The relation between joint erosion and forearm bone mineral density in female patient with rheumatoid arthritis

Romatoid Artritli bayan hastalarda eklem erozyonları ile ön kol kemik mineral yoğunluğu arasındaki ilişki

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Abstract

Purpose: Rheumatoid arthritis (RA) is a disease that characterized by joint damage including periarticular osteoporosis and focal bone erosion. Despite the fact that periarticular osteoporosis and erosions are known as radiographic hallmarks of RA, there is a lack of data on the relationship between forearm bone loss and radiographic damage. For this reason, we aimed in this study to determine whether there is a relationship between focal erosions and OP in RA patients.

Materials and methods: We evaluated 49 female patients with RA. Anteroposterior hand and foot radiographs and bone mineral density measurement of forearm, hip and lumbar spine with dual x-ray absorptiometry of all patients were taken at simultaneously. Radiographs were analyzed using the Larsen method. Disease activity was evaluated by DAS-28 and functional ability was measured with Health Assessment Questionnaire and Duruöz Hand Index.

Results: Patients had the mean age 53.9±11.8 and an average disease duration of 7.9±5.9 years. The erosion score was correlated with bone mineral density of forearm, but not with lumbar spine and hip. The disease activity and functional ability were not correlated with Larsen score. Both osteoporosis in all evaluated area and correlations were not affected by the menopause status and disease duration.

Conclusion: Our results demonstrated that bone mineral density of forearm indicate the erosion severity in female patients with RA.

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Key words: Rheumatoid arthritis, forearm osteoporosis, erosion, dual X-ray absorptiometry

Özet

Amaç: Romatoid artrit (RA) periartiküler osteoporoz ve erozyonların dahil olduğu eklem hasarı ile karakterize bir hastalıktır. Periartiküler osteoporoz ve erozyonlar RA'da iyi bilinen radyolojik bulgular olmasına rağmen, ön kol kemik mineral yoğunluğu ile radyografik hasar arasındaki ilişkiye dair çok az veri mevcuttur. Bu nedenle çalışmamızda RA'da fokal erozyonlar ile osteoporoz arasında ilişki olup olmadığını belirlemeyi amaçladık.

Gereç ve yöntem: Romatoid artritli 49 bayan hasta değerlendirildi. Hastaların tümünün el ve ayak grafileri ile ön kol, lomber ve kalça dual-x ray absorbsiyometri ölçümleri yapıldı. Radyografiler Larsen yöntemi ile değerlendirildi. Hastalık aktivitesi DAS-28 ile ve fonksiyonel durum Genel Sağlık anketi ve Duruöz El İndeksi ile değerlendirildi.

Bulgular: Hastaların yaş ortalaması 53.9±11.8 ve ortalama hastalık süresi 7.9±5.9 yıldı. Erozyon skoru, ön kol kemik mineral dansitesi ile korele iken lomber vertebra ve kalça ile korele değildi. Hastalık aktivitesi ve fonksiyonel durum Larsen skoru ile korele değildi. Gerek değerlendirilen bölgelerdeki osteoporoz, gerekse korelasyonlar menopoz durumu ve hastalık süresinden etkilenmedi.

Sonuç: Sonuçlarımız RA'lı bayan hastalarda ön kol kemik mineral dansitesinin erozyon şiddetini gösterdiğini belirtmektedir.

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Anahtar sözcükler: Romatoid artrit, önkol osteoporoz, erozyon, dual X-ray absorbsiyometri

Introduction

Rheumatoid arthritis (RA) is a common chronic inflammatory disease that characterized by joint damage [1]. Joint damage is periarticular osteoporosis and focal bone erosion. In patients with RA, systemic osteoporosis is also seen, as well as periarticular osteoporosis. Osteoporosis is more frequent in patients with RA than the general population [2].

The radiological evaluation was used to assess the joint damage such as periarticular osteoporosis and erosions. The assessment of joint damage with radiograms was used several radiological scoring methods. Since this methods require time and expertise, they are rarely used in everyday practice. In addition, the radiography has many drawbacks, such as the fact that evaluation is depended on the quality of graphy, the early erosion can not be detected and the high radiation exposure. Dual-X ray absorptiometry (DXA) is a technique used to determine the loss of axial and appendicular bone mass in patients with RA [3].

The appendicular bone loss in the distal radius occurs earlier than generalized osteoporosis and may be associated with subsequent progressive joint destruction in patients with RA [4,5].

Despite the fact that periarticular osteoporosis and erosions are known as radiographic hallmarks of RA, there is a lack of data on the relationship between forearm bone loss and radiographic damage. For this reason, we aimed to determine whether there is a relationship between focal erosions and OP in RA patients.

Methods

Fourty-nine females patients who diagnosed to have RA according to 1987 American College of Rheumatology (ACR) criteria were included in the study [6]. The patients with additional diseases which causes osteoporosis and who received antiresorptive treatment in the last one year were excluded from the study. The Institutional Ethics Committee approved the study, and all participants provided their written informed consent to participate in the study. Patient's age, duration of disease, medications and menopause status were recorded. The duration of disease less than 24 months was classified as early RA and longer than 24 months as late RA. History of glucocorticoid usage was questioned and calculated of cumulative dose. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and rheumatoid factor (RF), were evaluated. The disease activity was assessed with disease activity score by using 28-joint Disease Activity Score (DAS-28). DAS-28 was calculated on the based of the number of swollen and tender joints over 28 joints, ESR and a general health assessment on a visual analog scala [7]. Functional ability is measured by the Turkish validated Health Assessment Questionnaire (HAQ) and Duruöz Hand Index (DHI) [8,9].

Anteroposterior hand and foot radiographs of all patients were taken at simultaneously. Radiographs were analyzed using the Larsen method, by two rheumatologists. Briefly, 40 joints were scored in each patient from 0 (normal) to 5 (maximal destruction) and then the scores for each patient were summed [10].

Dual-X ray absorptiometry is a gold standart for the measurement of bone mineral density (BMD). BMD measurements of nondominant forearm, total hip, and L1-4 vertebrae were taken by a Hologic Discovery Bone Densitometer (Hologic, Bedford, MA) and t score was used to evaluation. The t-score compares the patient's bone density to the peak bone density of young adults. It is the number of standard deviations of the BMD measurement above or below of young adults of the same sex [1].

SPSS-18 is used for istatistical analyses. The results were expressed as mean±standard deviation (SD). Categorical data were analysed with the x^2 test. Correlations between the variables were estimated by Spearman's correlation coefficient method. For group comparison, we used t-test for continuous variables if normal distributed and Mann–Whitney U test if not normal distributed and chi-square test for categorical variables. All P values refer to two sided tests; P values less than 0.05 were considered significant.

Results

The total study cohort consisted of 49 female RA patients. The mean age was 53.9±11.8 years (25-76 years). Average disease duration was 7.9±5.9 years (10 patients early RA and 39

patients late RA). Thirteen of the patients were premenopausal and 36 were postmenopausal. All patients were using the DMARDs (synthetic (87.8%) and biological (12.2%). The clinical, laboratory and radiographic findings and cumulative dose of steroid are shown in Table 1.

The results of BMD in patients with pre- and postmenopausal were shown Table 2. Only the lumbar spine t score was significantly different between the two groups (p<0.05). The age and cumulative steroid doses were similar in both groups (p>0.05). There were no statistically differences between the results of BMD in both early and late RA patients (Table 3). The age, menopause status and cumulative steroid doses were similar in these groups (p>0.05). The correlation between clinical, laboratory and radiographic measurements with the results of BMD were shown Table 4. It was determined that Larsen score was strongly negative correlated with forearm BMD (p<0.001). This correlation was not affected neither menopause (pre- and post-menopausal respectively r:-0.76, p<0.05; r:-0.64, p<0.001) nor disease duration (early and late RA respectively r:-0.71, p<0.001; r:-0,63, p<0.05) in RA patients.

Table1. Laboratory and clinical characteristics of the 57 patients who received bone mineral density measurement

Evaluated Measurements	Mean ± SD
Lumbar spine t score	-1.72±1.26
Lumbar spine z score	-.67±1.21
Femur t score	-1.43 ± .99
Femur z score	-.61± .97
Forearm t score	-1.95±1.66
Forearm z score	-.87 ±1.47
Larsen score	18.04±18.75
DAS28	3.88±1.14
ESR	44.46 ±19.89
CRP	18.07±33.94
RF	85.23±99.6
HAQ	14.54±10.22
DHI	16.18±14.06
Cumulative dose of steroid	5.48±3.82

(DAS28: Disease activiy score28; ESR: eritrosit sedimentation rate; CRP: C-reactive protein; RF: Rheumatoid factor; HAQ: Health Assessment Questionnaire; DHI: Duruöz Hand Index)

Table 2. Prevalence of osteoporosis and osteopenia

	Normal		Osteopenia		Osteoporosis	
	n	%	n	%	n	%
Lumbar spine (L1-4)	17	29.8%	23	40.4%	17	29.8%
Total Hip	23	40.4%	22	38.6%	12	21.1%
Forearm	13	22.8%	25	43.9%	19	33.3%

Table 3. Comparison of the bone mineral density of patients using biological and synthetic disease-modifiying antirheumatic drugs (DMARDs) with early and late rheumatoid arthritis (RA)

	Early RA (n:11)	Late RA (n:46)	p
Lumbar spine t score	-1.89±0.91	-1.68±1.33	**
Lumbar spine z score	-0.74±0.73	-0.66±1.31	**
Femur t score	-1.41±0.98	-1.44±0.99	**
Femur z score	-0.58±0.66	-0.62±1.03	**
Forearm t score	-1.89±1.88	-1.96±1.62	**
Forearm z score	-0.77±1.25	-0.89±1.52	**
	Synthetic DMARDs (n:51)	Biological DMARDs (n:6)	
Lumbar spine t score	-1.75±1.31	-1.42±0.64	**
Lumbar spine z score	-0.65±1.25	-0.89±0,79	**
Femur t score	-1.41±1.02	-1.63±0.72	**
Femur z score	-0.57±0.99	-0.96±0.79	**
Forearm t score	-2.05±0.69	-1.04±1.05	**
Forearm z score	-0.92±1.50	-0.42±1.18	**

**. $p>0.05$ level (2-tailed).

Table 4. Clinical, laboratory and radiographic measurements correlation with BMD

	BMD, lumbar spine r	BMD, total hip r	BMD, forearm
Larsen score	-.17	-.33*	-.49**
DAS28	-.10	-.19	-.23
DHI	-.21	-.17	-.19
HAQ	-.15	-.22	-.23
Usage of steroid	-.03	-.04	-.02
Cumulative steroid dose	-.06	-.16	-.12
CRP	-.11	-.04	-.09
ESR	-.03	-.11	-.20
RF	.23	.30*	.34*

(BMD: Bone mineral density; DAS28: Disease activiy score28; ESR: eritrosit sedimentation rate; CRP: C-reactive protein; RF: Rheumatoid factor; HAQ: Health Assessment Questionnaire; DHI: Duruöz Hand Index) *. Correlation is significant at the 0.05 level (2-tailed).
 **. Correlation is significant at the 0.01 level (2-tailed).

Discussion

Rheumatoid arthritis is the most common form of inflammatory arthritis in adults. The skeletal system is a major target organ and is characterized by focal bone erosions, local and systemic osteoporosis [1,2,11]. Radiological scoring methods to evaluated the erosion severity is rarely used in daily practice of a physicians. Wheras, the determination of severity in erosions is very important to follow the disease and evaluation in seriousness [10]. In our study, we determined that forearm BMD was correlated with erosion score. Therefore,

we think that the forearm BMD may be a subjective and reliable method of assesing the erosion severity. Similar to our study, Desai et al. [18] had investigated the relation between osteoporosis and erosions. But, in their study, BMD of the forearm and hand, which is the most common areas for erosions, have not been evaluated. Previous studies have shown that hand BMD correlates with the severity of radiographic erosions [12-14]. However, in RA patients, the severe hand deformity can lead to change of hand position in DXA, thus causes an incorrect evaluation of the BMD. Also reference values of the hand BMD in ethnic groups is

not determined [3]. So it is more precious to evaluate the BMD of forearm instead of the hand in RA patients, as in our study. This relationship may be due to focal erosions and OP may be occured the similar inflammatory cascade. The inflammatory cytokines, such as tumor necrosis factor-α and RANKL, play important roles in both processes. The osteoprotogerin that stimulated by these proinflammatory cytokines causes erosion and osteoporosis via stimulating formation and activation of osteoclasts [15]. Lumbar spine and hip joint is less affected by RA-induced inflammation. For this reason erosive changes rarely ocur [1]. On the other hand, BMD measurements of lumbar vertebrae and hip may be erroneous results depending on degenerative joint disease, especially in older patients as in our study. It may be due to these factors that we have not determinated the relationship between BMD of lumbar vertebrae and hip and erosion severity.

In early RA, periarticular osteoporosis may occur before the erosions visible [16]. For this reason the relationship between hand or forearm bone loss and erosions can be expected and have also been shown in various studies [12,16,17]. Whereas in our study, this relationship was not only early but also in the late RA. In this case, we thought it might be that the forearm BMD is an indicator of erosion severity regardless of the duration of RA.

Menopause is an important risk factor in the development of osteoporosis [18]. However in our study, we determined that only lumbar vertebrae BMD is affected by menopause, there is no change in others. This result may be due to the periarticular bone loss occured especially in patients with RA [5,19-21]. The correlation between forearm BMD and erosion score was also present both premenopausal and postmenopausal RA patients.

Glucocorticoids supress of inflammation in RA and reduce the rate of joint destructions as seen on radiography, but they may cause osteoporosis [22]. On the other hand, RA-induced osteoporosis is caused by systemic inflammation [23]. For this reason immunsuppressive treatment, including glucocorticoids, can prevent disease related bone loss in RA [22-24]. We also determined that osteoporosis was not affected by the cumulative dose of glucocoricoids in RA patients, similar to previous studies [25,26]. We did not find the correlation between the bone loss and RF, disease activity, and disability, as in some previous studies [13,27-29].

In conclusion, our study demonstrated that forearm BMD measurement indicate the erosion severity in female patients with RA. The monitoring of erosion severity is very important especially in follow-up of these patients. For this reason, when considering the limitations of radiographic evaluation of erosions, we believe that forearm BMD can be used instead of radiography in following the disease.

Conflict of interest: The authors declared that there was no conflict of interest.

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