



The influence of anatomical location on the accuracy of tonsillolith diagnosis on panoramic radiographs

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ABSTRACT. This study aimed to analyze the influence of anatomical location regarding the accuracy of the diagnosis of tonsilloliths on panoramic radiographs. Of 2022 digital panoramic radiographs analyzed, 181 presented tonsilloliths. The images were reevaluated and classified according to six anatomical regions. The findings were related to gender and age. Variables were tested using the Chi-square test. The Receiver Operational Characteristic Curve (ROC) evaluated the performance in identifying the region that presented tonsilloliths. The Kappa test was used for intra and inter-examiner agreement ($p < 0.05$). Of the 181 patients (8.95%) with tonsilloliths, 104 (57.46%) were male ($p < 0.05$). The most prevalent age group was ≥ 49 years ($p < 0.05$). Unilateral/bilateral ratio was 2.5:1. The Kappa values for intra and inter-examiner showed substantial to almost perfect scores. The most common location of the tonsilloliths was the mandible ramus, superimposed on the soft palate ($p < 0.05$), presenting the largest area under the curve (AUC) and the greatest accuracy (AUC= 0.70; 0.66) as well. Likewise, this location and the location postero-inferior to the mandible angle showed greater sensitivity and specificity. In the panoramic radiographs image, tonsilloliths are most often superimposed on the mandible ramus, with greater accuracy and sensitivity for its detection.

Keywords: panoramic radiography; diagnosis; prevalence; sensitivity and specificity.

Received on November 4, 2022.
Accepted on September 29, 2023.

Introduction

Tonsilloliths are the most common soft tissue dystrophic calcifications in the maxillofacial region (Garay, Netto, & Olate, 2014; Missias et al., 2017; Takahashi et al., 2017; Icoz & Akgunlu, 2019). They are calcified masses that develop within the tonsils and other soft tissues of the pharyngeal airspace (Lo, Chang, & Chu, 2011; Nasseh, Sokhn, Noujeim, & Aoun, 2016; Aoun, Nasseh, Diab, & Bacho, 2018). They are caused by depositions of inorganic salts (Moura et al., 2007; Ghabanchi, Haghnegahdar, Khojastehpour, & Ebrahimi, 2015), calcium phosphate, carbonated calcium, magnesium (Cooper, Steinberg, Lastra, & Antopol, 1983; Caldas et al., 2007; Bangi, Tejaswi, Avinash, & Chittaranjan, 2013; Oliveira, Amaral, Abdo, & Mesquita, 2013; Bamgbose, Ruprecht, Hellstein, Timmons, & Qian, 2014), hydroxyapatite, oxalate and ammonium radicals (Ghabanchi et al., 2015), and are also associated with accumulation of necrotic material and bacterial and fungal growth (Bangi et al., 2013; Oda et al., 2013; Bamgbose et al., 2014).

Although dysphagia, halitosis, swelling, pain, foreign body sensation, dyspnea, otalgia and enlarged cervical glands may be reported (Mesolella et al., 2004; Caldas et al., 2007; Lo et al., 2011; Bangi et al., 2013; Bamgbose et al., 2014; Lincot et al., 2016), patients are usually asymptomatic (Aoun et al., 2018), and those calcifications are classified as incidental findings in imaging exams, mainly on panoramic radiographs (PR) (Oda et al., 2013; Aoun et al., 2018).

On PR, tonsilloliths can be single or multiple, unilateral or bilateral, and generally small (Bangi et al., 2013; Aoun et al., 2018), with an average size of 5 mm (Oliveira et al., 2013). Due to the angulation of the X-ray beam projection, the images are usually presented as small radiopaque structures superimposed, below or near to the mandible ramus (Bangi et al., 2013; Nasseh et al., 2016; Aoun et al., 2018). The differential diagnosis includes other calcified pathologies in this region, such as sialoliths and phlebolith (Takahashi et al., 2017).

The position of tonsilloliths in imaging exams, especially in PR, can vary, interfering with the diagnosis. Therefore, the aim of this study was to analyze the influence of anatomical location on the accuracy of detecting tonsilloliths in PR. The null hypothesis was that there is no statistically significant difference for the accuracy in detecting these calcifications in PR at different regions.

Material and methods

Image acquisition and sample selection

After ethics approval (CAAE: 30365520.6.0000.0104), this retrospective cross-sectional study was developed according to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) initiative (Elm et al., 2014) and followed the principles of the STARD (Standards for Reporting Diagnostic Accuracy Studies) (www.stard-statement.org). It was carried out according to the standards described in the Declaration of Helsinki.

Tonsilloliths were investigated in a total of 2022 RPs from a Brazilian population (863 males and 1159 female, aged between 18 and 90 years), belonging to the image sample of a Dental Radiology and Imaging Clinic, from January 2018 to July 2019. All images were acquired on the Orthopantomograph® OP300 device (Instrumentarium Dental, Tuusula, Finland) with a standardized protocol (tube voltage of 57 - 90 kV, maximum tube current of 16 mA, and exposure time of 16.1 seconds). All exams were performed with the patients positioned with the head stabilized, so that the median sagittal plane was perpendicular to the horizontal plane and the Frankfurt horizontal plane was parallel to the ground. Images of patients under 18 years old, with history of facial trauma, congenital craniofacial syndromes, pathologies in the maxillofacial region and images containing artifacts in the region of interest were excluded.

All images were exported in TIFF format and analyzed using JPEG View 1.0.35.1 software (public domain software). The imaging diagnosis of tonsilloliths was consensually performed by two experienced specialists (over 20 years) in Oral and Maxillofacial Radiology, if there was no consensus, the PR was discarded. They also divided the sample according to gender and age groups (18-32 years; 33-48 years; \geq 49 years).

Image preparation and analysis

Subsequently, the 181 selected images were evaluated by five examiners (postgraduate students, with experience ranging from 2 to 5 years in Oral and Maxillofacial Radiology), who underwent calibration and training. The calibration consisted of the theoretical presentation of the aim of the study, accomplished by two responsible researchers, who instructed and established criteria for the detection of tonsilloliths according to laterality (right/left or bilateral) and anatomical location (Takahashi et al., 2017). For training, the five examiners performed 15 evaluations in the presence of the responsible researchers. At that point, the examiners were able to ask questions. These initial assessments were discarded.

The locations of the tonsilloliths on the PR were classified according to Takahashi et al. (2017) into two categories – (1) superimposed on the ramus of the mandible or (2) calcifications superimposed on the soft tissue, and into six regions – category 1: superior to the soft palate (region 1); coincident with the soft palate (region 2); inferior to the soft palate (region 3); category 2: inferior to the body of the mandible (region 4); postero-inferior to the angle of the mandible (region 5); and posterior to the ramus of the mandible (region 6) (Figure 1 and 2). If multiple tonsilloliths were detected in two or more regions, each region was classified individually.

The analysis was performed on a high-resolution screen in a quiet room, with subdued light, individually and at different times. A maximum of 30 evaluations were carried out per day. Software brightness and contrast tools could be used, as well as imaging zoom. The evaluations were performed using a 5-point diagnostic scale, with the options (1) absent, (2) probably absent, (3) uncertain, (4) probably present and (5) present. After 15 days, 30% of the sample was reevaluated under the same conditions, to assess intra-examiner agreement.

Statistical analysis

The Kappa test was used to assess intra and inter-examiner agreement. To assess the prevalence of tonsilloliths regarding location, gender and age groups, the Chi-Square test was used. To compare the diagnostic capacity of the examiners, from 5-point scale the Receiver Operational Characteristic Curve (ROC) was used. The significance level was set at $p < 0.05$. Statistical analyzes were performed using software R version 3.6.2 (R., Auckland, NZL).

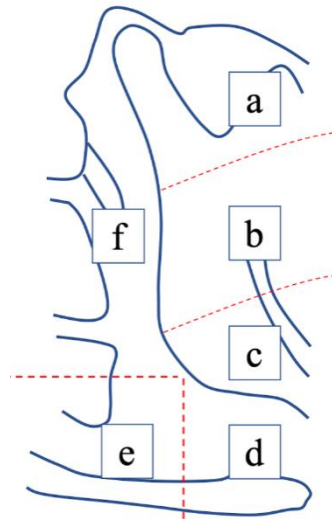


Figure 1. Illustration of the PR regions' division according to Takahashi et al. (2017). Category 1: superimposed on the ramus of the mandible – (a) Region 1: superior to the soft palate; (b) Region 2: coincident with the soft palate; (c) Region 3: inferior to the soft palate. Category 2: calcifications superimposed on the soft tissue – (d) Region 4: inferior to the body of the mandible; (e) Region 5: postero-inferior to the angle of the mandible; (f) Region 6: posterior to the ramus of the mandible.

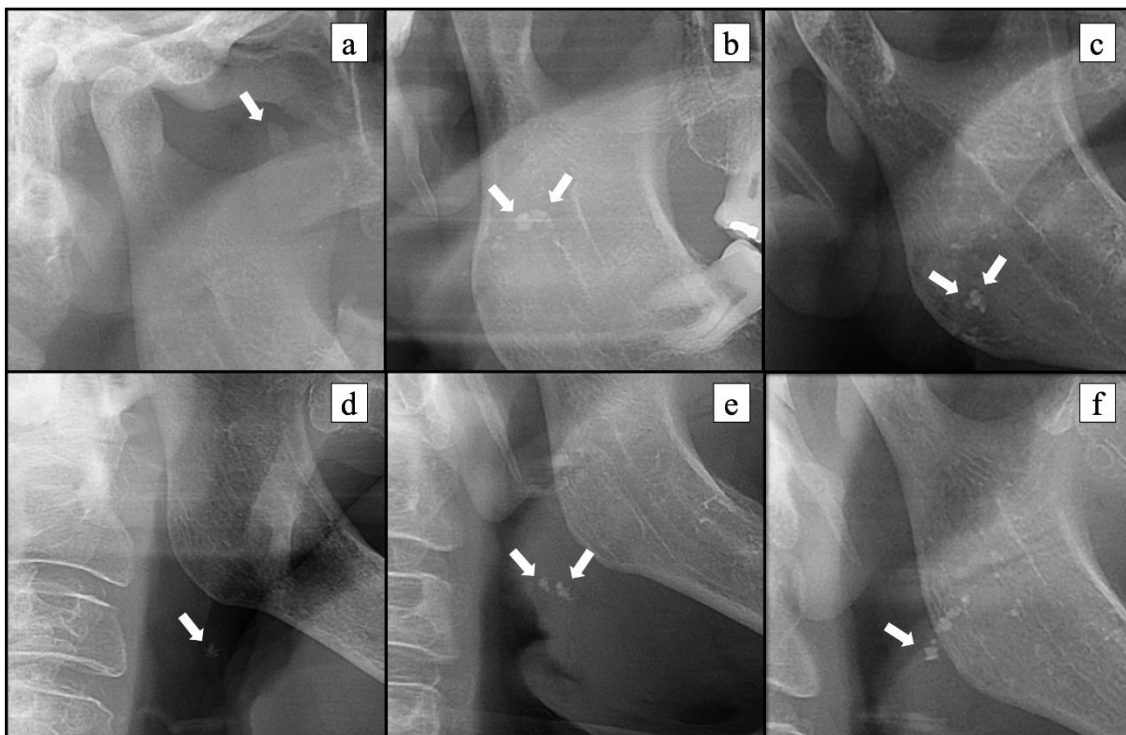


Figure 2. Panoramic radiographs showing the presence of tonsilloliths (white arrow) according to the regions (Takahashi et al., 2017): (a) Region 1; (b) Region 2; (c) Region 3; (d) Region 4; (e) Region 5; (f) Region 6.

Results

Of the 181 patients (8.95% of the total 2022) who had tonsilloliths, 77 (42.54%) were female and 104 (57.46%) were male. The mean age was 58.46 ± 14.40 years. Intra-examiner Kappa values showed scores ranging from substantial to almost perfect (0.61-0.99) and inter-examiner values with almost perfect scores (0.78-0.97) (Landis & Koch, 1977). The prevalence of tonsilloliths *per* region regarding gender and laterality showed significant differences ($p < 0.05$), with men being more affected (57.46%; $p < 0.05$). The unilateral/bilateral ratio was 2.5:1 ($p < 0.05$), but without differences between the right and left sides. There was a higher prevalence of calcifications in region 2 in both genders (Table 1). Concerning the prevalence of tonsilloliths *per* region regarding age, there were significant differences ($p < 0.05$), with a higher prevalence in patients ≥ 49 years. Once again, there was a higher prevalence of calcifications in region 2 in all age groups (Table 2).

Table 1. Prevalence of tonsilloliths per region according to gender.

Sex	Region	Tonsillolith Prevalence				
		Right Side		Left Side		Bilateral Presence
		Presence	p-value	Presence	p-value	
Men (n = 104)	Region 1	1 (1%)		0 (0%)		
	Region 2	41 (39%)		43 (41%)		
	Region 3	14 (13%)	<0.05*1	8 (8%)	< 0.05*1	29 (28%)
	Region 4	4 (4%)		9 (9%)		
	Region 5	17 (16%)		20 (19%)		
	Region 6	16 (15%)		13 (12%)		
Women (n = 77)	Region 1	0 (0%)		1 (1%)		
	Region 2	31 (40%)		27 (35%)		
	Region 3	5 (6%)	<0.05*1	6 (8%)	< 0.05*1	22 (29%)
	Region 4	4 (5%)		8 (10%)		
	Region 5	12 (16%)		11 (14%)		
	Region 6	11 (14%)		12 (16%)		

*p-value considered significant if < 0.05; 1Chi-square test.

Table 2. Prevalence of tonsilloliths per region according to age.

Age Groups	Region	Tonsillolith Prevalence				
		Right Side		Left Side		Bilateral Presence
		Presence	p-value	Presence	p-value	
18-32 (n = 12)	Region 1	0 (0%)		0 (0%)		
	Region 2	4 (33%)		5 (42%)		
	Region 3	0 (0%)	< 0.05*1	1 (8%)	< 0.05*1	1 (8%)
	Region 4	0 (0%)		0 (0%)		
	Region 5	0 (0%)		1 (8%)		
	Region 6	2 (17%)		2 (17%)		
33-48 (n = 25)	Region 1	0 (0%)		1 (4%)		
	Region 2	11 (44%)		7 (28%)		
	Region 3	2 (8%)	< 0.05*1	2 (8%)	< 0.05*1	4 (16%)
	Region 4	0 (0%)		2 (8%)		
	Region 5	1 (4%)		2 (8%)		
	Region 6	7 (28%)		3 (12%)		
≥ 49 (n = 144)	Region 1	1 (1%)		0 (0%)		
	Region 2	57 (40%)		58 (41%)		
	Region 3	17 (12%)	<0.05*1	11 (8%)	< 0.05*1	46 (32%)
	Region 4	8 (6%)		15 (10%)		
	Region 5	28 (19%)		28 (19%)		
	Region 6	18 (13%)		20 (14%)		

*p-value considered significant if < 0.05; 1Chi-square test.

For accuracy, only region 2 showed values above 70%. Regarding sensitivity, regions 2 and 5 showed values above 80%, and in relation to specificity, region 5 showed values above 70%. Table 3 shows the values of accuracy, sensitivity, specificity and AUC for all regions.

Table 3. Values of accuracy, sensitivity, specificity, and areas under the curve (AUC) per region.

Region	1		2		3		4		5		6	
	Right Side	Left Side	Right Side	Left Side	Right Side	Left Side	Right Side	Left Side	Right Side	Left Side	Right Side	Left Side
Accuracy(%)	0.55 ±0.04 (0.52-0.61)	0.56 ±0.04 (0.51-0.62)	0.72 ±0.03 (0.68-0.76)	0.71 ±0.03 (0.68-0.78)	0.59 ±0.04 (0.52-0.64)	0.54 ±0.04 (0.50-0.60)	0.57 ±0.02 (0.54-0.60)	0.63 ±0.06 (0.56-0.74)	0.58 ±0.07 (0.51-0.67)	0.55 ±0.04 (0.50-0.60)	0.58 ±0.05 (0.53-0.68)	0.59 ±0.07 (0.52-0.69)
Sensitivity (%)	0.59	0.74	0.80	0.91	0.63	0.64	0.37	0.33	0.82	0.83	0.53	0.70
Specificity (%)	0.42	0.60	0.49	0.42	0.42	0.50	0.18	0.25	0.72	0.72	0.38	0.59
AUC	0.57 (0.44-0.69)	0.53 (0.43-0.62)	0.70 (0.54-0.77)	0.66 (0.56-0.84)	0.56 (0.43-0.69)	0.52 (0.44-0.61)	0.51 (0.29-0.73)	0.51 (0.39-0.62)	0.50 (0.39-0.61)	0.51 (0.42-0.61)	0.55 (0.46-0.63)	0.52 (0.43-0.61)

Figure 3 illustrates the ROC curve of the joint performance of the examiners for each region. The ROC curve and the AUC showed high accuracy for region 2 for the right (AUC, 0.70) and left (AUC, 0.66) sides (Figure 3b).

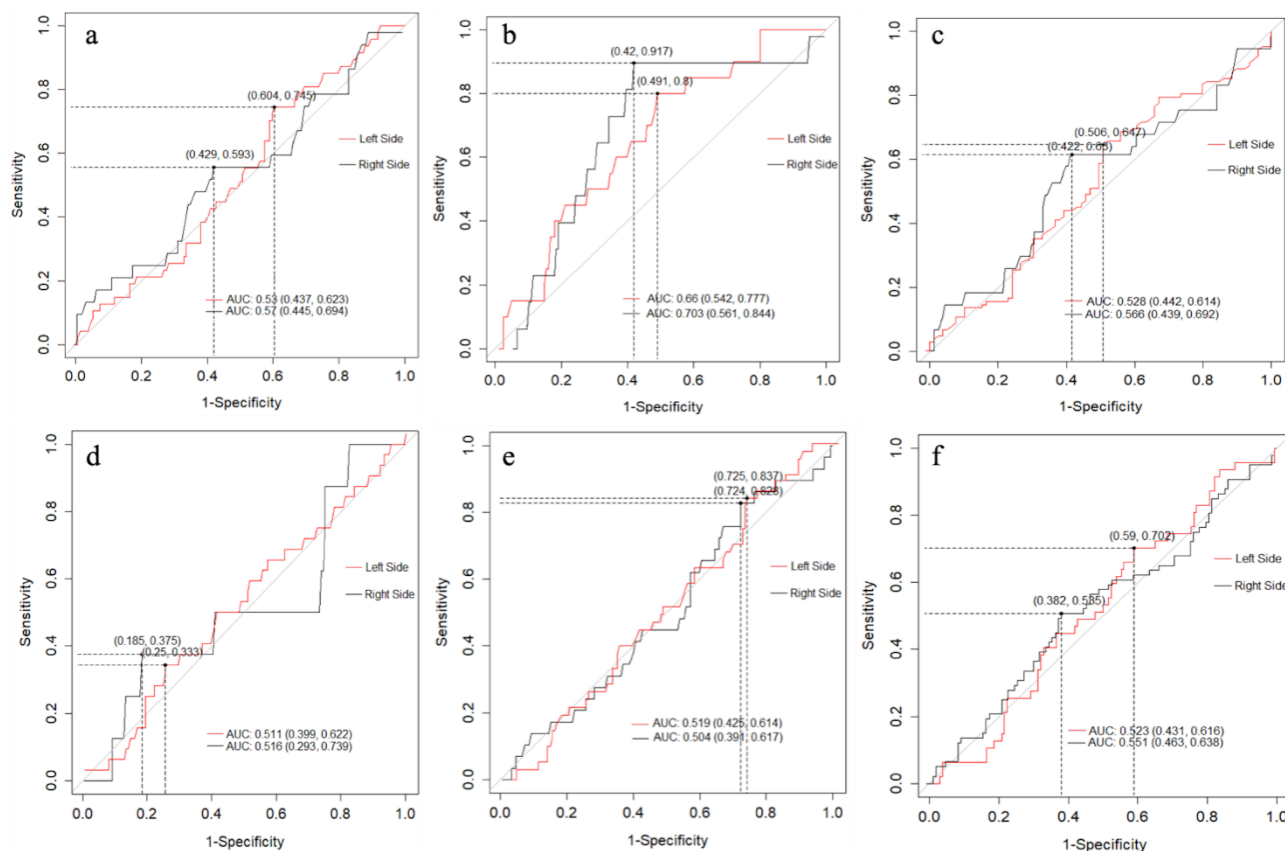


Figure 3. ROC curve according to the joint performance of the examiners for all regions considering the right and left sides, expressed by the colors black and red, respectively. (a) Region 1; (b) Region 2; (c) Region 3; (d) Region 4; (e) Region 5; (f) Region 6.

Discussion

The main objective of the study was to evaluate the influence of the anatomical location of tonsilloliths on the accuracy of diagnosis in PR. Calcifications in soft tissues of the head and neck region are generally common and are usually detected in imaging exams ordered for several dental purposes (Aoun et al., 2018). It is well known that the shape, number, distribution and location are fundamental to outline the diagnosis (Thomas, 1974; Garay et al., 2014). In PR, tonsilloliths appear as radiopaque structures, in oval, rounded or ill-defined shapes, single or multiple, superimposed or close to the ramus of the mandible (Bangi et al., 2013; Aoun et al., 2018).

The present study, conducted in an adult Brazilian population and using digital PR, showed a prevalence of tonsilloliths of 8.95%. Similar values were found by Aoun et al. (2018) (7.2%), Bamgbose et al. (2014) (8.14%), Oda et al. (2013) (7.3%) and Takahashi et al. (2017) (13.4%). On the other hand, the prevalence of tonsilloliths in 3D imaging is significantly higher, ranging from 16% to 46% (Fauroux, Mas, Tramini, & Torres, 2013; Takahashi et al., 2017; Kim et al., 2018; Ozdede, Akay, Karadag, & Peker, 2020) in computed tomography (CT) and in 5 to 34% (Price, Thaw, Tyndall, Ludlow, & Padilla, 2012; Moshfeghi, Navabi, Soltani, & Moaddabi, 2017; Ozdede et al., 2020) cone-beam computed tomography (CBCT). Besides the difference in the type of image exams, an explanation for this range in prevalence may be due to the population studied (Takahashi et al., 2017).

We found a predominance of tonsilloliths in men (57.46%), corroborating other studies (50.9% -60.4%) (Ghabanchi et al., 2015; Takahashi et al., 2017; Sutter et al., 2018;). On the other hand, some authors report that there is no significant difference between genders (Fauroux et al., 2013; Oda et al., 2013; Aoun et al., 2018). In our study, for both genders, region 2 showed a higher prevalence of these calcifications ($p < 0.05$).

In relation to laterality, the unilateral/bilateral ratio was 2.5: 1 ($p < 0.05$), a value very close to that showed in the literature (Aghdasi, Valizadeh, Amin-Tavakoli, & Bakhshandeh, 2012; Oda et al., 2013; Bamgbose et

al., 2014; Ghabanchi et al., 2015; Takahashi et al., 2017; Ozdede et al., 2020). There was no predilection for right or left side, corroborating previous studies (Oda et al., 2013; Takahashi et al., 2017).

Tonsilloliths can be seen at any age (Ozdede et al., 2020); however, the highest incidence is among 40 and 50 years of age (Özcan, Ural, Öktemer, & Alpaslan, 2006; Oda et al., 2013; Garay et al., 2014; Takahashi et al., 2017; Sutter et al., 2018; Ozdede et al., 2020). In our study, most calcifications were found in patients with a mean age of 58.46 (\pm 14.40) years, with a higher prevalence in patients \geq 49 years. Over the years, the human body is several times subjected to inflammatory processes in response to injury or infection. When these processes occur frequently, they can cause irreversible local changes, such as crypts in the tonsils, which becomes larger and deeper, favoring the accumulation of inorganic material and consequently the formation of tonsilloliths (Caldas et al., 2007; Bangi et al., 2013; Ghabanchi et al., 2015; Icoz & Akgunlu, 2019). The presence of persistent chronic inflammation in older patients, smoking and poor oral hygiene have also been linked to tonsillolith formation (Takahashi et al., 2017). In all age groups, region 2 was also the most affected.

The present study is the first to assess the accuracy in detecting tonsilloliths according to the location (Takahashi et al., 2017) on PR. Region 2, that coincides with the soft palate (Figure 1), showed an AUC significantly higher than the other regions, corroborating Takahashi et al. (2017). In addition to the prevalence in region 2 being higher, the examiners' diagnostic capability for this region was also superior. Calcifications superimposed on the ramus of the mandible (region 2) are easier to identify (Oda et al., 2013; Bamgbose et al., 2014;). Although the prevalence in this region is consolidated, our study evaluated the diagnostic capacity and, in this context, the other regions did not present similar ROC curve values. We assume that, even with experience in Oral and Maxillofacial Radiology, the examiners may have underestimated the presence of tonsilloliths in other regions.

Likewise, region 5 (Figure 1), with tonsilloliths overlapping the soft tissue and postero-inferior to the mandible angle, also showed higher sensitivity and specificity values when compared to the other regions (Table 3). Tonsilloliths in this region can be easily identified, as there is no overlap of the hard tissues of the face; however they are less prevalent (Özcan et al., 2006). As in other regions (1, 3, 4 and 6), the lower frequency should not lead to the negligence of these calcifications.

The findings of this investigation refute the null hypothesis, as there existed a statistically significant disparity in the accuracy of tonsillolith detection across various locations in PR. It is imperative to emphasize that the cross-sectional design of this study restricts information regarding the incidence and other behavioral aspects of the condition, which hold clinical significance. Further research endeavors, incorporating sample size calculation and employing CT/CBCT as the gold standard, are warranted to corroborate the true accuracy of bi-dimensional exams to detect these calcifications while ensuring a more representative sample of the population under study. Nevertheless, as the pioneering study assessing the diagnostic capabilities for tonsilloliths in digital PR, this research has furnished additional insights concerning their localization in PR images, thereby offering valuable guidance to clinicians, in order to prevent misdiagnosis during radiographic interpretation.

Conclusion

In the panoramic radiography images, tonsilloliths are most often superimposed on the mandible ramus (Region 2), with greater accuracy and sensitivity for its detection. The authors encourage radiologists and dentists to perform a more detailed assessment of the entire PR and do not underestimate the presence of tonsilloliths in less common regions. Sensibility sensitivity.

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