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Accuracy of Grayscale Value in Diagnosis of Odontogenic Keratocyst and Radicular Cyst

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A B S T R A C T

Objectives: Radicular cyst (RC) and odontogenic keratocyst (OKC) are among the most commonly identified cysts in both the maxilla and mandible. With the advancements in 3D imaging techniques such as cone-beam computed tomography (CBCT), there is an opportunity to thoroughly examine the boundaries of these lesions and quantify the grayscale of CBCT images, known as the grayscale value (GSV). This study investigated the reliability of CBCT GSV in distinguishing between RC and OKC.

Materials and Methods: A total of 60 specimens with confirmed pathological diagnoses of RC and OKC were meticulously selected. Before surgical biopsy of each lesion, CBCT images were obtained and analyzed using Romexis version 2.9.2 software to compute the mean GSV of each lesion. Statistical analysis was then conducted using SPSS version 1.0.0.1406, and a linear, backward regression model was used to analyze the differences in GSV between lesion categories (alpha=0.05).

Results: Upon extracting the mean GSV of the selected sections of each type of lesion, no statistically significant difference was observed between the mean GSVs of the two lesion categories (P>0.05).

Conclusion: The present findings regarding lack of a significant difference in the mean GSV between RC and OKC were substantial, and suggest that the GSV may not be a reliable index for differentiating these cystic lesions from each other, a conclusion that could potentially impact future diagnostic practices.

Keywords: Cone-Beam Computed Tomography; Jaw Cysts; Odontogenic Cysts; Radicular Cyst

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INTRODUCTION

Odontogenic cysts constitute a group of intrabony cavities characterized by an odontogenic epithelium originating from the tooth-forming apparatus. The lumen of these cysts may contain an accumulation of air, fluid, and viscous or caseous material. Odontogenic cysts are broadly categorized into developmental and inflammatory types [1]. Among these, odontogenic keratocysts (OKCs) represent a distinct type of developmental cysts, comprising approximately 10% of all jaw cysts, with a notable preference for the posterior region of the mandible. Microscopically, OKCs exhibit a uniformly thin keratinized epithelium, typically measuring six to eight cells thick, with minimal reddish ridges discernible. The luminal surface shows wavy, refractile, flattened, parakeratotic epithelial cells, with palisade-like arrangements of cuboidal or cylindrical cells in the underlying basal cell layer. Keratinous and viscous deposits may fill the lumen.

Unlike other odontogenic cysts, OKCs display

a high propensity for recurrence, potentially attributed to the presence of small daughter cysts or residual epithelial fragments following surgical excision. These satellite cysts and islands of odontogenic epithelium are frequently observed in patients diagnosed with nevoid basal cell carcinoma syndrome [2,3]. Radiographically, OKCs manifest as well-defined unilocular or multilocular radiolucencies, often demonstrating a propensity to invade bone without significant expansion [2-4].

Radicular cyst (RC) is the most prevalent odontogenic cyst of the jaws. RCs originate from the hydropic degeneration of the epithelial cell rests of Malassez following stimulation of non-vital teeth, and develop in the periapical region; thus, they are classified as inflammatory odontogenic cysts. RCs present as pathological cavities lined with non-keratinized, stratified squamous epithelium. The cyst wall's connective tissue exhibits varying degrees of infiltration of inflammatory cells, and features small blood vessels [3,5,6]. Radiographically, RCs typically manifest as well-defined, round radiolucencies adjacent to the apex of an untreated tooth with a non-vital pulp [5,6]. Clinical examinations, such as vitality tests and radiographic evaluations, are pivotal in achieving precise diagnosis and implementing appropriate treatment strategies. Notably, RCs were not included in the roster of odontogenic cystic lesions of the maxilla in the latest classification of the World Health Organization released in 2017. However, as the most prevalent maxillary cysts, they have consistently attracted the attention of oral and maxillofacial pathologists and surgeons [7]. As previously mentioned, OKC and RC often exhibit similar imaging characteristics but necessitate distinct treatment modalities. Therefore, additional imaging details are imperative to accurately assess lesion characteristics. Techniques such as computed tomography (CT) or cone-beam computed tomography (CBCT) can provide valuable insights into the extent of lesion, its relationship with the surrounding tissues, and internal structure. In cases of diagnosing OKC with an increased propensity for recurrence, surgeons may consider peripheral osteotomy of the bony cavity using a bone drill as a necessary step to diminish the likelihood of recurrence [3].

Furthermore, both CT and CBCT enable the evaluation of gray levels, providing insights into the primary features of the lesion. Gray values are quantified by the Hounsfield units (HUs) in CT scans and grayscale values (GSVs) in CBCT, reflecting the X-ray attenuation coefficient and internal density of structures [8,9]. Radiologists can discern tissue types and lesion densities by measuring the HUs and GSVs, enhancing diagnostic accuracy [9,10]. While histopathological examination remains the gold standard for identifying lesion types, using CBCT for lesion detection is increasingly prevalent considering characteristics such as periphery, location, and internal structures depicted on images. This modality represents a less invasive diagnostic approach than surgical biopsy [11].

The advantages of CBCT over CT include reduced radiation exposure, shorter image acquisition time, cost-effectiveness, and submillimeter resolution [12-14]. In a previous study, the utility of HUs in differentiating odontogenic cysts was explored, yielding satisfactory results [9]. Additionally, numerous investigations have demonstrated a linear correlation between the HU of CT scans and GSV of CBCT, suggesting that CBCT voxel values can approximate bone density [15]. Considering the absence of similar research in this domain, and the abundance of studies focusing on distinguishing between cysts and granulomas despite the high prevalence of developmental cysts [16,17], this study aimed to investigate this differentiation using CBCT imaging and GSV. Thus, this study sought to evaluate the diagnostic accuracy of GSV of CBCT in distinguishing between RC and OKC.

MATERIALS AND METHODS

This retrospective study involved the review of patient records of 60 individuals, consisting of 30 patients diagnosed with RCs and 30 with OKCs. The diagnoses were confirmed through

pathology reports obtained from the Department of Pathology, Faculty of Dentistry, Tehran University of Medical Sciences from June 2022 to May 2023, ensuring a reliable diagnostic foundation for the comparative analysis. Ethical approval for the study was granted by the Ethics Committee of Tehran University of Medical Sciences (approval number IR.TUMS.DENTISTRY.REC.1401.053).

The sample size was determined using the one-way ANOVA power analysis feature of PASS 11. To ensure statistical robustness, a significance level (α) of 0.05 and a desired statistical power (β) of 0.2 were carefully selected to mitigate the risks of type I and type II errors. Moreover, a mean standard deviation of 11.2 and an effect size of 0.33 were considered to estimate the magnitude of observed differences. This rigorous analysis led to a sample size of 30 patients for each group.

To ensure the primary nature of the lesions, patients diagnosed with inflamed odontogenic cysts and those with previous pathological lesions at the same site were excluded from the study. Additionally, cases lacking complete demographic information, displaying artifacts on CBCT images—such as motion artifacts, beam hardening, scatter, and cupping artifacts or metal streaks—that could interfere with accurate grayscale measurements, or featuring lesions smaller than 10mm were not included.

Confirmation of diagnosis as either RC or OKC was based on the pathology reports of the examined patients, ensuring the completeness of their pathological records. The CBCT images were obtained using the WhiteFox CBCT scanner (Acteon, Paris, France) with the following parameters: 105kVp, 8mAs, full-arch mode, 150×130mm field of view, and 0.25mm voxel size. Axial slices corresponding to the lesions were retrieved from the radiology department archives of the enrolled patients. The evaluation was performed by an oral and maxillofacial pathologist who was blinded to the original reports and re-examined all specimens to confirm the definitive diagnosis.

To determine the gray scale value (GSV) of the CBCT images in the axial slice at the lesion's center (approximately 1–2mm from the lesion borders), two oral and maxillofacial radiologists independently analyzed the images using Romexis software, version 2.9.2 (Planmeca, Helsinki, Finland). Within each lesion, they delineated 3–5 spherical regions of interest (ROI) with a volume of 10mm^3, and the software automatically calculated the GSV of each ROI. Measurements were obtained from multiple axial slices as described, and the mean GSV values were recorded. Both radiologists were blinded to the patients' final histopathological diagnoses (Fig. 1). Intra- and inter-examiner reliability were assessed using intraclass correlation coefficients (ICC), which demonstrated excellent agreement (ICC>0.90) for all measurements.

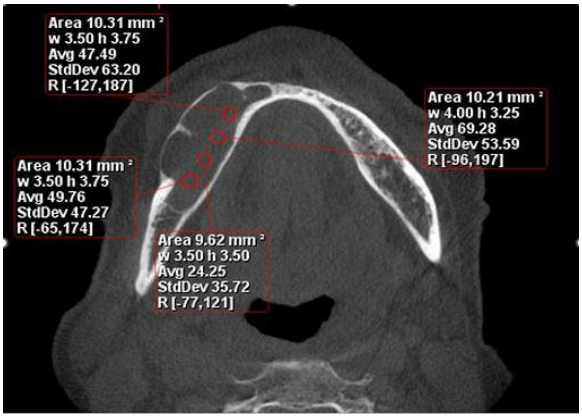

Fig 1. An illustration of the methodology for calculating the mean grayscale value (GSV) in the cases

Subsequently, the collected data were analyzed using SPSS software, version 26.0 (IBM Corp., Armonk, NY, USA), employing a linear backward regression model. The Pearson's Chi-square test was applied to evaluate associations between lesion characteristics and the categorical variables of age and gender. A p-value of <0.05 was considered statistically significant. The statistical consultant remained blinded to the definitive histopathological diagnoses, ensuring a double-blind design throughout the analytical process [9,18].

RESULTS

In this study, 60% of the RC cases were observed in males, and 40% in females. Similarly, of the OKC cases, 53.33% were in

males and 46.66% were in females. In general, 56.66% of the cases were males, and 43.33% were females. The Pearson's Chi-square test showed no statistically significant difference between males and females in the prevalence of lesions (P=0.845).

The mean age of patients with RC and OKC was 43.00±11.26 years and 56.32±14.18 years, respectively, while the mean GSVs were 118.81±35.42 for RC and 82.35±28.67 for OKC. Statistical analysis revealed no significant difference between RC and OKC regarding either the mean age of patients (P=0.163) or the mean GSV (P=0.205). To further evaluate the potential confounding effects of age and sex on GSV, a linear backward regression model was applied. The analysis demonstrated no significant confounding effect of these factors on GSV (P>0.05).

Gender (P=0.872), age (P=0.355), and GSV (0.205) did not exhibit a statistically significant association with lesion type. It is noteworthy that for the GSV, the P value was computed similarly, regardless of whether or not the regression model was employed, indicating consistency in the results regardless of the consideration of confounding factors.

DISCUSSION

The current findings suggested that the GSV alone cannot serve as a definitive parameter for distinguishing between OKC and RC, corroborating the results of a prior investigation [11]. Nasim et al. [19] conducted a study on 60 patients, using both 2D and 3D imaging to measure GSV at the epicenter of each lesion. They examined cystic and solid lesions, using radiological criteria like location, shape, and internal structure, followed by the GSV measurements. They concluded that GSV effectively differentiated cystic lesions such as RC and OKC from solid tumors, suggesting that GSV could be a reliable diagnostic tool without requiring biopsy or histopathological analysis. The difference in the results of Nasim et al, [19] and the current study may stem from variations in methodology and the diverse nature of the lesions (tumorous) under investigation. In contrast, AlMadi et al. [11] examined 57 patients and reported that the GSV index lacked diagnostic efficacy, aligning with the current findings. Notably, their study solely focused on peri-radicular lesions.

De Rosa et al. [20] investigated the usability of the gray spectrum between white and absolute black in CBCT images. In their study, 25 lesions were examined; of which, 14 were RCs and 11 were granulomas. They suggested that this method could be used as an auxiliary method for the differential diagnosis of these two lesions. The difference between their results and the current findings is due to differences in sample size and CBCT scanners. Also, they examined only two peri-radicular inflammatory lesions.

Simon et al. [16] undertook a study to distinguish between 17 large RCs and giant granulomas using the GSV index. Their investigation yielded 13 accurate diagnoses, with four misdiagnoses attributed to errors in the pathology diagnosis or small biopsy specimens. Consequently, they concluded that this non-invasive diagnostic approach was reliable. The current study's sample size exceeded that of Simon et al, [16] by more than three times, which not only enhances the statistical power of analysis but also increases the robustness of the present conclusion regarding poor diagnostic accuracy of the GSV in differentiating between RC and OKC.

Guo et al. [17] investigated the diagnostic accuracy of CBCT for distinguishing between RC and granulomas using six indicators: location, extent, shape, internal structure, and impact on surrounding structures. They determined that four indicators demonstrated relatively good accuracy and were thus considered the gold standard for diagnosis. The study encompassed 36 periapical lesions, representing a smaller sample size than the present study. Given the findings of Simon et al, [16] it was deemed appropriate to explore these proposed six indicators in GSV analyses.

Kruse et al. [21] conducted a systematic review on the diagnosis of RC and granulomas. Their study included articles evaluating the use of CBCT in diagnosing periapical lesions published from 2000 to 2013, totaling 25 articles. The study's conclusion suggested that

the routine use of CBCT as a diagnostic imaging modality lacks justification compared to conventional radiography. However, it is noteworthy that among these 25 articles, only 4 utilized histopathological analysis as the gold standard for diagnosis, which is essential for accurately diagnosing these lesions. Additionally, only one of these articles incorporated GSV as a diagnostic factor to differentiate periapical lesions. Therefore, despite the systematic nature of the review, its findings should be interpreted cautiously.

A study by Etoez et al. [22] shared similarities with an earlier investigation by Guo and colleagues [17]. Their study aimed to differentiate between RC and periapical granulomas. They used GSV along with anatomical indices. Their findings underscored the optimal efficacy of anatomical indices in accurately discerning between the two lesion types. However, the results also revealed that GSV did not serve as a reliable indicator for distinguishing between these specific lesions, corroborating the present findings.

Uehara et al. [9] conducted an evaluation utilizing ready-to-use HU derived from CT scans to differentiate among RCs, dentigerous cysts, and OKCs. Their study had a relatively large sample size of 164 lesions, including 64 RCs, 57 dentigerous cysts, and 43 OKCs, representing a notable strength. They concluded that the HU index can effectively distinguish OKC from the other two types of cysts. Conversely, the current study used the GSV index derived from CBCT imaging, and revealed no statistically significant difference in GSV between OKC and RC. It is important to note that previous research has demonstrated a strong correlation between HU and GSV [15,23].

Wang et al. [24] conducted a study to distinguish between OKC and ortho-keratinized odontogenic cystic lesions utilizing CBCT images and various indicators including lesion location, lesion size, cortical bone destruction, presence of an impacted tooth, root resorption, and displacement. They evaluated 36 OKCs and 12 ortho-keratinized odontogenic cystic lesions. Following statistical analysis of the results, they identified a statistically significant difference between these two lesions using the abovementioned indicators. Despite the radiographic similarities in the appearance of these lesions, with ortho-keratinized odontogenic cystic lesions often presenting as a unilocular (single compartment) lesion and OKC seldom causing root displacement, they did not incorporate the GSV index for distinguishing between them.

Yalçin et al. [25] investigated three types of lesions, namely RCs, OKCs, and dentigerous cysts, utilizing CT and magnetic resonance imaging to discern between them and establish distinct diagnoses. Given the popularity of CBCT in dentistry, the researchers also examined CBCT images of these lesions. The study encompassed 17 lesions, including 3 cases of RCs, 9 cases of OKCs, and 5 cases of dentigerous cysts. Factors evaluated included the reaction of surrounding bone, presence of edema or air around the lesions, presence of impacted teeth, location of the lesion, and its shape. However, it is noteworthy that this study had a smaller sample size than the present investigation, constituting a limitation. Nonetheless, the findings suggested that CT and magnetic resonance imaging, in conjunction with conventional radiographs, may aid pathologists and surgeons in arriving at a more definitive diagnosis. It is essential to mention that this study did not explore CBCT imaging or factors such as HU and GSV.

The present study has several limitations that should be acknowledged. First, the retrospective design inherently limited control over image acquisition parameters and lesion selection, which may have introduced selection bias. Second, the study was conducted in a single institution, which may restrict the generalizability of the findings. Additionally, only two lesion types—RC and OKC—were analyzed; inclusion of other odontogenic cysts or tumors might provide a more comprehensive assessment of the diagnostic utility of GSV. Future studies with multicenter collaboration and standardized imaging protocols are recommended to validate these results and

further clarify the diagnostic potential of CBCT-derived GSV in differentiating odontogenic lesions.

CONCLUSION

Upon examining the statistical analysis of the GSVs, it became evident that relying solely on this index may not differentiate between RC and OKC. While GSV offers valuable insights and aids in understanding the radiographic characteristics of the lesions, it should not serve as the sole basis for arriving at a definitive diagnosis. Histopathologic analysis remains the gold standard for diagnosing these lesions. Therefore, although GSV contributes valuable data to the diagnostic process, it is imperative to complement its findings with histopathologic examination. Combining GSV with histopathological findings may enhance the diagnostic accuracy, enabling physicians to make well-informed patient management and treatment planning decisions. A holistic approach is recommended to integrate radiographic imaging and histopathological assessments for a comprehensive and reliable diagnosis, enhancing patient care.

CONFLICT OF INTEREST STATEMENT

None declared.

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