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The bone mineral density of hip joint was reduced in the initial stage of ankylosing spondylitis?

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Abstract

The osteoporosis was common complication of ankylosing spondylitis (AS), but it was frequently unrecognized in the initial stage of the disease. This study was to compare areal bone mineral density (BMD) of hip joints in early AS patients with that in healthy controls, to explore the progress of bone loss in cortex and spongiosa in early AS.

Quantitative computed tomography (QCT) of hip was performed in 60 AS patients (modified New York criteria for AS, with grade 2 sacroiliitis in computed tomography) and 57 healthy controls. The QCT measurements of AS patients were compared with the measurements of healthy controls.

The AS patients had lower areal BMD in cortical bone and total bone of proximal femur in early AS patients ($P < .01$), than the controls. But there were not significant different of areal BMD in spongiosa of proximal femur between the early AS patients and healthy controls. Strong correlations were found between body mass index BMI, areal BMD in cortical bone ($r_s = 0.410$, $P < .001$; $r_s = 0.422$, $P < .001$) and total bone ($r_s = 0.368$, $P < .001$; $r_s = 0.266$, $P = .003$) both in AS patients and healthy controls.

The results indicate that osteopenia/osteoporosis is general in early stage of AS. What is more, the osteopenia/osteoporosis in cortex is earlier than in spongiosa of proximal femur in early AS.

Abbreviations: AS = ankylosing spondylitis, BMD = bone mineral density, BMI = body mass index, QCT = quantitative computed tomography.

Keywords: ankylosing spondylitis, bone mineral density, cortex, osteopenia, osteoporosis, spongiosa

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PLC and YYY had the same contribution as the first author to this work.

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We authors confirmed that this article is not under consideration for publication elsewhere. We provided full contact details for each author.

Publication was approved by all authors and the responsible authority (the ethics committee of the Third Hospital of Hebei Medical University) where the work was carried out.

We conform that the all patients have given their written consent for the article to be published.

The datasets used during the current study are available from the corresponding author on reasonable request.

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1. Introduction

Ankylosing spondylitis (AS) is an inflammatory disease, with new bone formation and ossification of the ligamentous apparatus as the primary pathological changes. The osteoporosis is coexisting with new bone formation, becoming the early feature of AS, particularly pronounced in active disease.[1–3] The mechanisms of inflammation, new bone formation and osteopenia/osteoporosis in AS are incompletely understood. The inflammation may play a dominant role in early AS,[1,4] and low bone mineral density (BMD) of the lumber spine and femoral neck is accompanying with inflammation in early AS and mild disease.[5] In late AS, ankylosis of joints result in decreased mobility inducing disuse osteoporosis.[6] In the past few decades, the data measured by dual-energy X-ray suggested that the inflammation may be an etiologic factor of bone loss in AS.[7,8] At present, there are a lot of different methods for monitoring the BMD in AS.[9–11]

Osteoporosis is well known a common complication in AS. Low BMD of femoral neck has been observed in early AS, while the bone loss begins from the cortex or the spongiosa is unknown. Our aim is to investigate the progress of bone loss in cortex and spongiosa by quantitative computed tomography (QCT) in early AS, compared with the health controls in similar age.

2. Methods

2.1. Participants

From October 2016 to January 2018, 60 patients (44 men and 16 women, age range 19 to 45 years, mean age 29.6 years) were recruited from the rheumatic immunity clinic. The inclusion criteria were AS according to modified New York criteria, and age more than18 years old. What was more, the sacroiliitis was grade 2 in computed tomography (CT), that was small localized area with

Table 1

Clinical characteristics and areal BMD of AS patients and health controls.

	Control group	AS group	*P* value
Demographic			
Male%	68.4%	75%	.68
Age, yr	32.5±10.3	29.6±7.7	.09
BMI (kg/m^2)	24.1±3.6	23.7±3.6	.55
Cortical bone (g/cm^2)			
femoral neck	0.47±0.16	0.39±0.13	.00
femoral trochanter	0.27±0.11	0.20±0.07	.00
femur intertrochanteric	0.77±0.17	0.68±0.16	.00
Total	0.56±0.12	0.47±0.11	.00
Spongy bone (g/cm^2)			
femoral neck	0.38±0.13	0.38±0.13	.88
femoral trochanter	0.41±0.07	0.40±0.07	.31
femur intertrochanteric	0.33±0.06	0.33±0.06	.66
Total	0.36±0.05	0.36±0.06	.84
Total bone (g/cm^2)			
femoral neck	0.88±0.20	0.80±0.19	.00
femoral trochanter	0.68±0.13	0.60±0.11	.00
femur intertrochanteric	1.09±0.17	1.01±0.18	.00
Total	0.92±0.14	0.85±0.22	.005

AS = ankylosing spondylitis, BMD = bone mineral density.

erosion or sclerosis, without alteration in the joint width.[12] Exclusion criteria were psoriasis, inflammatory bowel disease, dementia, pregnancy, joint surgery, and intraarticular injection. All of the patients had suffered from 2 or more of the following symptoms: insidious onset of pain/discomfort, morning stiffness, improvement of symptoms with exercise, or pain at night. None of the patients was treated with tumor necrosis factor α inhibitors or other biologic agents during the 3 months preceding the examination. Fifty-seven health controls (39men and 18 women, age range 19 to 45 years, mean age 31.8 years) were collected.

2.2. Equipment and scanning techniques

All patients and health controls underwent hip QCT examinations, performed by the same radiologist who had >5 years of work experience. All subjects were scanned using CT (Somatom Sensation 16, Siemens, Erlangen, Germany). The scanning parameters were as follow: 120Kv, 125mAs, 1 mm slice thickness, and 500Mm field of view. QCT studies were performed using the QCT Pro calibration phantom. The scanning region was from the iliac crest to mid-thigh.

2.3. Image analysis and data collection

One musculoskeletal radiologist with more than 5 years of musculoskeletal imaging experience, blinded to the diagnosis and patient demographics, evaluated all QCT images. Features evaluated included the presence or absence of: bone sclerosis, bone cortex erosion, and hip space narrowing.

The QCT allows measurement of areal BMD measured in g/cm^2 and volumetric BMD measured in mg/cm^3. In order to better measure cortical BMD, areal BMD was adopted as the quantitative parameter. Quantitative parameters were included as follow:

(1) Areal BMDs of cortex at femoral neck, tuberosity, intertrochanteric, and total hip;
(2) Areal BMDs of spongiosa at femoral neck, tuberosity, intertrochanteric, and total hip;
(3) Areal BMDs of bones at femoral neck, tuberosity, intertrochanteric, and total hip.

2.4. Statistical analysis

We summarized categorical and continuous variables as frequencies (percentages) and means (standard deviations) respectively. Two-sample *t* tests, or chi-square tests were used to compare intergroup differences. Multivariable linear regression analysis (adjusted for sex, age and body mass index [BMI]) was performed to study the effect of AS and health control on QCT parameters. We also examined the association between BMI and bone parameters using Pearson or Spearman correlation coefficients. A *P* value $<.05$ was considered statistically significant. The study was approved by institutional research ethics board. All subjects gave written informed consent.

3. Results

No statistically significant differences were identified between the AS patients and health controls with respect to age, sex, and BMI (Table 1). In 60 patients with AS, none had bone sclerosis, bone cortex erosion, and hip space narrowing. The disease durations of the patients were less than 5 years. There were 5 patients with peripheral joint involvement.

Intergroup comparisons performed using 2-sample *t* tests showed that AS patients had significant bone loss of areal BMD in cortical bones and total bones compared with the health controls. No statistically significant differences were identified between the AS patients and health controls with respect to areal BMD in spongy bones (Table 1).

Multivariable linear regression analyses assessing AS and health control with an independent predictor of areal BMD were shown in Tables 2 and 3. The BMI showed statistically significant positive correlations with the areal BMD of cortical bone and total bone of hip both in AS patients and health controls. The areal BMD of spongy bone showed statistically significant correlations with sex, age, and BMI in AS patients, but only showed statistically

Table 2

Multivariable linear regression analysis assessing AS patients with an independent predictor of areal BMD.

			sex		age		BMI	
QCT	Adj R^2	*P* value	*t*	*P*	*t*	*P*	*t*	*P*
Cortical bone	0.167	.000	1.179	.241	−0.004	.997	4.057	.000
Spongy bone	0.191	.000	3.611	.000	−3.959	.000	2.189	.031
Total bone	0.088	.003	1.805	.074	−1.409	.162	2.813	.006

The model was adjusted for differences in sex, age, and BMI.
Adj = adjusted, AS = ankylosing spondylitis, BMD = bone mineral density, BMI = body mass index, QCT = quantitative computed tomography.

Table 3

Multivariable linear regression analysis assessing health controls with an independent predictor of areal BMD.

			Sex		Age		BMI	
QCT	Adj. R^2	*P* value	*t*	*P*	*t*	*P*	*t*	*P*
Cortical bone	0.175	.000	1.177	.242	−1.456	.148	4.762	.000
Spongy bone	0.085	.005	2.966	.004	−1.734	.086	0.639	.524
Total bone	0.198	.000	2.333	.021	−2.309	.023	0.369	.000

The model was adjusted for differences in sex, age and BMI.

Adj = adjusted, BMD = bone mineral density, BMI = body mass index, QCT = quantitative computed tomography.

significant correlations with sex in health controls. The areal BMD of total bone showed statistically significant correlations with sex, age, and BMI in health controls, but only showed statistically significant correlations with BMI in AS patients.

Strong correlations were found between BMI, areal BMD in cortical bone ($r_s = 0.410$, $P < .001$; $r_s = .422$, $P < .001$) and total bone ($r_s = .368$, $P < .001$; $r_s = 0.266$, $P = .003$) both in AS patients and healthy controls (Figs. 1 and 2).

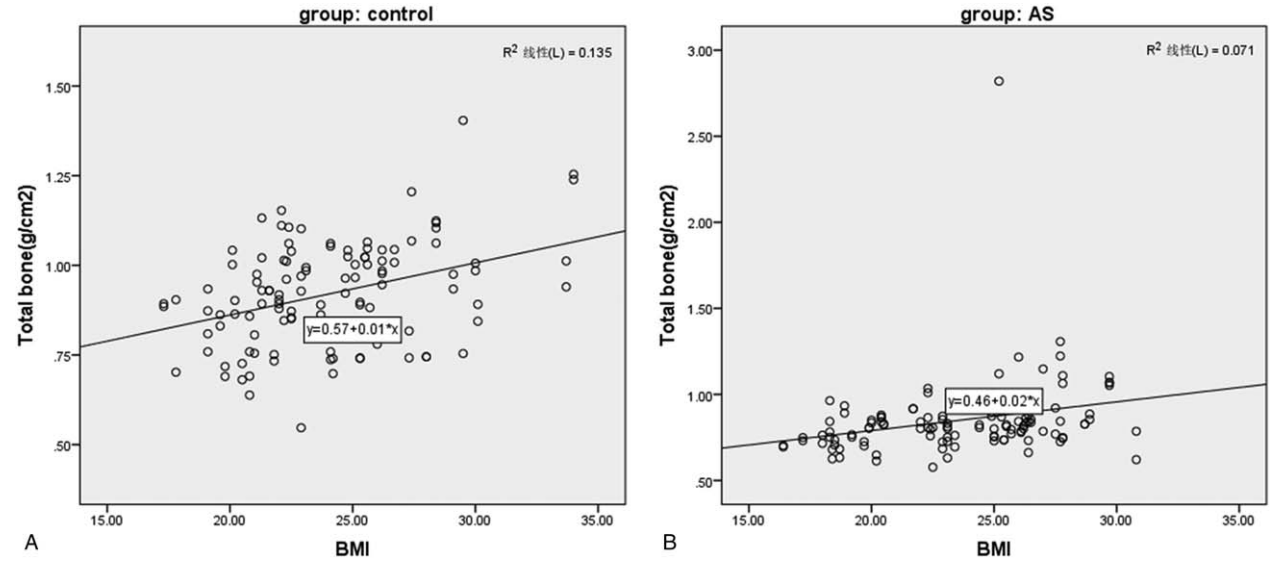

Figure 1. The correlations between areal BMD of total bone of hip joints with BMI in health controls (A) and AS patients (B). AS = ankylosing spondylitis, BMD = bone mineral density, BMI = body mass index.

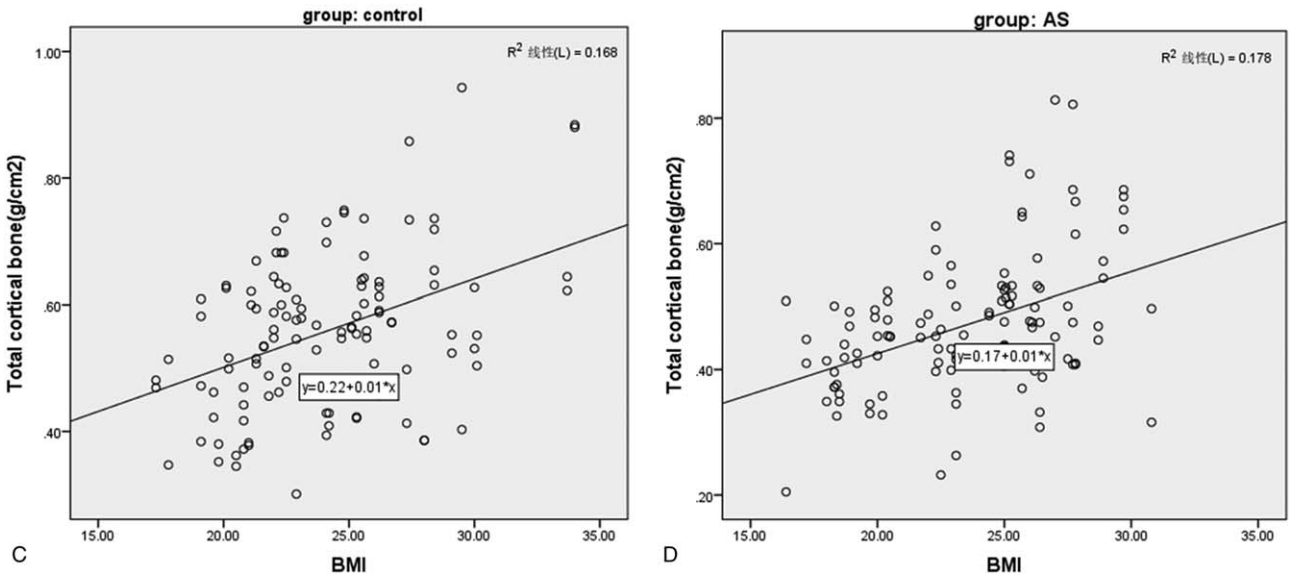

Figure 2. The correlations between areal BMD of total cortical bone of hip joints with BMI in health controls (C) and AS patients (D). AS = ankylosing spondylitis, BMD = bone mineral density, BMI = body mass index.

4. Discussion

The osteoporosis is a common complication of AS. High disease activity and hip involvement are the risk factors of bone loss in patients with AS. Patients with AS are at high risk of vertebral fractures, but not significant at risk of hip fractures, compared with controls.[13] Longitudinal study in early AS has suggested that spine and hip BMD decrease in early AS, especially in inflammatory activity stage.[2,8] Our results suggested that AS patients in early stage had lower cortical areal BMD and total areal BMD at hip joints, compared with the health controls. There was no significant difference of areal BMD in spongy bones of hip joints between AS patients and health controls. This was similar to the early study of QCT about BMD of AS patients. It reported that the bone density of the spongiosa was reduced in early AS, but this was not significant for the study group. This study conducted that reduction of cortical bone was evident parallel to spongiosa loss, and then in advanced stages, the cortical bone tented to increase because of the ankylosis.[14] There was not a definite answer about whether the cortical bone is firstly involved in early AS or is parallel to the spongiosa loss? Our study seems to support that the cortical bones tend to firstly decrease in early AS. Possible immobilization, especially in the initial inflammatory activity phases of AS, is 1 reason for bone loss in the early stage of AS. The mechanisms behind inflammation, bone loss and new-bone formation in AS are incompletely understood.

A previous study approved that the excess of adipose tissue in obesity may have immunomodulating properties and pharmacokinetic consequences.[15] It is already well known that the correlation between BMD and BMI. In this study, the BMI showed statistically significant positive correlations with the areal BMD of cortical bone and total bone of hip both in AS patients and health controls. While, related studies approved that the BMI did not influence the AS disease activity in axial spondyloarthritis. A high BMI positively correlated with syndesmophyte, but negatively influenced the response to infliximab in AS.[16–18] In this study, the areal BMD of spongy bone showed statistically significant correlations with sex, age, and BMI in AS patients. The areal BMD of total bone showed statistically significant correlations with BMI in AS patients.

The main limitations of this study included the cross-sectional design, small sample size, and lack the data of indices of disease activity and physical activity. Despite the small size of our study, it is the largest study of areal BMD of hip joints of early AS patients (including both men and women). Our results may guide further research on the prediction and management of bone loss in initial AS patients.

5. Conclusions

We conclude that the bone loss of hip joint is distinct in early AS. What is more, the bone loss in the cortex of hip joints is earlier than spongiosa in early AS. The BMI is an important factor for the areal BMD of the AS patients and health controls.

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