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The serum level of sclerostin decreases in radiographic axial spondyloarthritis patients with fatty lesions

Xuegang Li[1†], Haijian Jiang[1†], Xu Wang[1†] and Shuping Zhong[1*]

Abstract

Background Currently, the pathophysiology of new bone formation in radiographic axial spondyloarthritis (r-axSpA) remains unclear. Cellular elements and their secreted bone turnover markers might be one of the underlying mechanisms that drive the new bone formation. Our study aimed to investigate the role of bone turnover markers in r-axSpA patients with fatty lesions.

Methods 73 r-axSpA patients were enrolled in this study. 48 and 25 patients were divided into r-axSpA group with and without fatty lesions. Clinical variables were collected and all patients received comprehensive rheumatologic assessment for disease activity, including Modified Stoke Ankylosing Spondylitis Spine Score (mSASSS), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Axial Spondyloarthritis Disease Activity Score (ASDAS). Fatty lesions in the sacroiliac joints (SIJs) were scored independently by two radiologists. Serum levels of bone turnover markers, including sclerostin, osteoprotegerin (OPG), procollagen I N-terminal propeptide (PINP), cross linked C-telopeptide of type I collagen (CTX-I), osteocalcin (OC), were measured using enzyme-linked immunosorbent assays.

Results There were no significant differences between two groups in terms of gender, age, body mass index (BMI), duration, smoking, HLA-B27 positivity rate, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), BASDAI, ASDAS-ESR, ASDAS-CRP, biological disease-modifying anti-rheumatic drugs (bDMARDs) rate. No significant differences were observed in terms of OPG, PINP, CTX-I or OC between two groups. The mSASSS were higher in fatty lesions group than in those without fatty lesions ($p < 0.001$). The serum sclerostin levels were significantly lower in r-axSpA patients with fatty lesions than in those without fatty lesions ($p < 0.001$). There were correlations between BMI, mSASSS and sclerostin with the comprehensive Berlin scoring method (CBM) scores in the univariate analysis ($\rho = 0.311$, $\rho = 0.306$, $\rho = -0.920$, respectively). However, only sclerostin had correlation with the CBM scores in multivariate analysis ($\rho = -0.040$, $p < 0.001$).

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Conclusions In the r-axSpA patients with fatty lesions, serum sclerostin levels are declined. Serum sclerostin might be useful as a biomarker to predict the progression of the chronic inflammation in SIJs in r-axSpA.

Keywords Sclerostin, Radiographic axial spondyloarthritis, Fatty lesions

Background

Radiographic axial spondyloarthritis (r-axSpA) is a chronic inflammatory disease and mainly affects the sacroiliac joints (SIJs) and axial skeleton joints, together with additional extra-musculoskeletal manifestations such as uveitis, psoriasis and inflammatory bowel disease [1].

The physiological state of the human skeleton is constantly in a process of bone destruction by osteoclasts and bone remodeling by osteoblasts. During this process, osteoblasts and osteoclasts continuously release proteins and protein metabolites, which respond dynamically to the state of bone remodeling. These substances are also known as bone turnover markers [2, 3]. Structural damage in individuals with r-axSpA is characterized by the formation of new bone in the spine. However, the pathophysiology of new bone formation in r-axSpA remains unclear. Cellular elements and their secreted bone turnover markers might be one of the underlying mechanisms that drive the new bone formation [4]. Previous research has identified several classical bone turnover markers, including cross linked C-telopeptide of type I collagen (CTX-I), procollagen I N-terminal propeptide (PINP), osteocalcin (OC) and (osteoprotegerin) OPG. OC and PINP were considered to be associated with bone formation, and CTX-I was associated with bone resorption. However, OPG was considered to inhibit the process of bone resorption. Sclerostin, a relatively new biomarker, has been identified as an important inhibitor of the canonical Wnt-β catenin signaling pathway and thus inhibiting bone formation, which was considered a biomarker that may be able to predict the stage of r-axSpA disease activity [5, 6]. Furthermore, chronic inflammation and pathological remodelling of the bone tissue in r-axSpA might finally result in syndesmophytes formation and ankylosing. It was suggested in a cohort study that magnetic resonance imaging (MRI) vertebral corner inflammation followed by fat deposition was the strongest contributor to the development of new bone at the same vertebral corner, addressing the hypothesis that vertebral corner inflammation 'leads to' fat deposition, which in turn 'leads to' bone formation [7]. The mechanism of interaction between chronic inflammation and new bone formation is still not completely understood.

The aim of this study was to investigate the role of bone turnover markers in r-axSpA patients with fatty lesions and to examine the relationship between the serum levels of bone turnover markers and the severity of fatty lesion.

Methods

Study population

Seventy-three patients with r-axSpA were enrolled in this study. All these patients were admitted for moderate or severe back pain after the initial assessment was made by rheumatologists. Only those who might had active disease would be admitted. All the patients fulfilled the Modified New York Criteria [8]. Among these patients, forty-eight and twenty-five patients were classified into the group of r-axSpA with and without fatty lesion, respectively. Patients with recent infection, current pregnancy, a history of neoplasm or any chronic inflammatory diseases were excluded. All the clinical data were collected from the medical records.

Blood sample collection and processing

6 mL of peripheral venous blood was taken in the early morning from these patients after fasting for at least eight hours at the Department of Rheumatology of the Fifth Affiliated Hospital of Sun Yat-sen University from May 2022 to February 2024. All the blood samples were processed within one hour. Blood samples were centrifuged, and serum was isolated and stored at -80℃ before use.

Clinical assessment and marker measurement

The demographic data were gathered from the patient charts. The erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and human leukocyte antigen (HLA)-B27 were also collected. Serum levels of sclerostin (E-EL-H1544c, Elabscience, Wuhan, China), osteoprotegerin (OPG) (CHE0074, 4Abio, Beijing, China), procollagen I N-terminal propeptide (PINP) (E-EL-H0185c, Elabscience, Wuhan, China), cross linked C-telopeptide of type I collagen (CTX-I) (E-EL-H0835c, Elabscience, Wuhan, China) and osteocalcin (OC) (E-EL-H1343c, Elabscience, Wuhan, China) were measured with a specific sandwich enzyme-linked immunosorbent assay (ELISA). A percentage coefficient of variation (CV%) ≤ 10% between duplicate samples was considered acceptable, and samples were re-tested until CV% ≤ 10% was attained. Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Axial Spondyloarthritis Disease Activity Score (ASDAS) was used to assess the disease activity scores [9].

Imaging assessment

All the patients underwent the magnetic resonance imaging (MRI) examination of the SIJs. Imaging scores were measured by two experienced radiologists. Fatty lesions

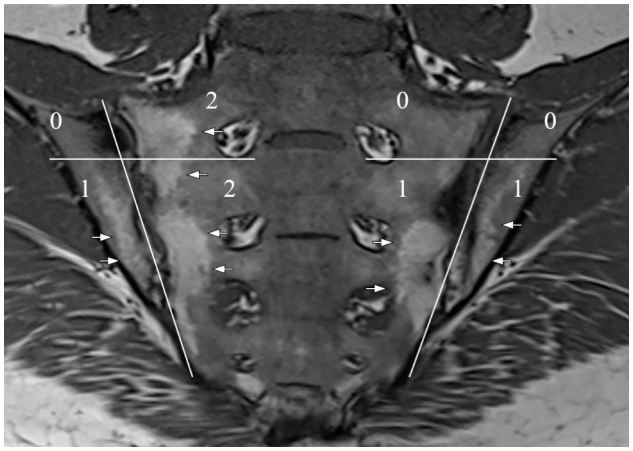

Fig. 1 The CBM scores to evaluate fatty lesions by MRI in the SIJs. The figure shows a T1w TSE sequence and a coronal slice of the SIJs. Each of the SIJs was divided into four quadrants by the joint space and a horizontal fictitious line passing below the first sacral neural foramina. The comprehensive Berlin scoring method quantifies fatty lesions on a 0–3 scale (0: no fatty lesions, 1: ≤ 33%, 2: 33–66%, 3: > 66% of the subchondral bone area in the respective quadrant), adding up to a total score of 0–24

were scored using the comprehensive Berlin scoring method (CBM) on unenhanced T1-weighted (T1W) turbo spin-echo (TSE) sequence of MRI images. Each of the sacroiliac joints was divided into four quadrants using the SIJ space and a fictitious horizontal line passing below the first sacral neural foramina [10]. Figure 1 shows the scoring method for dividing each SIJ into quadrants. The CBM quantifies fatty lesions on a 0–3 scale (0: no fatty lesions, 1: ≤ 33%, 2: 33–66%, 3: > 66% of the subchondral bone area in the respective quadrant). The sum score of the CBM was calculated by adding up the 8 quadrants scores, ranging from 0 to 24 [11, 12].

Statistical analysis

The numerical variable results were described as the means ± standard deviation (SD) or the median (interquartile range: first - third quartile) for normally distributed or non-normally distributed data. Categorical variables were assessed by the chi-square test. Normally distributed variables were compared using independent-sample t-test. Nonnormally distributed variables were compared using the Mann-Whitney U test. The correlation analysis was evaluated by Spearman's correlation coefficient. Analysis for clinical characteristics, bone turnover biomarkers and the CBM scores, was performed using univariate analysis. The multivariate analysis was further performed to correct the potential confounders. For all the analysis, the p value of < 0.05 was considered to indicate statistical significance. Intra- and inter-observer reliability was assessed by intraclass correlation coefficient (ICC). The statistical analysis was performed using Statistical Package of Social Science (SPSS) version 27.0.

Table 1 Comparison of demographic and clinical characteristics between r-axSpA with and without fatty lesions

	Fatty lesions ($n=48$)	No fatty lesions ($n=25$)	p value
Male (%)	40 (83.3%)	17 (68.0%)	0.133
Age (year)	34.2 ± 7.5	33.2 ± 8.6	0.598
BMI (kg/m^2)[a]	23.2 (20.5–25.5)	23.9 (21.3–26.5)	0.450
Duration (year)[a]	5.3 (3.0-11.5)	8.0 (2.3–10.0)	0.701
Smoking status (%)	10 (20.8%)	7 (28.0%)	0.492
HLA-B27 positive (%)	45 (93.8%)	23 (92.0%)	1.000
ESR (mm/H)[a]	17.0 (9.0-27.8)	13.0 (6.0-28.5)	0.436
CRP (mg/L)[a]	4.7 (1.9–13.3)	5.3 (0.8–11.6)	0.613
ASDAS-ESR[a]	2.0 (1.2–2.9)	1.6 (1.0–3.0)	0.429
ASDAS-CRP[a]	1.8 (1.1–2.9)	1.6 (0.9–2.8)	0.475
BASDAI[a]	1.8 (0.8–3.2)	0.9 (0.4–3.1)	0.317
bDMARDs rate	42 (87.5%)	21 (84.0%)	0.727
mSASSS[a]*	4 (2–9)	1 (0–3)	< 0.001
Sclerostin (pg/ml)*	254.2 (204.8-341.3)	462.1 (360.4-631.7)	< 0.001
OPG (pg/ml)	412.4 ± 289.1	370.2 ± 271.6	0.548
PINP (pg/ml)	2639.5 ± 1298.7	2979.5 ± 1306.7	0.293
CTX-I (ng/ml)[a]	0.42 (0.27–0.68)	0.34 (0.21–0.54)	0.313
OC (ng/ml)[a]	57.6 (35.7–95.1)	54.5 (26.6-112.6)	0.857

r-axSpA = radiographic axial spondyloarthritis; BMI = body mass index; HLA-B27 = human leukocyte antigen B27; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; ASDAS = Axial Spondyloarthritis Disease Activity Score; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; bDMARDs = biological disease-modifying anti-rheumatic drugs; mSASSS = Modified Stoke Ankylosing Spondylitis Spine Score; OPG = Osteoprotegerin; PINP = Procollagen I N-Terminal Propeptide; CTX-I = Cross Linked C-telopeptide of Type I Collagen; OC = Osteocalcin

[a]Median (Interquartile range)

*Statistical significance

Results

Assay and observer reliability

Each of all the biomarkers achieved an acceptable inter-assay CV% (≤ 10%). Excellent intra-observer reliability for two radiologists was achieved (ICC = 0.825, ICC = 0.849, respectively). Good inter-observer reliability was also achieved (ICC = 0.779).

Comparison of clinical characteristics of r-axSpA subgroups

Table 1 lists the baseline data of r-axSpA patients with and without fatty lesion. There were no significant differences in terms of sex, age, body mass index, duration, smoking or HLA-B27 between two groups. In addition, no significant differences were observed in terms of ESR, CRP, ASDAS-ESR, ASDA-CRP, BASDAI or biological disease-modifying anti-rheumatic drugs (bDMARDs) rate between the two groups ($p = 0.436$, $p = 0.613$, $p = 0.429$, $p = 0.475$, $p = 0.317$, $p = 0.727$, respectively). However, the Modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) of the group with fatty lesions were significantly higher than the group without fatty lesions ($p < 0.001$).

Comparison of bone turnover markers between two groups

There were no significant differences between two groups in terms of serum levels of OPG, PINP, CTX-I and OC. However, the serum levels of sclerostin in the group with fatty lesions were significantly lower than those in the group without fatty lesions ($p < 0.001$) (Fig. 2).

Univariate and multivariate analysis between clinical variables, bone turnover markers and CBM scores

Table 2 presents the correlation between clinical variables, bone turnover markers and the CBM scores. In r-axSpA patients with fatty lesions group, there were correlations between body mass index (BMI), mSASSS and sclerostin with the CBM scores in the univariate analysis ($\rho = 0.311$, $\rho = 0.306$, $\rho = -0.920$, respectively). However, the serum levels of OPG, PINP, CTX-I or OC were not correlated with the CBM scores ($\rho = -0.081$, $\rho = 0.079$, $\rho = -0.054$, $\rho = 0.022$, respectively), and all the p values were > 0.05. In the multiple linear regression analysis, only sclerostin had correlation with the CBM scores [B (95%CI) = -0.040 (-0.049, -0.032), $p < 0.001$]. Figure 3 shows that serum sclerostin levels correlated negatively with CBM scores ($\rho = -0.920$, $p < 0.001$). Multiple linear regression analysis models were conducted to investigate whether the CBM score was an independent variable of BMI, mSASSS and sclerostin level. The CBM scores were independently associated with sclerostin level [B (95%CI) = -17.227 (-20.825, -13.628), $p < 0.001$]. However, the CBM score was not an independent variable of BMI and mSASSS ($p = 0.705$, $p = 0.630$, respectively) (Table 3).

Discussion

In this study, serum sclerostin levels decreased in the r-axSpA patients with fatty lesions. Negative association was detected between the serum levels of sclerostin and the comprehensive Berlin scoring method scores in r-axSpA patients with fatty lesions.

Different clinical parameters, including gender, age, duration, life style factors, body mass index, ESR and

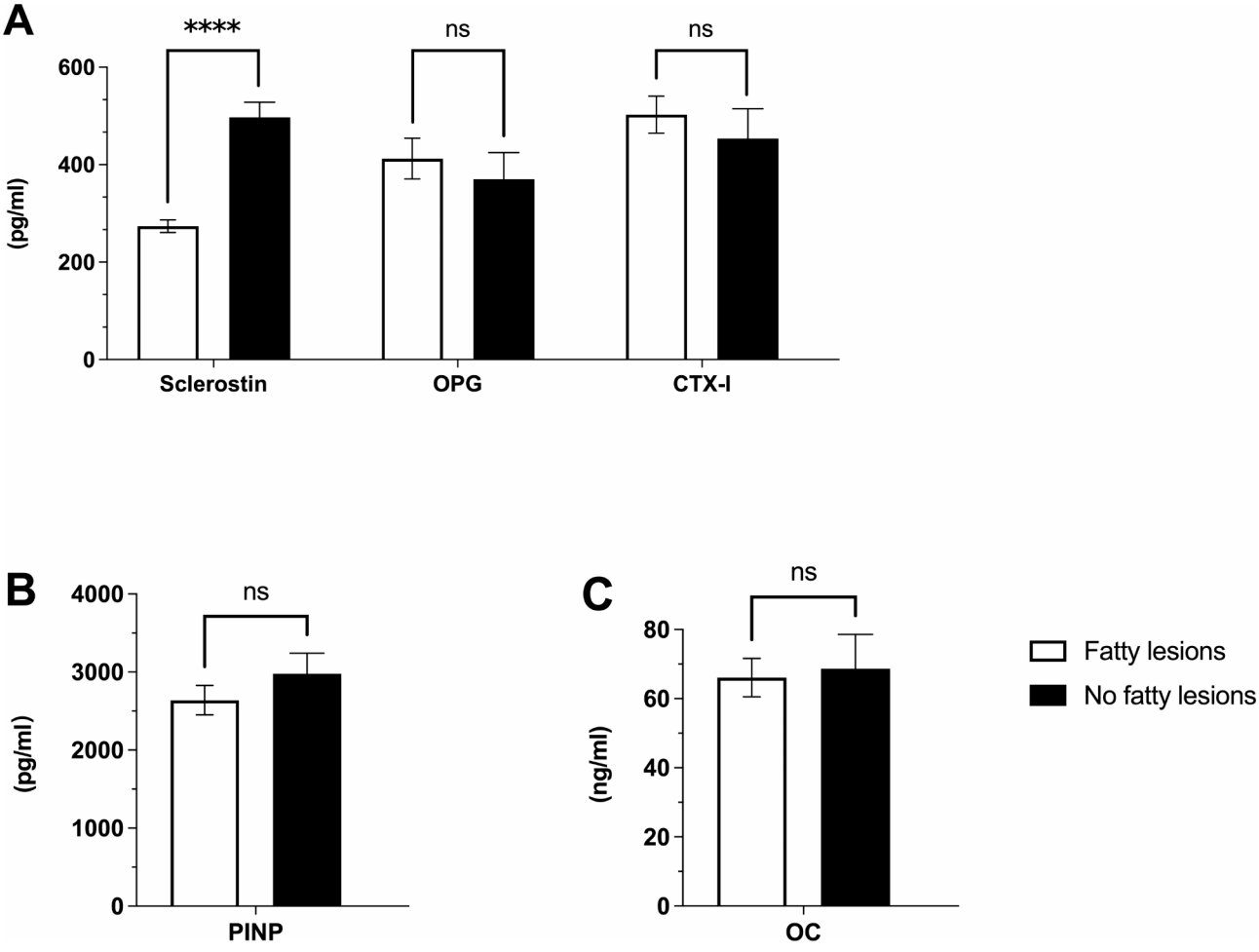

Fig. 2 Comparison of bone turnover markers levels between r-axSpA with and without fatty lesions. The serum levels of sclerostin were significantly lower in r-axSpA patients with fatty lesions than in those without fatty lesions ($p < 0.001$). No significant differences were observed in terms of OPG, PINP, CTX-I or OC between two groups

Table 2 Univariate and multivariate analysis between CBM scores and clinical variables and biomarkers in r-axSpA with fatty lesions

	Univariate analysis		Multivariate analysis		
Variables	**ρ**	***p* value**	**B (95%CI)**	**β**	***p* value**
Age (year)	0.133	0.366			
BMI (kg/m^2)	0.311	0.031*	0.015 (-0.121, 0.151)	0.019	0.825
Duration (year)	0.025	0.864			
ESR (mm/H)	0.058	0.694			
CRP (mg/L)	0.182	0.216			
ASDAS-ESR	0.022	0.883			
ASDAS-CRP	0.104	0.483			
BASDAI	0.041	0.784			
mSASSS	0.306	0.034*	-0.021 (-0.076, 0.034)	-0.066	0.448
Sclerostin (pg/ml)	-0.920	< 0.001*	-0.040 (-0.049, -0.032)	-0.840	< 0.001*
OPG (pg/ml)	-0.081	0.582			
PINP (pg/ml)	0.079	0.595			
CTX-I (ng/ml)	-0.054	0.715			
OC (ng/ml)	0.022	0.880			
			Adjusted $R^2 = 0.669$		

r-axSpA = radiographic axial spondyloarthritis; ρ = Spearman's correlation coefficient; B = Unstandardized coefficient; β = Standardized coefficient; CI = confidence interval ; CBM = the comprehensive Berlin scoring method; BMI = body mass index; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; ASDAS = Axial Spondyloarthritis Disease Activity Score; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; SIJ = Sacroiliac joint; mSASSS = Modified Stoke Ankylosing Spondylitis Spine Score; OPG = Osteoprotegerin; PINP = Procollagen I N-Terminal Propeptide; CTX-I = Cross Linked C-telopeptide of Type I Collagen; OC = Osteocalcin; R^2 = coefficient of determination

*Statistical significance

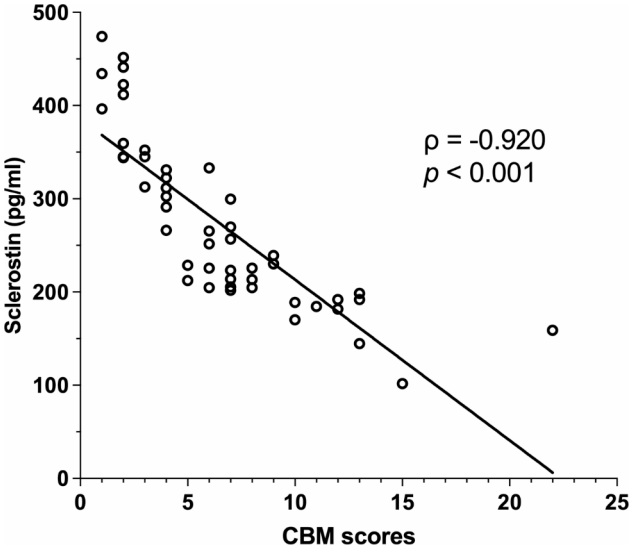

Fig. 3 Correlation between serum sclerostin levels and CBM scores in r-axSpA with fatty lesions. The serum sclerostin levels correlated negatively with CBM scores (ρ = -0.920, $p < 0.001$)

CRP, were reported to be associated with radiographic progression in r-axSpA patients [13–15]. Besides these clinical parameters, different biomarkers were also found to predict radiographic progression in r-axSpA patients, among them were markers of inflammation, bone turnover biomarkers and adipokines [16, 17]. The role of bone turnover markers for predicting the radiographic progression has been paid more and more attention in the recent years [16, 18, 19]. Additionally, it was found that MRI vertebral corner inflammation followed by fat deposition could contribute to the new bone formation at the same vertebral corner. Therefore, it would be of great importance to identify the relationship between bone turnover markers and the severity of fatty lesions

Table 3 Multiple linear regression analysis models showing independent variables associated with sclerostin levels in r-axSpA patients

	Dependent variable			
Independent variable	**Adjusted R^2**	**B (95%CI)**	**β**	***p* value**
Model 1	0.055		BMI	
Age (year)		0.209 (-0.004, 0.422)	0.289	0.054
ASDAS-CRP		1.013 (-0.472, 2.498)	0.198	0.176
CBM scores		0.069 (-0.298, 0.436)	0.055	0.705
Model 2	0.005		mSASSS	
Age (year)		0.438 (-0.111, 0.987)	0.241	0.115
ASDAS-CRP		0.528 (-3.299, 4.355)	0.041	0.782
CBM scores		0.227 (-0.718, 1.173)	0.072	0.630
Model 3	0.689		Sclerostin	
Age (year)		0.127 (-1.963, 2.218)	0.011	0.903
ASDAS-CRP		-4.519 (-19.082, 10.043)	-0.053	0.535
CBM scores		-17.227 (-20.825, -13.628)	-0.827	< 0.001*

r-axSpA = radiographic axial spondyloarthritis; R^2 = coefficient of determination; B = Unstandardized coefficient; β = Standardized coefficient; CI = confidence interval ; BMI = body mass index; ASDAS = Axial Spondyloarthritis Disease Activity Score; ESR = erythrocyte sedimentation rate; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; CBM = the comprehensive Berlin scoring method; mSASSS = Modified Stoke Ankylosing Spondylitis Spine Score; CRP = C-reactive protein;

*Statistical significance

in r-axSpA patients. In this study, there was only significant difference in terms of sclerostin among these bone turnover markers between groups with and without fatty lesions and r-axSpA patients with fatty lesions exhibited lower serum levels of sclerostin than those without fatty lesions. The serum levels of sclerostin in all r-axSpA patients in our research were different from previous studies. In a meta-analysis, the mean sclerostin levels varied greatly even in different studies, from 7.41 to 427.69 pg/ml [20]. These huge differences might be attributed to race, use of different ELISA kits and different disease status of the patients. The serum levels of sclerostin in r-axSpA still remain controversial. Several studies demonstrated that serum sclerostin levels were significantly lower in r-axSpA patients than in healthy controls [4, 21–24]. No significant difference was also reported in sclerostin levels between r-axSpA and healthy controls in another study [25]. However, there is still little concentration about sclerostin levels in r-axSpA subgroups.

MRI vertebral corner inflammation followed by fat deposition could contribute to the development of new bone at the same vertebral corner [7], indicating patients with r-axSpA might experience acute inflammation, fatty deposition and then bone formation sequentially. It was reported that the sclerostin serum level had a weak negative correlation with the active inflammatory MRI SIJ lesions by SpondyloArthritis Research Consortium of Canada (SPARCC) [23]. Serum sclerostin was significantly higher in axSpA without syndesmophytes growth than in axSpA with new syndesmophytes [21]. Moreover, the serum level of sclerostin was also correlated with syndesmophytes and modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) [26, 27]. However, there were few studies focusing on the relationship between fatty lesions and serum sclerostin level. In this research, r-axSpA patients with fatty lesions had lower serum levels of sclerostin. Thus, we speculate that lower serum levels of sclerostin might participate in the whole process of new bone formation and the progression of inflammation might lower the levels of serum sclerostin. Nevertheless, the mechanism remains unknown. The serum sclerostin level significantly increased over time after initiation of TNF inhibitor [24]. Furthermore, the serum levels of sclerostin were increased after the treatment of imrecoxib or celecoxib in r-axSpA and a decrease in ESR was significantly correlated with the levels of sclerostin being significantly elevated in the SPARCC-reduced group [28]. Further studies should focus on how the inflammation could drive the change of sclerostin and then promote the new bone formation.

There are still limitations to this study. First, it had a relatively small sample and was a cross-sectional design. Longitudinal cohort studies with larger samples should be needed to confirm whether the serum level of sclerostin may be a useful marker to predict fatty lesion in r-axSpA. Second, not all the bone turnover markers were included in this study. Third, the relationship between pathological studies of SIJs with fatty lesions and sclerostin should also be investigated to further ascertain the role of bone turnover markers in r-axSpA. Finally, the use of different bDMARDs might have effects on the radiographic imaging and the serum level of biomarkers and the use of bDMARDs should be investigated in the further study.

Conclusions

This research reported the serum levels of sclerostin decreases in r-axSpA patients with fatty lesions. These results provide important implications for physicians to understand the role of bone turnover markers in the fatty lesion in r-axSpA. Future studies should focus on monitoring the change of the serum level of sclerostin in r-axSpA patients with fatty lesions.

Abbreviations

r-axSpA	Radiographic axial spondyloarthritis
SIJs	Sacroiliac joints
CTX-I	Cross linked C-telopeptide of type I collagen
PINP	Procollagen I N-terminal propeptide
OC	Osteocalcin
CV	Coefficient of variation
OPG	Osteoprotegerin
MRI	Magnetic resonance imaging
ESR	Erythrocyte sedimentation rate
CRP	C-reactive protein
HLA-B27	Human leukocyte antigen B27
ELISA	Enzyme-linked immunosorbent assay
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
ASDAS	Axial Spondyloarthritis Disease Activity Score
CBM	Comprehensive Berlin scoring method
T1W	T1-weighted
TSE	Turbo spin-echo
SD	Standard deviation
ICC	Intraclass correlation coefficient
SPSS	Statistical Package of Social Science
bDMARDs	Biological disease-modifying anti-rheumatic drugs
mSASSS	Modified Stoke Ankylosing Spondylitis Spine Score
BMI	Body mass index
SPARCC	SpondyloArthritis Research Consortium of Canada
CI	Confidence interval

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13075-025-03479-x.

Supplementary Material 1

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Author contributions

SZ, HJ and XW collected all the data and performed statistical analyses. XL had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. HJ prepared Figs. 1, 2 and 3 and XL prepared Table 1, and 2. All authors were involved in

drafting the article or revising it critically for important content, and all authors approved the final version to be submitted for publication.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Patients were informed of the clinical requirements and potential risks associated with all operations before this study. Informed consent forms were obtained and any details that could potentially reveal the identity of the subjects under study were omitted. This study was approved by the Ethics Committee of the Fifth Affiliated Hospital of Sun Yat-Sen University (Approval number: K269-1).

Consent for publication
No individual person's data were used in this study.

Competing interests
The authors declare no competing interests.

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References

1. Bautista-Molano W, Fernández-Ávila DG, Brance ML, Ávila Pedretti MG, Burgos-Vargas R, Corbacho I, Cosentino VL, Díaz Coto JF, Giraldo Ho E, Gomes Resende G, et al. Pan American League of Associations for Rheumatology recommendations for the management of axial spondyloarthritis. Nat Rev Rheumatol. 2023;19(11):724–37.
2. Tian A, Ma J, Feng K, Liu Z, Chen L, Jia H, Ma X. Reference markers of bone turnover for prediction of fracture: a meta-analysis. J Orthop Surg Res. 2019;14(1):68.
3. Takada J, Dinavahi R, Miyauchi A, Hamaya E, Hirama T, Libanati C, Nakamura Y, Milmont CE, Grauer A. Relationship between P1NP, a biochemical marker of bone turnover, and bone mineral density in patients transitioned from alendronate to romosozumab or teriparatide: a post hoc analysis of the STRUCTURE trial. J Bone Min Metab. 2020;38(3):310–15.
4. Perrotta FM, Ceccarelli F, Barbati C, Colasanti T, De Socio A, Scriffignano S, Alessandri C, Lubrano E. Serum Sclerostin as a possible biomarker in Ankylosing spondylitis: a case-control study. J Immunol Res. 2018;2018:9101964.
5. Chen XX, Baum W, Dwyer D, Stock M, Schwabe K, Ke HZ, Stolina M, Schett G, Bozec A. Sclerostin inhibition reverses systemic, periarticular and local bone loss in arthritis. Ann Rheum Dis. 2013;72(10):1732–6.
6. Soós B, Szentpétery Á, Raterman HG, Lems WF, Bhattoa HP, Szekanecz Z. Effects of targeted therapies on bone in rheumatic and musculoskeletal diseases. Nat Rev Rheumatol. 2022;18(5):249–57.
7. Machado PM, Baraliakos X, van der Heijde D, Braun J, Landewé R. MRI vertebral corner inflammation followed by fat deposition is the strongest contributor to the development of new bone at the same vertebral corner: a multilevel longitudinal analysis in patients with ankylosing spondylitis. Ann Rheum Dis. 2016;75(8):1486–93.
8. 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(4):361–8.
9. Lukas C, Landewé R, Sieper J, Dougados M, Davis J, Braun J, van der Linden S, van der Heijde D. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. Ann Rheum Dis. 2009;68(1):18–24.
10. Althoff CE, Feist E, Burova E, Eshed I, Bollow M, Hamm B, Hermann KG. Magnetic resonance imaging of active sacroiliitis: do we really need gadolinium? Eur J Radiol. 2009;71(2):232–6.
11. Althoff CE, Sieper J, Song IH, Haibel H, Weiß A, Diekhoff T, Rudwaleit M, Freundlich B, Hamm B, Hermann KG. Active inflammation and structural change in early active axial spondyloarthritis as detected by whole-body MRI. Ann Rheum Dis. 2013;72(6):967–73.
12. Krohn M, Braum LS, Sieper J, Song IH, Weiss A, Callhoff J, Althoff CE, Hamm B, Hermann KG. Erosions and fatty lesions of sacroiliac joints in patients with axial spondyloarthritis: evaluation of different MRI techniques and two scoring methods. J Rheumatol. 2014;41(3):473–80.
13. Min HK, Lee J, Ju JH, Park SH, Kwok SK. Alcohol consumption as a predictor of the progression of spinal structural damage in axial spondyloarthritis: data from the catholic Axial Spondyloarthritis COhort (CASCO). Arthritis Res Ther. 2019;21(1):187.
14. Poddubnyy D, Haibel H, Listing J, Märker-Hermann E, Zeidler H, Braun J, Sieper J, Rudwaleit M. Baseline radiographic damage, elevated acute-phase reactant levels, and cigarette smoking status predict spinal radiographic progression in early axial spondylarthritis. Arthritis Rheum. 2012;64(5):1388–98.
15. Ramiro S, Stolwijk C, van Tubergen A, van der Heijde D, Dougados M, van den Bosch F, Landewé R. Evolution of radiographic damage in ankylosing spondylitis: a 12 year prospective follow-up of the OASIS study. Ann Rheum Dis. 2015;74(1):52–9.
16. Rademacher J, Tietz LM, Le L, Hartl A, Hermann KA, Sieper J, Mansmann U, Rudwaleit M, Poddubnyy D. Added value of biomarkers compared with clinical parameters for the prediction of radiographic spinal progression in axial spondyloarthritis. Rheumatology (Oxford). 2019;58(9):1556–64.
17. Rademacher J, Siderius M, Gellert L, Wink FR, Verba M, Maas F, Tietz LM, Poddubnyy D, Spoorenberg A, Arends S. Baseline serum biomarkers of inflammation, bone turnover and adipokines predict spinal radiographic progression in ankylosing spondylitis patients on TNF inhibitor therapy. Semin Arthritis Rheum. 2022;53:151974.
18. Arends S, Spoorenberg A, Efde M, Bos R, Leijsma MK, Bootsma H, Veeger NJ, Brouwer E, van der Veer E. 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(6):e99685.
19. Serdaroğlu Beyazal M, Erdoğan T, Türkyılmaz AK, Devrimsel G, Cüre MC, Beyazal M, Sahin I. Relationship of serum osteoprotegerin with arterial stiffness, preclinical atherosclerosis, and disease activity in patients with ankylosing spondylitis. Clin Rheumatol. 2016;35(9):2235–41.
20. Yang J, Xu S, Chen M, Yuan Y, Zhang X, Ma Y, Wu M, Han R, Hu X, Liu R, et al. Serum sclerostin and bone morphogenetic Protein-2 levels in patients with Ankylosing spondylitis: a Meta-analysis. Calcif Tissue Int. 2019;105(1):37–50.
21. Appel H, Ruiz-Heiland G, Listing J, Zwerina J, Herrmann M, Mueller R, Haibel H, Baraliakos X, Hempfing A, Rudwaleit M, et al. Altered skeletal expression of sclerostin and its link to radiographic progression in ankylosing spondylitis. Arthritis Rheum. 2009;60(11):3257–62.
22. Gómez-García I, Ladehesa-Pineda ML, Diaz-Tocados JM, López-Medina C, Abalos-Aguilera MC, Ruiz-Vilches D, Paz-Lopez G, Gonzalez-Jimenez A, Ranea JAG, Escudero-Contreras A, et al. Bone metabolism and inflammatory biomarkers in radiographic and non-radiographic axial spondyloarthritis patients: a comprehensive evaluation. Front Endocrinol (Lausanne). 2024;15:1227196.
23. Iaremenko O, Shynkaruk I, Fedkov D, Iaremenko K, Petelytska L. Bone turnover biomarkers, disease activity, and MRI changes of sacroiliac joints in patients with spondyloarthritis. Rheumatol Int. 2020;40(12):2057–63.
24. Saad CG, Ribeiro AC, Moraes JC, Takayama L, Goncalves CR, Rodrigues MB, de Oliveira RM, Silva CA, Bonfa E, Pereira RM. Low sclerostin levels: a predictive marker of persistent inflammation in ankylosing spondylitis during anti-tumor necrosis factor therapy? Arthritis Res Ther. 2012;14(5):R216.
25. Gercik O, Solmaz D, Coban E, Iptec BO, Avcioglu G, Bayindir O, Kabadayi G, Topal FE, Kozaci D, Akar S. Evaluation of serum fibroblast growth factor-23 in patients with axial spondyloarthritis and its association with sclerostin, inflammation, and spinal damage. Rheumatol Int. 2019;39(5):835–40.
26. Descamps E, Molto A, Borderie D, Lories R, Richard CM, Pons M, Roux C, Briot K. Changes in bone formation regulator biomarkers in early axial spondyloarthritis. Rheumatology (Oxford). 2021;60(3):1185–94.

27. Sun W, Tian L, Jiang L, Zhang S, Zhou M, Zhu J, Xue J. Sclerostin rather than Dickkopf-1 is associated with mSASSS but not with disease activity score in patients with ankylosing spondylitis. Clin Rheumatol. 2019;38(4):989–95.
28. Guo Y, Jiang D, Mai Z, Chen Y, Li T, Gao G. Imrecoxib and celecoxib affect sacroiliac joint inflammation in axSpA by regulating bone metabolism and angiogenesis. Clin Rheumatol. 2023;42(6):1585–92.

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