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Analysis of the effects of metabolic syndrome and periodontitis on cortical-trabecular bone structure of the mandible and periodontal inflammation

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To evaluate the effects of metabolic syndrome (MetS) and periodontitis on mandibular cortical and trabecular bone structure and their association with periodontal inflammatory burden, 80 individuals were allocated to four groups: systemically and periodontally healthy (MetS − P−, *n* = 20), periodontitis only (MetS − P+, *n* = 20), MetS only (MetS + P−, *n* = 20), and both conditions (MetS + P+, *n* = 20). Trabecular bone was assessed by fractal dimension (FD) analysis in three regions, while cortical morphology was evaluated on panoramic radiographs using radiomorphometric indices: symphysis index (SI), anterior index (AI), molar index (MI), panoramic mandibular index (PMI), and Klemetti index (KI). Periodontal inflamed surface area (PISA) and periodontal epithelial surface area (PESA) were calculated to quantify inflammatory load. Condyle and angulus FD values were higher in MetS groups ($p < 0.05$). AI and SI were highest in MetS + P+ and lowest in MetS − P− ($p < 0.05$). MI and PMI showed no intergroup differences ($p > 0.05$). KI distribution differed significantly, with more C1 in controls and more C2 in MetS + P+ ($p < 0.05$). PISA was greatest in MetS + P+ ($p < 0.05$). Positive correlations were observed between PESA and AI, and between PISA and both AI and SI ($p < 0.05$). Coexistence of MetS and periodontitis is associated with regional mandibular trabecular and cortical bone alterations and increases periodontal inflammatory burden, suggesting a combined effect of metabolic stress and periodontal inflammation on bone microarchitecture.

Keywords Fractal analysis, Metabolic syndrome, Radiomorphometric indices

Periodontitis is a progressive, multifactorial and chronic inflammatory disease that occurs as a result of the interaction between pathogens in dental plaque and the host's immune system. Although microbial biofilm is a necessary factor for the onset of infection, the immune response is mainly responsible for the destruction caused by the disease. The host immune response is not solely dependent on microbial load, it is also significantly influenced by factors such as smoking, genetic predisposition, hormonal changes, and systemic conditions including diabetes mellitus (DM) and obesity[1].

Metabolic syndrome (MetS) is a clinical picture characterized by the coexistence of a number of metabolic disorders such as abdominal obesity, insulin resistance, hypertension, hyperglycemia, and dyslipidemia, and poses a risk for cardiovascular diseases[2]. Insulin resistance, increased free fatty acids, oxidative stress, and lipid profile disorders accompany this picture, is associated with increased levels of pro-inflammatory cytokines and supporting the inflammatory process. The persistence of chronic inflammation and disruptions in insulin signal transduction have significant effects on the physiologic balance of bone tissue. This condition is associated with

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a decrease in bone mineral density and an acceleration of resorptive processes. In parallel with these changes in the production-destruction cycle, an adaptive bone response may develop in bone tissue aimed at adapting to environmental and biomechanical conditions[3–6].

The relationship between periodontitis and MetS, which is attracting considerable interest today, is gaining importance due to the shared inflammatory pathways, increased oxidative stress, and changes in insulin resistance, highlighting the potential for interaction that could affect the outcomes of both diseases[2,7–9]. In studies conducted in this context, periodontal clinical parameters of patients with periodontitis and MetS are more negative than those of systemically healthy individuals with periodontitis. Furthermore, the longitudinal studies summarized by Kaye et al.[10] indicate an increased risk of developing components of MetS later in life in individuals with impaired periodontal health[11,12]. The interaction between these two diseases, particularly their potential effects on bone metabolism, stands out as a noteworthy area requiring investigation.

Fractal analysis is a measurement technique used to determine numerical values that characterize the complex structure of the trabecular bone using digital radiographs. This technique is used to evaluate the possible effects of systemic diseases and treatments on the jawbone by determining the complex architecture of bone tissue with the increase in fractal dimension (FD) values obtained non-invasively[13,14]. In addition to this quantitative evaluation, radiomorphometric measures such as the symphysis index (SI), anterior index (AI), molar index (MI), panoramic mandibular index (PMI), and Klemetti index (KI) are also potential tools in determining the risk of osteoporosis by evaluating the characteristics of the mandible, such as cortex morphology and mineral density[13–16].

Routine periodontal clinical parameters are insufficient to measure the total inflammatory load surface area generated by periodontitis. However, evaluating periodontitis as a risk factor for systemic diseases requires determining the amount of inflamed tissue. For this reason, periodontal epithelial surface area (PESA) and periodontal inflammatory surface area (PISA) criteria have been developed. PISA quantitatively expresses the amount of inflamed periodontal tissue and thus the systemic inflammatory burden of periodontitis. The widespread use of PISA aims to provide more definitive results on the relationship between periodontitis and other systemic diseases[17].

This study was planned based on the hypothesis that statistically significant differences in PISA values and mandibular bone structure would be observed in individuals with MetS and periodontitis compared with others. The aim of this study was to evaluate mandibular trabecular and cortical bone characteristics using FD analysis and radiomorphometric indices on panoramic radiographs, to compare these parameters among groups defined by MetS and periodontitis status, and to investigate their association with periodontal inflammatory burden quantified by PISA.

Methods

Ethical statement

The study was conducted in full adherence to the 1975 Declaration of Helsinki, which was revised in 2013. Ethics approval was obtained from the interventional ethics committee of Recep Tayyip Erdogan University, Faculty of Medicine with the decision numbered 2025/371. Each participant was provided with detailed information about the purpose and content of the study and their consent was obtained.

Study population

The data in this study were collected retrospectively between January 2020, and July 2025, by examining the anamnesis, digital panoramic radiographs, and periodontal index values of patients aged 18–65 years who presented to the Faculty of Dentistry Recep Tayyip Erdogan University, for dental examinations due to various dental complaints and who had previously been diagnosed with metabolic syndrome by an internal medicine specialist.

To determine the appropriate sample size during the planning phase of the study,, an a priori power analysis was conducted using G*Power (v3.1.9.7). Based on a one-way ANOVA model ($f = 0.40$, $\alpha = 0.05$, power = 0.80), the required total sample size was determined to be 76 participants (≥ 19 per group). To enhance statistical power and ensure balanced group allocation, a total of 80 participants (20 per group) were included: systemically and periodontally healthy control group (MetS-P-) ($n = 20$), systemically healthy with periodontitis group (MetS-P+) ($n = 20$), periodontally healthy with MetS group (MetS + P-) ($n = 20$), and the MetS with periodontitis group (MetS + P+) ($n = 20$).

Inclusion criteria were determined as being between the ages of 18–65 years, panoramic radiographs of sufficient diagnostic quality in the evaluation of mandibular bone, and intraosseous pathology in the areas where FD analysis and radiomorphometric indices were examined, and no diagnosis of osteoporosis/osteopenia according to dual energy X-ray absorptiometry (DEXA) values. The exclusion criteria were as follows: use of drugs known to affect bone density (except drugs used in relation to MetS), conditions and diseases that affect bone density (e.g. osteomalacia, kidney diseases, hypothyroidism, hyperparathyroidism), having mandibular pathologies such as cystic tumors, having periodontal treatment in the last 6 months, smoking, having an autoimmune disease or cancer. In addition, the age ranges of the participants in the control and study groups were matched to ensure compatibility. To eliminate the potential confounding effects of smoking, both current and former smokers were excluded from the study, and all participants were lifelong non-smokers.

The grouping of the participants was based on the 2017 classification[18] for periodontal condition and the 2009 guideline of the Turkish Society of Endocrinology and Metabolism[19] for the diagnosis of MetS. Accordingly, the diagnosis of MetS was deemed sufficient if at least two of the following criteria were present: hypertension (systolic blood pressure > 130 mm Hg, diastolic blood pressure > 85 mm Hg, or using antihypertensive medication), dyslipidemia (triglyceride levels > 150 mg/dL or high-density lipoprotein (HDL) levels < 40 mg/dL in men, < 50 mg/dL in women), or abdominal obesity (body mass index (BMI) > 30 kg/m^2 or waist circumference:

>94 cm in men, > 80 cm in women), with one of the following being mandatory: DM, impaired glucose tolerance, or insulin resistance. Periodontitis (stage III–IV and grade C periodontitis) and periodontal health were determined according to the 2017 classification diagnostic criteria[18]. Periodontal health was defined as probing pocket depth (PPD) ≤ 3 mm, absence of clinical attachment loss (CAL), no radiographic evidence of alveolar bone loss, and bleeding on probing affecting ≤ 10% of sites. The periodontitis group exhibited PPD ≥ 6 mm, interdental CAL ≥ 5 mm, and radiographic bone loss extending to the middle or apical third of the root, along with a history of ≥ 1 teeth lost due to periodontitis. In addition, the bone loss/age ratio was calculated for each patient, and all cases were classified as grade C, with a bone loss/age ratio > 1.0. The control group consisted of systemically healthy individuals recruited from the same clinical population who presented for routine dental examination, met the criteria for periodontal health, and whose systemic health status was confirmed through medical records. Panoramic radiographs of all participants were performed by the same operator using the same device (Planmeca Promax 2D S2, Planmeca Oy, Helsinki, Finland) with a constant exposure protocol (66 kVp, 8 mA, 16.6 s). The positioning of the patients during imaging was performed in accordance with the instructions for use. Standard positioning was applied ensuring that the Frankfurt plane was parallel to the ground and the sagittal plane coincided with the vertical plane of the device.

Measurements

Clinical measurements

Periodontal evaluation of all participants was performed in a standardized manner by the same periodontist (S.A.B) using William's periodontal probe (Hu-Friedy®, Chicago, IL, USA). Excluding third molars, probing pocket depth (PPD), amount of recession, and clinical attachment loss (CAL) were measured from six different surfaces (mesiobuccal, distobuccal, midbuccal, mesiolingual/mesiopalatal, distolingual/distopalatal, and midlingual/midpalatal) of each tooth; bleeding on probing (BOP) was also assessed from four surfaces (mesial, distal, buccal, and palatal/lingual). These measurements were used by plotting them in a standard calculation table developed by the researchers and accessible online (www.parsprototo.info) for determining PESA and PISA values. PESA calculates the total surface area of pocket epithelium. PISA, on the other hand, reflects the surface area of bleeding pocket epithelium in mm^2, calculated using CAL, recession, and BOP measurements. The calculation tool allowed for the systematic recording of measurements and was also used for the quantitative assessment of individual inflammatory burden[17].

Radiographic measurements

Fractal analysis Panoramic radiographs were analyzed using Image J (v1.52) software, developed by the National Institutes of Health (Bethesda, MD, USA) and available for free at https://imagej.nih.gov/ij/download.html (Fig. 1). For each patient, a total of six regions of interest (ROIs) of 30 × 30 pixels each, located on the right and left sides of the radiographs, were evaluated using the box-counting method. The average of the measurements for both sides was used to calculate the overall FD value. The analyzed regions included the distal part of the mental foramen (FD1), the condyle (FD2), and the angulus region below the mandibular canal (FD3). These regions were selected to evaluate the effects of metabolic syndrome and periodontitis on mandibular bone structure while ensuring standardized and reproducible ROI placement by excluding root superposition and anatomical variations. (Fig. 2). To examine the image quality optimally, the panoramic radiographs were converted to JPEG format, then cropped and reproduced for analysis. A Gaussian turbidity filter was applied to minimize brightness differences based on changes in soft tissue and bone thickness[13]. The processed radiographs were obtained by subtracting them from the original radiographs. Grayscale values (128) were assigned to the pixels to highlight the trabecular structures and bone marrow cavities, then, steps such as binarization, erosion, dilation, inversion, and skeletonization were performed to make them suitable for fractal analysis[13]. The FD value was obtained by dividing the areas representing the trabecular structures in the image into square pixel boxes of different sizes and calculating the total number of boxes for each dimension[13].

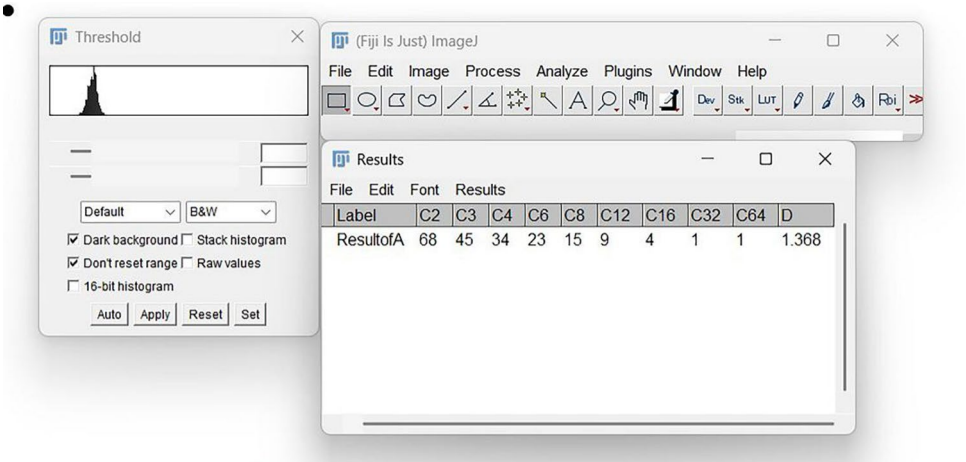


Fig. 1. Fractal dimension analysis performed using ImageJ software.

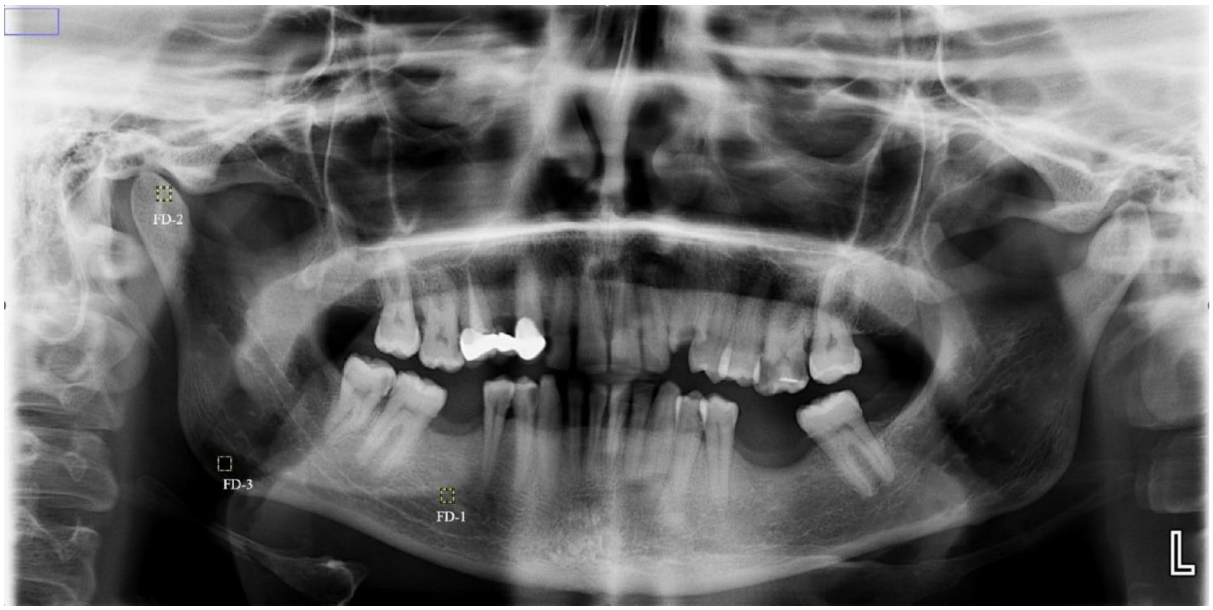


Fig. 2. Selected regions for fractal analysis in panoramic radiography: distal part of the mental foramen (FD1), condyle (FD2), and the angulus region under the mandibular canal (FD3).

Radiomorphometric index

Radiomorphometric analyses were performed using the Planmeca Romexis 4.6.2.R (Planmeca, Helsinki, Finland) software. In this study, based on the cortical thickness measurement method described by Barra et al.[16] in cone-beam computed tomography, and considering that these radiomorphometric indices have also been adapted for use in panoramic radiographs in previous studies[14,15,20], measurements were calculated on panoramic radiographs by separately evaluating the symphysis, right and left anterior, and molar regions of the mandible. The SI was measured perpendicular to the inferior cortex of the mandible, at a point equidistant from the centers of the right and left mental foramina. The AI was determined parallel to the long axis of the mandible, 1 cm anterior to the mental foramen, and perpendicular to the inferior cortex of the mandible. The MI was determined 1 cm distal to the mental foramen, parallel to the long axis of the mandible, and perpendicular to the inferior cortex of the mandible[15](Fig. 3). All linear radiomorphometric measurements (SI, AI, and MI) were recorded as cortical thickness values in millimeters (mm) using digital image analysis software.

The PMI is a measurement method used to evaluate the structural condition of the mandibular cortical bone, based on the ratio between cortical thickness and mandibular height. PMI was calculated by dividing the mandibular cortical height at the level of the mental foramen by the distance to the lower border of the mandible. In each panoramic radiograph, the perpendicular distance (a) between the inferior border of the mental foramen and the lower cortical border of the mandible, and the thickness of the mandibular cortex (b) at the same level were measured, and the PMI value was determined using the formula a/b. Measurements were performed with 0.01 mm accuracy using digital image analysis software[14](Fig. 3).

The Mandibular Cortical Index (MCI) or KI are indices designed to qualitatively assess the quality of the subcortical bone tissue located behind the mental foramen. Our measurements were classified into three categories according to the parameters of this index: C1 - cortical structure with a continuous and smooth endosteal surface; C2 - moderately eroded cortex characterized by crescent-shaped defects or cortical bone remnants resulting from lacunar resorption; C3 - highly porous cortical structure characterized by prominent cortical remnants and marked porosity[14].

All radiologic analyses were performed by an experienced oral and maxillofacial radiologist (T.E.K) with 10 + years of experience who had no access to the participants' clinical information. To ensure interobserver reliability, 20% of the panoramic images were randomly selected and re-evaluated two weeks after the initial assessment (T.E.K.).

Statistical analysis

In calculating the sample size for this study, a power of at least 80% and a type-1 error of 5% were used for each variable. The normality of the continuous measurements in the study was examined using the Kolmogorov-Smirnov and skewness-kurtosis tests. Parametric tests were used because the measurements were normally distributed. Descriptive statistics for the variables in the study are expressed as mean, standard deviation, number (n), and percentage (%). One-way analysis of variance (ANOVA) was used to compare continuous measurements across groups. Following the ANOVA, post hoc pairwise comparisons were performed using the Bonferroni correction. The Chi-square test was used to determine the relationships between categorical variables. Pearson correlation coefficients were calculated to determine the relationships between continuous

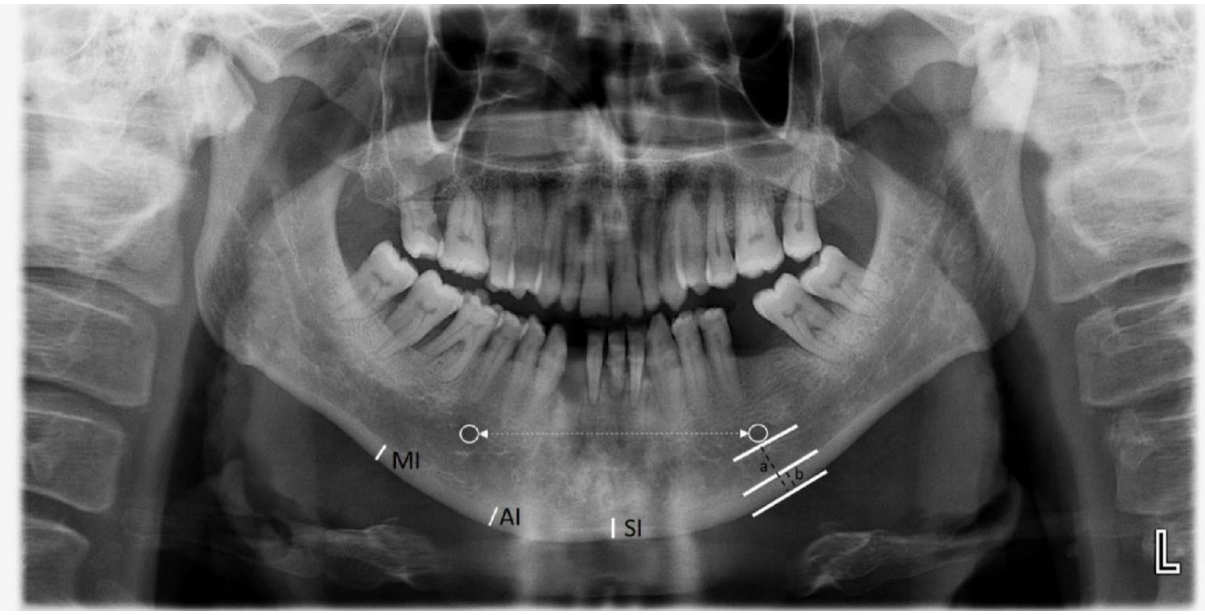


Fig. 3. Assessment of radiomorphometric indices on panoramic radiographs: SI: symphysis index, MI: molar index, AI: anterior index, PMI: panoramic mandibular index, The perpendicular distance (a) between the inferior border of the mental foramen and the lower cortical border of the mandible, and the thickness of the mandibular cortex (b) at the same level were measured, and the PMI value was determined using the formula a/b.

measurements. The SPSS (IBM SPSS for Windows, ver. 26) statistical package program was used for all analyses. The statistical significance level was set at $p < 0.05$.

Additional statistical procedures were performed to further explore group differences and control for assumption violations. Homogeneity of variances was assessed using Levene's test. In cases where the homogeneity assumption was violated, Welch's ANOVA was applied as a robust alternative to the standard one-way ANOVA. Effect sizes for ANOVA analyses were calculated using eta-squared (η^2) and interpreted according to conventional thresholds (small, medium, large). For categorical variables with low expected cell counts, Fisher's Exact Test was used instead of the Chi-square test.

Results

The mean ages ± standard deviations of the MetS − P−, MetS − P+, MetS + P−, and MetS + P+ groups were 50.20 ± 6.26, 50.15 ± 5.49, 52.30 ± 6.25, and 53.20 ± 5.44 years, respectively, and no statistically significant difference was observed among the groups in terms of age ($p = 0.262$). In addition, the numbers of female and male participants were similarly distributed across the groups, with no significant difference between them ($p = 0.385$).

Table 1 presents the results of fractal analysis examining the effect of MetS and periodontitis on bone trabeculation in the angulus, condyle, and mental distal region. Intergroup comparisons revealed statistically significant differences in the condyle and angulus measurements ($p < 0.05$), whereas no significant difference was observed in the mental distal region ($p > 0.05$).

Fractal analysis values of the angulus and condyle regions were found to be statistically significantly higher in individuals with metabolic syndrome compared to those without ($p < 0.05$). Additionally, in individuals without metabolic syndrome, fractal values were higher in the presence of periodontitis compared to those without periodontitis; however, this difference was not statistically significant ($p > 0.05$) (Table 1).

SI and AI values showed statistically significant differences between the groups ($p < 0.05$). Specifically, the SI values of the MetS − P− group were found to be significantly lower compared to the MetS + P− and MetS + P+ groups ($p < 0.05$). No statistically significant difference was found between the groups in terms of MI and PMI values ($p > 0.05$) (Table 2). When the CI classification was evaluated, the C2 ratio increased significantly in the MetS + P+ group compared with the control group ($p < 0.05$) (Table 3).

Periodontal clinical parameters showed statistically significant differences among all groups ($p < 0.001$). PI, BOP, GI, and CAL values were significantly higher in the MetS − P+ and MetS + P+ groups compared to the MetS − P− and MetS + P− groups ($p < 0.001$). GI values differed significantly among all groups ($p < 0.001$), with the highest values observed in the M + P+ group. PPD values were significantly higher in the MetS + P− group compared to the MetS − P− group ($p < 0.001$), while the highest values were observed in the MetS − P+ and MetS + P+ groups (Table 4).

PESA and PISA values were found to be statistically significantly higher in the Mets + P+ group than in the other groups ($p < 0.05$). In addition, these values were statistically significantly higher in the periodontitis groups compared to the non-periodontitis groups ($p < 0.05$)(Table 4).

Measure	MetS- P– (*n* = 20)		MetS – P+ (*n* = 20)		MetS + P– (*n* = 20)		MetS + P+ (*n* = 20)		*p*	η^2
	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI		
FD1	1.452 ± 0.057	[1.425. 1.478]	1.447 ± 0.047	[1.425. 1.469]	1.463 ± 0.038	[1.445. 1.481]	1.460 ± 0.066	[1.429. 1.490]	0.766	0.015
FD2	1.334 ± 0.080c	[1.297. 1.372]	1.377 ± 0.081b.c	[1.339. 1.415]	1.409 ± 0.063a	[1.380. 1.438]	1.393 ± 0.082a.b	[1.355. 1.432]	**0.019***	0.122
FD3	1.367 ± 0.077b	[1.330. 1.403]	1.394 ± 0.077a.b	[1.357. 1.430]	1.422 ± 0.057a	[1.395. 1.449]	1.422 ± 0.081a	[1.384. 1.460]	**0.049***	0.093

Table 1. Comparison of Fractal Dimension Values (FD1, FD2, FD3) Between Groups. Group abbreviations: MetS – P–: systemically and periodontally healthy controls; MetS – P+: systemically healthy with periodontitis; MetS + P–: Metabolic Syndrome without periodontitis; MetS + P+: Metabolic Syndrome with periodontitis. Post hoc: Bonferroni correction applied for multiple comparisons. Different superscript letters (a. b, c) indicate statistically significant differences between groups ($p < 0.05$). 95% CI: Effect size: η^2 (eta-squared): <0.06 = small, 0.06–0.14 = medium, > 0.14 = large (Cohen, 1988). Homogeneity of variance: Levene's test confirmed equal variances across all groups for all measures (all $p > 0.05$), * $p < 0.05$ (statistically significant), FD1: distal part of the mental foramen, FD2: condyle, FD3: the angulus region under the mandibular canal, n: sample size, SD: Standart Deviation.

Measure	MetS – P– (*n* = 20)		MetS – P+ (*n* = 20)		MetS + P– (*n* = 20)		MetS + P+ (*n* = 20)		*p*	η^2
	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI		
SI	0.235 ± 0.037c	[0.218, 0.252]	0.282 ± 0.094b.c	[0.238, 0.325]	0.309 ± 0.068a.b	[0.277. 0.341]	0.327 ± 0.068a	[0.295, 0.359]	0.001*	0.206
MI	0.306 ± 0.048	[0.283, 0.329]	0.318 ± 0.043	[0.298, 0.338]	0.312 ± 0.049	[0.289. 0.335]	0.331 ± 0.055	[0.305, 0.356]	0.441	0.037
AI	0.309 ± 0.058c	[0.281, 0.336]	0.322 ± 0.064b.c	[0.292, 0.351]	0.351 ± 0.051a.b	[0.327. 0.375]	0.381 ± 0.047a	[0.359, 0.403]	0.001*	0.214
PMI	0.340 ± 0.071	[0.307, 0.373]	0.341 ± 0.073	[0.307, 0.375]	0.379 ± 0.105	[0.330. 0.428]	0.382 ± 0.055	[0.356, 0.408]	0.163	0.065

Table 2. Comparison of Mandibular Morphometric Indices (SI, MI, AI in mm; PMI as ratio) Between Groups. Group abbreviations: MetS – P–: systemically and periodontally healthy controls; MetS – P+: systemically healthy with periodontitis; MetS + P–: Metabolic Syndrome without periodontitis; MetS + P+: Metabolic Syndrome with periodontitis.Post hoc: Bonferroni correction applied for multiple comparisons. Different superscript letters (a, b, c) indicate statistically significant differences between groups ($p < 0.05$). 95% CI: Effect size: η^2 (eta-squared): <0.06 = small, 0.06–0.14 = medium, > 0.14 = large (Cohen, 1988). Homogeneity of variance: Levene's test confirmed equal variances across all groups for all measures (all $p > 0.05$). * $p < 0.05$ (statistically significant), mm: milimeter, SI: symphysis index, MI: molar index, AI: anterior index, PMI: panoramic mandibular index, n: sample size, SD: Standard Deviation.

		MetS -P-		MetS -P+		MetS + P-		MetS + P+		*p.
		N	%	N	%	N	%	N	%	
Sex	Male	9	27.3%	6	18.2%	7	21.2%	11	33.3%	*0.385*
	Female	11	23.4%	14	29.8%	13	27.7%	9	19.1%	
KI	C1	20	31.7%	17	27.0%	14	22.2%	12	19.0%	***0.006****
	C2	0	0.0%	3	17.6%	6	35.3%	8	47.1%	

Table 3. Distribution of Klemetti Index Between Groups. MetS -P-: patients who were systemically and periodontally healthy, MetS -P+: patients who were systemically healthy but with periodontitis, MetS + P-: patients with Metabolic Syndrome who were periodontally healthy, MetS + P+: patients with Metabolic Syndrome and periodontitis, N: sample size, %: percentage, KI: Klemetti Index, C1: Klemetti Index 1, C2: Klemetti Index 2, *p:<0.05. Fisher's Exact Test was used due to low expected cell counts (4 cells [50%] had expected count < 5).

In our findings, no correlation was observed between age and FD and radiomorphometric parameters ($p > 0.05$). In addition, a positive correlation was observed between PESA and AI and PISA and AI and SI values ($p < 0.05$), but no significant correlation was observed between PESA and PISA values and FD values ($p > 0.05$) (Table 5).

The agreement between the first and second measurements of FD, cortical thickness, and PMI values was very high. All ICC values exceeded 95%, indicating excellent reliability ($p < 0{,}001$) (Table 6)[21].

Discussion

To the best of our knowledge, there are no studies evaluating FD values and radiomorphometric parameters in individuals affected by both MetS and periodontitis. The current study aimed to investigate the relationship between FD and radiomorphometric values based on changes in mandibular bone structures in patients with

Measure	MetS – P– ($n = 20$)		MetS – P+ ($n = 20$)		MetS + P– ($n = 20$)		MetS + P+ ($n = 20$)		*P*	η^2
	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI	Mean ± SD	95% CI		
PESA	925.8 ± 65.2b	[895.3. 956.3]	1850.4 ± 590.7c	[1574.0. 2126.9]	833.0 ± 95.9a	[788.1. 877.8]	2502.9 ± 400.6d	[2315.4. 2690.4]	< 0.001*	0.793
PISA	32.0 ± 15.5b	[24.7. 39.3]	1359.8 ± 433.2c	[1157.0. 1562.5]	12.8 ± 8.8a	[8.6. 16.9]	2202.9 ± 405.5d	[2013.1. 2392.7]	< 0.001*	0.911
PI	0.856 ± 0.495 a	[0.624. 1.088]	2.418 ± 0.318 b	[2.269. 2.566]	0.838 ± 0.211 a	[0.739. 0.936]	2.383 ± 0.298 b	[2.243. 2.522]	< 0.001*	0.841
GI	0.772 ± 0.428 b	[0.572, 0.972]	2.328 ± 0.360 c	[2.159, 2.497]	0.534 ± 0.169 a	[0.455, 0.613]	2.572 ± 0.256 d	[2.452, 2.691]	< 0.001*	0.895
BOP	3.706 ± 1.634 a	[2.941, 4.471]	77.745 ± 17.444 b	[69.581, 85.909]	2.738 ± 0.827 a	[2.350, 3.125]	81.885 ± 15.182 b	[74.780, 88.991]	< 0.001*	0.920
PPD	1.757 ± 0.137 a	[1.693, 1.821]	3.462 ± 0.574 c	[3.193, 3.731]	2.411 ± 0.293 b	[2.274, 2.548]	3.502 ± 0.743 c	[3.154, 3.850]	< 0.001*	0.699
CAL	0.040 ± 0.179 a	[-0.044, 0.124]	3.510 ± 0.561 b	[3.248, 3.773]	0.033 ± 0.101 a	[-0.015, 0.080]	3.537 ± 0.770 b	[3.176, 3.897]	< 0.001*	0.931

Table 4. Comparison of Periodontal Inflammatory Burden (PESA and PISA) and Periodontal Clinical Parameters Between Groups. Group abbreviations: MetS – P–: systemically and periodontally healthy controls; MetS – P+: systemically healthy with periodontitis; MetS + P–: Metabolic Syndrome without periodontitis; MetS + P+: Metabolic Syndrome with periodontitis. Post hoc: Bonferroni correction applied for multiple comparisons. Different superscript letters (a, b, c, d) indicate statistically significant differences between groups ($p < 0.05$). 95% CI: 95% confidence interval. Effect size: η^2 (eta-squared): <0.06 = small, 0.06–0.14 = medium, > 0.14 = large (Cohen, 1988). Homogeneity of variance: Levene's test indicated unequal variances across groups for all measures (all $p < 0.05$); therefore, Welch ANOVA was applied as a robust alternative. *$p < 0.05$ (statistically significant), PESA: Periodontal epithelial surface area, PISA: Periodontal inflamed surface area, n: sample size, SD: Standart Deviation.

		PESA	PISA	Age
FD1	r	– 0.065	– 0.004	0.151
	p.	0.568	0.973	0.182
FD2	r	0.080	0.092	– 0.070
	p.	0.480	0.418	0.538
FD3	R	0.168	0.176	– 0.020
	p.	0.135	0.118	0.857
SI	r	0.202	0.260*	– 0.058
	p.	0.073	0.020	0.608
MI	r	0.109	0.124	– 0.057
	p.	0.336	0.272	0.616
AI	r	0.229*	0.238*	– 0.095
	p.	0.041	0.033	0.402
PMI	r	0.052	0.094	– 0.038
	p.	0.647	0.406	0.739
Age	r	0.068	0.107	
	p.	0.550	0.345	

Table 5. Correlation Between Mandibular Radiomorphometric Parameters, Age, and Periodontal Inflammatory Indices (PESA, PISA). FD1: distal part of the mental foramen, FD2: condyle, FD3: the angulus region under the mandibular canal, r: correlation coefficient, PESA: Periodontal epithelial surface area, PISA: Periodontal inflamed surface area, SI: symphysis index, MI: molar index, AI: anterior index, PMI: panoramic mandibular index, *p:<0.05.

MetS and periodontitis. The findings show that in individuals with coexisting metabolic stress and periodontal inflammation, increased FD values, especially in the condyle and angulus regions, and increased SI and AI values in the anterior region of the mandible, suggest that the mandibular bone undergoes changes at both the trabecular and cortical levels.

Different results have been reported in the literature regarding the effects of metabolic factors on trabecular bone microarchitecture[5,22–24]. Kurşun-Çakmak and Bayrak[22], evaluated fractal dimension (FD) measurements obtained from the anterior, premolar, molar, and condylar regions. In the type 1 diabetes group, FD values were higher in the control group across all regions, although the differences were not statistically significant. In the type 2 diabetes group, FD values were higher in the control group in the anterior region, whereas lower FD values were observed in the control group in the other regions. The authors attributed these findings to impaired bone metabolism associated with chronic hyperglycemia and insulin deficiency, suggesting that this process disrupts the organization of the trabecular network and weakens bone microarchitecture. In our study, FD values in the condylar and angulus regions were significantly higher in the MetS groups compared to the controls, while FD

		95%CI		
	ICC	Lower	Upper	*p*
FD1	0.976	0.954	0.987	< 0.001**
FD2	0.989	0.979	0.994	< 0.001**
FD3	0.984	0.970	0.991	< 0.001**
MI	0.998	0.996	0.999	< 0.001**
AI	0.998	0.997	0.999	< 0.001**
PMI	0.999	0.997	0.999	< 0.001**
SI	1.000	0.999	1.000	< 0.001**

Table 6. Intra-Observer Reliability (Test–Retest) ICC Results for Measurement Parameters. CI, confidence interval; ICC: intraclass correlation coefficient, FD1: distal part of the mental foramen, FD2: condyle, FD3: the angulus region under the mandibular canal,, SI: symphysis index, MI: molar index, AI: anterior index, PMI: panoramic mandibular index.

values in the distal region of the mental foramen were also higher in the MetS groups, although the difference did not reach statistical significance.

Although there is no study in the literature examining MetS and periodontitis together, there are studies evaluating fractal size analysis in individuals with MetS or diabetes[13,24,25]. In support of our findings, Tassoker et al.[23] detected elevated FD values in the gonial and interdental domains in individuals with type 1 diabetes and associated this increase with compensatory restructuring triggered by metabolic stress. However, the interpretation of increased FD values requires careful consideration. Fractal dimension reflects trabecular complexity rather than bone quantity or strength alone[13,14]. Therefore, increased FD values should not be directly interpreted as improved bone quality. From a biological perspective, metabolic syndrome (MetS) is a complex condition characterized by insulin resistance, visceral obesity, dyslipidemia, and chronic low-grade inflammation, and this pro-inflammatory state plays a critical role in bone metabolism. Increased levels of pro-inflammatory cytokines and oxidative stress may promote bone resorption by enhancing osteoclastic activity while simultaneously impairing osteoblastic function. This imbalance may, lead to structurally more complex but less organized trabecular patterns[3,6,26]. Accordingly, these microarchitectural changes should not be interpreted as a physiologically favorable adaptation, but rather as a reflection of dysregulated bone remodeling under metabolic stress conditions.

Furthermore, the effects of metabolic syndrome on bone are not unidirectional. Obesity, one of its major components, may exert a protective effect on bone mineral density through increased mechanical loading and hormonal influences[3,6,26,27]. Bagherzadeh et al.[5] reported that the impact of MetS on the skeleton is heterogeneous, with findings ranging from a positive association with bone mineral density to negative or no associations with bone quality. In this context, bone remodeling processes occurring under metabolic and inflammatory stress conditions do not necessarily indicate a physiologically favorable state; instead, they may result in a structurally more complex but less organized bone architecture. Accordingly, the increased FD values observed in metabolic syndrome may reflect a disorganized and remodeled trabecular structure developing under metabolic stress rather than a healthy bone architecture.

Kayaaltı-Yüksek et al.[24] compared FD values in patients with diabetes and periodontitis and in systemic healthy and periodontitis patients and reported that the highest FD values were in systemic healthy patients and patients with gingivitis (control group). They also reported that patients with periodontitis had the lowest FD value and that there was no significant difference between the diabetic or systemically healthy groups in all patients with periodontitis, regardless of the stage. In contrast, in our study, FD values were significantly higher in individuals with MetS—both with periodontitis and periodontally healthy—compared to the MetS – P– group, and although not statistically significant, they were also higher compared to the MetS – P+ group.

Several studies found that individuals with periodontitis had lower FD values than periodontally healthy individuals[13,25,28]. Unlike these, Dosdoğru et al.[29] reported that FD values obtained in the interdental regions in individuals with advanced periodontitis did not differ significantly from healthy individuals and emphasized that FD might have limited sensitivity in distinguishing inflammatory changes alone. In our own work, similar to that study[29] no significant difference was observed between the groups in terms of FD values distal to the mental foramen. In the condyle and angulus regions, FD values were significantly higher in individuals with MetS compared to systemically healthy individuals; however, no significant difference was observed between individuals with periodontitis and those who were periodontally healthy.

In the literature, some studies performed on panoramic radiographs have used radiomorphometric measurements such as MCI, PMI, and Mandibular Cortical Width (MCW) to evaluate BMD. In our study, instead of the traditional MCW measurement, we used the MCW measurement described by Barra et al.[16] In this study, an increase was detected in the SI and AI values, but there was no significant change in the MI and PMI values. However, this result differs from the literature reporting that MCIs remain largely stable in patients with type 2 DM. Both Kurşun-Çakmak and Bayrak et al.[22] and Dedeoğlu et al.[15] reported that PMI and MCW did not change in individuals with T2DM. The study also reported that the AI, SI, MI, and PMI indices showed no significant differences in long-term follow-ups. While a decrease in PMI values was reported in the child population due to obesity, another component of MetS[30], an increase in PMI values has been reported in adolescents[31]. In addition, in a study evaluating the effect of hyperlipidemia on mandibular bone, no significant

differences were observed in cortical thickness measurements such as AI, SI, PI and PMI[14] In the current study, although a significant increase in AI and SI was observed in the groups with MetS and periodontitis, the lack of significant difference between the groups in PMI and MI values may be due to regional adaptive remodeling triggered by metabolic-inflammatory load in the anterior region.

According to our findings, CI values differed significantly between the groups; C1 was highest in healthy individuals, and C2 was most pronounced in the group with MetS and periodontitis. Günaçar et al.[14] also reported that C2 ratios increased in individuals with hyperlipidemia, whereas C1 was mostly seen in healthy individuals, explaining this by hyperlipidemia increasing osteoclastogenesis and suppressing LDL-mediated mineralization[32,33]. In the literature, it is reported that MCI shows limited change in similar metabolic states. For example, Kurşun-Çakmak and Bayrak[22] found that the MCI distribution of the T2DM group was similar to that of the control group Temur et al.[30] reported that MCI did not differ between obese and non-obese individuals. Therefore, the increased C2 ratios found in individuals with MetS in our current study suggest that MetS, particularly with the combined effects of dyslipidemia and periodontal inflammation, may affect the mandibular cortical surface more significantly compared with other metabolic disorders.

This study found no association between age and either FD or radiomorphometric parameters. Similar to our findings, there are studies that found no significant correlation between age and FD values[13,24] Furthermore, although we observed a positive correlation between PESA and AI values, and between PISA and AI and SI values, no significant correlation was observed between PESA and PISA values and FD values. Kayaaltı Yüksek et al.[24] reported no correlation between clinical attachment loss and FD values, supporting our findings. Mishra et al.[34] reported a negative correlation between bone loss percentage and FD values.

According to our findings, periodontal clinical parameters were higher in groups with periodontitis compared to those without. Except for GI and PPD, metabolic syndrome alone did not lead to a significant increase in the other parameters. Similarly, Senkal et al.[35] reported that periodontal clinical parameters were significantly higher in the periodontitis groups compared to the other groups, in line with our results. We found PISA scores to be highest in the MetS + P+ group, consistent with studies reporting that MetS worsens periodontal condition[2,35,36]. Studies have shown that MetS exacerbates periodontal inflammation by increasing vascular permeability and cytokine production[8,35,37]. The increase in PISA suggests that MetS may be associated with an enhanced inflammatory response associated with periodontitis through systemic mechanisms and that periodontal inflammatory burden may become more visible. In addition, this finding supports the usability of PISA and PESA values in examining the effects of systemic diseases on periodontal tissues.

This study has certain limitations that should be considered when interpreting the findings. First, the cross-sectional design limits the ability to establish causal relationships between metabolic syndrome, periodontitis, and mandibular bone alterations. In addition, the relatively small sample size and single-center design may restrict the generalizability of the findings to broader populations with different clinical and systemic characteristics. Another limitation is the use of two-dimensional panoramic radiographs instead of three-dimensional imaging modalities such as cone-beam computed tomography. Due to inherent characteristics of panoramic imaging, including magnification, geometric distortion, limited resolution, and anatomical superposition, measurement accuracy may be affected. Although widely used, fractal analysis performed on two-dimensional images may also be influenced by projection-related limitations; therefore, the findings should be interpreted with caution. Furthermore, the inclusion of patients with advanced periodontitis may have introduced confounding effects related to tooth loss. Altered occlusal loading patterns, chewing-side preference, and potential temporomandibular joint adaptations particularly in functionally loaded regions may have contributed to the observed bone changes. In addition, regional differences in tooth distribution may have affected the standardization of periodontal inflammatory burden across measurement sites.Finally, although care was taken in group formation, several clinical and lifestyle-related variables such as the duration and severity of metabolic syndrome, medication use (e.g., antihypertensive or lipid-lowering agents), diet, physical activity, hormonal status, and microbial profile could not be fully standardized or comprehensively evaluated. Therefore, the interaction between systemic and periodontal factors may not have been entirely isolated, and these factors may have influenced the observed associations. Further studies with larger populations and more controlled designs are warranted.

Conclusion

This study shows that individuals with MetS and periodontitis were associated with regional and measurable changes in mandibular trabecular and cortical bone structure and that these changes are associated with increased periodontal inflammatory load. The fractal analysis findings, especially in the condyle and angulus regions, and the increase in anterior mandibular cortical indices suggest that metabolic and inflammatory stress may be associated with adaptive remodeling process on bone microarchitecture. From a clinical perspective, these findings indicate that metabolic syndrome may influence mandibular bone microarchitecture and should be considered during radiographic evaluation fractal and radiomorphometric parameters derived from panoramic radiographs may serve as adjunctive tools in assessing the effects of metabolic and periodontal conditions; however, they should not be used as standalone diagnostic measures.To better understand the complex interaction between metabolic syndrome, periodontitis, and mandibular bone structure, further studies with larger populations and more detailed periodontal classification are warranted.

Data availability

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

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Author contributions

SAB conceptualized and designed the study, performed the periodontal examinations, calculated PESA and PISA values, contributed to data interpretation, and drafted the manuscript. HY contributed to the study design and data acquisition and critically revised the manuscript. AHK and FO participated in data collection and statistical analysis. RS assisted in clinical data interpretation and contributed to manuscript revision TEK performed all radiological and radiomorphometric analyses and ensured the methodological accuracy of the imaging procedures. BK, as an internal medicine specialist, was responsible for the metabolic syndrome–related evaluations and contributed to the interpretation of systemic findings. OK participated in data analysis and critically revised the manuscript. NY contributed to the literature review, data organization.

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Declarations

Competing interests

The authors declare no competing interests.

Ethics declerations

All procedures performed in this study were conducted in accordance with the principles of the Declaration of Helsinki. The study was approved by the Interventional Clinical Research Ethics Committee of Recep Tayyip Erdogan University, Faculty of Medicine (Approval No. 2025/371). Written informed consent was obtained from all participants prior to their inclusion in the study.

Additional information

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