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PrevALEnce of CALCIFICATIONS in soft tissues VISIBLE on a dental PANTOMOGRAM:

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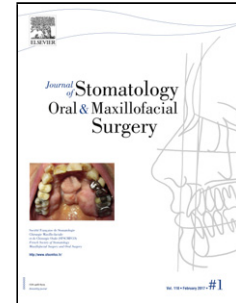
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Title: Prevalence of CALCIFICATIONS in soft tissues
VISIBLE on a Dental PANTOMOGRAM: a retrospective
analysis<!--<RunningTitle>Prevalence of Calcifications in
soft tissues on dental Pantomogram</RunningTitle-->



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TITLE: PREVALENCE OF CALCIFICATIONS IN SOFT TISSUES VISIBLE ON A DENTAL PANTOMOGRAM: A RETROSPECTIVE ANALYSIS

SHORT TITLE: PREVALENCE OF CALCIFICATIONS IN SOFT TISSUES ON DENTAL PANTOMOGRAM

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ABSTRACT

Objectives: To determine the frequency and spectrum of soft tissues calcifications identified on Dental Pantomograms (DPT) at a University Dental Clinic in the northern region of Portugal and to compare the data obtained with those published in the literature.

Methods: We conducted a 3-year descriptive analysis (2012-2014) of DPT calcifications within soft tissues at the University Clinic (CESPU), in Oporto, Portugal. Information on gender, age, location of the lesions and the radiographic diagnosis were analysed. DPTs were interpreted by two examiners (Kappa test 0.8). Data were entered into a database and analysed with Chi-square and Fisher exact tests. Statistical analysis was performed using the Kolmogorov-Smirnov and Shapiro-Wilk test.

Results: 2375 DPTs were analysed, with 468 calcifications observed in the radiographs of 420 individuals. Calcifications of the stylohyoid and stylomandibular ligament were most common, with atheroma, sialoliths, tonsilloliths rhinololiths and antrololiths also identified. A statistically significant relationship was observed between the presence of calcifications of the stylohyoid and stylomandibular ligaments, atheromatous calcifications in the carotid artery and tonsilloliths in individuals older than 40.

Conclusions: This is the largest sample analysis ever done in Portugal, providing useful information about the incidence and distribution of soft tissue calcifications identifiable on DPTs, allowing valuable comparison with other countries.

Advances in knowledge: Despite mostly being incidental findings, panoramic radiography can be the first relevant test that aids dental practitioners in the process of requesting other imaging techniques or forwarding to the correct specialty.

Keywords: soft tissues calcification; heterotopic calcification; panoramic radiograph; carotid artery calcification.

INTRODUCTION

Dental Pantomograms (DPT) are clinically useful for the diagnosis of problems that require extensive visualization of the jaws. They are commonly used as the initial image of an evaluation for allowing adequate visualization or assisting in the indication of other radiological images [1].

Radiographically soft tissue calcifications are present in about 4% of DPTs and usually correspond to radiographic findings in routine examinations [1-5].

The diagnosis of incidental calcified lesions and some diseases in the oral soft tissues can be challenging [6]. It is important that the dentist knows how to identify them properly, as some calcifications be associated with an increased mortality [7]. An understanding of these lesions can therefore facilitate appropriate referral for further investigation if necessary.

A few descriptive studies have attempted to answer this; however, these have small sample sizes, no inter-reliability scores or no set criteria about for the calcifications of the soft tissues [3,4,6,7]. The aim of this study was to determine the spectrum and the frequency of soft tissues calcifications visible on DPTs in a Portuguese University clinic population, comprising patients of all ages and genders and then to compare the results with other studies reported worldwide.

Additionally, we wish to evaluate the occurrence of tonsil stones, salivary gland stones, phleboliths, calcified lymph nodes, stylohyoid ligament, rhinoliths and antroliths and carotid artery calcification using panoramic radiographs.

MATERIALS AND METHODS

We performed a retrospective, descriptive analysis over 3 years (2012-2014) of DPTs at the University Clinic (CESPU), in Oporto, Portugal. Patients from the Oporto community were self-referred, or referred by their general practitioner to the centrally based University clinic.

The study was reviewed and approved by the Institutional Review Board of the University CESPU. The study was performed in full accordance with the World Medical Association Declaration of Helsinki.

Data regarding diagnosis and respective clinical information were retrieved from patient hospital records and transferred into a Microsoft® Excel database. The data were anonymized before analysis. In the analysis, information on gender, age, DPT diagnostic quality grade and diagnosis were included. Exclusion criteria included: non-diagnostic DPTs, sectional DPTs, other type of films and cases with unclear or missing data, or with an inconclusive diagnosis. There was no gender or age restriction.

Prior to analysis, authors reached a consensus on the radiographic appearance of possible findings based on previous studies and relevant literature as described in table 1. DPTs were collected and simultaneously interpreted by two dentally qualified examiners. Comparing the

records of the two examiners, the degree of confidence in the results obtained through the Kappa Test was 0.8 (degree of substantial agreement).

The calcifications were evaluated according to their anatomical location, distribution, quantity and the format. Only obvious calcifications and clear differential diagnoses were considered. In addition, this study utilised digital imaging which allowed the modification of characteristics such as density and contrast, allowing better identification and visualisation of low-density calcifications.

The data collected was subsequently entered and statistically analysed using IBM SPSS Statistics® for Macintosh, version 23.0.0.2 (IBM, New York, USA), for which a significance level of 5 % was adopted as decision criteria. Statistical analysis was performed using the Kolmogorov-Smirnov and Shapiro-Wilk test, where it was verified that the numerical variable "age" did not follow the normal standards (Figure 1). Comparison of proportions were performed using the Chi-Square test in cases where its use was appropriate and Fisher's exact test when the frequencies obtained were very low.

RESULTS

Of a total of 2375 DPTs analysed, 1324 were females (55.7%) and 1051 males (44.3%). The corresponding ages ranged from 3 years to 90 years, with an average age of 38 years (figure 1).

468 calcifications (19.7%) were found in 420 DPTs in the study sample (table 2).

Of the calcifications found, 159 were in individuals under 40 years old (34%), and 309 in individuals over 40 years old (66%) (table 3), thus verifying a significant difference in the presence of calcifications with the increase of age by the Chi-Square test ($p < 0.05$).

Of those who presented with visible calcifications, 273 individuals were female (58.3%), and 195 were male (41.7%) (table 4). There were no significant differences in this variable.

Calcifications found in this study include calcifications of the styloid complex (stylomandibular and stylohyoid ligaments), atheroma of the carotid artery, salivary stones, tonsil stones, antroliths and rhinoliths. The distribution of our findings is demonstrated in table 3.

There were no radio-opacities in the sample which suggested a calcified lymph node or phleboliths.

There was a statistically significant increase in the number of calcifications of the styloid and stylomandibular ligament, carotid artery atheroma and tonsil stones in individuals older than 40 (Table 3). The only significant difference observed between males and females was the presence of tonsil stones. These calcifications were more prevalent in males ($p = 0.03$) (Table 4).

DISCUSSION

This study demonstrates the classic limitations of cross-sectional studies; it is not possible to obtain the entire history of the patient. Additionally, there are a limited number of published articles regarding calcifications to corroborate the findings via panoramic radiography, with a particularly limited amount of literature on the presence of calcified lymph nodes, salivary stones, and phleboliths.

Previous studies showed the prevalence of calcifications within soft tissues identifiable on DPTs between 2.61% and 8% [3,4,6]. In the present study, a higher prevalence of 19.7% was observed (table 2), which may be due to the fact that the DPTs are digitally visualised, with possibility for adjustment of the image density whenever necessary, unlike the study carried out by Monsour et al [4]. In addition, calcification of the carotid artery was not included in the same study.

Calcification of the styloid complex shows great variability in the population [8]. The elongation of the styloid process was considered when it exceeded 30mm from the inferior border of the external acoustic meatus using the digital DPT editing tool [8-13]. In our study, this calcification was the most prevalent, and was encountered in a total of 310 cases (13.1%) (table 3 and 4), differing from other radiographic studies found in the literature, where prevalence rates range from 52.1%, 38.57%, 3.7% [8,13,14]. No relationship was found regarding gender, but there was a

statistically significant relation with increasing age ($p < 0.05$) (table 3). Some studies consider panoramic radiography as the best method of evaluation of this calcification, as it allows the visualisation of both sides simultaneously with its medial angulation [8-10]. More than 50% of patients are clinically asymptomatic [1]. An example of this calcification can be seen in figure 2.

Tonsil stones were observed in 21 radiographs (0.9%) (table 3 and 4), which is lower than that found in Takahashi's study comparing the prevalence of tonsil stones in DPTs and computerized tomography with a prevalence of 13.4% [15]. Our study obtained a prevalence that is closer to that obtained in the Garay study (1.4%) [3]. In addition, there was also a higher prevalence in males and an increase in occurrence in those older than 40 years of age. These differences are statistically significant (tables 2 and 3).

Patients with tonsil stones may be asymptomatic and, they are often chance finding on DPTs (figure 3). When they are symptomatic, patients may display signs and symptoms such as halitosis and odynophagia, foreign body sensation upon swallowing and reflex otalgia [7, 15-18].

Of the soft tissue calcifications, 13 (0.5%) presented as radio-opacities, characteristic of sialolithiasis (table 3 and 4). It has been reported in the literature that sialolithiasis affect 0.01% to 1% of the general population, which is consistent with our results [3]. Garay et al. [3] obtained a higher percentage of salivary stones in females, whereas in our study there were no significant differences observed between genders ($p = 0.890$) (Table 3). In terms of age, there was homogeneity across our data and the Garay et al. [3] study; there were no significant differences between the presence of these calcifications and an increase in age ($p = 0.161$) (table 3).

The submandibular gland is the most affected (83% to 94%), followed by the parotid gland (4% to 10%) [19]. They may rarely appear in the sublingual and minor salivary glands, (1% to 7%), which is probably due to the fact that the submandibular gland duct is longer and more twisted, with ascending flow in its proximal portion, alongside having viscous saliva with a high mineral content [1]. Sufferers of sialolithiasis do not typically display symptoms, but they may be associated with pain and swelling of the submandibular gland (figure 4) [16].

Only one antrolith and rhinolith were visualised (0.1%) (table 3 and 4). These are rare calcifications, and there are no studies in the literature with an approach of panoramic radiography alone [2]. Patients with these calcifications may be asymptomatic for long periods of time, although expansion of the lesion may penetrate the mucosa causing pain, congestion and ulceration (figure 5) [1].

One-hundred and twenty-two cases (5.1%) identified calcified carotid artery atheroma (tables 2 and 3). This type of calcification has been the subject of many studies in recent years, due to the fact this calcification is implicated with an increase in morbidity and mortality, particularly cerebrovascular disease (e.g ischaemic stroke). A number of studies point to a prevalence ranging from 3% to 5%, showing our data to be consistent [3,6,20,21]. "Bayer et al. [20] reported in their study that the presence of calcified carotid atheromas were more common in females than males. There were similar findings in our data, however the results were not statistically significant ($p = 0.093$) (Table 3).

Carotid artery atheromas are often misdiagnosed as calcification of the triticeous cartilage, thyroid cartilage, salivary stones, hyoid bone, lymph nodes and stylomandibular and stylohyoid ligaments [3,20-27]. Kamikawa et al. [14] undertook a study on cadavers, which determined a great variability between the observers in the distinction between these anatomical structures. Additionally, Ahmad et al. [26] studied the prevalence of calcification of triticeous cartilage and radiographic differences in comparison to calcification of carotid atheromas; he concluded that these calcifications have characteristics that make it possible to differentiate between them radiographically since cartilage calcification is more circular or oval, with regular borders, whereas calcification of the atheroma is more irregular and tends to be linear (figures 6,7,8).

Our results are consistent with previous studies in which highlighted the relevance of DPTs in the detection of carotid calcifications [27].

Since ischaemic stroke is associated with high morbidity and mortality, early detection and appropriate management is key. This makes DPTs a key tool at the disposal of dentists to potentially reduce the prevalence of this disease [28]. The dentist may therefore help save lives with a radiograph taken for the purpose of dental care [25].

Conclusion

In conclusion, stylohyoid and stylomandibular ligament calcifications were the most common calcifications found in our sample of DPTs. This is the largest sample ever done within a Portuguese population, with relevant Kappa scores, providing useful information about the incidence and

distribution of these calcifications. This facilitates valuable comparison in calcification rates with other studies from authors in different countries.

Further studies are needed to determine the validity of DPTs in the early detection of carotid calcification, and the potential for associated reduction in cerebrovascular disease.

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Figure Legends

Figure 1. Sample distribution by age.

Figure 2. DPT where the arrows indicate biliary calcification of the stylohyoid ligament.

Figure 3. DPT where arrows indicate the presence of tonsil stones.

Figure 4. DPT where the arrow indicates a salivary stone of the submandibular gland.

Figure 5. DPT where the arrow indicates the presence of an antrolith.

Figure 6. Diagram demonstrating the most common region of atheroma appearance on panoramic radiography (Left, White [1]), and DPT where arrows indicate physiological calcification of thyroid cartilage (T) and triticeous cartilage (S) (Right).

Key:: C1, C2, C3 and C4 = cervical vertebrae; H = hyoid bone; C = carotid artery; T = triticeous cartilage; E = epiglottis; B = mandibular base; S = Superior horn of thyroid cartilage.

Figure 7. DPT where arrows indicate the presence of carotid artery calcifications.

Figure 8. DPT where arrows indicate the presence of carotid artery calcifications.

Table 1: Characteristics of calcifications in the maxillofacial region

Table 2. Prevalence of soft tissue calcifications in the study performed.

Table 3. Distribution of calcifications per age.

Table 4. Distribution of calcifications by gender.

Table 1: Characteristics of calcifications in the maxillofacial region

Type of Calcification	Location	Radiographic Appearance
Lymph Node Calcification	The most common site is the submandibular region, below the lower edge of the mandible, in close proximity to the angle of the mandible. ^{1,4,6} Calcification may affect a single node or a linear series of nodes, which are known as lymph node chains [1,2].	Varying degrees of radio-opacity Well-defined periphery, which may times give it a lobular appearance similar to a cauliflower [1,2,6,16]
Tonsil Stones	<ul style="list-style-type: none"> Multiple small calcifications typically overlap the middle portion of the ascending ramus, [1,15,17] or; Superimposed on the soft tissues (postero-inferior to the angle of the mandible or posterior to the ramus) [15]. Visible as single or multiple nodular radiopaque images, non-continuous, at the point the intervertebral junction C3 and C4 or; [2,20,22-25,28,30]	<ul style="list-style-type: none"> Multiple poorly defined radio-opacities which may be oval, round or irregular in shape [2]. The borders are poorly defined and of slightly greater radiopaque density than the spongy bone [1,16]. Multiple, irregular radio-opacities
Calcification of the Carotid Artery	1-4cm postero-lateral to the angle of the mandible [25] or; Vertical radiopaque lines representing fine calcifications of the vascular walls [2,20,25,28,29].	Multiple, irregular radio-opacities
Salivary Stones	<ul style="list-style-type: none"> The submandibular gland is the most affected (83% to 94%), observed overlying the angle of the mandible and mandibular ramus [3,6]. The parotid gland is affected second most commonly, with parotid lithiasis the main cause of calcifications in the parotid space [19]. 	<ul style="list-style-type: none"> Oval or elongated radio-opaque plaques. May present with varying degrees of opacity depending on the amount of inorganic material deposited within the calcification [2].
Phleboliths	The mandibular jaw is the most common site in the posterior region of the body and the posterior branch, and in the interior of the inferior alveolar canal [1,6].	Multiple circular or oval layers with a characteristic appearance of a radiopaque “target” at the periphery, which is radiolucent in its midsection [2].
Rhinoliths/Anthroliths	<ul style="list-style-type: none"> Rhinoliths form in the nasal cavity Anthroliths form in the antrum of the maxillary sinus [1,2,6]. 	<ul style="list-style-type: none"> Varied appearance depending on their location Homogeneous or heterogeneous radio-opacities and have a laminar appearance [1,2].
Stylohyoid Ligament	<ul style="list-style-type: none"> When the styloid process exceeds 30mm in length, measured from the lower edge of the external acoustic meatus, it is considered to be elongated [8-13] Radiographically, the ossification extends anterior to the mastoid process and crosses the posterolateral portion of the mandibular branch towards the hyoid bone [8,10,11] 	<ul style="list-style-type: none"> The styloid process appears as a pointed, thin, conical and radiopaque structure with central base and forwardly inclined projections. Ossification of the ligament is seen in a rough, straight, and flat line, but in some cases, certain irregularities may be noted on its outer surface [1,2]

Table 2. Prevalence of soft tissue calcifications in the study performed.

420 dental pantomograms	N	Percentage
Soft tissue calcifications	468	19.7%
Total in sample	2375	100%

Table 3. Distribution of calcifications per age.

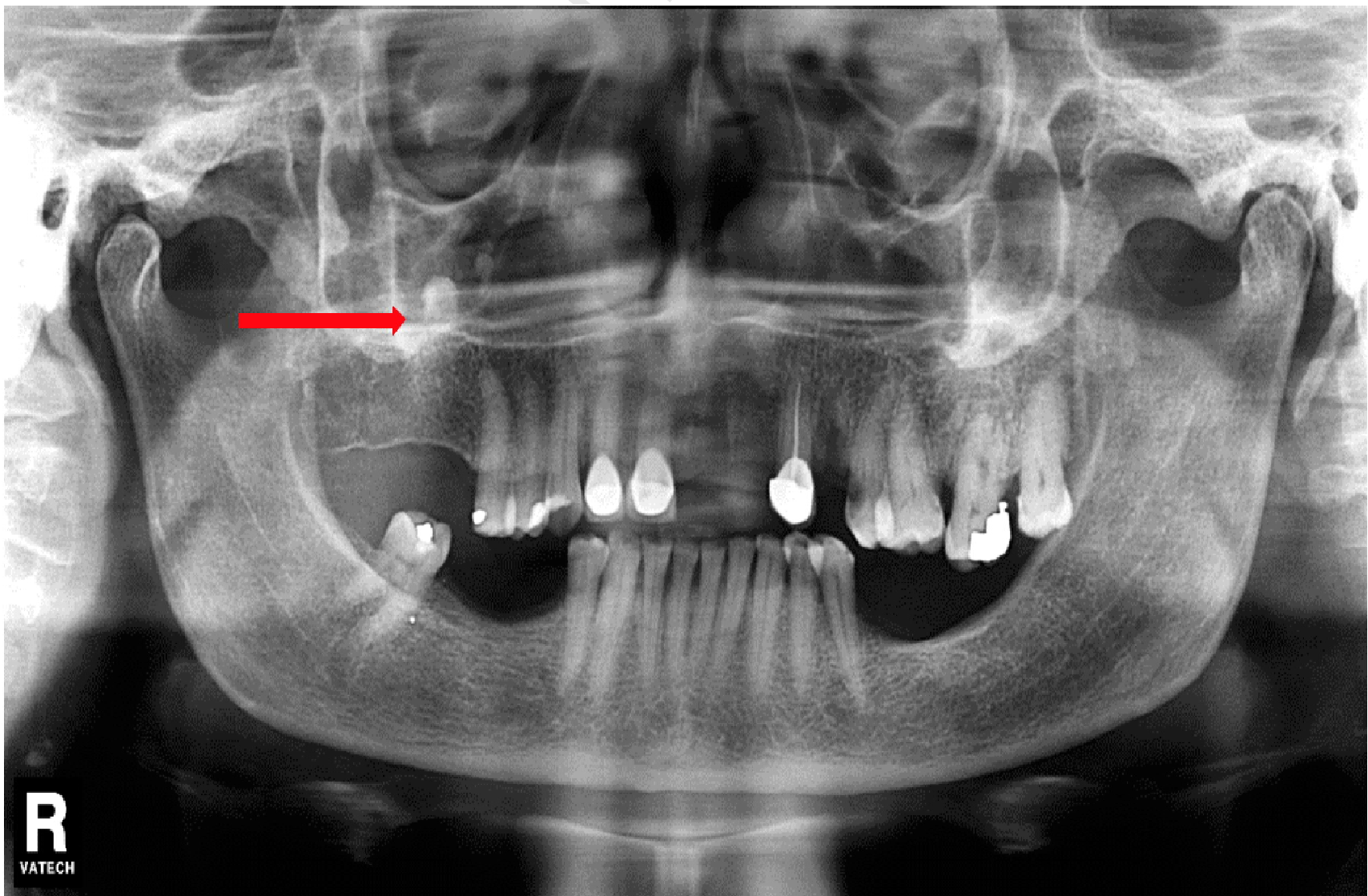
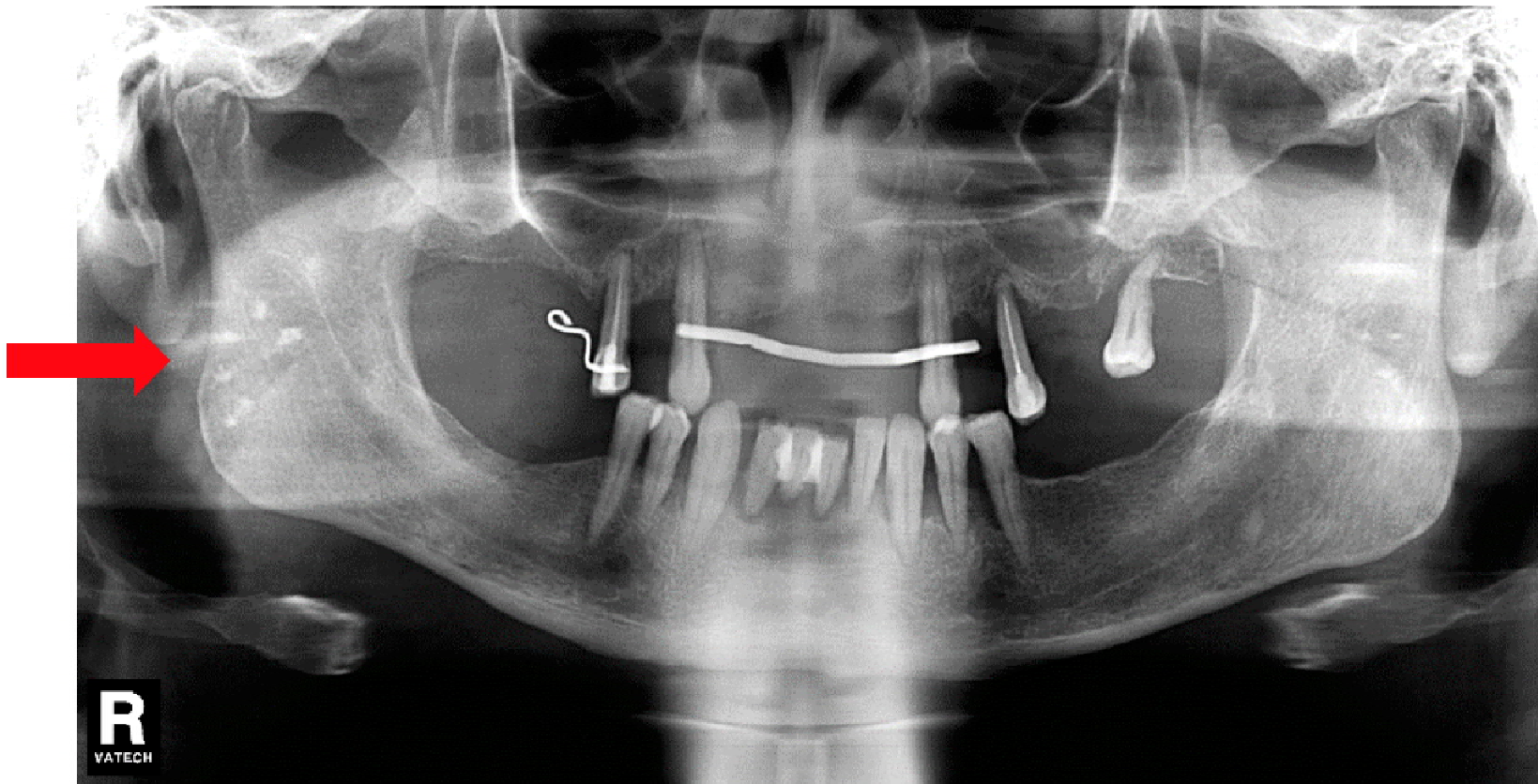
CALCIFICATION (<40>)	PATIENT AGE		P VALUE		
	TOTAL	% OF TOTAL (N=2375)			
	<40 years	>= 40 years			
STYLOID LIGAMENT	N	135	175	310	≈13.1% 0.000* ¹
	% of calc. of ligament % of age (<40>)	43.5%	56.5%	56.6%	
CAROTID ARTERY ARETHOMA	N	18	104	122	≈5.1% 0.000* ¹
	% of calc. of carotid artery % of age (<40>)	84.9%	14.8%	85.2%	
TONSIL STONES	N	2	19	21	≈0.9% 0.000* ¹
	% of calc. of tonsil stones % of age (<40>)	9.5%	1.3%	90.5%	
SALIVARY STONES	N	4	9	13	≈0.5% 0.161*
	% of calc. of salivary stones % of age (<40>)	30.8%	2.5%	69.2%	
ANTHROLITHS	N	0	1	1	0.463**
	% of calc. of anthroliths % of age (<40>)	0.0%	0.0%	100.0%	≈0.1%
RHINOLITHS	*Chi-square test N*Fisher's exact test	0.0%	0.0%	0.3%	0.463**
	% of calc. of rhinoliths % of age (<40>)	0.0%	0.0%	100.0%	
TOTAL		159	309	468	19.7%
% OF TOTAL		34.0%	66.0%	100.0%	

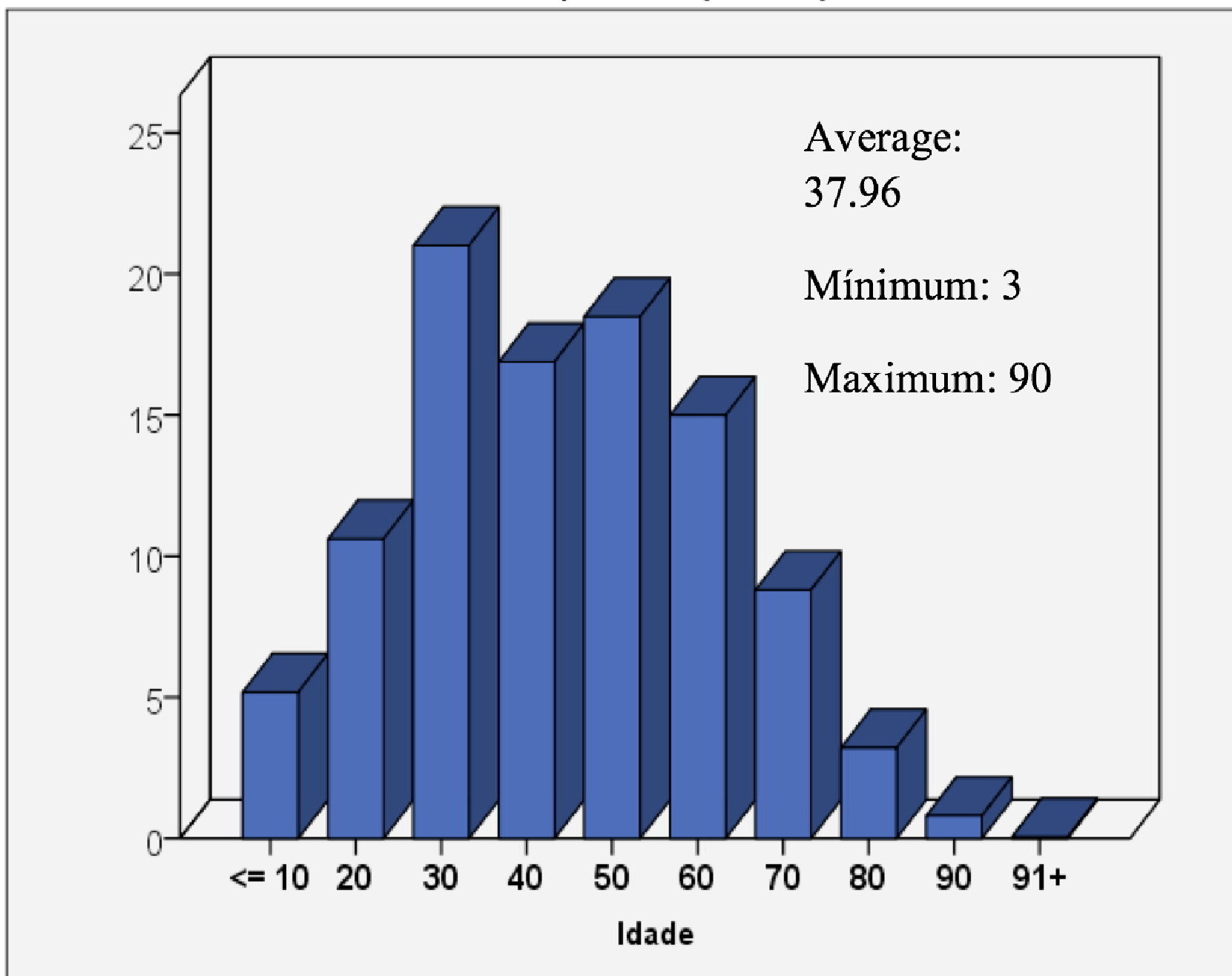
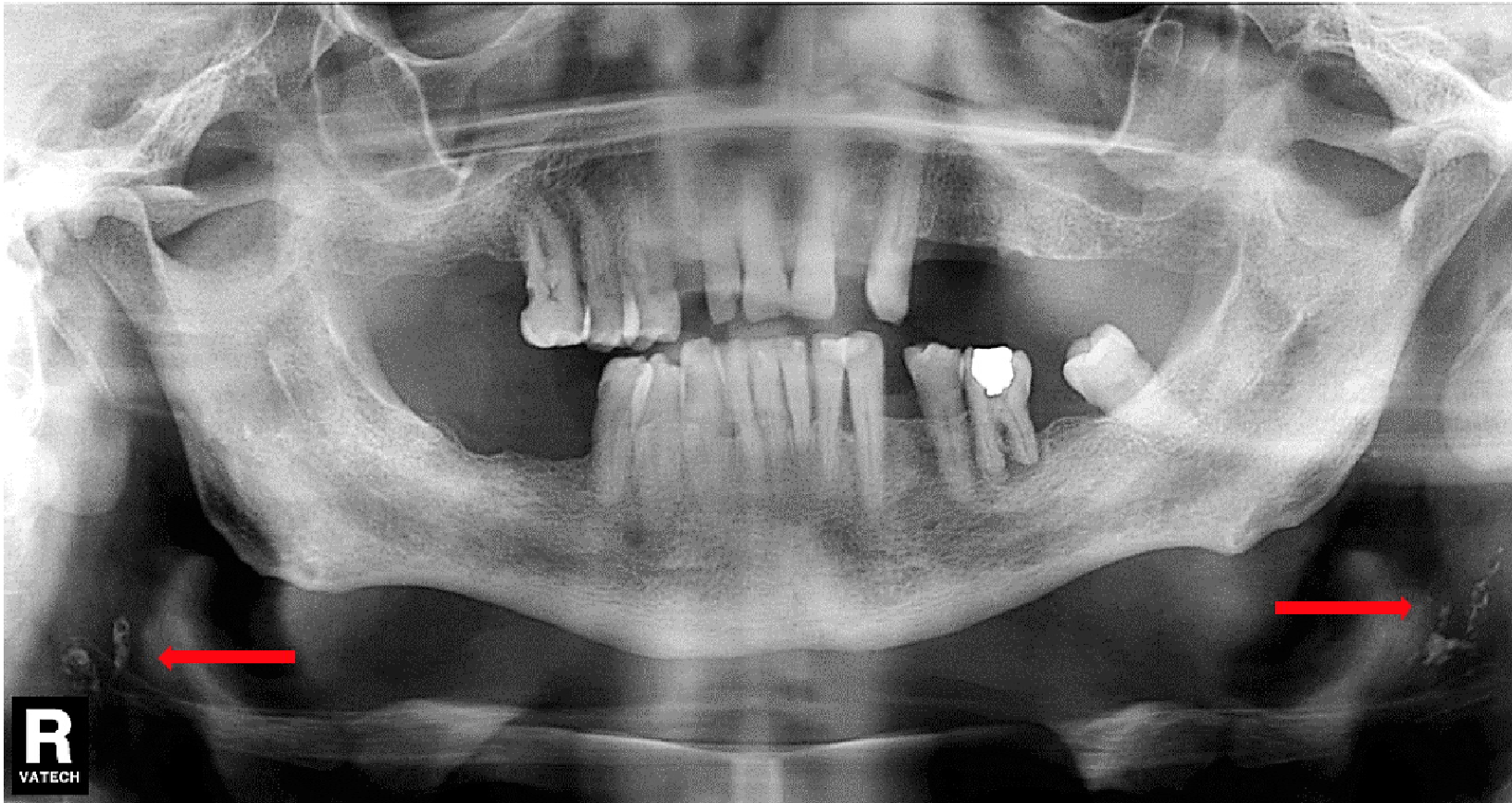
Table 4. Distribution of calcifications by gender.

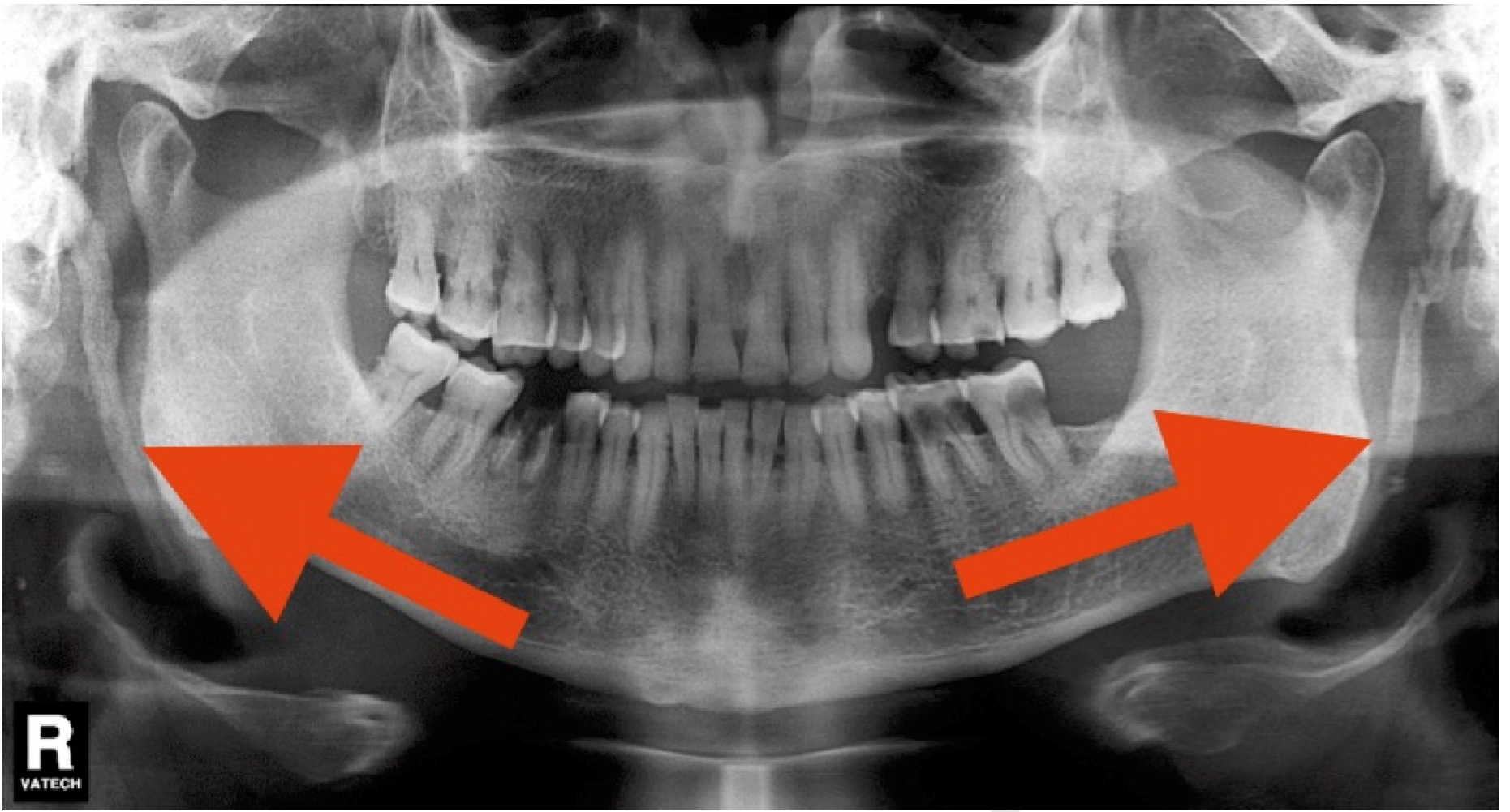
CALCIFICATION	GENDER	TOTAL	% OF TOTAL (N=2375)	P VALUE	
STYLOID LIGAMENT	Female	Male			
	N	183	127	310	≈13,1% 0,212*
	% of calc. of ligament % by gender	59.0%	41.0% 65.1%		
CAROTID ARTERY ARETHOMA	N	77	45	122	≈5,1% 0,093*
	% of calc. of carotid artery % by gender	63.1%	36.9% 23.1%		
TONSIL STONES	N	5	16	21	≈0,9% 0,03* ¹
	% of calc. of tonsil stones % by gender	23.8%	76.2% 8.2%		
SALIVARY STONES	N	7	6	13	≈0,5% 0,890*
	% of calc. of salivary stones % by gender	53.8%	46.2% 3.1%		
ANTHROLITHOS	N	1	0	1	1,000**
	% of calc. of anthroliths % by gender	100.0%	0.0% 0.0%		
RINOLITOS	N	0	1	1	0,443**
	% of calc. of rhinoliths % by gender	0.0%	100.0% 0.5%		
TOTAL	273	195	468	19,7%	
% OF TOTAL	58.3%	41.7%	100%		

*Chi-square test**Fisher's exact test¹statistically significant test value









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