Imaging Science in Dentistry 2024; 54: 345-53
https://doi.org/10.5624/isd.20240065

Fractal analysis of jawbone structure in patients with rheumatoid arthritis

Elif Celebi[1,*], Ozlem Gormez[2], Atalay Dogru[3], Turgay Aydogan[4], Hikmet Orhan[5]

[1]*Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Bahçeşehir University, Istanbul, Turkey*
[2]*Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Suleyman Demirel University, Isparta, Turkey*
[3]*Department of Rheumatology, Faculty of Medicine, Suleyman Demirel University, Isparta, Turkey*
[4]*Department of Computer Engineering, Faculty of Engineering and Natural Sciences, Suleyman Demirel University, Isparta, Turkey*
[5]*Department of Biostatistics and Medical Informatics, Faculty of Medicine, Suleyman Demirel University, Isparta, Turkey*

ABSTRACT

Purpose: Periarticular and generalized osteoporosis are well-known comorbidities of rheumatoid arthritis (RA), associated with either the disease itself or glucocorticoid therapy. This study was performed to quantitatively evaluate changes in the jawbones of patients with RA using fractal analysis (FA).

Materials and Methods: The study comprised 186 participants, including 144 women and 42 men. Of these, 93 were patients with RA and 93 were healthy controls. For the RA group, disease duration, laboratory findings, and medication use were recorded. Measurements of fractal dimension (FD), lacunarity (Lac), bone area fraction (BA/TA), and trabecular thickness (Tb.Th) were taken at the mandibular condyle and angle. These measurements were obtained from panoramic radiographs using ImageJ version 1.52p (National Institutes of Health, Bethesda, MD, USA).

Results: Relative to control participants, patients with RA exhibited higher FD values for both mandibular condyle and angle regions ($P<0.05$). Conversely, the RA group displayed lower Lac values for both regions ($P<0.05$). Similarly, Tb.Th values were significantly lower in the RA patient group for both the condyle and the angle ($P<0.05$). Furthermore, a significant negative correlation was identified between disease duration and FD at the mandibular condyle ($P<0.05$).

Conclusion: The results demonstrate that FA can be used to quantitatively assess changes in trabecular bone in the jawbones of patients with RA. Image analysis parameters derived from panoramic radiographs, including FA, Lac, BA/TA, and Tb.Th, hold promise in guiding patients with RA toward appropriate medical examinations. ***(Imaging Sci Dent 2024; 54: 345-53)***

KEY WORDS: Arthritis, Rheumatoid; Radiography, Panoramic; Fractals; Radiography, Dental

Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by chronic synovitis, progressive cartilage and bone damage, and ultimate loss of function. The most common manifestations include symmetrical pain and swelling in the hands, wrists, feet, and knees, although other joints may also be affected.[1,2] While RA predominantly targets the joints, some patients experience extra-articular complications such as rheumatoid nodules, vasculitis, pericarditis, interstitial lung disease, bronchiectasis, and pleural effusion during the clinical course.[3,4]

Either RA activity or glucocorticoid therapy can result in osteopenia and osteoporosis, which are characterized by reduced bone mineral density (BMD). Consequently, RA may lead to both periarticular and generalized osteoporosis. Particularly in its severe form, RA can affect the temporomandibular joint (TMJ), leading to clinical symptoms such as pain, swelling, crepitation, and limited mouth opening.[5,6] However, in RA cases, early detection of TMJ involvement with radiographic evaluation re-

Received March 31, 2024; Revised June 10, 2024; Accepted July 2, 2024
Published online August 12, 2024
*Correspondence to : Prof. Elif Celebi
Department of Dentomaxillofacial Radiology, Faculty of Dentistry, Bahçeşehir University, Gayrettepe, Barbaros Boulevard. No:153, 34357 Beşiktaş/İstanbul, Turkey
Tel) 90-539-396-1911, E-mail) celebielifin@gmail.com

mains challenging. Patients with RA face around double the risk of developing osteoporosis, as well as hip and vertebral fractures, compared to the general population. This elevated risk is independent of the adverse effects of glucocorticoid therapy on bone mass.[3,7]

The primary method for evaluating bone strength is BMD assessment using dual-energy X-ray absorptiometry (DXA). This technique is used to measure the loss of bone mass. However, the current understanding acknowledges that bone strength is determined by the bone's microarchitecture - that is, its structure and shape - as well as its mass. Consequently, increasing emphasis is being placed on the need to evaluate both bone quality and quantity.[8,9] Image processing techniques applicable to radiographs have been developed to estimate trabecular microarchitecture. Among these, fractal analysis (FA) is particularly noteworthy. FA is used to characterize complex shapes and structural models, quantified as the fractal dimension (FD). FD is a numerical parameter that reflects complexity, with higher values indicating greater structural intricacy.[10-13] However, fractal sets with the same FD can exhibit markedly different textures.[9] Lacunarity (Lac) is another metric that describes the features of fractals with the same dimension but different textures. Lac relates to the distribution of gap sizes within the structure: objects with low Lac appear more uniform due to consistent gap sizes, whereas those with high Lac display greater heterogeneity. Thus, Lac is a scale-dependent indicator of texture heterogeneity. In addition to FD and Lac, quantitative methods can also assess bone microarchitecture by measuring the space between trabeculae (Tb.Sp), the trabecular thickness (Tb.Th), and the bone volume fraction (BV/TV). BV/TV represents the proportion of bone volume within a given area, indicating the amount of mineralized bone per unit volume. For 2-dimensional radiographs, this is calculated as the bone area fraction (BA/TA).[8,14,15]

FA has diverse applications across various disciplines, including dentistry. In the dental field, FA is primarily used to evaluate the morphological features of the jawbones and to assess trabecular changes resulting from diseases, medications, or treatments.[16] Several studies have demonstrated the promise of FD in distinguishing individuals diagnosed with osteoporosis from healthy controls. Given the fractal nature of bone tissue, FA may represent an optimal non-invasive technique for detecting and quantifying changes in bone mineral content and architectural shifts within the jawbone.[17] The calculation of FD on hand radiographs has been employed to investigate alterations in bone structure resulting from RA. Prior research has focused on using FA to substantiate radiographic changes observed in the metacarpophalangeal finger joints (I-III).[2] Decreased FD values in the mandibular condyles of patients with RA have been observed using both cone-beam computed tomography (CBCT) and panoramic radiography.[6,18]

In this study, the authors hypothesized that the application of FA to panoramic radiographs could represent a valuable tool to quantify changes in the jawbones of individuals with RA. Thus, the objective of the study was to investigate potential associations between the FD of the jawbones and RA. The fractal box-counting method was used to evaluate the trabecular bone structure of the mandible and maxilla on dental panoramic radiographs. Additionally, other microarchitectural parameters, including Lac, BA/TA, and Tb.Th, were evaluated. The study also explored the potential relationships between medication use and serological indices in patients with RA, with the goal of promoting a broader understanding of this condition.

Materials and Methods

Study population

This investigation was designed as a retrospective case-control study, with approval granted by the Clinical Research Ethics Committee of the Faculty of Medicine at Suleyman Demirel University (project number 02.04.2020/97). The study was performed in accordance with the principles of the 1964 Helsinki Declaration and its subsequent amendments.

Patients with RA were selected from the records of the Department of Rheumatology at Suleyman Demirel University, Faculty of Medicine. All participants were diagnosed with RA according to the 2010 American College of Rheumatology/European League Against Rheumatism criteria by a rheumatologist with over 10 years of experience. The study included only individuals who had completed examinations and for whom panoramic radiographs were taken, for various reasons, at the Department of Dentomaxillofacial Radiology of the Faculty of Dentistry at the same university. The exclusion criteria encompassed the presence of cystic or tumoral lesions, a history of trauma or surgery leading to bone loss, and other conditions affecting bone health aside from RA, such as hyperparathyroidism, hypoparathyroidism, Paget disease, osteomalacia, renal osteodystrophy, osteogenesis imperfecta, multiple myeloma, or bone metastasis. Additionally, patients with other rheumatologic conditions such as psoriatic arthritis, ankylosing spondylitis, systemic lupus erythematosus, and other connective tissue diseases were

Fig. 1. Regions of interest, measuring 70×70 pixels, were selected for fractal analysis of the trabecular bone in the mandibular condyles (white boxes) and mandibular angles (black boxes) on panoramic radiograph.

excluded. Patients who had used bisphosphonates were also excluded from the study.

For each patient, the duration of RA disease was recorded, along with the presence of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA). Patients who were negative for both ACPA and RF (ACPA–RF–) were categorized as seronegative. Those positive for ACPA, RF, or both were classified as seropositive. Medications prescribed between the time of RA diagnosis and the date of panoramic radiography were documented.

Image analysis

Patient information and the availability of suitable panoramic radiographic images were verified using a picture archiving and communication system and Romexis version 3.8.3 (Planmeca, Helsinki, Finland). All radiographs were captured using the Planmeca ProMax device (Planmeca; 66-68 kVp, 7-13 mA, and 16 s). To ensure accurate measurements, the image quality of the panoramic radiographs was confirmed to be high. Images with patient positioning errors or artifacts were excluded from the study. Panoramic images were exported in TIFF format with a 16-bit depth and then analyzed using ImageJ version 1.52p (National Institutes of Health, Bethesda, MD, USA).

Four regions of interest (ROIs) were identified, with 2 ROIs located on each side and representing the mandibular condyle and angle (Fig. 1). The dimensions of the ROIs were set at 70×70 pixels. The FD values of the regions were calculated by averaging the measurements obtained from the left and right sides. Measurement followed the methodology described by White and Rudolph in 1999 (Fig. 2).[19] Initially, the ROIs were cropped, and the image was converted to an 8-bit format. The image was then duplicated, and a Gaussian filter was applied to the duplicate. This blurred image was subtracted from the original image. Subsequently, 128 gray values were added to all pixel positions of the resulting image, which was then thresholded at a brightness value of 128 to produce a binarized image. That image underwent erosion and dilation, inversion, and finally skeletonization. In skeletonized images, the skeletal structure represents the trabecular bone pattern, while the extraskeletal structure corresponds to the bone marrow. The box-counting method was used, in which the image is divided into squares of varying dimensions: 2, 3, 4, 6, 8, 12, 16, 32, and 64 pixels. The analysis for each square involves identifying the frames that contain trabeculae and calculating the total number of such frames in the image. These values are plotted on a logarithmic scale, and a line of best fit is drawn through the points on the graph. The slope of this line yields the FD value, which reflects the complexity of the trabecular structure. FD measurements were repeated 1 month later by the same oral radiologist to assess intraobserver reliability.

Lac evaluation involves a non-binarization technique that represents the distribution of gaps, or lacunae, in an object or image. A higher Lac indicates greater variability in the distribution of these gaps. FracLac is a downloadable plugin that can be used with ImageJ to perform FA on grayscale images. The FracLac plugin also enables the direct computation of Lac on these images. Within the plugin, the "Gray1: Differential" option was selected. The box-counting method in the FracLac plugin was chosen for the Lac calculations.[14] Lac was computed for each radiograph on both sides, and the average of these values was used for statistical analysis.

The analysis of BA/TA and Tb.Th was conducted using the BoneJ plugin in ImageJ. BoneJ is a free and user-friendly program designed for the evaluation of bone geometry through the measurement of various trabecular

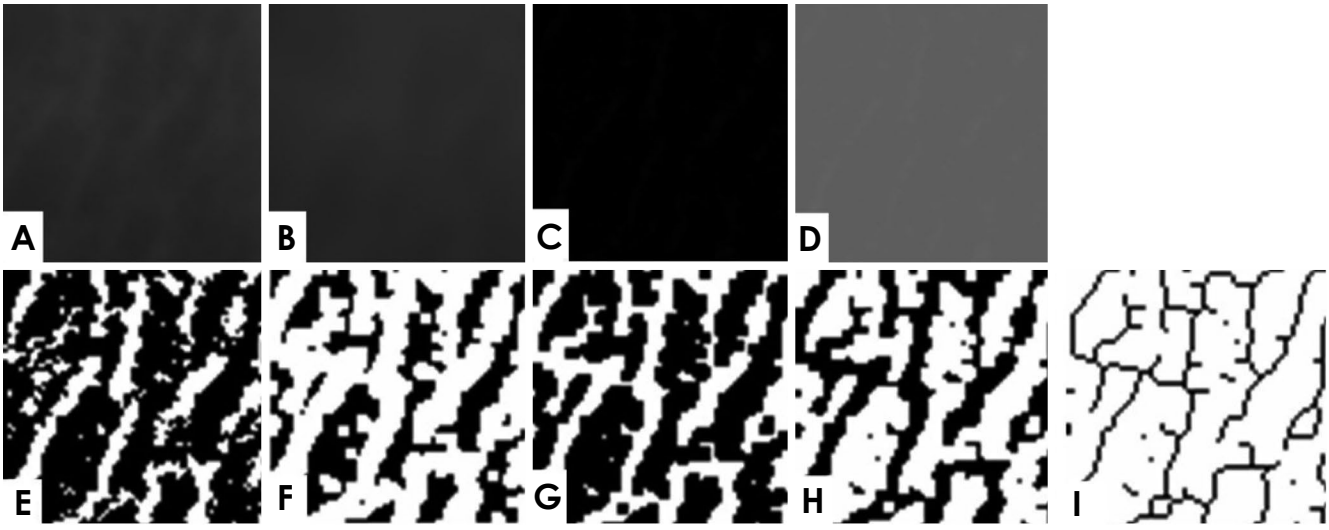

Fig. 2. Steps of fractal analysis. A. Cropped original region of interest. B. Duplicated and blurred image. C. Subtraction of the blurred image from the original image. D. Addition of 128 gray values. E. Binarization using a threshold value of 128. F. Erosion. G. Dilation. H. Inversion. I. Skeletonization.

parameters, including BA/TA and Tb.Th. These parameters were assessed on binary images.[8] Tb.Th was measured in pixels.

Statistical analysis

Statistical analysis was conducted using SPSS version 29.0 (IBM Corp, Armonk, NY, USA). The normal distribution of the examined features was assessed using the Kolmogorov-Smirnov test. To compare the control and patient group averages, the *t*-test was employed, while for 3-group comparisons that displayed a normal distribution, 1-way analysis of variance was applied with the Tukey honestly significant difference test. For features that did not follow a normal distribution, the Mann-Whitney *U* test was used. The Pearson correlation coefficient was utilized to determine the association between continuous variables. The outcomes were presented as numbers and percentages for categorical variables and as mean ± standard deviation for continuous variables. *P*-values of less than 0.05 were considered to indicate statistical significance. One month after the initial analysis, the measurements were repeated in a sample of 62 patients to evaluate intraobserver agreement using Cronbach alpha statistics.

Results

In the FD analysis for each ROI, the intraclass correlation coefficients ranged from 0.883 to 0.943, indicating high reproducibility.

This study consisted of 186 individuals, 144 female and 42 male. The patient group included 93 individuals with RA, while the control group comprised 93 individuals without RA. The mean age of the patient group was 40.45 ± 9.45 years, with an age range of 20 to 56 years. The control group had an average age of 40.55 ± 9.5 years, with ages also ranging from 20 to 56 years.

The serological characteristics, disease duration, and medication use information for the patient group are presented in Table 1. Of the patients, 54 (58%) were seronegative and 39 (42%) were seropositive. The average disease duration was 4.44 ± 3.04 years. RF positivity was observed in 29% of the patients with RA, while ACPA positivity was found in 31.2%.

Without distinguishing between cases in which 1 or more drugs were used concurrently, 65.6% (n = 61) of the patients with RA used glucocorticoids, 63.4% (n = 59) used conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), and 14% (n = 13) used biological disease-modifying antirheumatic drugs (bDMARDs). Furthermore, 29% of the patients (n = 27) did not use any of these drugs.

In the study, a statistically significant difference was observed in the FD values of the mandibular condyle and angle regions ($P < 0.05$), which were higher in the RA cohort than in the control group (Table 2). A significant difference was also identified in the Lac values of the mandibular condyle and angle regions ($P < 0.05$), which were lower in the RA group. No significant distinction in BA/

TA was noted between the groups for either the mandibular condyle or the angle.

A significant difference was observed in the Tb.Th values for both mandibular condyle and angle regions, with the RA group displaying lower values than the control participants ($P<0.05$).

Upon stratifying the FD values by sex, no significant difference in FD was detected between the RA and control groups for male participants. However, among female participants, FD measurements were higher in the RA group, with significant differences observed for both condylar and angle values ($P<0.05$). The Lac for the angle and the Tb.Th for the mandibular condyle and angle differed between patients with RA and healthy women, with the latter group exhibiting higher values ($P<0.05$). In contrast, only the Tb.Th angle demonstrated a significant difference in male participants, with higher values observed in the control group ($P<0.05$).

When comparing healthy, seropositive, and seronegative participants, the Lac and Tb.Th mandibular condyle values were significantly lower in the seropositive group compared to the healthy controls ($P<0.05$ for both). Additionally, the FD and Tb.Th of the angle differed significantly for the seropositive and seronegative patients relative to the control group ($P<0.05$ for both). However, the FD of the mandibular condyle, the BA/TA of the condyle, and the BA/TA of the angle did not exhibit significant differences across groups (Table 3).

No significant differences were observed in the FD values of the mandibular condyle and angle according to the use of bDMARDs, csDMARDs, or glucocorticoids. Similarly, no significant difference was noted in FD between patients with RA who used all of the specified medications (n = 13) and those who used none (n = 27). However, patients using glucocorticoids exhibited significantly higher BA/TA values for the mandibular condyle and angle, as well as the Tb.Th of the angle, than those not taking these medications ($P<0.05$). Additionally, the BA/TA and Tb.Th of the angle were higher in the group using

Table 1. Serological characteristics, disease duration, and medication use in patients with rheumatoid arthritis

	Rheumatoid arthritis (n = 93)
Age, years	40.00 ± 9.56
Female, n (%)	72 (77.4%)
Seropositive, n (%)	39 (41.9%)
Disease duration, years	4.44 ± 3.04
Medication use, n (%)	66 (71.0%)
Glucocorticoid use, n (%)	61 (65.6%)
csDMARDs, n (%)	59 (63.4%)
bDMARDs, n (%)	13 (14.0%)

csDMARDs: conventional synthetic disease-modifying antirheumatic drugs, bDMARDs: biological disease-modifying antirheumatic drugs

Table 2. Comparison of fractal dimension (FD), lacunarity (Lac), bone area fraction (BA/TA), and trabecular thickness (Tb.Th) between rheumatoid arthritis and control groups in the mandibular condyle and angle regions

	Rheumatoid arthritis (n = 93)	Control (n = 93)
FD, mandibular condyle	1.43 ± 0.03	1.42 ± 0.04*
FD, angle	1.43 ± 0.04	1.41 ± 0.04*
Lac, mandibular condyle	0.12 ± 0.04	0.13 ± 0.05*
Lac, angle	0.11 ± 0.04	0.14 ± 0.07*
BA/TA, mandibular condyle	0.37 ± 0.03	0.37 ± 0.02
BA/TA, angle	0.31 ± 0.05	0.31 ± 0.05
Tb.Th, mandibular condyle	4.51 ± 0.43	4.71 ± 0.43*
Tb.Th, angle	4.13 ± 0.29	4.30 ± 0.29*

*$P<0.05$ compared with the rheumatoid arthritis group

Table 3. Comparison of fractal dimension (FD), lacunarity (Lac), bone area fraction (BA/TA), and trabecular thickness (Tb.Th) across 3 groups: control, seropositive rheumatoid arthritis (RA), and seronegative RA

	Control (n = 93)	Seronegative (n = 54)	Seropositive (n = 39)
FD, mandibular condyle	1.42 ± 0.04	1.43 ± 0.03	1.43 ± 0.03
FD, angle	1.41 ± 0.04[a]	1.42 ± 0.04[b]	1.43 ± 0.04[b]
Lac, mandibular condyle	0.13 ± 0.05[a]	0.12 ± 0.04[a,b]	0.11 ± 0.04[b]
Lac, angle	0.14 ± 0.07[a]	0.11 ± 0.05[b]	0.12 ± 0.04[a,b]
BA/TA, mandibular condyle	0.37 ± 0.02	0.37 ± 0.03	0.37 ± 0.03
BA/TA, angle	0.31 ± 0.05	0.31 ± 0.05	0.31 ± 0.05
Tb.Th, mandibular condyle	4.71 ± 0.43[a]	4.57 ± 0.48[a,b]	4.44 ± 0.34[b]
Tb.Th, angle	4.30 ± 0.29[a]	4.13 ± 0.31[b]	4.12 ± 0.26[b]

[a, b]: $P<0.05$ between the groups labeled with different letters in the row

Table 4. Differences in fractal dimension (FD), lacunarity (Lac), bone area fraction (BA/TA), and trabecular thickness (Tb.Th) among patients according to medication use

	Glucocorticoids		csDMARDs		bDMARDs	
	(+) n=61	(−) n=32	(+) n=59	(−) n=34	(+) n=13	(−) n=80
FD, mandibular condyle	1.43±0.03	1.43±0.03	1.43±0.03	1.43±0.03	1.42±0.03	1.43±0.03
FD, angle	1.42±0.04	1.43±0.03	1.43±0.03	1.43±0.04	1.41±0.03	1.43±0.03
Lac, mandibular condyle	0.11±0.04	0.11±0.04	0.11±0.04	0.12±0.04	0.12±0.05	0.11±0.04
Lac, angle	0.11±0.04	0.12±0.04	0.11±0.04	0.12±0.04	0.12±0.05	0.11±0.04
BA/TA, mandibular condyle	0.37±0.03	0.36±0.03*	0.37±0.03	0.36±0.03	0.37±0.03	0.37±0.02
BA/TA, angle	0.32±0.05	0.29±0.04*	0.32±0.05	0.30±0.04*	0.31±0.06	0.31±0.04
Tb.Th, mandibular condyle	4.53±0.35	4.48±0.54	4.51±0.35	4.51±0.54	4.49±0.43	4.66±0.37
Tb.Th, angle	4.19±0.30	4.00±0.23*	4.20±0.28	4.01±0.27*	4.26±0.25	4.11±0.30

csDMARDs: conventional synthetic disease-modifying antirheumatic drugs, bDMARDs: biological disease-modifying antirheumatic drugs, *$P<0.05$

Table 5. Correlation analysis of disease duration with fractal dimension (FD), lacunarity (Lac), bone area fraction (BA/TA), and trabecular thickness (Tb.Th)

	Disease duration	
	Pearson correlation	*P*-value (2-tailed)
FD, mandibular condyle	−0.279	0.007
FD, angle	−0.201	0.053
Lac, mandibular condyle	0.118	0.262
Lac, angle	0.124	0.236
BA/TA, mandibular condyle	0.031	0.768
BA/TA, angle	−0.049	0.64
Tb.Th, mandibular condyle	0.203	0.052
Tb.Th, angle	0.223	0.031

csDMARDs compared to those not using csDMARDs, and this difference was also significant ($P<0.05$). No significant differences were observed in any parameter regarding the use of bDMARDs (Table 4).

The analysis revealed no significant correlation between FD and age ($P>0.05$). However, a negative correlation was observed between disease duration and condylar FD ($r=-0.279$; $P<0.05$). Additionally, a positive correlation was identified between disease duration and Tb.Th ($r=0.223$; $P<0.05$) (Table 5).

Discussion

In this study, trabecular changes resulting from RA were investigated, as were several factors associated with the disease process. These factors included sex, medication use, disease duration, and serological characteristics. The RA group differed significantly from the healthy control group in FD, Lac, and Tb.Th, indicating structural changes in the mandibular bone across the 2 evaluated regions of the mandible. Additionally, when stratified by sex, female patients with RA exhibited higher FD values for both ROIs, a lower Lac for the angle, and a lower Tb.Th for the condyle and angle compared to controls. In contrast, only the Tb.Th for the angle differed significantly for male participants; as in women, this parameter displayed higher values in the control group. The findings suggest that RA has a more pronounced impact on bone metabolism in female patients, even during the premenopausal phase.

Changes detected by FA may be attributed to osteopenia, a common clinical feature of RA. Local osteopenia can manifest early in the disease progression, with some individuals showing signs within a few months after symptom onset, prior to the development of erosive bone changes and synovial thickening. In RA, bones distant from inflamed joints are frequently affected by generalized osteoporosis, a common comorbidity.[3,7] The present study involved evaluation of both the mandibular condyle region, to determine potential RA involvement in the TMJ area, and the jawbone, to assess general osteoporosis.

Osteopenia and osteoporosis, which are characterized by a systemic reduction in BMD, can stem from RA itself or from glucocorticoid therapy. RA contributes to the development of both localized (periarticular) and generalized osteoporosis.[20] A recent systematic review revealed that FA has a sensitivity of approximately 86% and a specificity of about 73% for detecting osteoporosis compared to normal BMD, highlighting its potential value as a supplementary screening tool in craniofacial im-

aging for osteoporosis.[21] However, findings from studies evaluating FA and osteoporosis vary. Some studies have reported lower FD values,[22-24] while others have found no significant differences[25,26] or reported higher values.[12,27,28] Here, FD measurements were higher in the RA group than in the control group, which aligns with studies that employed FA and reported greater FD values in individuals with osteoporosis.[12,27,28] Current evidence does not strongly support the use of FA for diagnosing osteoporosis.[17] In the present study, DXA results were not available for the patients, precluding correlation of the findings with an osteoporosis diagnosis. Nonetheless, employing FA in populations at elevated risk of osteoporosis may facilitate the early detection of bone changes in RA.

Serological indicators of RA, such as RF and/or ACPA positivity in the serum, are well-established biomarkers of the disease. RF and ACPA are widely recognized as independent predictors of joint erosion and can indicate the potential progression of RA. Studies suggest that patients with seropositive RA may have similar or even more erosive disease than those with seronegative RA.[29,30] One study that examined the metacarpophalangeal joints (I-III) of seropositive and seronegative RA patients, as well as a control group, revealed a correlation between FD values and ACPA.[2] In the present research, similar FD values were observed for the seropositive and seronegative groups. However, the Lac and Tb.Th of the mandibular condyle were lower in the seropositive group than in the healthy controls, while no such differences were observed in seronegative patients. In contrast, Lac angle values were lower in seronegative patients compared to both seropositive and healthy groups. These findings suggest that ACPA and/or RF positivity may influence the trabecular bone structure of the jaws, although further research is needed to confirm these results.

Patients with RA often experience TMJ involvement, which can impair the function of the chewing system. Yilmaz et al.[5] highlighted the involvement of the TMJ in RA, noting the associated osteoarthritic features. In other research, CBCT was used to identify osteoarthritic changes in the TMJ, with a significantly higher prevalence of radiographic signs—such as erosion, flattening of the condylar head, osteophyte formation, and subchondral cysts—in patients with RA compared to control participants.[31,32] Yesiltepe et al.[18] explored the influence of RA on TMJ structure using CBCT images and observed lower FD values in the TMJs of patients with RA. In their study of panoramic radiographs, Türkmenoğlu et al.[6] reported markedly lower FD values in the mandibular condyles of individuals with RA. However, in the present study, the condylar FD in patients with RA was significantly higher than that in the control group. Condylar FD values were observed to decrease as the disease duration increased. Since this study was retrospective and lacked a clinical evaluation of the TMJ, the relationship between this parameter and temporomandibular disorders (TMDs) could not be evaluated. The presence and severity of degenerative changes may explain the negative correlation with disease duration.

Most patients with RA take prednisone or other comparable glucocorticoid formulations, which have been shown to alleviate symptoms. However, long-term glucocorticoid use raises concerns about cardiovascular risk and osteoporosis.[33] Research has indicated that longer-term and continuous use of oral glucocorticoids increases the risk of fractures, especially in the hip and vertebrae, with higher cumulative doses linked to a greater risk of fracture.[34] In the present study, no significant changes in FD values were observed among patients undergoing treatment with glucocorticoids, csDMARDs, or bDMARDs. However, in the examination of specific parameters, the BA/TA ratio of the mandibular condyle, the BA/TA of the angle, and the Tb.Th of the angle were higher in the patients using glucocorticoids compared to those not using them. Similarly, the BA/TA and Tb.Th of the angle were higher in the group using csDMARDs. Interestingly, no significant differences were noted in any parameters regarding the use of bDMARDs. Contrasting with these results, a prior study reported lower FD values in patients using corticosteroids.[35] Nevertheless, more data, such as dosage and method of administration, must be collected to draw a conclusion, which is a limitation of this study.

Another limitation of the study is that, although clinical data of patients with RA—including disease duration and the presence of RF and ACPA antibodies—were obtained from patient records, parameters related to disease activity, such as erythrocyte sedimentation rate, C-reactive protein level, clinical joint involvement, and DAS28 score, could not be evaluated. Furthermore, the effects of bruxism and TMDs were not included in the data. Future research should evaluate the effect of the clinical course of the disease, medication characteristics, and determinants of disease activity, while incorporating a larger patient sample.

In conclusion, this study demonstrated changes in the jawbones of patients with RA using image analysis methods to quantify trabecular parameters, including FD, Lac, Tb.Th, and BA/TA. This assessment provided an objective

evaluation of the bone. Thus, such analyses of panoramic radiographs, taken during routine dental examinations, can reveal bone changes in patients with RA and thereby offer insights into disease prognosis. Early detection of these impacts on bone can improve the quality of life for these patients. Furthermore, the findings of the study may inform future research in this area.

Conflicts of Interest: This article presents refined results from an academic thesis study by E.C., which was presented during specialty training.

References

1. Moshayedi S, Tasorian B, Almasi-Hashiani A. The prevalence of osteoporosis in rheumatoid arthritis patient: a systematic review and meta-analysis. Sci Rep 2022; 12: 15844.
2. Zandieh S, Haller J, Bernt R, Hergan K, Rath E. Fractal analysis of subchondral bone changes of the hand in rheumatoid arthritis. Medicine (Baltimore) 2017; 96: e6344.
3. Zerbini C, Clark P, Mendez-Sanchez L, Pereira R, Messina O, Uña C, et al. Biologic therapies and bone loss in rheumatoid arthritis. Osteoporos Int 2017; 28: 429-46.
4. Conforti A, Di Cola I, Pavlych V, Ruscitti P, Berardicurti O, Ursini F, et al. Beyond the joints, the extra-articular manifestations in rheumatoid arthritis. Autoimmun Rev 2021; 20: 102735.
5. Yilmaz HH, Yildirim D, Ugan Y, Tunc SE, Yesildag A, Orhan H, et al. Clinical and magnetic resonance imaging findings of the temporomandibular joint and masticatory muscles in patients with rheumatoid arthritis. Rheumatol Int 2012; 32: 1171-8.
6. Türkmenoglu A, Yüksel HT, Karahan AY. Evaluation of mandibular condyle trabecular structure in patients with rheumatoid arthritis using fractal analysis. Oral Surg Oral Med Oral Pathol Oral Radiol 2022; 133: 229-37.
7. Dougados M. Comorbidities in rheumatoid arthritis. Curr Opin Rheumatol 2016; 28: 282-8.
8. Diba SF, Gracea RS, Shantiningsih RR, Hidjah K. Analysis of mandible trabecular structure using digital periapical radiographs to assess low bone quality in postmenopausal women. Saudi Dent J 2021; 33: 997-1003.
9. Yasar F, Akgünlü F. Fractal dimension and lacunarity analysis of dental radiographs. Dentomaxillofac Radiol 2005; 34: 261-7.
10. Göller Bulut D, Bayrak S, Uyeturk U, Ankarali H. Mandibular indexes and fractal properties on the panoramic radiographs of the patients using aromatase inhibitors. Br J Radiol 2018; 91: 20180442.
11. Jolley L, Majumdar S, Kapila S. Technical factors in fractal analysis of periapical radiographs. Dentomaxillofac Radiol 2006; 35: 393-7.
12. Bollen AM, Taguchi A, Hujoel PP, Hollender LG. Fractal dimension on dental radiographs. Dentomaxillofac Radiol 2001; 30: 270-5.
13. Smith TG Jr, Lange GD, Marks WB. Fractal methods and results in cellular morphology - dimensions, lacunarity and multifractals. J Neurosci Methods 1996; 69: 123-36.
14. da Silva ME, Dos Santos HS, Ruhland L, Rabelo GD, Badaró MM. Fractal analysis of dental periapical radiographs: a revised image processing method. Oral Surg Oral Med Oral Pathol Oral Radiol 2023; 135: 669-77.
15. Santos IG, Ramos de Faria F, da Silva Campos MJ, de Barros BÁ, Rabelo GD, Devito KL. Fractal dimension, lacunarity, and cortical thickness in the mandible: analyzing differences between healthy men and women with cone-beam computed tomography. Imaging Sci Dent 2023; 53: 153-9.
16. Kato CN, Barra SG, Tavares NP, Amaral TM, Brasileiro CB, Mesquita RA, et al. Use of fractal analysis in dental images: a systematic review. Dentomaxillofac Radiol 2020; 49: 20180457.
17. Franciotti R, Moharrami M, Quaranta A, Bizzoca ME, Piattelli A, Aprile G, et al. Use of fractal analysis in dental images for osteoporosis detection: a systematic review and meta-analysis. Osteoporos Int 2021; 32: 1041-52.
18. Yeşiltepe S, Yılmaz AB, Kurtuldu E, Sarıca İ. Fractal analysis of temporomandibular joint trabecular bone structure in patients with rheumatoid arthritis on cone beam computed tomography images. Meandros Med Dent J 2018; 19: 345-51.
19. White SC, Rudolph DJ. Alterations of the trabecular pattern of the jaws in patients with osteoporosis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1999; 88: 628-35.
20. Gullick NJ, Scott DL. Co-morbidities in established rheumatoid arthritis. Best Pract Res Clin Rheumatol 2011; 25: 469-83.
21. Cavalcante DS, Silva PG, Carvalho FS, Quidute AR, Kurita LM, Cid A, et al. Is jaw fractal dimension a reliable biomarker for osteoporosis screening? A systematic review and meta-analysis of diagnostic test accuracy studies. Dentomaxillofac Radiol 2022; 51: 20210365.
22. Hua Y, Nackaerts O, Duyck J, Maes F, Jacobs R. Bone quality assessment based on cone beam computed tomography imaging. Clin Oral Implants Res 2009; 20: 767-71.
23. Southard TE, Southard KA, Jakobsen JR, Hillis SL, Najim CA. Fractal dimension in radiographic analysis of alveolar process bone. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996; 82: 569-76.
24. Güngör E, Yildirim D, Çevik R. Evaluation of osteoporosis in jaw bones using cone beam CT and dual-energy X-ray absorptiometry. J Oral Sci 2016; 58: 185-94.
25. Tosoni GM, Lurie AG, Cowan AE, Burleson JA. Pixel intensity and fractal analyses: detecting osteoporosis in perimenopausal and postmenopausal women by using digital panoramic images. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2006; 102: 235-41.
26. Yaşar F, Akgünlü F. The differences in panoramic mandibular indices and fractal dimension between patients with and without spinal osteoporosis. Dentomaxillofac Radiol 2006; 35: 1-9.
27. Law AN, Bollen AM, Chen SK. Detecting osteoporosis using dental radiographs: a comparison of four methods. J Am Dent Assoc 1996; 127: 1734-42.
28. Ruttimann UE, Webber RL, Hazelrig JB. Fractal dimension

from radiographs of peridental alveolar bone. A possible diagnostic indicator of osteoporosis. Oral Surg Oral Med Oral Pathol 1992; 74: 98-110.
29. Choi S, Lee KH. Clinical management of seronegative and seropositive rheumatoid arthritis: a comparative study. PLoS One 2018; 13: e0195550.
30. Barra L, Pope JE, Orav JE, Boire G, Haraoui B, Hitchon C, et al. Prognosis of seronegative patients in a large prospective cohort of patients with early inflammatory arthritis. J Rheumatol 2014; 41: 2361-9.
31. Cordeiro PC, Guimaraes JP, de Souza VA, Dias IM, Silva JN, Devito KL, et al. Temporomandibular joint involvement in rheumatoid arthritis patients: association between clinical and tomographic data. Acta Odontol Latinoam 2016; 29: 123-9.
32. Youssef Mohamed MM, Dahaba MM, Farid MM, Ali Elsayed AM. Radiographic changes in TMJ in relation to serology and disease activity in RA patients. Dentomaxillofac Radiol 2020; 49: 20190186.
33. Kirwan JR, Bijlsma JW, Boers M, Shea BJ. Effects of glucocorticoids on radiological progression in rheumatoid arthritis. Cochrane Database Syst Rev 2007; 2007: CD006356.
34. Steinbuch M, Youket TE, Cohen S. Oral glucocorticoid use is associated with an increased risk of fracture. Osteoporos Int 2004; 15: 323-8.
35. Aktuna Belgin C, Serindere G. Fractal and radiomorphometric analysis of mandibular bone changes in patients undergoing intravenous corticosteroid therapy. Oral Surg Oral Med Oral Pathol Oral Radiol 2020; 130: 110-5.