OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS DIFFER IN THEIR EXTENT AND PATTERNS OF BONE QUALITY AND QUANTITY ALTERATIONS AS REVEALED BY AN ANIMAL MODEL SYSTEM

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INTRODUCTION

Osteoarthritis (OA) and rheumatoid arthritis (RA) are now the most common types of joint disorders. OA is a degenerative disease characterized by joint discomfort, loss of articular cartilage, and is associated with low level inflammation with progressive bone destruction. In contrast, RA causes more powerful chronic and systemic inflammation [1-3]. Researchers’ present focus is on evaluating bone quantity, especially bone mineral density (BMD) in OA or RA. However, differences between OA and RA related to the extent and pattern of alterations in both bone quality and quantity have not been extensively investigated, especially in longitudinal studies. Bone quality depends on multiple factors, including structural characteristics (bone macro- and micro-architecture) and bone mineralization [4-6]. Thus, the aim of this study was to investigate the differences between OA and RA by assessing the extent and pattern of alterations in bone quality and quantity by longitudinal tracking using micro-computed tomography (µ-CT).

METHODS

Animal models for human OA and RA were employed. Twenty-one 8-week-old female Sprague–Dawely rats were divided randomly into 3 groups: control (CON) (n = 7), osteoarthritis (OA) (n = 7), and rheumatoid Arthritis (RA) (n = 7). OA was mimicked by injecting 1 mg mono-iodoacetate (MIA) in 50 µl saline into the knee joint cavity [7-8]. RA was mimicked using the collagen-induced arthritis (CIA) method. Rats were injected twice intradermally with bovine type II collagen [9-10]. The tibial joints of the rats were scanned using a SkyScan1076 in vivo micro-CT (µ-CT) (SKYSCAN, Belgium) on day 0 (before treatment) and then 4 and 8 weeks after treatment. Trabecular bone with a 600-µm slice thickness on the tibial epiphysis was primarily analyzed. Bone quality and quantity, bone mineralization, micro-architecture, and bone mineral density (BMD) were evaluated. Specifically, we assessed trabecular bone micro-architecture, bone volume fraction (BV/TV, %), thickness (Tb.Th, mm), number (Tb.N, 1/mm), separation (Tb.Sp, mm), and pattern factor (Tb.Pf, 1/mm). A paired t-test and a one-way ANOVA test were performed to identify the difference in the rats between 0 to 8 weeks. The experimental protocol was approved by the Yonsei University School of Animal Care and Ethics Committee.

RESULTS

Bone mineralization

Bone mineralization in the OA group, reflected by the distribution of x-ray attenuation, gradually increased to high levels until week 4 and then decreased during the next 4 weeks. Compared with the OA group, bone mineralization in RA rats decreased continuously during the study (Figs. 2, 3, 4).

BMD and structural parameters (0–4 weeks)

Alterations of BMD and micro-architecture are summarized and shown, respectively, in Fig. 5. Trabecular bone BMD increased significantly in the CON and OA groups (+36.36% and +30.92%) compared with the RA group (-4.39%) (p < 0.05). The increased rate of BV/TV in CON and OA groups (+25.74% and 22.88%) were also significantly higher than those of the RA group (-8.83%) (p < 0.05). Tb.Th values in CON and OA (+29.13% and +25.40%) increased markedly versus the RA group.
group (−3.53%) \((p < 0.05)\). The rate of decrease in Tb.N values was higher in the RA (−5.81%) than CON or OA groups (−2.20% and −1.55%) \((p < 0.05)\). Tb.Sp values did not differ significantly among the groups. The increased Tb.Pf rates in the RA group (+13.32%) were significantly higher than those of the CON and OA groups (−58.15% and −38.02%) \((p < 0.05)\).

Figure 1: X-ray attenuation in the tibial knee joint at week 8. 3D images of tibiofemoral joint (lower row) and cross sectional images of tibial epiphysis (Upper row) are shown. Each column represents the results for control (A,D) osteoarthritis (B,E) and rheumatoid arthritis (C,F) groups.

BMD and structural parameters (4–8 weeks)

BMD significantly decreased in the OA and RA groups (−31.38% and −47.83%) compared with the CON group (−2.51%) \((p < 0.05)\). BV/TV decreased markedly in the OA and RA groups (−27.46% and −54.76%) \((p < 0.05)\). The rate of Tb.Th decrease in OA and RA groups was significantly higher (−25.38% and −22.77%) than that of the CON group (+1.42%) \((p < 0.05)\). The rate of Tb.N decrease was significantly higher in the RA group (−41.62%) than that of the other 2 groups \((p < 0.05)\). The Tb.Sp rate markedly increased in OA and RA groups (+13.28% and +41.29%) \((p < 0.05)\). Increased rates of Tb.Pf in OA and RA groups (+74.40% and +270.59%) were significantly higher than in the CON group (+2.78%) \((p < 0.05)\).

Figure 2: Bone mineralization, week 0

Figure 3: Bone mineralization, week 4

Figure 4: Bone mineralization, week 8

Figure 5: Alterations in relative variations of structural parameters (* group difference; †, †† respective differences between weeks 0–4 and weeks 4–8 \((p < 0.05)\).
DISCUSSION

Bone quality and quantity in both OA and RA models were reduced during the study. However, the degree and pattern of bone quality and quantity were significantly different ($p < 0.05$). Figures 1 and 5 show decreases in BMD and structural features in the overall region and callus on the boundary area in the RA model. In contrast, OA induced localized BMD decreases and changes in structural features within the damaged area and no callus growth on the boundary area. This resulted in bone growth in the undamaged area and increasing bone mineralization until week 4. These results indicate that bone strength properties in RA may be different from those in OA. We conclude, therefore, that a new strategy should be devised for preventing and/or treating fractures at risk for OA and RA. To our knowledge, this study is the first to simultaneously track, as a function of time, the extent and patterns of alterations of both bone quality and quantity in OA and RA.

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