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Radiomorphometric Analysis of Patients With Osseous Dysplasia

Osseöz Displazili Hastaların Radyomorfometrik Analizi

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ABSTRACT

Objective: The aim of this study was to examine the radiomorphometric parameters of trabecular and cortical bone of the mandible in patients of osseous dysplasia.

Methods: A total of 43 patients (40 females and 3 males) patients of osseous dysplasia and age-gender matched healthy 43 individuals (control group) were included in this study. The analyzed radiomorphometric parameters were fractal dimension, mandibular cortical width, and mandibular cortical index.

Results: There were not significant differences in the mean fractal dimensions of selected regions between the two groups (*P*>.005). However in mandible, especially bone quality of condyle region was significantly lower in patients of osseous dysplasia (*P*<.005). There were no significant differences in mandibular cortical width between the two groups (*P*> .05). The mean mandibular cortical width was 2.3 mm in the patients of osseous dysplasia and 2.4 mm in the control group. Therefore there were no significant differences in mandibular cortical index between the two groups (*P*> .05).

Conclusion: Especially fractal dimension of condyle region was significantly lower in patients of osseous dysplasia. Therefore, precaution is needed before surgical interventions in this region. It was also observed that the bone quality of the patients with the three variants of cemental dysplasia in the mandible was similar.

Keywords: Osseous Dysplasia, Panoramic radiography, Fractal, Jaw, Mandible

ÖZ

Amaç: Bu çalışmanın amacı osseöz displazi hastalarında mandibulanın trabeküler ve kortikal kemiğinin radyomorfometrik parametrelerini incelemektir.

Yöntemler: Toplamda 43 osseöz displazi hastası (40 kadın ve 3 erkek) ve yaş-cinsiyet açısından eşleşmiş 43 sağlıklı birey (kontrol grubu) bu çalışmaya dahil edilmiştir. Analiz edilen radyomorfometrik parametreler fraktal boyut, mandibular kortikal genişlik ve mandibular kortikal indeks idi.

Bulgular: İki grup arasında değerlendirilen dört bölgenin ortalama fraktal boyutları arasında anlamlı fark yoktu (*P*>,005). Ancak mandibulada, özellikle kondil bölgesinin kemik kalitesi osseöz displazi hastalarında anlamlı derecede daha düşüktü (*P*< ,005). İki grup arasında mandibular kortikal genişlikte anlamlı bir fark bulunmamıştır (*P*> ,05). Osseöz displazi hastalarında ortalama mandibular kortikal genişlik 2.3 mm, kontrol grubunda ise 2.4 mm olarak ölçülmüştür. Bu nedenle, iki grup arasında mandibular kortikal indekste de anlamlı bir fark bulunmamıştır (*P*>,05).

Sonuç: Mandibulada, özellikle kondil bölgesinin kemik kalitesi osseöz displazi hastalarında anlamlı derecede düşüktü. Bu nedenle, bu bölgeye yapılacak cerrahi müdahalelerden önce önlem alınması gerekmektedir. Ayrıca, mandibulada semental displazinin üç varyantına sahip hastaların kemik kalitesinin benzer olduğu gözlendi.

Anahtar Kelimeler: Fraktal, Mandibula, Osseöz Displazi, Panoramik radyografi

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INTRODUCTION

Osseous dysplasia, a medical entity alternatively recognized as cemento-osseous dysplasia (COD), represents a relatively rare and benign fibro-osseous lesion primarily localized within the osseous structures of the jaw. This pathological condition is typified by an aberrant proliferation of bone and fibrous tissue, which often supplants the physiological architecture of normal bone. Osseous dysplasia exhibits a predilection for tooth-bearing regions of the jawbones, and it is frequently discernible through the utilization of routine dental radiographic imaging or during comprehensive dental examinations.[1] The application of fractal dimension analysis introduces an innovative computational methodology for the quantitative assessment of the intricate and inherently irregular structural characteristics frequently encountered within osseous dysplasia lesions.

Within the scope of osseous dysplasia, three cardinal subtypes merit investigation. One of these, periapical osseous dysplasia, primarily localizes to the anterior mandible and typically manifests as circumscribed radiolucent lesions enveloped by radiopaque margins. It is noteworthy that this subtype predominantly affects middle-aged African and American women and generally remains clinically asymptomatic. In contradistinction, focal osseous dysplasia preferentially affects the posterior regions of the mandible and maxilla. Its identification often stems from serendipitous discovery during routine dental radiographic assessments. Analogous to periapical osseous dysplasia, focal osseous dysplasia tends to present as an asymptomatic condition, with a higher prevalence among the female population. Conversely, florid osseous dysplasia, comprising the third variant, is hallmarked by its dissemination across multiple quadrants of the jaws. This subtype primarily affects middle-aged African and American women. However, it presents with symptoms such as infection and pain.[2]

Although the precise etiological underpinnings of osseous dysplasia remain enigmatic, prevailing conjecture posits an association with perturbations in the normative bone remodeling processes. Diagnosis conventionally relies on radiographic imaging modalities complemented by meticulous clinical evaluation, and interventions are typically reserved for instances where complications ensue.[1]

The present introduction aspires to elucidate the multifaceted dimensions of osseous dysplasia, encompassing its various subtypes, clinical attributes, diagnostic paradigms, and potential avenues for therapeutic intervention. Notably, it underscores the imperative for individuals diagnosed with osseous dysplasia to undertake periodic dental follow-up regimens, thereby facilitating the vigilant monitoring of potential evolving pathology and ensuing complications.

Fractal dimension, an enthralling mathematical construct that emanates from the field of fractal geometry, confers a novel paradigm for the quantitative assessment of intricate, irregular phenomena and configurations prevalent in the natural world. This mathematical parameter, fractal dimension, serves as a robust analytical tool when applied to the complex and multifaceted nature of osseous dysplasia lesions. Through fractal dimension calculations, scholars and practitioners alike attain profound insights into the intricate patterns and self-similarities embedded within these pathological entities. This computational approach holds substantial promise in fostering a deeper understanding of osseous dysplasia, thus culminating in its enhanced characterization, diagnosis, and the refinement of therapeutic stratagems.[3]

These divergent observations underscore the exigency of further scholarly inquiry aimed at elucidating the intricate relationship between mandibular fractal dimension analysis and the presence or progression of cemental, focal, and florid osseous dysplasia. In the interim, fractal dimension analysis remains an auspicious investigative tool for the evaluation of mandibular osseous structures across a spectrum of maladies, encompassing cemental, focal, and florid osseous dysplasia. Possessing attributes characteristic of a non-invasive, quantitative modality, it harbors substantial potential for the early detection and dynamic monitoring of osseous changes. Such capabilities augur considerable contributions to the management and prognostication of cemental, focal, and florid osseous dysplasia, along with other mandibular pathologies. The overall aim of this retrospective pilot study was to clarify whether osseous dysplasia leads to noticeable structural changes in the mandible.

METHODS

This retrospective cross-sectional study was conducted in accordance with the provisions of the Declaration of Helsinki and informed consent was obtained from the individuals included in the study. A comparative analysis was conducted on panoramic radiographs obtained from patients diagnosed with cemento-osseous dysplasia, focal osseous dysplasia, and florid osseous dysplasia, alongside age and gender-matched controls, at the Oral and Maxillofacial Radiology Department of the Faculty of Dentistry, during the period spanning 2019 to 2023. Each group comprised 2 male and 41 female subjects, ensuring gender parity across the study cohorts. Ethical clearance for the study was obtained from the Ethics Committee of Van Yüzüncüyıl University, under approval number 2023/13-07, date 08/12/2023.

The inclusion criteria were no systemic disease affecting bone development and metabolism except any osseous dysplasia and sufficient image quality. Lesions that are well-defined and appear as radiolucent, mixed, or radiopaque areas around the tips of lower front teeth were categorized as cemento osseous dysplasia (COD). Similar lesions affecting only one area around the back teeth were labeled as focal COD, whereas those found in multiple areas across different sections were termed florid COD.[4]

The study's exclusion criteria comprised individuals with a history of pharmaceutical intervention or systemic illnesses that may influence bone development or metabolism, images containing artifacts, the presence of syndromes affecting the oral or maxillofacial region, and cases where the diagnosis of osseous dysplasia was uncertain.

Panoramic radiographic images were captured utilizing an ORTHOPHOS XG device (Sirona, USA), with exposure parameters set at 60 kV, 3 mA, and a duration of 14.1 seconds. Subsequent to image acquisition, conversion to DICOM format was undertaken, followed by meticulous analysis employing ImageJ software (U.S. National Institutes of Health, Bethesda, MD, USA). The analysis was executed by two proficient oral and maxillofacial radiologists, each possessing ten and six years of clinical experience, with inter-examiner reliability being evaluated through an additional examiner proficient in the field.

For the assessment of fractal dimension, following the methodology outlined by Kato et al.,[5] nine distinct regions of interest (ROIs) were delineated for fractal analysis. These ROIs were manually drawn using ImageJ's Rectangle tool, encompassing the condyle (1), angulus of mandible (2), molar (3), premolar (4) regions bilaterally, along with the anterior (5) region (Figure 1). Additionally, ROIs were demarcated in the cortical bone bilaterally, extending from the mental foramen to the posterior region of the third molar. Fractal analysis was conducted according to the protocol established by White and Rudolph,[6] involving a series of steps including image duplication, Gaussian filtering, image subtraction, binarization, noise elimination, sharpening of external lines, inversion, and skeletonization (Figure 2). The fractal dimension was determined by counting 2–30 pixel-sized boxes on the skeletonized image using the Fractal box count plugin of ImageJ. Interexaminer reliability was assessed by analyzing 20% of the total sample.

Mandibular cortical width (MCW) was measured bilaterally surrounding the mental foramen, with two parallel lines drawn from the upper and lower borders of the cortex, and a third line perpendicular to these lines passing through the center of the mental foramen. The length of the third line between the other two lines was recorded as the mandibular cortical width (Figure 3). Interexaminer reliability was again assessed through analysis of 20% of the total sample.

The mandibular cortical index (MCI) was determined in accordance with the classification proposed by Klemetti et al.[7], categorizing erosion patterns of mandibular cortical bone into three groups: C1, C2, and C3. Each side was evaluated independently, with the highest category recorded (Figure 4). Inter- and intra-examiner reliability were evaluated using Cohen's kappa coefficient based on analysis of 20% of the total sample.

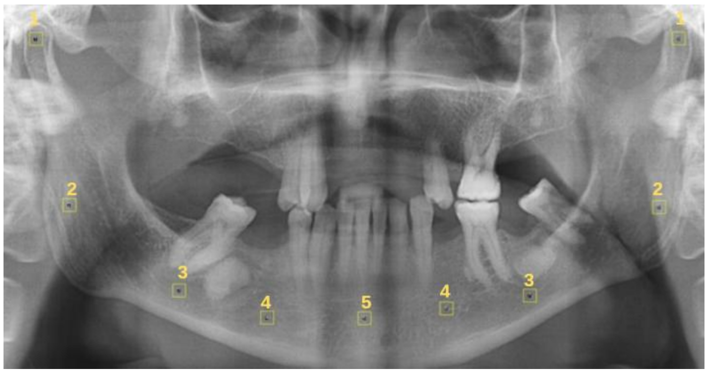

Figure 1. Selected ROIs for FA. Manually drawn squares of 30 × 30 pixels in the condyle, angulus of mandible, molar, premolar, and anterior region. Also, manually drawn bilateral ROIs of cortex.

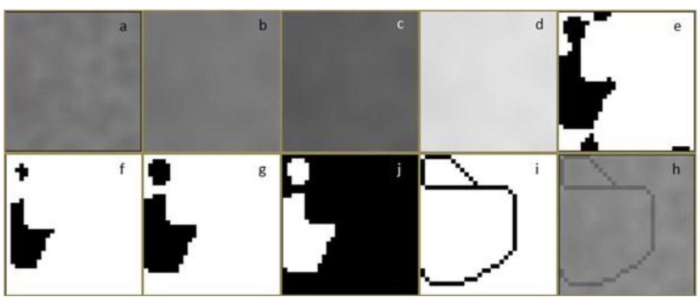

Figure 2. The process begins with the duplication of the original image post-cropping (a). Subsequently, a Gaussian filter is applied to induce blur with a sigma value of 35 (b). This blurred image is then subtracted from the original (c), followed by the addition of 128 Gy values (d). Binarization of the resulting image follows suit (e), succeeded by erosion (f) and dilation (g) operations. An inversion step is then performed (h), followed by skeletonization (i). Finally, the skeletonized image is superimposed onto the cropped image (j).

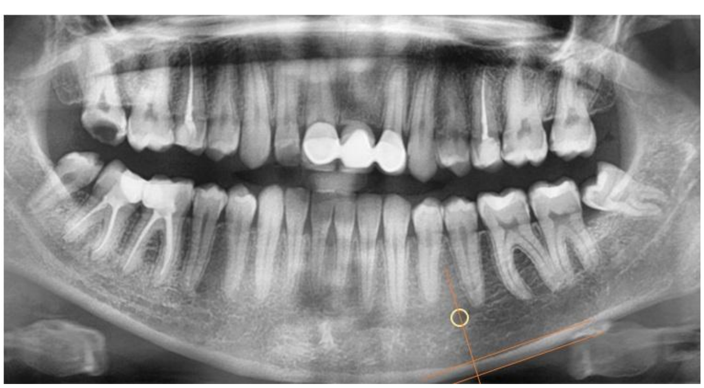

Figure 3. Two parallel lines passing from the upper and lower borders of the cortex were drawn. Then, a third line passing through the center of the mental foramen perpendicular to the two lines was drawn. The length of the third line between the other two lines was considered the MCW .

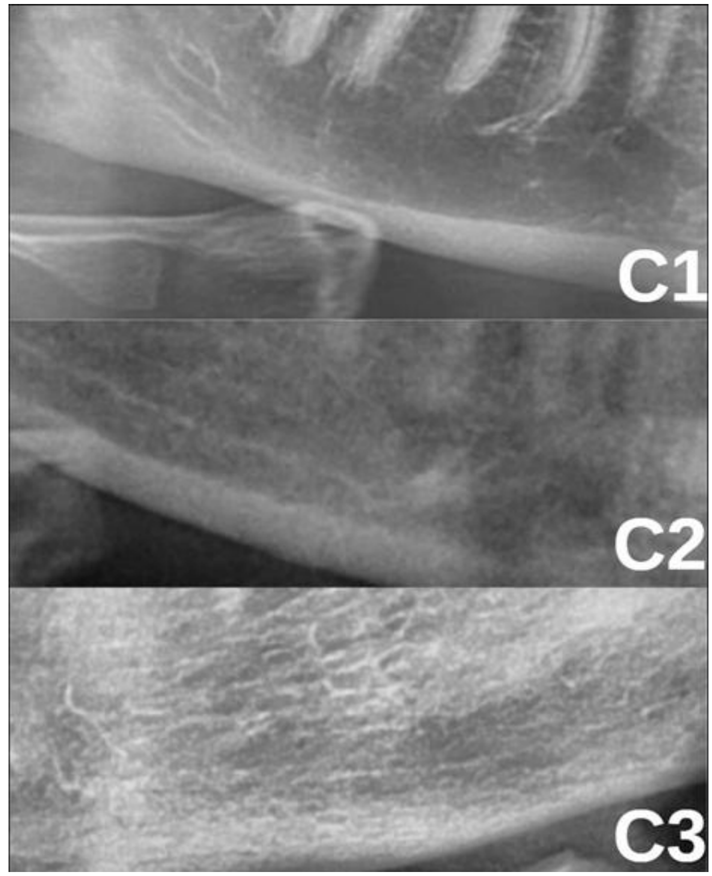

Figure 4. Radiographic presentation of mandibular cortical index classification. C1, C2, and C3.

Statistical analysis involved descriptive statistics to evaluate the distribution of each variable in each group. The McNemar–Bowker test was utilized to compare MCI distributions between osseous dysplasia patients and control groups. Student's t-test was employed to compare mean mandibular cortical width and fractal dimension values between osseous dysplasia and control groups, as well as to compare mean mandibular cortical width across different MCI subgroups. Differences in fractal dimension and mandibular cortical width values among patients with different types of osseous dysplasia were analyzed using the One-Way ANOVA test. All statistical analyses were performed using IBM SPSS V23 (IBM Co., Armonk, NY) software with a confidence interval of 95% and statistical significance was set at $P < .05$.

RESULTS

The study encompassed individuals with an average age of 40.6 years (± 11.4 years), ranging from 19 to 68 years, inclusive of patients diagnosed with various forms of osseous dysplasia and a control group. Specifically, among the cases 20 (46.5%) were afflicted with cemento-osseous dysplasia, 6 (14%) with focal osseous dysplasia and 17 (39.5%) with florid osseous dysplasia. Table 1 delineates a comparative analysis of fractal dimension (FD) values across various anatomical regions between the two cohorts. Noteworthy is the observation that patients with osseous dysplasia exhibited comparatively lower mean FD values in the condyle and anterior regions, whereas higher mean values were discerned in other regions when juxtaposed with the control group. However, these differences did not achieve statistical significance, except in the condyle regions, as indicated in Table 1. In mandible, especially bone quality of condyle region was significantly lower in patients of osseous dysplasia. Additionally, Table 1 presents a comparative examination of mandibular cortical width (MCW) between the two cohorts, illustrating a slightly greater mean MCW in the control group, albeit lacking statistical significance (*P> .05*). Moreover, Table 1 also depicts the distribution of mandibular cortical index (MCI) classifications between patients with osseous dysplasia and the control group, indicating no statistically significant variance (*P> .05*) across the observed C1, C2, and C3 categories. Furthermore, Table 2 provides an overview of FD and MCW values stratified by osseous dysplasia types, revealing no statistically significant differences in any of the radiomorphometric parameters concerning the various osseous dysplasia types.

Reliability analysis indicated commendable inter-examiner agreement for FD assessment (intraclass correlation coefficient [ICC]= 0.743), excellent inter-examiner reliability for MCW measurement (ICC= 0.902), and good inter-examiner reliability for MCI determination employing Cohen's kappa coefficient (κ=0.659).

Table 1. Comparison of fractal dimensions of anatomic regions, mandibular cortical width, mandibular cortical index between the patients of osseous dysplasia and control groups.

Region	Groups	N	Mean	Std. deviation	Std. error mean	P^{*}
Anterior	Osseous Dysplasia	43	.84	.31	.069	.453
	Control	43	.94	.33		
Premolar	Osseous Dysplasia	43	.97	.22	.056	.057
	Control	43	.91	.29		
Molar	Osseous Dysplasia	43	.95	.24	.55	.427
	Control	43	.89	.27		
Angulus	Osseous Dysplasia	43	.95	.19	.041	.815
	Control	43	.95	.19		
Condyle	Osseous Dysplasia	43	.8	.36	.069	.007
	Control	43	.93	.28		
MCW	Osseous Dysplasia	43	22.58	12.11	1.15	.919
	Control	43	24.05	13.06		
		C1	C2	C3	N(%)	P^{**}
MCI	Osseous Dysplasia	23	16	4	43 (100)	
	Controls	29	11	3	43 (100)	
						.413
	Total	52	27	17	86 (100)	

N, number of measurements, MCW, mandibular cortical width, MCI, mandibular cortical index, P^{*} Student's t test, P^{**} McNemar–Bowker Test.

Table 2. Comparison of anterior, premolar, molar, angulus, condyle region FD and MCW by osseous dysplasia type.

	Cemento Osseous Dysplasia (M±Sd)	Focal Osseous Dysplasia (M±Sd)	Florid Osseous Dysplasia (M±Sd)	**P****
Premolar	1.03±.076	.87±.23	.93±.31	.243
Molar	1.02±.17	.75±.38	.94±.21	.062
Angulus	.93±.16	.81±.30	1.02±.15	.060
Condyle	.85±.34	.71±.37	.79±.38	.718
MCW	24.37±5.05	22.37±3.93	21.07±6.31	.280

***One-way analysis of variance, M±Sd : Mean ± Standart deviation, P<.05*

DISCUSSION

Panoramic radiographs offer multiple forms of information despite their limitations in distortion and image overlap.[8] The panoramic radiograph, due to its low-dose X-radiation and affordability, is often requested in clinical practice to assess the oral and maxillofacial region. It serves as a dependable and cost-effective means of screening for low bone mineral density (BMD) in patients, especially as the high cost of DXA limits its evaluation to select female cases.[9] Furthermore, aside from their fractal dimension of radiographs non-invasive nature and ease of application, these methods offer crucial clinical insights into significant bone changes.[5]

Eser et al.[10] assessed changes in fractal dimension by identifying triangular-shaped regions of interest (ROIs) on the mesial and distal interradicular surfaces of the first molar teeth in panoramic radiographs of individuals with gingivitis and periodontitis. Korkmaz et al.[11] evaluated the effects of vitamin D deficiency on mandibular bone patterns using fractal analysis, assessing a total of eight distinct regions: the condyle, the angulus and the areas anterior and posterior to the mental foramen.

Balkan et al.[12] evaluated changes in fractal dimension observed in the mandibular condyle, ramus, and angulus regions on panoramic radiographs following botulinum toxin injection into the masseter muscle in individuals with bruxism.

Yavuz et al.[13] compared imaging methods for trabecular bone fractal dimension analyses, with each group consisting of 15 radiographs (digital periapical radiographs, panoramic radiographs, and cone-beam computed tomography). They found no statistically significant difference between the digital periapical radiography technique and the panoramic radiography technique. However, they concluded that the cone-beam computed tomography method did not correlate with the other methods in the fractal dimension analysis of trabecular bone.

Software and studies are available for conducting fractal dimension analyses on both two-dimensional and three-dimensional radiographs. Each type of radiograph has its own advantages and disadvantages. A significant disadvantage is the radiation dose administered to the patient. However, the major advantage is that they provide information about the three-dimensional structure of tissues.[14] Therefore, radiographic indications are established considering clinical benefit. Two-dimensional radiographs are commonly used in bone assessments with fractal analysis, which is why this study evaluated changes in fractal dimensions across nine distinct regions of interest (ROIs). This approach aims to represent changes occurring in each anatomical region of the mandible.

De Oliveira et al.[15] conducted a fractal analysis on cone-beam computed tomography images of six individuals diagnosed with fibrous dysplasia and six individuals diagnosed with ossifying fibroma. In their study, they found that the bone quality of fibrous dysplasia patients was higher in both two-dimensional and three-dimensional radiographs compared to those with ossifying fibroma. However, in this study, no significant differences were observed among the FD, MCW, and MCI values in three different types of osseous dysplasia.

In Arsan's[16] study, a fractal analysis was conducted on cone-beam computed tomography images of 28 patients diagnosed with cemento osseous dysplasia in five different regions. There was no statistically significant difference observed between the cemento osseous dysplasia group and the control group. Similarly, Kato et al.[5] performed fractal analysis on panoramic radiographs of 30 female patients with cemento osseous dysplasia. The FD value, similar to Arsan's study, did not show a statistically significant difference, while the MCW and MCI values were found to be lower in the cemento osseous dysplasia group compared to the healthy group.Unlike Kato's study, in our research, although cortical bone thickness and porosity in COD patients were similar to the healthy group, it was observed that the bone quality in the condylar region of COD patients was significantly weaker.

When looking at the pathogenesis of Cemento Osseous Dysplasia (COD), Haefliger et al.[17] observed "pathogenic hotspot mutations involving the RAS-MAPK signaling pathway" in 28% of the 30 COD cases they studied.[17] However, they argued that these mutations still do not explain the mechanism of spontaneous growth.In a study by Lv et al.[18], they discovered an "ANO5 missense mutation" in a family with three generations of florid COD. The authors emphasized that this discovery could lead to better clinical management and genetic counseling for FCOD cases.

Klemm et al.[19] reported that in the case of a very rare disease known as "Camurati–Engelmann disease" or alternatively referred to as "progressive diaphyseal dysplasia," mutations in the transforming growth factor-beta 1 gene were observed. It was noted that in this disease, bilateral osteosclerosis can be observed in the cranial base and mandible.

Cheng et al.[20] have identified that Kenny-Caffey syndrome is a bone dysplasia related to the FAM111A protein. In this syndrome, they observed features such as frontal bossing, relative macrocephaly, triangular face, narrow nasal ridge and micrognathia or microretrognathia. Additionally, dental manifestations including oligodontia, enamel hypoplasia, retention of primary dentition, and delayed eruption of secondary dentition were also noted. When all of these studies analyzing osseous dysplasias are interpreted, it can be concluded that there is a possibility of pathogenesis related to gene mutations in these respective bone dysplasias.

In a review where Kato et al.[21] analyzed 66 cases of Cemento Osseous Dysplasia, they found that the most common cause of COD-related local infections was the extraction of adjacent teeth. Additionally, in this review, the factors most commonly reported to contribute to the development of COD-related osteomyelitis were, in order, tooth extraction, prosthesis trauma, and root canal treatment. Therefore, it was emphasized that clinicians should differentiate between periapical pathology and COD to prevent such complications.

Consolaro et al.[22] have emphasized that orthodontic treatment can be contraindicated in some cases of Cemento Osseous Dysplasia. The reason for this is the potential for bacterial contamination from oral microbiota due to surgical procedures such as the installment of mini-implants or mini-plates and the application of traction to impacted teeth in the hypovascular bone tissue. Additionally, it was mentioned that tooth movement is not possible in this disorganized bone area, and remodeling does not occur in this abnormal mineralized and unorganized bone tissue. Whitt et al.[23], in their follow-up study on cases of segmental odontomaxillary dysplasia, have reached the opposite conclusion. They found that there were no problems with orthodontic tooth movement or dental implant osseointegration in these patients.

Colak[24] found that in patients with ectodermal dysplasia, another type of dysplasia observed in the jaws, the bone mineral density was lower in cone-beam computed tomography images. Leet et al.[25] reported that in patients with polyostotic fibrous dysplasia, the incidence of bone fractures is higher in the first decades of life, and in cases where "phosphaturia" is observed, there is a higher likelihood of bone fractures occurring earlier and more frequently.

Apolinário et al.[26] conducted radiomorphometric analysis before and after the use of pamidronate (PAM) in 62 children with osteogenesis imperfecta. They observed a statistically significant increase in FD and MCW values after the use of the medication. This indicates that fractal analysis can be used as an effective, reliable, and easy analysis method in diseases causing resorption and during medication usage.

Limitations of our study is the need to examine the changes caused by osseous dysplasias and other bone-affecting diseases in the jawbones from both a fractal dimension and genetic perspective using larger sample sizes. Additionally, similar studies can be conducted using both two-dimensional and three-dimensional radiographs to compare the results. This would allow for an investigation into the adequacy of two-dimensional radiographs in this conditions.

CONCLUSION

In conclusion, it has been determined that cortical bone porosity and bone thickness in COD patients are similar to those in healthy individuals. However, it should be kept in mind that the quality of bone, especially in the condylar region of COD patients, may not be equivalent to that of healthy individuals. Clinicians should approach surgical procedures in the joint area of these patients more cautiously. Additionally, patients with the three variants of segmental dysplasia in the mandible were found to have similar bone quality.

Ethics Committee Approval: Approval for this study was obtained from Van Yüzüncü Yıl University Non-Interventional Clinical Research Ethics Committee (Approval number: 2023/13-07, date 08/12/2023).
Informed Consent: In this study, panoramic radiographs used during routine radiologic examination of patients admitted to our clinic were used. Therefore, no consent form was obtained.
Peer-review: Externally peer-reviewed.
Author Contributions: Concept – S.K,A.K; Design - S.K,A.K; Supervision - A.K; Resources - A.K; Materials – S.K; Data Collection and/or Processing – S.K; Analysis and/or Interpretation - S.K,A.K; Literature Search - S.K,A.K; Writing Manuscript - S.K,A.K; Critical Review -A.K.
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