http://periodicos.uem.br/ojs/acta
ISSNon-line:1807-8648
Doi:10.4025/actascihealthsci.v47i1.70607

ODONTOLOGIA / DENTISTRY ARTICLES

Fractal analysis of bone trabeculae from the mandible of patients with chronic kidney disease

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ABSTRACT. The aim of this study was to investigate the characteristics of the bone trabeculae pattern in the mandible of patients with chronic kidney disease (CKD) using fractal dimension analysis in cone beam computed tomography (CBCT) exams. The sample comprised 20 adult patients, divided into two groups: a group of 10 individuals with CKD and a control group of 10 people matched for sex and age similar to the first group. The software ImageJ was used to do fractal analysis on the mandibular condyle and body of each individual. Statistical analysis included the use of the intraclass correlation coefficient (ICC) for the examiner's standardization and the student t-test for fractal analysis. The results showed a lower complexity of bone microarchitecture in the CKD group compared to the healthy patients. The fractal values found in the mandible of individuals were significantly lower for both body and condyle in the CKD group. The decrease in bone quality interferes directly in the planning of clinical and surgical interventions, therefore, fractal analysis appears to be a potential, simple, and economic method for examining bone quality through imaging exams.

Keywords: Cone beam computed tomography; fractals; chronic kidney insufficiency.

Received on December03, 2023.
Accepted on March14, 2024.

Introduction

Kidney disease can be associated with several pathologies, such as heart valve disease, periodontal disease, thyroid dysfunction, modifications in taste, and even calcifications in soft tissues (Çağlayan et al., 2015). In addition, kidney disease can cause bone changes, known as renal osteodystrophy. This condition can be described as an increase in the porosity of the bone microarchitecture and can be identified in imaging exams (McNerny & Nickolas, 2017; Allen et al., 2020).

More specifically in dentistry, there are studies that use panoramic radiographs to assess bone changes in patients with kidney diseases (Massahud et al., 2018). Abnidian and collaborators (2020) conducted an analysis of the bone trabeculae of the mandible in patients with chronic kidney disease (CKD) and compared it with a control group of healthy patients (Abdinian et al., 2020). In that work, they classified the trabeculae as dense, heterogeneous, sparse or sparse with a "ground glass" appearance. The authors concluded that the bone trabeculae of patients with CKD had decreased mineral density compared to healthy patients (Abdinian et al., 2021). Similarly, Massahud et al. (2018) used the same methodology to assess bone trabeculae and concluded that a decrease in bone trabeculae is associated with altered parathyroid hormone levels in chronic renal patients.

In the literature, several studies use fractal analysis to assess the quality of bone trabeculae (Massahud et al., 2018; Abdinian et al., 2021). Besides that, many studies demonstrate how this calculation, in cone beam computed tomography (CBCT) scans, can be an important tool for evaluating changes in bone trabeculae (Mostafa et al., 2016). Fractals aim to measure the complexity of a figure that cannot be explained by conventional geometry. Thus, trabecular bone has complex and self-similarity characteristics that allows the measurement of its complexity through fractal analysis (Mandelbrot, 1983; Messent et al., 2005).

A work by Gumussoy and collaborators (2016), evaluated, in panoramic radiographs, the ability of fractal calculation to identify changes in the bone trabeculae of the mandible in patients with CKD. The authors concluded that renal patients had a lower value, in other words less bone complexity, than the control group and that fractal analysis is a simple and low-cost procedure, which can be efficient to assess trabecular alterations in patients who have kidney diseases (Gaalaas et al., 2014; Kwak et al., 2016). However, no studies were found in the literature that use the calculation of fractals in CBCTs in this group of patients.

Some of the alterations caused by CKD can be seen in the head and neck region and can be identified by the dental surgeon. Changes in bone density in the dentomaxillofacial region can also be identified by CBCT, a tool widely used in dental practice. Clinically, changes in bone density can mainly affect the success in placing dental implants and the periodontal health of these patients, causing greater clinical attachment loss (Güngör et al., 2016). Thus, it is important for dentists to be aware of these differences in the pattern of bone trabeculae in patients with CKD and to take this into account during dental treatment.

Whereas the possibility of the presence of bone alterations in patients with CKD and how this can affect dental practice, this study aims to conduct a fractal analysis of the trabecular bone of the mandible of patients with CKD and compare it with the bone trabeculae from healthy patients. The established null hypothesis is that there is no difference in the bone trabeculae of patients with renal failure compared to healthy patients.

Material and methods

Ethics committee

This is a retrospective and observational study with a convenience sample, approved by the Permanent Ethics Committee of Research Involving Human Beings of the State University of Maringá (SUM) in Brazil (CAEE: 58882022.0.0000.0104).

Sample

This study included the CBCT exams of 10 individuals with CKD, who attended the extension project "Oral attention to pre and post kidney transplant patients" in SUM. The CBCT scans were executed as necessary during the dental treatment required in the project. Besides that, 10 CBCT scans of healthy patients were selected, which were executed during their dental treatment for various reasons. These control group individuals were carefully selected to match the CKD group in gender and age as closely as possible. The average age of the included patients was 67 years.

Obtaining the Images

Every CBCT image was obtained in the Clinical Research Imaging Laboratory (CRIL) of the Health Technology Center (HTC), of the Research Support Central Complex (RSCC), located in the Department of Dentistry of the State University of Maringá by the same oral and maxillofacial radiology specialist and then archived. The images were obtained by the equipment i-CAT Next Generation® (Imaging Sciences International, Hatfield, PA, EUA), with a volume of 300µ of isometric voxels, FOV (Field of View) of 17 × 23 cm, tube tension of 120 kVp and tube current of 3-8 mA. During image acquisition, the patients were instructed to be seated and maintain their heads in a natural position, keeping tongue and lips at rest.

Examiners and Image Region Selection

The analysis was performed by two examiners using the software *ImageJ* (*version* 2.0.0), of public domain (*National Institutes of Health, Bethesda, Md, EUA*, https://imagej.nih.gov/ij) (Gaalaas et al., 2014; Oliveira-Santos et al., 2019). For calculating inter-examiner agreement, the Intraclass Correlation Coefficient was used.

In each axial reconstruction, with cut thickness of 0.3 mm, regions of interest were selected in both the right and the left sides. In ImageJ, each region was cropped in a square shape of 10x10 pixels for analysis. The first region of interest was the trabecular bone in the center of the mandibular condyle, in the largest area of its mediolateral dimension, avoiding the cortical bone (Figure 1). The second region involves the mandibular body, below the apex of the 1st and 2nd inferior molars and above the mandibular channel (Figure 2).

Fractal evaluation of bone trabeculae of chronic kidney disease patients' mandible

Under low light ambience, the evaluations were made in a computer with Microsoft Windows XP Professional SP2 operating system (Microsoft Corp., Redmond, WA, EUA), Intel® Core™ 2 Duo 1.86 Ghz-e6300 processor (Intel Corporation, EUA), NVIDIA GeForce 6200 turbocache video card (NVIDIA Corporation, EUA) and EIZO - S2000 FlexScan monitor, 1600 x 1200 pixels resolution (EIZO Nanao Corporation, Hakusan, Japan).

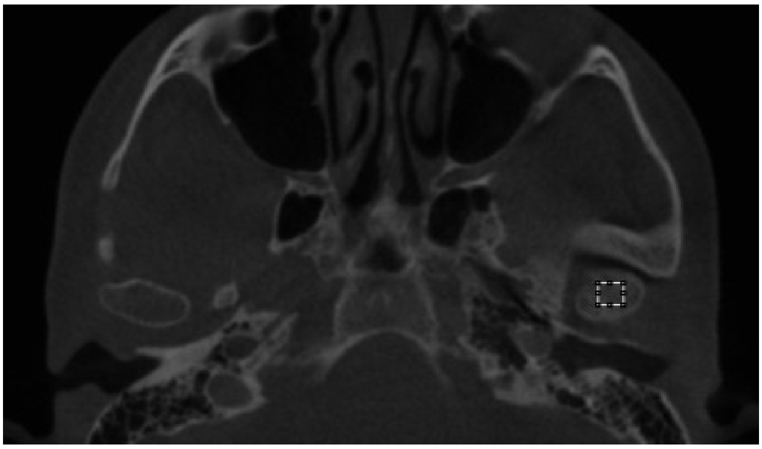

Figure 1. Region of interest 1 – Mandibular condyle.

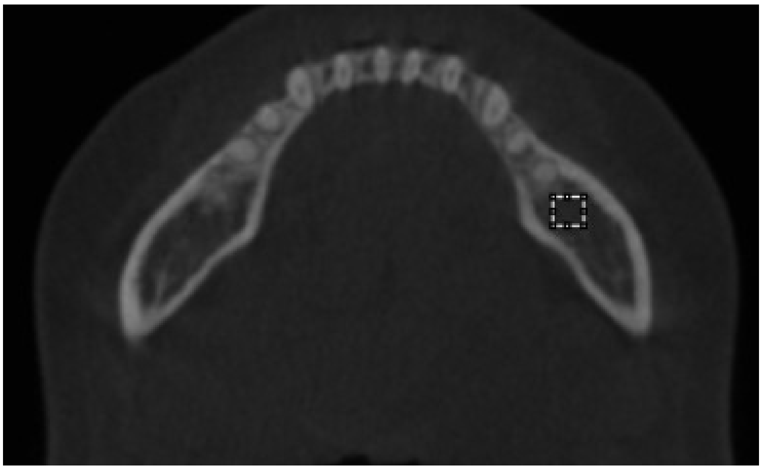

Figure 2. Region of interest 2 – Mandibular body.

In ImageJ, the regions of interest underwent fractal analysis using the method described by White and Rudolph (1999), in the following steps: duplicating original image and applying Gaussian Filter to remove low and medium structures, keeping only significant density variations, in other words, producing high-contrast images. Then, the second image was subtracted from the first image and added a gray value of 128 in each pixel, resulting in an image with the same gray value, no matter the initial intensity in the image. The goal of this process was to make the individual brightness variations in the image to represent only the specific characteristics of bone trabeculae.

Next, it was necessary to binarize the image, segmenting it to highlight the components similar to bone trabeculae. Then, the image was eroded and dilated for noise reduction and, finally, skeletonized, which means, eroded until only a central line of pixels remained. After the processing, the fractal calculation was performed using the "Fractal Box Count" tool in ImageJ (Gaalaas et al., 2014; Oliveira-Santos et al., 2019).

Statistical analysis

The analyses were performed in the Bioestat 5.0 software (Mamirauá Institute). The Shapiro-Wilk test was used to verify the assumption of normality in the variables of mandibular body and condyle for both CKD and control groups. Levene's test was used for homogeneity. Pearson's correlation test was used to do inter-examiner correlation. Aiming to verify potential differences between the measurement of the mandibular body and condyle variables, the independent t-student test was used. The paired t-student test was used to compare the measurements of the right and left sides of CKD and control groups.

Results and discussion

The results of the Shapiro-Wilk and Levene's test demonstrated normality and homogeneity, in this order. For the inter-examiner correlation, Pearson's correlation test showed a very strong inter-examiner correlation: r (*Pearson*) = 0.945.

In Table 1, mandibular body and condyle variables were divided and organized in right and left sides. Statistically significant differences were observed between the CKD and control groups in the right side (0.516 ± 0.210) and left side (0.537 ± 0.199) of the body, as well as the left mandibular condyle (0.417 ± 0.171), respectively, with p-values of0.019, 0.033 e 0.029. In particular, the fractal values were reduced in the CKD group compared to the control group, suggesting that the regions of the mandibular body (right and left side) and condyle of the investigated patients showed less complexity and quantity of bone trabeculae.

Table 1. Comparison of the measures studied between the CKD and control groups presented with statistical average (± standard deviation) and t-test application.

	CKD		Control		
	Average	SD	Average	SD	*p-value
Mandibular body (right)	0.516	± 0.210	0.709	± 0.110	*0.01
Mandibular body (left)	0.537	± 0.199	0.695	± 0.086	*0.033
**p-value	0.818		0.757		
Mandibular condyle (right)	0.433	± 0.281	0.619	± 0.217	0.057
Mandibular condyle (left)	0.417	± 0.171	0.616	± 0.230	*0.029
**p-value	0.881		0.973		

*p value for t-test between groups ($p \leq 0.05$, statistically significant difference). **p value for t-test between the right and left sides for different groups. SD = standard deviation. CKD = chronic kidney disease.

The Table 2 presents the average fractal dimensions for the analysis of the mandibular body and condyle, without distinction between sides. There were statistically significant differences between the groups for the measurements of the mandibular body, where the CKD patients average (0.526 ± 0.226) was lower compared to the control group (0.702 ± 0.096), with a p-value of 0,001. The same occurred with the condyle, where the CKD group average (0.425 ± 0.239) was lower than the control group (0.618 ± 0.205), with p value of 0.007. In short, the table indicates that the bone density of both the body and condyle are lower in the CKD patients in comparison with the control group.

Table 2. Comparison of the studied measures between the CKD and control groups presented with statistical average (± standard deviation) and t-test application.

	CKD		Control		
	Average	SD	Average	SD	*p value
Mandibular body	0.526	± 0.226	0.702	± 0.096	*0.001
Mandibular condyle	0.425	± 0.239	0.618	± 0.205	*0.007
** p value	0.142		0.102		

*p value for t-test between groups ($p \leq 0.05$, statistically significant difference). **p value for t-test between the right and left sides for different groups. SD = standard deviation. CKD = chronic kidney disease.

This research represents the first utilization of CBCT for fractal analysis in CKD patients. As presented in the results, the fractal values found in the mandible of individuals of both groups studied were compared, revealing a significant decrease in both the mandibular body (0.526 ± 0.226, p = 0.001) and condyle (0.425 ± 0.239, p = 0.007) in the CKD group. From this information, it is suggested that CKD may lead patients to bone trabeculae loss in the mandibular body and condyle.

Fractal analysis is a useful tool for mathematically evaluating complex structures, such as bone trabeculae, used widely in imaging studies for both dentistry and medicine (Saberi et al., 2021). It is a promising technique for bone quality evaluation, due to its easy access and execution, providing fast and precise results (Messent et al., 2005; Kwak et al., 2016). The result of this study is a unique and specific number, obtained by software-made calculations. The greater the complexity seen in the image, the closer the fractal value will be to 1, indicating more complexity of the analyzed structures.

This analysis can be implemented in the verification of periapical bone regeneration and in some systemic conditions, such as osteoporosis (Updike & Nowzari, 2008; De Molon et al., 2015). Although there are no other research in medical literature, besides Gumussoy et al. (2016), to which this study can be directly compared, other studies have been made using fractal analysis in systemic diseases related to bone structure alterations and have had similar results that corroborate with this present research. The studies found were able to conclude that the fractal values decrease in patients with systemic diseases with results varying depending on the studied condition. Therefore, executing more studies using the same technique in different groups of patients would be beneficial to confirm its utility (Southard et al., 2000; Demirbas et al., 2008; Ergün et al., 2009).

CKD, on the other hand, is a global health problem with crescent incidence and associated with severe complications for the affected population. During the progression of the disease, most patients suffer from oral complications. The repercussions of renal osteodystrophy manifest through morphologic qualitative alterations of the bones, which may interfere with orthodontic and orthognathic interventions (Nithin et al., 2021; Ceratti et al., 2022). Besides that, studies show that hypocalcemia is a common factor present in patients with advanced CKD causing orofacial pain due to muscular disturbance provoked by low levels of calcium. For this reason, being mindful of bone and systemic alterations in patients with CKD becomes highly important for a correct diagnosis of temporomandibular dysfunction and orofacial pain. Despite the necessity of clinical, laboratorial and imaging examinations for diagnosing renal osteodystrophy, a simple option would be the verification of bone quality of these individuals through fractal analysis (Santos et al., 2021).

In scientific literature, a strong correlation between CKD and periodontal disease is observed, as they are both multifactorial chronic diseases that mutually influence and support bone damage, leading to dental loss. Dental implants are a good option to restore these lost elements and reestablish life quality. Nevertheless, due to CKD complications such as infections, bone lesions, bleeding risks e drug-altered metabolism, the treatment using dental implants for CKD patients in dialysis is more challenging (Yuan et al., 2017). Therefore, the installation of implants in these patients requires the dentist to be aware of this condition facing the risk of post-surgical complications. Fractal analysis can be useful for verifying bone quality and predicting treatment prognosis, as observed in the present study, because CKD may be associated with lower bone trabeculae density.

The current study acknowledges certain limitations, such as the utilization of a convenience sample consisting of all available CBCT exams of CKD patients in the CRIL. Consequently, the authors recommend conducting future studies with larger sample sizes to delve deeper into bone quality assessment in CKD patients and validate the fractal analysis method. To ensure the method's reliability, it is essential to perform histopathological examinations.

Conclusion

This study provides relevant information for dentistry highlighting the possible repercussions of complexity decrease of bone trabeculae in the oral and maxillofacial complex of CKD patients. This information must be considered when planning clinical or surgical procedures, such as periodontal or orthognathic surgery, orthodontic treatment and implant installation. Based on the results and literature revision, fractal analysis is a promising, simple and economical method for examining bone quality through imaging exams. The results show that there is a minor bone trabeculae complexity in CKD patients in the mandibular body and condyle.

Acknowledgements:

We thank the State University of Maringa for all the invested resources in research promotion.

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