072502.
15. Grisar J, Bernecker PM, Aringer M, et al. Ankylosing spondylitis, psoriatic arthritis, and reactive arthritis show increased bone resorption, but differ with regard to bone formation. J Rheumatol 2002; 29: 1430–1436.
16. Park MC, Chung SJ, Park YB, Lee SK. Bone and cartilage turnover markers, bone mineral density, and radiographic damage in men with ankylosing spondylitis. Yonsei Med J 2008; 49: 288–294, DOI: 10.3349/ymj.2008.49.2.288.
17. Niu CC, Lin SS, Yuan LJ, et al. Correlation of blood bone turnover biomarkers and Wnt signaling antagonists with AS, DISH, OPLL, and OYL. BMC Musculoskelet Disord 2017; 18: 61, DOI: 10.1186/s12891-017-1425-4.
18. Huang J, Song G, Yin Z, Fu Z, Ye Z. Alteration of Bone Turnover Markers in Canonical Wingless Pathway in Patients With Ankylosing Spondylitis. Arch Rheumatol 2016; 31: 221–228, DOI: 10.5606/ArchRheumatol.2016.5857.
19. Muntean L, Rojas-Vargas M, Font P, et al. Relative value of the lumbar spine and hip bone mineral density and bone turnover markers in men with ankylosing spondylitis. Clin Rheumatol 2011; 30: 691–695, DOI: 10.1007/s10067-010-1648-3.
20. Taylan A, Sari I, Akinci B, et al. Biomarkers and cytokines of bone turnover: extensive evaluation in a cohort of patients with ankylosing spondylitis. BMC Musculoskelet Disord 2012; 13: 191, DOI: 10.1186/1471-2474-13-191.
21. Epsley S, Tadros S, Farid A, et al. The Effect of Inflammation on Bone. Front Physiol 2021; 11: 511799, DOI: 10.3389/fphys.2020.511799.
22. Ogasawara T, Yoshimine Y, Kiyoshima T, et al. In situ expression of RANKL, RANK, osteoprotegerin and cytokines in osteoclasts of rat periodontal tissue. J Periodontal Res 2004; 39: 42–49, DOI: 10.1111/j.1600-0765.2004.00699.
23. Perpétuo IP, Caetano-Lopes J, Vieira-Sousa E, et al. Ankylosing Spondylitis Patients Have Impaired Osteoclast Gene Expression in Circulating Osteoclast Precursors [published correction appears in Front Med (Lausanne) 2017; 4: 38, DOI: 10.3389/fmed.2017.00038]. Front Med (Lausanne) 2017; 4: 5, DOI: 10.3389/fmed.2017.00005
24. Arends S, Spoorenberg A, Efde M, et al. Higher bone turnover is related to spinal radiographic damage and low bone mineral density in ankylosing spondylitis patients with active disease: a cross-sectional analysis. PLoS One 2014; 9: e99685, DOI: 10.1371/journal.pone.0099685
25. Gamez-Nava JI, de la Cerda-Trujillo LF, Vazquez-Villegas ML, et al. Association between bone turnover markers, clinical variables, spinal syndesmophytes and bone mineral density in Mexican patients with ankylosing spondylitis. Scand J Rheumatol 2016; 45: 480–490, DOI: 10.3109/03009742.2016.1152399.