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AN ALTERNATIVE TRABECULAR BONE STRUCTURE ANALYSIS ON PANORAMIC RADIOGRAPHS OF PATIENTS WITH SCOLIOSIS

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ABSTRACT

Objective: *The aim of this study was to evaluate the mandibular trabecular bone of patients with scoliosis using fractal analysis (FA), and to compare these patients to a healthy control group.*

Material and Method: *Six regions of interest (ROIs) were chosen on the mandible. FA was performed using a box-counting method on panoramic radiographs of 105 patients with adolescents' idiopathic scoliosis, and 105 control subjects.*

Results: *Fractal dimension (FD) values of the patients with scoliosis (1.2136) were found to be lower than the control subjects (1.2654). The results were statistically significant ($p<0.05$). Although there was no significant correlation between the FD values of ROI-1, 2, 5 and 6 and the Cobb angle of the patients, there was a correlation between the FD values of ROI-3 and 4 and the Cobb angle.*

Conclusion: *The FD values of the patients with scoliosis were found to be lower than those in the control group. These findings suggest a promising result for similar research that focuses on the evaluation of bone microstructure on panoramic radiography using the FA method.*

Keywords: *Scoliosis, trabecular bone, fractal, panoramic radiography.*

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SKOLYOZLU HASTALARIN PANORAMİK RADYOGRAFLARINDA ALTERNATİF TRABEKÜLER KEMİK YAPISI ANALİZİ

ÖZET

Amaç: Bu çalışmanın amacı, skolyozlu hastaların mandibular trabeküler kemiğini fraktal analiz (FA) ile değerlendirmek ve bu hastaları sağlıklı bir kontrol grubuyla karşılaştırmaktır.

Materyal ve Metot: Mandibulada altı ilgi bölgesi (ROI) seçildi. FA, idiyopatik skolyozlu adolesan 105 hasta ve 105 kontrol deneğinin panoramik radyografilerinde kutu sayma yöntemi kullanılarak yapıldı.

Bulgular: Skolyozlu hastaların (1,2136) fraktal boyut (FD) değerleri kontrol deneklerinden (1,2654) daha düşük bulundu. Sonuçlar istatistiksel olarak anlamlıydı (p<0,05). Hastaların ROI-1, 2, 5 ve 6 FD değerleri ile Cobb açısı arasında anlamlı bir korelasyon olmamasına rağmen ROI-3 ve 4'ün FD değerleri ile Cobb açısı arasında korelasyon vardı.

Sonuç: Skolyozlu hastaların FD değerleri kontrol grubuna göre daha düşük bulundu. Bu bulgular, FA yöntemi kullanılarak panoramik radyografide kemik mikro yapısının değerlendirilmesine odaklanan benzer araştırmalar için umut verici bir sonuç ortaya koymaktadır.

Anahtar kelimeler: Skolyoz, trabeküler kemik, fraktal, panoramik radyografi.

INTRODUCTION

Adolescent idiopathic scoliosis (AIS) is an orthopedic deformity that is defined as the lateral curvature of the spine. It is the most common structural deformity of the spine. Spine curvatures that have a Cobb angle (the angle between lines drawn end plates of end vertebrae) of over ten degrees on an anteroposterior radiograph are diagnosed as scoliosis.[1] AIS is a complex curvature that causes deformity in all three planes. It is a pathology that can cause cardiopulmonary complications in the advanced stage of the disease, as well as deformation in the spine. It also causes emotional disorders and cosmetic deformities.[2] While the incidence rate of AIS varies between 1-3% globally, the incidence rate of AIS cases of over 30 degrees that require treatment is much lower (0.15-0.3%).[3,4]

The basic hypotheses proposed to explain the etiology of scoliosis are: genetic and hormonal factors, autonomic nervous system dysfunction, abnormal bone and connective tissue structure.[5] A decrease or deficiency of the estrogen receptors alpha and beta in bone cells have been shown to be effective in scoliosis curvature.[6] Another etiological factor is the melatonin hormone, which causes an increase in osteoblastic activity. In an experimental study, it was found that scoliosis developed due to a decrease of the melatonin hormone after the removal of the pineal glands.[7] It is also known to have osteopenia in the spinal bone structure in patients diagnosed with AIS. One of the causes of osteopenia is a polymorphism in the Vitamin D receptor gene. In conclusion, these factors that cause deformity in the vertebral bone structure in scoliosis patients may also affect the trabecular structure of the whole skeletal system, as well as jaw bones.[8-10]

The trabecular structure of bone presents fractal properties such as self-similarity, complexity, and a characteristic length due to its natural architecture. The texture of images consist of many small components that present fractal features. Many methods have been developed by researchers for the analysis of this texture. Fractal application is a method of texture analysis that is used to define complex shapes and structures.[11] In recent years the use of fractal analysis (FA) has increased in many scientific disciplines, especially biology and medicine.[12] In many studies in the literature, it has been reported that the FA of cancellous bone is a practical, low-cost, and promising tool for the evaluation of bone tissue.[13-16] Researchers have used the FA method to evaluate jaw bones in osteoporosis and various osteoporotic diseases, such as periodontitis and diabetes mellitus. It is also used to examine the effect of bisphosphonate intake. They noted that FA is capable to discriminate the patients with osteoporotic pathologies from healthy individuals.[11,17-19] In dentistry, it is especially important to evaluate the bone quality of osteopenic patients during the pre-surgical implant planning stage. Suer *et al*. indicated that FA of panoramic radiographs is capable of aiding the prediction of bone quality during the pre-surgical implant planning stage.[20]

In this study, we hypothesized that the trabecular structure of the mandible would decrease in patients with scoliosis when compared to healthy individuals. In order to verify this, the trabecular structure of the mandible was examined on dental panoramic radiographs using the fractal box-counting method. Although there were many studies on the evaluation of the osteoporotic effects of various metabolic and endocrine diseases on jaw bones, there were no studies

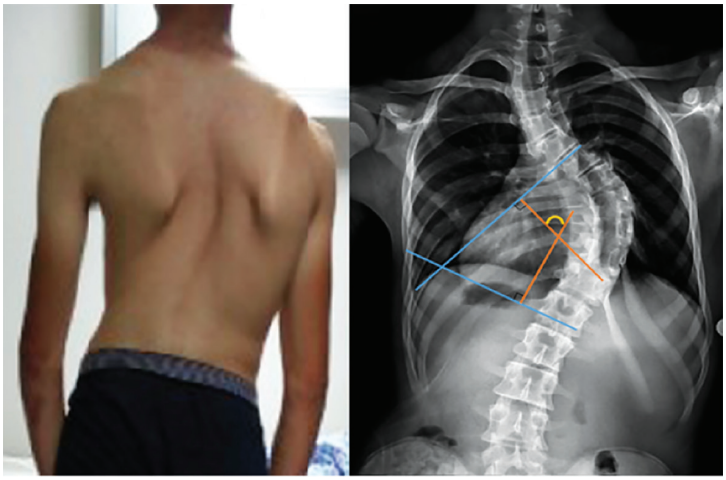

Figure 1. Back side of patient with scoliosis is seen on the right figure. Cobb angle measurement on antero-posterior radiography of patient with scoliosis is seen on the left figure.

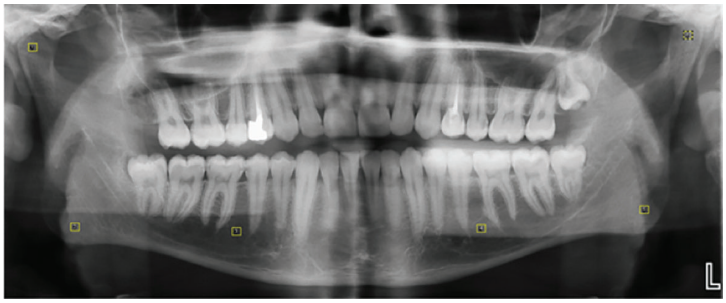

Figure 2. ROI selection on panoramic radiography to be used for FA.
ROI-1 and 6: on the head of the mandibular condyle **ROI-2 and 5:** on the mandibular gonial region **ROI-3 and 4:** between the first molar and second premolar tooth apexes of the mandible

related to scoliosis. To the best of our knowledge, this paper is the first study related to the FA method and the evaluation of mandibular bone structure in patients with AIS.

MATERIAL AND METHOD

Study Group

This study was performed using a panoramic radiography of patients diagnosed with AIS in the Orthopedics Service. The study was approved by the local ethics committee (decision number: 5/2018), and all participants completed the written informed consent. A number of patients with osteoporotic pathologies that could affect bone metabolism, such as endocrine system diseases (hyperparathyroidism, hyperthyroidism, and diabetes mellitus), hematological system disorders (multiple myeloma and lymphoproliferative disease), drug use (steroids, anticoagulants, chemotherapy/ immunosuppressive medications, bisphosphonates, and anticonvulsants), sex hormone less secreted disorders (hypopituitarism and hypogonadal disease syndrome), and genetic diseases (Marfan syndrome, Ehlers-Danlos syndrome, hypophosphatemia and osteogenesis imperfecta), as well as those with renal failure and those who received radiation therapy, were not included due to their medical condition. Of the 107 patients, two were excluded. In total, 105 AIS patients with a curvature of ten degrees or over were included in this study. The Cobb angle was used to measure scoliosis curves. The control group consisted of 105 patients. Participants who had no systemic diseases who underwent a radiographic examination for various dental problems were matched by age and sex. All procedures performed in this study were in accordance with the Helsinki Declaration of 1964 and its later versions.

Measurement of the Cobb Angle

Cobb's method was used to measure the degree of spinal curvature. The Cobb angle is the most common method used to determine the degree of scoliotic curvature in the frontal plane. An anteroposterior (AP) radiograph was used to evaluate the Cobb angle of patients with AIS. The measurement begins with the determination of the end vertebrates. On the concave side of the curvature, the intervertebral spaces are narrower. The levels at which the intervertebral spaces begin to expand are at the end vertebrae. The Cobb angle is defined as the angle between the line extended parallel to the upper edge of the cephalic end vertebra, and the line extended parallel to the lower edge of the caudal end vertebrae. Patients with a curvature of ten degrees or more were diagnosed with scoliosis.

Patients with AIS were classified into three separate subgroups according to the Cobb measurements, and as reported by Bridwell *et al*. (Figure 1).[21] According to Bridwell *et al*.: 10-25 degrees cases (10 or greater than 10, and less than 25) are mild.[21] These patients can be treated with exercise. Patients with 25-45 degree curves are moderate cases (25 or greater than 25, and less than 45). These patients can be treated with bracing. Patients who have an angle of 45 degrees and over are severe cases. These patients need surgery.

Images and Fractal Analysis

All dental radiographic examinations were performed using the same panoramic radiography device (ProMax®; Planmeca Oy, Helsinki, Finland) and the same X-ray technician. The exposure parameters were set on average as 62 kVp, 4 mA and 16.2 s.

The box counting method as designed by White and Rudolph was used to perform the FA on the mandible.[17] Six regions of interest (ROIs) were chosen on both

sides of the mandible. The size of every ROI was set to 35x30 pixels. ROI-1 and 6 were chosen on the head of the mandibular condyle, ROI-2 and 5 were chosen on the mandibular gonial region, and ROI-3 and 4 were chosen between the first molar and second premolar tooth apexes of the mandible (Figure 2). Boundaries of compact bone and anatomical structures such as tooth root, mandibular foramen, and mandibular canal were not included to ROIs. Only cancellous bone was selected. The FA transactions (Figure 3-4) were performed by the same person. ImageJ 1.52b image analysis software (National Institutes of Health, Bethesda, MD; http://rsb.info.nih. gov/nih-image). The software was obtained free of charge from the website "http: rsb.info.nih.gov". First, the ROI was cropped and duplicated. The duplicated image was blurred by applying the Gaussian filter (sigma = 35 pixels). Thus, fine and medium scale variations in the image were eliminated, leaving only the high-scale variations. The blurred image was extracted from the original image by using the 'subtraction' process. 128 were added to each pixel location, and was set as the threshold value regardless of the initial intensity degree of the image. After thresholding, the image was converted to a binary format. In order to remove the noise in the image, the erosion and dilatation process was applied to the image. The inverted image was skeletonized so that only the central parts of the trabeculae remained. Finally, FA was performed on the skeletonized image by using the box-counting method.

Statistical Analysis

A single investigator (fourth author of article, research assistant who has been studying for a doctorate in oral and maxillofacial radiology for four years) evaluated all of the parameters. After 20 days, in order to evaluate the intra-observer reliability, the image analysis was repeated twice on 40 randomly selected radiographs by the same investigator. The reliability of the intraviewer was 0.930 (Cohen's kappa coefficient).

Results were analyzed using SPSS statistic program (IBM, SPSS VERSION 22.0, Armonk, NY, USA). Whether the data of the FD measurements were distributed normally was determined by a Kolmogorov-Smirnov test. The Student's t-test was performed to compare the FD values of patient with scoliosis and the control subjects. The Pearson correlation was performed in the analysis of the correlation between the Cobb angle and the FD value of the patients. An ANOVA statistical test was performed to assess the FD values and subgroups of the Cobb angle. Results were reported as mean ± standard deviation, and a level of $p<0.05$ was accepted as statistically significant.

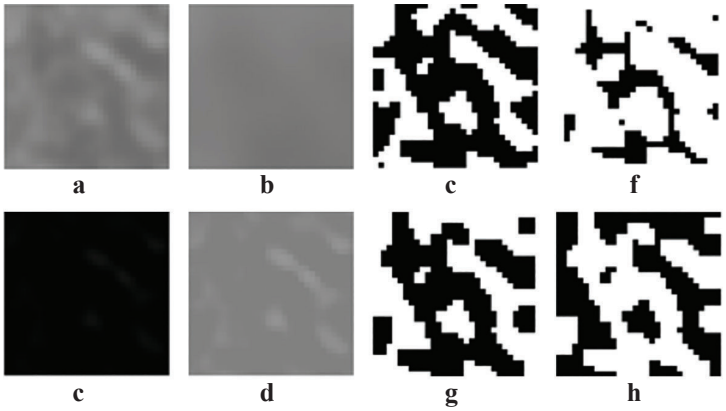

Figure 3. FD analysis transactions. **a**. Cropped and duplicated ROI, **b.** Blurred image of the cropped and duplicated ROI, **c.** The blurred image was then subtracted from the original image, **d.** Adding 128 to the result, **e.** Application of 128 threshold value and binarizing, **f.** Erosion process, **g.** Dilatation process, h. Reversing.

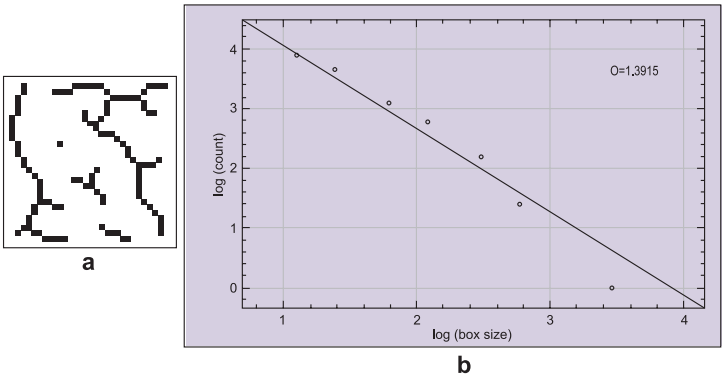

Figure 4. The last step of FD analysis transactions: **a.** Skeletonizing, **b.** Calculation of fractal dimension.

RESULTS

The age range of the patients was 11-20 years (mean age: 16 years). Thirty-four patients were male (mean age: 15 years) and 71 patients were female (mean age: 16 years). The age range of the control group was 11- 20 years, with a mean age of 16 years (34 male and 71 female). The average Cobb angles of the patients with scoliosis were 41.5 in total. According to Cobb angle's classification system, there were 39 patients (13 male and 26 female) with a Cobb angle between 10-25 degrees (mean: 19.6 degrees), 35 patients (10 male and 25 female) with a Cobb angle between 25-45 degrees (mean: 38.3 degrees), and 31 patients (11 male and 20 female) with a Cobb angle above 45 degrees (mean: 65.3 degrees).

According to the results, the FD values of the patients with scoliosis were found to be lower than the control subjects, and the results were statistically significant ($p<0.05$). In total, the average FD value was 1.2136 ± 0.11 in patients with scoliosis, and the average FD value in the control group was 1.2654 ± 0.08. The average FD values of each ROI in the patient group and the control group are outlined in

Table 1. The descriptive and statistical data of fractal dimension (FD) values of the patients with scoliosis and the control subjects.

ROI	N	Mean FD±SD		*p*-value
		Patient	Control	
1	105	1.2322±0.12	1.2825±0.08	0.001
2	105	1.2078±0.10	1.2430±0.09	0.013
3	105	1.2122±0.11	1.2720±0.08	<0.001
4	105	1.2191±0.11	1.2673±0.08	<0.001
5	105	1.1843±0.11	1.2529±0.08	<0.001
6	105	1.2264±0.11	1.2748±0.08	0.001

SD: Standard deviation, **FD:** fractal dimension

Table 2. Correlations between the Cobb angle and FD value of patients

	Correlations					
	ROI.1	ROI.2	ROI.3	ROI.4	ROI.5	ROI.6
N	105	105	105	105	105	105
Pearson Correlation	-0,023	-0,012	-0,257*	-0,233*	-0,141	-0,161
Sig. (2-tailed)	0,819	0,903	0,008	0,017	0,150	0,101

*: Correlation is significant at the 0.05 level, **FD:** fractal dimension

Table 3. Fractal dimension (FD) values of ROI-3 and 4 in accordance with subgroup of Cobb angle

		ROI-3		ROI-4	
Subgroup of Cobb angle	n	Mean±SD	*p*-value	Mean±SD	*p*-value
10 ≤ n < 25	39	1.2482±0.10		1.2420±0.08	
25 ≤ n < 45	35	1.2129±0.12	0.15	1.2222±0.09	0.39
45 ≤ n	31	1.1662±0.11		1.1867±0.09	

SD: standard deviation

Table 1. Although there was no correlation between the FD values of ROI-1, 2, 5, and 6, and the Cobb angle of the patients (p=0.846, p=0.851), there was a correlation between the FD values of ROI-3 and 4 and the Cobb angle of the patients (p=0.008) (Table 2).

When the FD values and the three subgroups of the Cobb angle were compared, there was no significant correlation between ROI-1, 2, 5, and 6. There was a significant correlation between ROI-3 and 4 (Table 3).

DISCUSSION

In this study, the microstructural evaluation of the mandibular trabecular bone was performed using the FA method on panoramic radiographs of patients with AIS. This information was then compared to the healthy control subjects. According to the results of this study, the mean FD values of patients with scoliosis were lower than the control subjects. There was a statistically significant difference.

In the field of dental radiology, numerous methods (such as radiomorphometric and densitometric measurements) have been used for the qualitative and quantitative evaluation of bone structure.[22-24] This is especially the case for osteoporotic individuals. Many studies have been conducted to investigate the use of bone mineral density (BMD) in different parts of the body. The literature has also reviewed the role of radiomorphometric analysis in diagnosing osteoporosis.[25] Bone quality depends on many factors, such as bone geometry, trabecular continuity, the microstructure of bone tissue, and the amount of mineralization and defects. Bone mineral density measurements have been used frequently in the analysis of bone structure in past decades.[26] However, recent studies have shown that only the density measurements are insufficient for evaluating bone quality, and that trabecular microstructure analysis must be taken into consideration.[26-28]

FA is a method that can provide the mathematical image analysis. Additionally, bone microstructure can be evaluated using this method.[12] From engineering to medicine, the use of the FA method is diverse, and it has also been used in plenty of dental research. In previous studies, the FA method has been used for the analysis of trabecular micro-architecture in patients with osteoporosis and hyperparathyroidism. It has also been used during the implant planning stage.[29-31] In a radiography study on the relationship between periodontal disease and bone destruction, it was reported that the destructive effects of periodontal pathology on trabecular bone can be successfully evaluated using the FA method. Researchers have stated that even small trabecular destructive changes in the early stages of the disease can be determined using the FA method before the effects of periodontal pathology have clearly emerged.[11,32] Moreover, in implantology and fractal based studies, researchers have stated that using the FA method based on two-dimensional dental radiographs of implant recipient sites prior to implant surgery is a promising, non-invasive and useful predictors on the evaluation of primary implant stability.[20,33]

While a number of hypotheses have been proposed for its etiopathogenesis, AIS is a complex spine disease with an unknown pathogenesis. However, the relationship between AIS and osteoporosis has been established in the previous studies. It was reported that patients with scoliosis present with low bone density. In these studies the dual X-ray absorptiometry (DXA) method was used, and BMD was evaluated by measuring femoral head density.[9,34,35] However, as mentioned above, only the density measurements

were insufficient for the evaluation of bone quality, and trabecular microstructure analysis must be taken into consideration. In one study, Lee *et al*. reported that the trabecular bone architecture weakened by osteopenia in patients with scoliosis may aggravate the spinal deformity.[36] Additionally, the relationship between scoliosis and the development of dentofacial asymmetries was investigated in recent studies. Ikemitsu *et al*. suggested the relationship between jaw deformities and scoliosis.[37] In our study, a significant difference was found in the FD values between the patients with AIS and the healthy control group. The FD values were found to be lower in patients with scoliosis. Although there have been many studies on the FA method in osteoporosis or osteoporotic diseases related to abnormal bone structure, there is no similar study in the literature to compare directly to this study. To the best of our knowledge, this study is the first in the literature to analyze mandibular bone quality in patients with scoliosis.

Our results are consistent with previous studies that involve patients with osteoporotic pathologies. Demirbas *et al*. performed on panoramic radiographs of patients with sickle cell anemia (SCA).[38] They stated that the FD values of the patients with SCA were found to be lower when compared to the healthy subjects. They associated this result with a loss of complexity in the trabecular structure. This led to a smoother form transformation because of the osteoporotic effect of SCA. Updike and Nowzari also reported that the resorption process that started with periodontal disease caused a decrease in trabecular complexity and thus lead to a decrease in the FD value.[11] In a similar study, Demiralp *et al*. performed on panoramic radiographs of 33 patients taking bisphosphonates.[39] They found that the FD values of the patients were higher than the FD values of the control subjects. The result of this study by Demiralp *et al*. may be related to the antiresorptive effect of bisphosphonates on bone tissue.[39]

In this study, the FD values obtained from all six ROIs of the patient group were significantly lower than in the control group. However, there was a correlation between the FD values and the Cobb angles for ROI-3 and 4. It was observed that the FD value decreased as the Cobb angle increased. Sadat-Ali *et al*. reported that scoliotic individuals with a Cobb angle above 30 degrees had significantly lower BMD values than those with a Cobb angle below 30 degrees.[9] Therefore, in this study, it may be said that the lower FD value of individuals with higher Cobb angles was related to the possibility of the existence of lower bone density in scoliotic individuals with high Cobb angles. For ROI-1, 2, 5, and 6, there were lower FD values in scoliotics compared to the control group. However, an unclear correlation with the Cobb angle may be related to the existence of superimpositions from many anatomic structures, especially in TMJ region of panoramic radiography or the multiplicity of artefacts in these regions of panoramic radiography. Therefore, the FD values obtained from these regions may not have fully reflected the trabecular microstructure. In addition, a possible correlation with the Cobb angle may not have emerged.

Many studies have pointed out that a higher value of fractal in the trabecular bone structure would indicate a more complex architecture.[40] With this in mind, there is no consensus on how destructive bone changes caused by diseases affect the complexity of the trabecular structure, and how it affects outcomes of FA. Therefore, different FA results have been obtained in different studies. For instance, researchers such as Hua *et al*. and Ruttimann *et al*. have stated that the FA values increased in pathologies that cause osteoporosis-like effect on trabecular bone.[41,42] Some other researchers, such as Updike *et al*., Southard *et al*., Ergün *et al*., and Demirbaş *et al*. have come to the conclusion that the FD decreases, which is the conclusion in our study.[11,16,38,43] Our argument is that dilution in trabeculae due to osteopenia in scoliosis decreases in the number of trabeculae and increases the dimension of lacunae between trabeculae. This decreases the complexity of the trabecular architecture, and thus the FD will be lower. However, changes in trabeculae that affect the FD values, such as thickening and resorption, depend on many factors in bone metabolism. The following issues can also contribute to the contradictory results found in FA studies: the method in which the images are obtained; the criteria for determining the ROI; anatomical variations; how diseases affect bone structure; how different bones in different parts of the body are affected by diseases; and finally, the different types of methods used to measure FD.

This study had a number of limitations. One of the limitations of the present study was the use of panoramic radiography. Of course, panoramic radiography is not the most appropriate tool to assess the structural changes of trabecular bone. "Cone beam computed tomography (CBCT)" is a reliable diagnostic tool that does not have many negative factors compared to panoramic radiographs when assessing bone structure. However, CBCT was not used in this study because it is not a routine radiographic method in dentistry. In addition, CBCT emits much more radiation compared to panoramic

radiography. Therefore, we preferred panoramic radiography because it is often used to examine jaw bones in dentistry. One of the major advantages of panoramic radiographs are its widespread and routine use. Panoramic radiography allows a general examination of the jaw bone morphology. It also allows many different kinds of analyses of the jaw bones using different measurement techniques. Panoramic radiography is the most preferred, simplest, practical and inexpensive imaging method for patients who consult a dentist for any reason. Another disadvantage in this study was that lack of histopathological assessment on how osteopenia-induced changes in bone metabolism affect the trabecular structure in patients with scoliosis.

CONCLUSIONS

There is still a need for an easy, predictable, and nondestructive method to predict bone quality prior to implant surgery in age-related osteoporosis or disorders caused by osteopenia. Especially in implant dentistry, bone quality is one of the main factors affecting the success of implant treatment. Regarding the success rate of osteointegration in cases where bone quality is insufficient, the success rate of the osteointegration increases in cases with good bone quality. The findings of this study suggest that FA might be a simple and cost-effective tool to reveal the microstructural changes in trabecular bone that is not visible to the naked eye. In addition, the FA of panoramic radiographs for osteopenic individuals, such as patients with scoliosis, might help to predict bone quality prior to implant surgery. Panoramic radiography is the most widely used imaging modality in dentistry, and it contains clinical data related to the bone structure of patients. By using the FA method, the data capacity of panoramic radiography might be utilized more in the evaluation of bone structure. Further studies with histopathological findings should be performed as the gold standard to demonstrate the clinical validity of the FA method.

*The authors declare that there are no conflicts of interest.

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