Do rheumatoid arthritis patients have low back pain or radiological lumbar lesions more frequently than the healthy population? – Cross-sectional analysis in a cohort study with age and sex-matched healthy volunteers

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Citation	The Spine Journal. 20(12); 1995-2002
Issue Date	2020-12
Type	Journal Article
Textversion	Author
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DOI	10.1016/j.spinee.2020.06.020

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Akinobu Suzuki, Koji Tamai, Shinji Takahashi, Kentaro Yamada, Kentaro Inui, Masahiro Tada, Tadashi Okano, Yuko Sugioka, Tatsuya Koike, Hiroaki Nakamura. Do rheumatoid arthritis patients have low back pain or radiological lumbar lesions more frequently than the healthy population? – Cross-sectional analysis in a cohort study with age and sex-matched healthy volunteers. *The Spine Journal*. 20, 2020, 1995-2002. doi:10.1016/j.spinee.2020.06.020.

Do rheumatoid arthritis patients have low back pain or radiological lumbar lesions more frequently than the healthy population?

-Cross-sectional analysis in a cohort study with age and sex-matched healthy volunteers

Abstract

Background Context: Rheumatoid arthritis (RA) can affect the spine; however, the epidemiology of lumbar lesions and/or low back pain (LBP) in RA patients has not been well-studied.

Purpose: The purpose of this study was to compare the prevalence of lumbar lesions and LBP in RA patients with that in healthy volunteers, and to elucidate the influence of RA on lumbar disease.

Study design: Cross-sectional analysis in a cohort study with age- and sex-matched healthy volunteers.

Patient Sample: This study included 185 patients with RA and 188 gender/age-matched healthy volunteers without RA.

Outcome Measures: Lumbar spondylolisthesis and prevalent vertebral fractures were evaluated using plain lateral X-ray images. Thoraco-lumbar scoliosis was evaluated using dual-energy X-ray absorptiometric images. LBP was assessed using the Visual Analogue Scale (VAS) and Rolland-Morris disability questionnaire (RDQ).

Methods: The prevalence of radiological lumbar lesion and LBP was compared between the RA and control groups. In the RA group, factors associated with lumbar lesion and LBP were analyzed using a multiple logistic regression model.

Results: The prevalence rates of spondylolisthesis and prevalent vertebral fracture were significantly higher in the RA group than in the control group; the prevalence of thoraco-lumbar scoliosis tended to be higher in the RA group. There was no significant difference in

the average LBP-VAS between the groups. However, the percentage of analgesic drug use was significantly higher, and RDQ scores tended to be worse in the RA group than the control group. Multivariate analysis revealed that age and disease activity score were both related to LBP in the RA group.

Conclusion: RA patients are more likely to have radiological lumbar lesions. LBP in RA patients is well controlled, similar to the level in the healthy population; however, disease activity was related to LBP in RA patients. These results suggest that disease control is important for lumbar care in RA patients.

Keywords: Low back pain, Lumbar spondylolisthesis, Vertebral fracture, Thoraco-lumbar scoliosis, Rheumatoid arthritis, Risk factors, Disease activity

Abbreviations: RA, rheumatoid arthritis; LBP, low back pain; MTX, methotrexate; DAS28-CRP, Disease Activity Score 28 – C-reactive protein; CRP, C-reactive protein; VAS, visual analogue scale; RDQ, Rolland-Morris disability questionnaire; HADS, hospital anxiety and depression scale; PSL, prednisolone; OP Meds, anti-osteoporotic medications

Introduction

Although rheumatoid arthritis (RA) is known for causing synovitis in peripheral joints, it can also affect the spine. Cervical lesions such as atlantoaxial subluxation or subaxial subluxation are known to be RA-specific lesions; in fact, their epidemiology has been extensively studied. In a cross-sectional study, Takahashi et al. reported that 42% of RA patients had radiological cervical lesions and that neck pain intensity was associated with vertical atlantoaxial subluxation [1]. Terashima et al. reported that the incidence of cervical spine instabilities increased from 41.3% to 76.9% during a 10-year follow-up; in addition, mutilating changes, corticosteroid administration, and previous joint surgery were demonstrated as predictive risk factors of cervical spine instabilities [2].

In the existing literature, several studies have focused on radiological lumbar lesions or low back pain (LBP) in RA patients. In 1952, Baggenstoss first reported destructive lumbar lesions as “rheumatoid granulomatous nodules” in RA patients [3]. Shortly thereafter, Lawrence et al. reported that spondylolisthesis, disc space narrowing without vertebral osteophytes, and osteoporosis were common in RA patients [4]. Kawaguchi et al. examined lumbar X-rays in 106 RA patients, and abnormal radiological findings in the lumbar spine were detected in 57% of the cases [5]. Supposedly, the prevalence of LBP is relatively high in RA patients; in fact, it has been reported to be as high as 65% [6–9]. However, degenerative changes similarly occur in the population without RA; in addition, there have been a few studies concerning the epidemiology of lumbar lesions and/or LBP compared to the healthy population. It remains unclear as to whether the prevalence of radiological lumbar lesion and LBP is higher in RA patients.

Therefore, the purpose of the present study was to compare the prevalence rates of radiological lumbar lesions and LBP in RA patients and healthy volunteers, as well as to clarify the relationship between RA and both lumbar lesions and LBP.

Patients and Methods

Study population

This study is part of a 10-year prospective cohort study (**T**otal **m**anagement **o**f **r**isk factors in **r**heumatoid arthritis patients to **l**ower morbidity and mortality [TOMORROW] study, UMIN000003876). This analysis included 185 patients with RA (RA group) and 188 age- and sex-matched healthy volunteers without RA (control group). The latter were recruited using mass media. All RA patients were between 20–79 years old and fulfilled the American College of Rheumatology (ACR) criteria for RA [10]. This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. This prospective study was approved by the Institutional Review Board, and all participants provided written informed consent beforehand.

Clinical assessments

Height and body weight were measured on a digital scale, and body mass index (BMI, kg/m²) was subsequently calculated. In addition, on-going treatment regimens were equally investigated. Corticosteroids, non-steroidal anti-inflammatory drugs, muscle relaxants, prostaglandin E1 derivatives, and opioids were selected as analgesic drugs in this study. For RA patients, the use of corticosteroids, methotrexate (MTX), biological agents, and anti-osteoporotic medication was individually recorded regardless of the related amount or type. The disease activity of RA was measured using the Disease Activity Score 28 – C-reactive protein (DAS28-CRP) composed of 28-tender joint count, 28-swollen joint count, visual analogue scale (VAS) of general health, and C-reactive protein (CRP) scores [11]. Regarding RA progression, joint destruction was classified based on bilateral hand X-rays, according to Steinbrocker's classification [12].

LBP in the preceding four weeks was assessed using both the VAS (100 mm) and Roland-Morris disability questionnaire (RDQ); patients with VAS scores for LBP greater than 40 mm were considered LBP-positive. Finally, statuses of anxiety and depression were evaluated using the Hospital Anxiety and Depression Scale (HADS) [13].

Imaging evaluation

Lumbar spondylolisthesis and prevalent vertebral fracture were both evaluated on plain lateral X-ray using imaging software (Synapse; Fujifilm, Tokyo, Japan). Spondylolisthesis was defined as an anterior/posterior slip greater than or equal to 3 mm. Vertebral fracture was defined as a decrease in vertebral height greater than 20% compared with caudal or cranial normal vertebrae by a semi-quantitative assessment [9]. Bone mineral density (BMD, g/cm²) was measured by dual-energy X-ray absorptiometry using a QDR 4500 system (Hologic, Waltham, MA). Quality control (for the device) was performed by the daily assessment of a spine phantom. BMD was scanned in a whole-body mode, and BMD of the lumbar spine BMD was analyzed. Thoraco-lumbar scoliosis, defined as a Cobb angle greater than 10°, was evaluated on the whole-body image obtained through dual-energy X-ray absorptiometry, which was performed using the QDR 4500 system (Hologic®, Waltham, MA).

Statistical analysis

Results were expressed as mean $\pm$ standard deviation. Continuous variables were compared using the Mann–Whitney U test, whereas categorical variables were compared using a chi-squared (χ^2) test. *P*-values less than 0.05 were considered statistically significant. In the assessment of the factors associated with LBP and radiological lumbar lesions, a multiple logistic regression model was used to obtain odds ratios (ORs) and their related 95% confidence intervals (CIs). In the comparison of the prevalence rates of LBP and radiological

lumbar lesions between the two groups, the multivariate model included age, gender, BMI, lumbar spine BMD, and the presence of RA. In the analysis of the factors related to LBP and radiological lumbar lesions within the RA group, the multivariate model included those which yielded p -values less than 0.10 in the univariate analysis. All statistical analyses were performed using SPSS version 21.0 (IBM-SPSS, Inc., Chicago, IL, USA).

Results

Patient characteristics

Demographics and patient characteristics are summarized in Table 1. The mean age was 58.4 years and 57.8 years in the RA and control groups, respectively; the proportions of female patients in the RA and control groups were 84.3% and 84.0%, respectively; the mean BMI was 22.5 kg/m² in the RA group and 22.7 kg/m² in the control group. Lumbar spine BMD was 0.94 g/cm² in the RA group and 0.95 g/cm² in the control group. No significant difference in age, gender, BMI, or lumbar spine BMD was between the groups. In the RA group, the mean disease duration was 19.1 years; 35 (18.9%), 147 (79.5%), and 89 (48.1%) patients were treated with corticosteroids, MTX, and biological agents, respectively.

Radiological lumbar lesions in RA group and control group

The prevalence rates of spondylolisthesis and prevalent vertebral fracture were both significantly higher in the RA group than in the control group (spondylolisthesis: 46.5% vs. 26.6%, $p < 0.01$, vertebral fracture: 45.9% vs. 33.9%, $p = 0.01$) (Table 2). The prevalence of thoraco-lumbar scoliosis tended to be higher in the RA group (29.7%) than in the control group (22.9%) ($p = 0.08$). In the multivariate analysis, RA was significantly related to both vertebral fracture ($p = 0.026$, adjusted OR = 1.670) and spondylolisthesis ($p < 0.001$, adjusted OR = 2.669), whereas age was related to all three lesions (spondylolisthesis: $p < 0.001$,

adjusted OR = 1.084, vertebral fracture: $p < 0.001$, adjusted OR = 1.072, scoliosis: $p < 0.001$, adjusted OR = 1.046) (Table 2). Sex and lumbar BMD were related only to vertebral fracture (Sex (Male): $p = 0.043$, adjusted OR = 0.510, Lumbar BMD: $p = 0.026$, adjusted OR = 0.243).

Factors related to radiological lumbar lesions within RA patients

In the univariate analysis, the factors related to spondylolisthesis were age ($p < 0.01$, crude OR = 1.086, 95% CI: 1.052–1.120), DAS28-CRP ($p = 0.053$, crude OR = 1.265, 95% CI: 0.997–1.605), and use of anti-osteoporotic medications ($p < 0.01$, crude OR = 2.854, 95% CI: 1.537–5.298). In addition, multivariate analysis showed that the only factor significantly related to spondylolisthesis was age ($p < 0.01$, adjusted OR = 1.076, 95% CI: 1.040–1.112).

Age ($p < 0.01$, crude OR = 1.090, 95% CI: 1.055–1.126), lumbar BMD ($p < 0.01$, crude OR = 0.065, 95% CI: 0.011–0.383), and the use of anti-osteoporotic medications ($p < 0.01$, crude OR = 2.680, 95% CI: 1.448–4.961) were all identified as factors related to prevalent vertebral fracture by univariate analysis. Multivariate analysis demonstrated that age was the only significant factor related to prevalent vertebral fracture ($p < 0.01$, adjusted OR = 1.073, 95% CI: 1.036–1.111).

Univariate analysis identified age ($p = 0.027$, crude OR=1.032, 95% CI: 1.004–1.062), disease duration ($p < 0.01$, crude OR = 1.036, 95% CI: 1.009–1.064), and use of anti-osteoporotic medications ($p = 0.025$, crude OR = 2.093, 95% CI: 1.098–3.991) as factors related to thoraco-lumbar scoliosis. On the contrary, multivariate analysis showed that only disease duration was significantly related to scoliosis ($p = 0.047$, adjusted OR = 1.014, 95% CI: 1.000–1.058).

LBP in the RA group and control group

The average VAS scores of LBP were 25.3 ± 25.6 and 21.3 ± 28.7 in the RA and control groups, respectively. In fact, no significant difference was observed between the two groups in terms of VAS score of LBP (Table 3); in addition, a similar distribution was observed between the two groups (Fig. 1). The RDQ score tended to be worse in the RA group. According to the χ^2 test, the patients in the RA group answered *YES* more frequently in 17 items of a total of 24 items. Nonetheless, the percentage of analgesic drug use was significantly higher in the RA group (43.8%) than in the control group (6.9%) ($p < 0.001$). Unexpectedly, according to the HADS, although the anxiety scores were similar in both groups, the depression score was slightly but significantly higher in the control group than in the RA group (Table 3).

In the multivariate analysis performed in all subjects, age was the only factor related to LBP ($p < 0.01$, adjusted OR = 1.031, 95% CI: 1.010–1.053) (Table 4).

Factors related to LBP within RA patients

The univariate logistic regression analysis showed that age, scoliosis, disease duration, DAS28-CRP, Steinbrocker's stage, use of steroids, and use of anti-osteoporotic medications were all associated with LBP-related VAS scores greater than 40 (Table 5). In addition, the multivariate logistic regression analysis revealed that age (OR = 1.052, 95% CI: 1.012–1.093) and DAS28-CRP (OR = 1.550 and 95% CI: 1.12–2.14) were both significantly related to LBP (Table 6).

Discussion

We investigated the prevalence of both LBP and radiological lumbar lesions in 185 RA patients and 188 age/gender-matched control subjects. To the best of our knowledge, this is

the first study to compare the prevalence of both LBP and radiological lumbar lesion between RA patients and healthy controls.

We found that the prevalence rates of spondylolisthesis and vertebral fractures in the RA group were 46.5% and 45.9%, respectively; in fact, these were higher than those in the control group (26.6% and 33.9%, respectively). Although no statistical significance was actually detected, the prevalence of thoraco-lumbar scoliosis tended to be higher in the RA group (29.7%) than in the control group (22.9%).

To date, several studies have been conducted concerning the prevalence of lumbar lesions in RA patients compared to that in control subjects. Hagege et al. investigated the prevalence of spondylolisthesis in LBP patients with and without RA, eventually reporting that the prevalence was significantly higher in the RA patients (41.8%) than in those without RA (18.1%) [14]. Ørstavik et al. investigated the prevalence of vertebral deformities in RA patients in comparison with population-based controls without RA and reported both the prevalence and the number of deformities to be significantly higher in RA patients than in controls [15]. Okano et al. similarly reported that vertebral fractures (vertebral height loss more than 20% through semi-quantitative assessment) were more frequently observed in RA patients (45.5%) than in control subjects (30.0%) [16]. In fact, the present results are consistent with those of previous studies, as all of them suggest that lumbar lesions can be identified more frequently in RA patients than in control subjects without RA.

There are several possible reasons for this higher incidence of lumbar lesions. First, RA patients have a higher risk of osteoporosis due to the disease itself, as well as due to low physical activity and glucocorticoid utilization [17]. Kim et al. conducted a population-based cohort study and reported that RA patients had a 25% higher risk of osteoporotic fracture — including hip, pelvis, humerus, and wrist fractures — compared to non-RA subjects [18]; this directly affects the incidence of vertebral fractures, and it may similarly affect that of thoraco-

lumbar scoliosis indirectly. Second, because intervertebral facet joints are synovial joints, they can actually be affected by RA-induced synovitis; furthermore, although the disc-vertebral joint is not a synovial joint, end plates can also be affected. Shichikawa et al. demonstrated that, according to the results of autopsies conducted on RA patients, the inflammation of both enthesis and peridiscal tissue could cause erosion of the end plate, as well as disc degeneration [19]. Sakai et al. investigated end plate erosion on both X-ray and MRI and reported that actual erosion was found in 45.2% of 104 RA patients [20]. In our previous study on lumbar MRI in RA patients [21], lumbar facet joints and end plate erosion were found in 76.6% and 70.6% of the RA patients, respectively. End plate erosion strongly correlated with adjacent vertebral body fracture or disc degeneration, whereas facet erosion correlated with spondylolisthesis. Nevertheless, facet erosion and end plate erosion can both occur in the patients without RA, and it remains unclear whether the prevalence of these erosions is higher in RA patients. However, in addition to facet or end plate erosions, less osteophyte formation and/or lower bone quality may affect the incidence of radiological lumbar lesions in patients with RA.

In the multivariate analysis of factors related to radiological lumbar lesions in the RA group, only age was identified as an independent risk factor for spondylolisthesis and prevalent vertebral fracture; in addition, disease duration was identified as a risk factor for thoraco-lumbar scoliosis. Several risk factors associated with lumbar lesions have been previously reported in RA patients: Sugimura et al. reported that higher serum CRP levels and history of joint surgery were both associated with lumbar spondylolisthesis [22]. Hagege et al. reported that age was the only independent risk factor for lumbar spondylolisthesis [14]. Ørstavik et al. investigated the factors associated with vertebral deformity in both RA patients and population-based control subjects and reported that BMD and long-term corticosteroid use were independent factors associated with vertebral deformities, in addition to RA [15].

Our previous MRI study showed that lower lumbar level, high disease activity, and Steinbrocker's stage were all associated with end plate erosion; in addition, lower lumbar level, age, and high disease activity were associated with facet erosion [21]. It is well known that RA equally affects bone quality and accelerates osteoporosis [23,24]. In summary, the data of previous literature and this study suggest that both age-related degeneration and disease-related inflammation/erosion affect the incidence of lumbar lesions in RA patients. Specifically, it can similarly be interpreted that RA accelerates aging through joint inflammation/erosion and osteoporosis in the lumbar spine.

In 1993, Helliwell et al. reported that 43.2% of RA patients had LBP and that 33.0% of all the RA patients complained of LBP lasting more than 3 months [8]. In 2006, Kothe et al. submitted a questionnaire to 281 patients with RA, 150 of whom (53.4%) reported an episode of LBP during the previous 6 months [6]. Although these rates have been considered relatively higher than the ones for healthy population in other studies, it remains unclear whether the rate is truly higher in RA patients due to the lack of control subjects and the difference in the evaluation method of LBP. In this study, the rate of patients with LBP-related VAS greater than 40 was 27.6% for RA patients and 25.5% for controls, and no statistically significant difference either in prevalence or average VAS was detected. These results can be interpreted as "*LBP rate in RA patients is similar to that in healthy population*"; however, two important points should not be overlooked. First, the rate of utilization of analgesic drugs was 43.8% in the RA group, i.e., significantly higher than that in the control group (6.9%). The reasons for utilizing analgesic drugs were not analyzed in this study; however, these drugs may be used for LBP in some patients and peripheral joint involvement in other patients. In either case, this study suggests that LBP in RA patients is well controlled similar to the level of the healthy population. Secondly, RDQ score tended to be worse in the RA group ($p = 0.068$). This implies that LBP is more likely to impair

activities of daily living in RA patients than in healthy subjects; this may be due to additional issues in other peripheral joints, particularly in the limbs.

In the present study, there were significant differences in age, scoliosis, disease duration, DAS28-CRP, Steinbrocker's stage, use of corticosteroids, and use of anti-osteoporotic medications between RA patients with LBP and those without LBP. Among those factors, the multivariate analysis revealed that higher age and higher DAS28-CRP were related to LBP in RA patients; interestingly, radiological lumbar lesions were not associated with LBP in RA patients. Yamada et al. reported that female gender, tobacco smoking habit, and moderate and high DAS28-erythrocyte sedimentation rate (ESR) were all significantly related to severe LBP. Recently, Miura et al. [25], through a cross-sectional study of a large number of RA patients, reported that BMI, multiple vertebral fractures, higher DAS28-CRP, vertebral end plate and/or facet erosion, higher BMI, longer disease duration, greater pelvic tilt, older age of disease onset, greater sagittal vertical axis, and lower MTX utilization were all identified as independent factors associated with dysfunctional LBP [9]. The discrepancies among these various studies may be due to the different definitions of LBP-positivity, the number of enrolled patients, and included factors in the analysis. Nevertheless, a factor in common is actually DAS28; there are two possible reasons for this relationship between DAS28 and LBP. Firstly, lumbar spine inflammation itself can cause LBP; in fact, it is well known that facet joint inflammation and erosion can both trigger LBP. Second, because DAS28 includes patient-reported VAS score concerning general health, severe forms of LBP may raise the VAS score. Nevertheless, because it remains unclear as to which one represents the cause and which the effect, further studies focused on lumbar spine inflammation, would be necessary to clarify this point.

This study has several limitations. First, the healthy volunteers were recruited using mass media; however, the HADS-anxiety score was significantly higher in the control group;

albeit, no significant difference was observed. Furthermore, the prevalence of vertebral fracture in the control group was higher than those previously reported. Therefore, the control group may have included more subjects who were highly conscious of their health than the general population; in addition, there could have been some other selection bias in the control subjects. Second, anterior-posterior spondylolisthesis was evaluated, rather than lateral-listhesis. Furthermore, scoliosis was evaluated using DEXA in the supine position, rather than antero-posterior X-ray, to reduce radiation exposure as much as possible; consequently, the prevalence of these lesions may have been underestimated. Lastly, the prevalence and risk factors related to lumbar lesion were analyzed in RA patients; however, the characteristics of lumbar lesion were not analyzed. Therefore, further study, including MRI and dynamic X-ray would be necessary for the investigation of RA-specific lumbar lesion.

In conclusion, RA patients are more likely to have radiological lumbar lesions, especially lumbar spondylolisthesis, and prevalent thoraco-lumbar vertebral fractures. Moreover, although LBP in RA patients was well controlled similar to the level of the healthy population, the activity of daily living may be more affected by LBP in the RA patients, and disease activity was related to LBP in RA patients. These results suggest that disease control is equally important for lumbar care in RA patients.

References

- [1] Takahashi S, Suzuki A, Koike T, Yamada K, Yasuda H, Tada M, et al. Current prevalence and characteristics of cervical spine instability in patients with rheumatoid arthritis in the era of biologics. *Mod Rheumatol* 2014;24:904–9.
- [2] Terashima Y, Yurube T, Hirata H, Sugiyama D, Sumi M, Hyogo Organization of Spinal Disorders. Predictive Risk Factors of Cervical Spine Instabilities in Rheumatoid Arthritis. *Spine (Phila Pa 1976)* 2017;42:556–64.
- [3] Baggenstoss AH, Bickel WH, Ward LE. Rheumatoid granulomatous nodules as destructive lesions of vertebrae. *J Bone Joint Surg Am* 1952;24 A:601–9.
- [4] Lawrence JS, Sharp J, Ball J, Bier F. Rheumatoid Arthritis of the Lumbar Spine. *Ann Rheum Dis* 1964;23:205–17.
- [5] Kawaguchi Y, Matsuno H, Kanamori M, Ishihara H, Ohmori K, Kimura T. Radiologic findings of the lumbar spine in patients with rheumatoid arthritis, and a review of pathologic mechanisms. *J Spinal Disord Tech* 2003;16:38–43.
- [6] Kothe R, Kohlmann T, Klink T, Rüther W, Klinger R. Impact of low back pain on functional limitations, depressed mood and quality of life in patients with rheumatoid arthritis. *Pain* 2007;127:103–8.
- [7] Baykara RA, Bozgeyik Z, Akgul O, Ozgocmen S. Low back pain in patients with rheumatoid arthritis: Clinical characteristics and impact of low back pain on functional ability and health related quality of life. *J Back Musculoskelet Rehabil* 2013;26:367–74.
- [8] Helliwell PS, Zebouni LN, Porter G, Wright V. A clinical and radiological study of back pain in rheumatoid arthritis. *Br J Rheumatol* 1993;32:216–21.
- [9] Yamada K, Suzuki A, Takahashi S, Yasuda H, Koike T, Nakamura H. Severe low back pain in patients with rheumatoid arthritis is associated with Disease Activity Score but

- not with radiological findings on plain X-rays. *Mod Rheumatol* 2015;25:56–61.
- [10] Arnett FC, Edworthy SM, Bloch DA, Mcshane DJ, Fries JF, Cooper NS, et al. The American rheumatism association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988;31:315–24.
- [11] Prevoo ML, Van 't Hof MA, Kuper HH, Van Leeuwen MA, Van de Putte LB, Van Riel PL. Modified Disease Activity Scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. *Arthritis Rheum* 1995;38:44–8.
- [12] Steinbrocker O, Traeger CH, Batterman RC. Therapeutic criteria in rheumatoid arthritis. *J Am Med Assoc* 1949;140:659–62.
- [13] Kitamura T. The Hospital Anxiety and Depression Scale (HADS). *Seishinka Shindangaku* 1993;4:371–2.
- [14] Hagege B, Tubach F, Alfaiate T, Forien M, Dieudé P, Ottaviani S. Increased rate of lumbar spondylolisthesis in rheumatoid arthritis: A case-control study. *Eur J Clin Invest* 2018;48:e12991.
- [15] Ørstavik RE, Haugeberg G, Mowinckel P, Høiseth A, Uhlig T, Falch JA, et al. Vertebral Deformities in Rheumatoid Arthritis. *Arch Intern Med* 2004;164:420.
- [16] Okano T, Inui K, Tada M, Sugioka Y, Mamoto K, Wakitani S, et al. High frequency of vertebral fracture and low bone quality in patients with rheumatoid arthritis—Results from TOMORROW study. *Mod Rheumatol* 2017;27:398–404.
- [17] Laan RF, Buijs WC, Verbeek AL, Draad MP, Corstens FH, Van de Putte LB, et al. Bone mineral density in patients with recent onset rheumatoid arthritis: influence of disease activity and functional capacity. *Ann Rheum Dis* 1993;52:21–6.
- [18] Kim SY, Schneeweiss S, Liu J, Daniel GW, Chang C-L, Garneau K, et al. Risk of osteoporotic fracture in a large population-based cohort of patients with rheumatoid

- arthritis. *Arthritis Res Ther* 2010;12:R154.
- [19] Shichikawa K, Matsui K, Oze K, Ota H. Rheumatoid spondylitis. *Int Orthop* 1978;2:53–60.
- [20] Sakai T, Sairyo K, Hamada D, Higashino K, Katoh S, Takata Y, et al. Radiological features of lumbar spinal lesions in patients with rheumatoid arthritis with special reference to the changes around intervertebral discs. *Spine J* 2008;8:605–11.
- [21] Yamada K, Suzuki A, Takahashi S, Yasuda H, Tada M, Sugioka Y, et al. MRI evaluation of lumbar endplate and facet erosion in rheumatoid arthritis. *J Spinal Disord Tech* 2014;27:E128–35.
- [22] Sugimura Y, Miyakoshi N, Miyamoto S, Kasukawa Y, Hongo M, Shimada Y. Prevalence of and factors associated with lumbar spondylolisthesis in patients with rheumatoid arthritis. *Mod Rheumatol* 2016;26:342–6.
- [23] Van Onna M, Boonen A. The challenging interplay between rheumatoid arthritis, ageing and comorbidities. *BMC Musculoskelet Disord* 2016;17:1–9.
- [24] Adami G, Saag KG. Osteoporosis pathophysiology, epidemiology, and screening in rheumatoid arthritis. *Curr Rheumatol Rep* 2019;21:34
- [25] Miura K, Morita O, Hirano T, Watanabe K, Fujisawa J, Kondo N, et al. Prevalence of and factors associated with dysfunctional low back pain in patients with rheumatoid arthritis. *Eur Spine J* 2019;28:976–82.

Figure legends

Figure 1. The distribution of Visual Analogue Scale (VAS) scores of low back pain in 20-mm increments in the control and RA groups.

Table 1. Demographic data of the study population.

	Control	RA	p-value
N	188	185	
Female, N (%)	158 (84.0)	156 (84.3)	1.000
Age (y)	57.8 ± 12.4	58.4 ± 12.5	0.539
BMI (kg/m ²)	22.7 ± 3.6	22.5 ± 3.6	0.837
Lumbar BMD	0.95 ± 1.88	0.94 ± 0.21	0.347
Background of RA			
Disease duration	-	19.1 ± 11.7	
Steinbrocker Stage			
I	-	34 (18.4%)	
II	-	46 (24.9%)	
III	-	65 (35.1%)	
IV	-	40 (21.6%)	
DAS28 CRP	-	2.7 ± 1.3	
>4.1	-	27 (14.6%)	
2.7–4.1	-	52 (28.1%)	
2.3–2.7	-	22 (11.9%)	
<2.3	-	84 (45.4%)	
Use of PSL	-	35 (18.9%)	
Use of MTX	-	147 (79.5%)	
Use of BIO	-	89 (48.1%)	

BMI, body mass index; BMD, bone mineral density; DAS28-CRP, Disease Activity Score in 28 joints – C-reactive protein; PSL, prednisolone; MTX, methotrexate; BIO, biological agents.

Table 2. Multivariate analysis of factors for radiological lumbar lesion in total study population.

	aOR (95%CI)	p value
Spondylolisthesis		
Age (Yr)	1.084 (1.058-1.110)	<0.001
Sex (Male)	1.475 (0.733-2.969)	0.276
BMI (kg/m ²)	0.304 (0.968-1.110)	0.304
RA	2.669 (1.661-4.289)	<0.001
Lumbar BMD (g/cm ²)	2.221 (0.593-8.318)	0.236
Vertebral fracture		
Age (Yr)	1.072 (1.048-1.096)	<0.001
Sex (Male)	0.510 (0.265-0.979)	0.043
BMI (kg/m ²)	1.023 (0.958-1.093)	0.496
RA	1.670 (1.062-2.628)	0.026
Lumbar BMD (g/cm ²)	0.243 (0.070-0.845)	0.026
Scoliosis		
Age (Yr)	1.046 (1.022-1.069)	<0.001
Sex (Male)	1.694 (0.788-3.640)	0.177
BMI (kg/m ²)	0.959 (0.893-1.029)	0.240
RA	1.465 (0.907-2.365)	0.118
Lumbar BMD (g/cm ²)	1.541 (0.450-5.283)	0.491

BMD, Bone mineral density

Table 3. Results of the questionnaires.

	Control	RA	p-value
LBP VAS	21.3 ± 25.6	25.3 ± 28.7	0.145
RDQ	1.8 ± 3.5	3.1 ± 5.2	0.068
HADS -anxiety	7.4 ± 2.4	7.7 ± 2.2	0.218
HADS-depression	10.5 ± 2.2	10.0 ± 2.0	0.047

LBP, low back pain; VAS, Visual Analogue Scale; RDQ, Rolland-Morris disability questionnaire; HADS, Hospital Anxiety and Depression Scale.

Table 4. Multivariate analysis of factors for low back pain and radiological lumbar lesion in total study population.

	aOR (95%CI)	p value
LBP		
Age (Yr)	1.031 (1.010-1.053)	0.004
Sex (Male)	1.878 (0.887-3.977)	0.100
BMI (kg/m ²)	1.037 (0.970-1.109)	0.285
RA	1.090 (0.682-1.740)	0.720
Lumbar BMD (g/cm ²)	1.363 (0.396-4.693)	0.623

BMD, Bone mineral density

Table 5. Univariate analysis of factors for low back pain in RA patients.

	LBP (-)	LBP (+)	p-value	Crude OR
	(95%CI)			
n	134	51		
Age, y	56.1 ± 12.8	64.5 ± 9.1	<0.001	1.072
	(1.035–1.11)			
Female, n (%)	110 (82.1)	46 (90.2)	0.182	2.007
	(0.722–5.584)			
BMI, kg/m ²	22.6 ± 3.4	22.9 ± 4.1	0.565	1.027
	(0.939–1.123)			
Lumbar BMD, g/cm ²	0.94 ± 0.22	0.93 ± 0.19	0.649	0.692
	(0.142–3.382)			
HADS anxiety	7.6 ± 2.3	7.9 ± 2.6	0.479	1.852
	(0.624–5.495)			
HADS depression	10.1 ± 2.2	10.0 ± 2.4	0.637	0.914
	(0.419–1.991)			
Lumbar Lesion, n (%)				
Fracture	58 (43.3)	23 (45.1)	0.158	1.595
	(0.834–3.052)			
Spondylolisthesis	61 (45.5)	25 (49.0)	0.507	1.245
	(0.652–2.374)			
Scoliosis	35 (26.1)	31 (60.8)	0.084	1.825
	(0.923–3.608)			
Disease duration, y				

LBP in rheumatoid arthritis

	17.8 ± 11.2	22.5 ± 12.5	0.018	1.033 (1.005–1.061)
DAS28–CRP	2.5 ± 1.2	3.3 ± 1.2	<0.001	1.67 (1.273–2.19)
Steinbrocker Stage, n (%)				
I	29 (21.6)	5 (9.8)	Ref	
II	30 (22.4)	16 (31.4)	0.049	3.093 (1.003–9.542)
III	49 (36.6)	16 (31.4)	0.257	1.894 (0.628–5.713)
IV	26 (19.4)	14 (27.5)	0.052	3.123 (0.989–9.865)
Medication, n(%)				
Use of steroids	19 (14.2)	35 (68.6)	0.009	0.944 (0.495–1.8)
Use of MTX	107 (79.9)	40 (78.4)	0.831	0.918 (0.417–2.021)
Use of BIO	65 (48.5)	24 (47.1)	0.860	2.767 (1.287–5.947)
Use of OP Meds	46 (34.3)	36 (70.6)	0.002	2.861 (1.472–5.558)

LBP, low back pain; BMI, body mass index; BMD, bone mineral density; HADS, Hospital Anxiety and Depression Scale; DAS28-CRP, Disease Activity Score in 28 joints – C-reactive protein; PSL, prednisolone; MTX, methotrexate; BIO, biological agents; OP Meds, anti-osteoporotic medications.

Table 6. Multivariate analysis of factors for low back pain in RA patients.

	aOR (95%CI)	p value
Age	1.052 (1.012–1.093)	0.011
Scoliosis	1.550 (0.698–3.444)	0.282
Disease duration	1.007 (0.972–1.042)	0.714
DAS28–CRP	1.550 (1.122–2.140)	0.008
Steinbrocker Stage, n (%)		
I	Reference	
II	2.532 (0.677–9.475)	0.168
III	1.063 (0.280–4.033)	0.928
IV	1.476 (0.352–6.191)	0.595
Use of PLS, n (%)	1.416 (0.570–3.520)	0.454
Use of OP Meds, n (%)	1.492 (0.686–3.247)	0.313

DAS28-CRP, Disease Activity Score in 28 joints – C-reactive protein; PSL, prednisolone;

OP Meds, anti-osteoporotic medications.