

Peri-Implant Diseases: an update for dentistry

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ABSTRACT

Objective: this study aims to present and describe the main pathological, benign and malignant alterations of the peri-implant mucosa. **Material and Methods:** an integrative review of the literature was carried out using the following descriptors: peri-implant pathology; reactive lesion dental implant; carcinoma dental implant; peri-implant disease dental implant; reactive lesion by dental implant; oral squamous cell carcinoma around dental implants; peri-implant disease; pathology; for the elaboration of the search strategy in the databases PubMed, LILACS, MEDLINE and SciELO to obtain the scientific productions. **Results:** conditions such as peri-implant mucositis and peri-implantitis are poorly reported in the literature, which makes it difficult to estimate their real prevalence. Among the benign reactive lesions, the pyogenic granuloma and peripheral giant-cell granuloma stand out, described as the most frequently associated with the implants. Regarding neoplasia, cases of hemangioma and OSCC were published, suggesting a possible influence of the implant in the development of these conditions. **Conclusion:** the occurrence of several pathologies associated with dental implants was observed in the literature, which demonstrates the importance of a detailed clinical examination, associated, in certain situations, with histopathological examination for an accurate diagnosis and adequate management of the various peri-implant diseases.

Keywords: Dental implant; Peri-implant mucositis; Peri-implantitis; Reactive lesion by dental implant; Squamous cell carcinoma.

Introduction

Attempts to replace teeth lost by prosthetic elements date back to the Mayan period (100-1500 A.D.). The dental implant is a titanium alloplastic material that has the root function of one or more teeth, used as a replacement for elements lost by trauma, periodontal diseases or caries.¹ Currently, oral rehabilitation with osseointegrated dental implants has become one of the best options for the treatment of edentulous patients, which has led to its universalization and, sometimes, its indication without adequate planning (Figure 1), leading to an increase in the number

of complications associated with its use (Figure 2), such as inflammatory processes affecting soft tissues and/or bones, known as peri-implant diseases (PIDs). The PIDs are subdivided into peri-implant mucositis and peri-implantitis. These processes are analogous to gingivitis and periodontitis in natural teeth, respectively.² Clinically, such conditions are presented as edema, erythema, hypertrophy and soft tissue ulcers, with characteristics that sometimes require a differential diagnosis with malignant lesions, such as oral squamous cell carcinoma (OSCC), for example (Figure 3).³

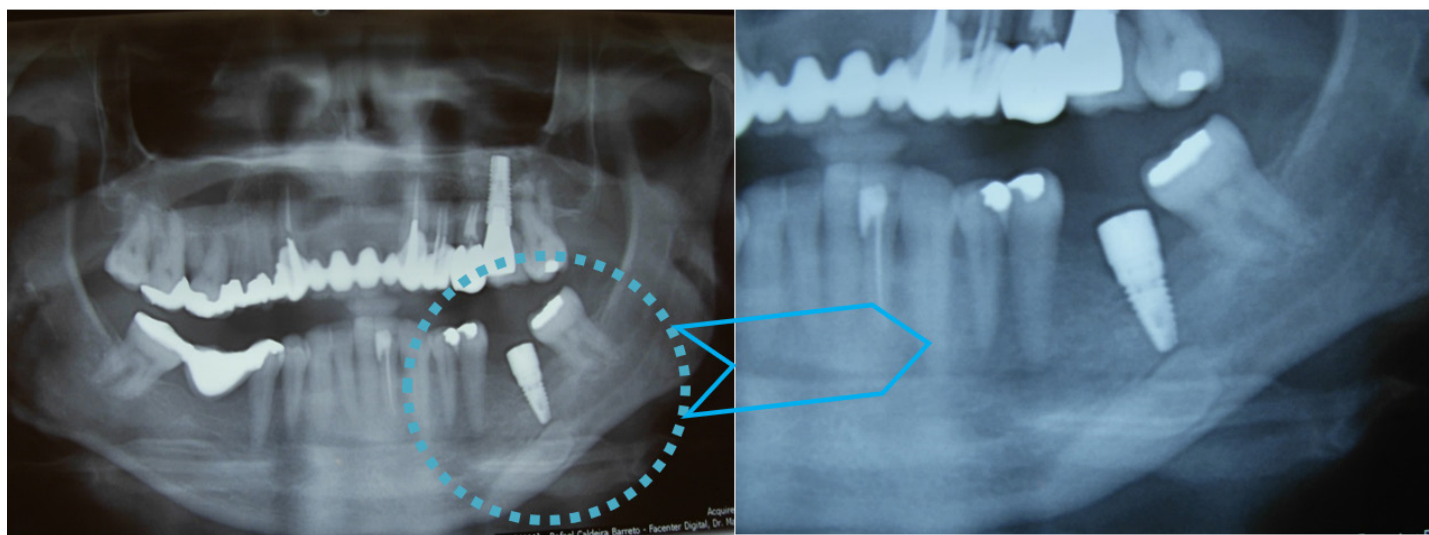


Figure 1. Panoramic radiography showing the general and enlarged image of the implant installation associated with included supernumerary tooth

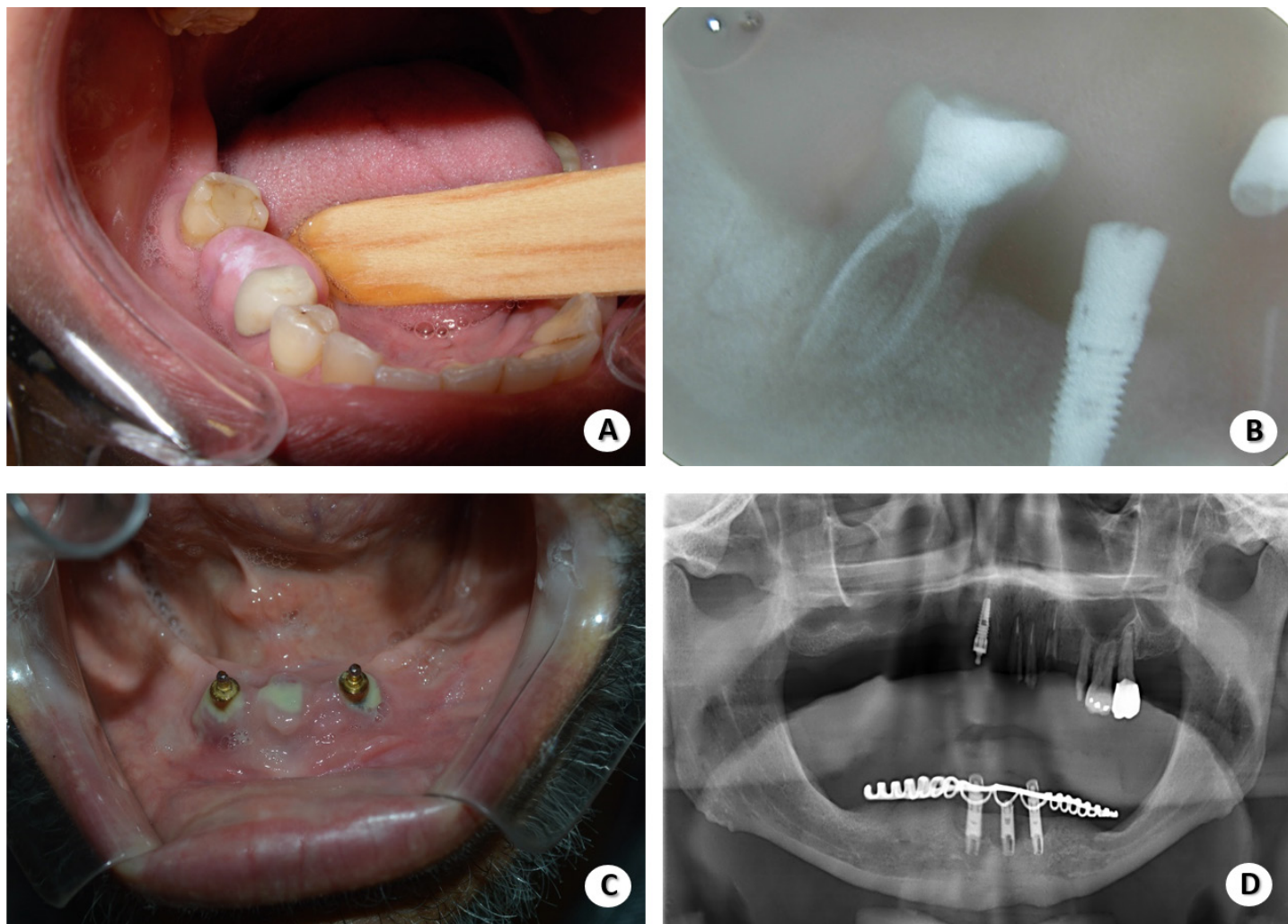


Figure 2. Examples of complications related to the installation of dental implants. "A" is the presence of a nodule located in the peri-implant region of element 46, suggestive of reactional lesion; in "B" we have the periapical showing nodule association directly linked to the constituent of the dental implant; in "C" we have a case of peri-implant mucositis with purulent secretion drainage; and in "D", panoramic radiograph of three implants associated with peri-implant mucositis



Figure 3. Ulcer with more than 30 days of evolution and no signs of healing, associated with the region of dental implants. Case to be investigated with biopsy examination followed by anatomopathological analysis

Reactive lesions are those characterized by excessive proliferation of connective tissue in response to chronic irritation. Among these are included focal fibrous hyperplasia, fibroepithelial hyperplasia, peripheral ossifying fibroma, peripheral giant-cell granuloma (PGCG), and pyogenic granuloma (PG). The last two are the most commonly diagnosed in the peri-implant mucosa.

In addition, some studies have reported the development of OSCC in the mucosa adjacent to the dental implant, which should be considered, therefore, as a diagnostic hypothesis in the case of peri-implant mucosal lesions, since it requires a precise and fast diagnosis for immediate treatment.⁴

Thus, in addition to the increase in the number of PID cases, such as mucositis and peri-implantitis, and the development of peri-implant mucosal lesions, this is associated with the fact that such conditions are little discussed in the training of dental surgeons and implant dentists. Therefore, this study aims to present and describe the main pathological, benign and malignant alterations of the peri-implant mucosa aiming to update the professionals who perform the clinical follow-up of patients rehabilitated with dental implants, thus assisting the detection, diagnosis and adequate management of the most frequent changes.

Material and Methods

The study consists of an integrative review of the literature, where the PubMed, LILACS, MEDLINE and SciELO databases were used to obtain the scientific productions. The bibliographic search was carried out in October 2016, establishing the time interval between 1989 and 2016 and using the following descriptors for the elaboration of the search strategy: peri-implant pathology; reactive lesion dental implant; carcinoma dental implant; peri-implant disease dental implant; reactive lesion by dental implant; oral squamous cell carcinoma around dental implants; peri-implant disease; pathology.

Scientific articles in English, Spanish and Portuguese that were relevant, current and published in indexed journals, with editorial board and ISSN (International Standard Serial Number) were selected. Publications that did not have the complete text available for reading, if in different languages from those previously mentioned and that did not address the object of study, were excluded.

Results

Non-neoplastic Lesions Associated with Implants

Peri-implant Mucositis

Ferreira *et al.*⁵ in a cross-sectional study, observed the prevalence of 64.6% of peri-implant mucositis and concluded that patients with periodontitis, diabetes and poor oral hygiene are more likely to develop such condition.

According to Berglundh *et al.*,⁶ studies on the prevalence of peri-implant diseases are scarce, apart from the fact that cross-sectional studies in implant-rehabilitated patients and bleeding on probing data are hardly published. Considering this, to evaluate the prevalence of this condition is highly difficult.

Peri-implantitis

Peri-implantitis is an inflammatory and destructive process that affects peri-implant soft and hard tissues. The histopathological features found in peri-implant tissues in regions of implants removed due to the disease consisted of the presence of bacterial biofilm on the implant surface and a chronic inflammatory infiltrate in the connective tissue. Such histopathological features were described by Piatteli *et al.*⁷ in a study of 230 implants recovered over a period of 8 years.

In their study, Roos-Jansåker *et al.*⁸ performed a clinical and radiographic examination of 999 implants in 218 patients between 9 and 14 years after the rehabilitation and observed a pocket depth greater than or equal to 4 mm, and bleeding on probing in 48% of the sites with dental implants.

Pyogenic Granuloma (PG)

The first reports of PG in association with dental implants were presented in the study by Olmedo *et al.*⁴ where 2 clinical cases of reactive lesions of peri-implant mucosa were diagnosed, both initially considered as epulis. To the histopathological examination, the cases were diagnosed as PG and PGCG, with the presence of metallic particles in the tissues, suggesting that the etiology of the lesions may be associated with the corrosion process of the metallic structure, as demonstrated by Rodrigues *et al.*⁹

Dojcinovic *et al.*¹⁰ reported the case of a 32-year-old male patient who had an exophytic and ulcerated nodular lesion of 1.0 cm in the left posterior maxillary gingiva associated with a dental implant. A clinical diagnosis of inflammatory fibrous hyperplasia was made, and the lesion excised and referred for histopathological analysis, and then diagnosed as PG. In this case, the etiology of the lesion was the inadequate choice of a healing abutment, which prevented the correct hygiene of the region, causing a chronic inflammatory process in the peri-implant tissue. Excision and replacement of the healing abutment were sufficient to resolve the case.

Peripheral Giant-Cell Granuloma (PGCG)

PGCG is an infrequent peri-implant soft tissue complication, with only 11 cases reported in the literature until 2010, according to Peñarrocha-Diago *et al.*¹¹ The first reported case of PGCG associated with dental implants was described by Hanselaer *et al.* in 1984 *apud* Rodrigues *et al.*⁹, and only 15 cases have been reported in the literature up

to 2015. Hirshberg *et al.*¹² reported PGCG in 12% of the 25 peri-implant soft tissue biopsies examined.

Bischof *et al.*¹³ described a case of PGCG in a 56-year-old female patient with three implants in the posterior region of the mandible. The patient in question reported difficulty in performing hygiene in the region, causing dental plaque accumulation.

In the cases analyzed by Brown *et al.*,¹⁴ a recurrence rate of 46.2% of PGCG associated with dental implants was observed, which is considerably higher than that of PGCG in general, where an average recurrence rate of 5 to 11% is reported.

Neoplastic Lesions Associated with Dental Implants Hemangioma

Kang *et al.*¹⁵ reported a case of hemangioma associated

with a dental implant (Figure 3). In their study, the co-development of PG and capillary hemangioma in the upper alveolar ridge associated with a dental implant in a patient using Warfarin was described. The lesion was excised and submitted to histopathological and immunohistochemical analysis, where PG and Hemangioma characteristics were observed. According to the authors, such different conditions coincidentally expanded in the same gingival mass.

Oral Squamous Cell Carcinoma (OSCC)

Jané-Salas *et al.*³ reviewed 13 articles published between 1996 and 2009 referring to 19 cases in which OSCC was developed in patients with osseointegrated implants (Table 1). Figure 4 shows the number of patients who developed OSCC and shows in which cases there were risk factors or history of cancer and/or pre-malignant lesions.

Table 1. Cases of OSCC in patients rehabilitated with osseointegrated implants reported in the literature

Authors	Publication	Type of study	Number of cases	Risk factors	History of cancer or pre-malignant lesion
Schache <i>et al.</i> 2008 ²⁸	Br J Oral MaxillofacSurg	Clinical case	1	No	No
Shaw <i>et al.</i> 2004 ³⁰	Int J Oral MaxillofacSurg	Clinical case	2	No	No
Chimenos-Küstener <i>et al.</i> 2008 ³¹	RevPortEstomatolCirMaxillofac	Clinical case	1	Yes	No
Eguiadel Valle <i>et al.</i> 2008 ³²	Med Oral Patol Oral Cir Bucal	Clinical case	1	No	No
Kwok <i>et al.</i> 2008 ³³	BrDent J	Clinical case	3	Yes	Yes (in 1 of the 3 cases)
Clapp <i>et al.</i> 1996 ⁴⁸	Arch Otolaryngol Head Neck Surg	Clinical case	3	Yes	Yes (2 cases)
Moxley <i>et al.</i> 1997 ⁴⁹	J Oral MaxillofacSurg	Clinical case	1	Yes	Yes
Block et Scheufler 2001 ³⁴	J Oral MaxillofacSurg	Clinical case	1	Yes	Yes
Abu El-Naaj <i>et al.</i> 2007 ³⁵	RevStomatolChirMaxillofac	Clinical case	1	Yes	Yes
Czerninski <i>et al.</i> 2006 ³⁶	QuintessenceInt	Clinical case	2	Yes	Yes
Dib <i>et al.</i> 2007 ³⁷	Clin Implant Dent Relat Res	Clinical case	1	No	No
Gallego <i>et al.</i> 2008 ³⁸	J AmDentAssoc	Clinical case	1	No	Yes
Gulati <i>et al.</i> 2009 ⁴⁰	Ann R Coll SurgEngl	Clinical case	1	Yes	Yes

Source: Jané-Salas *et al.*, 2015.¹⁸

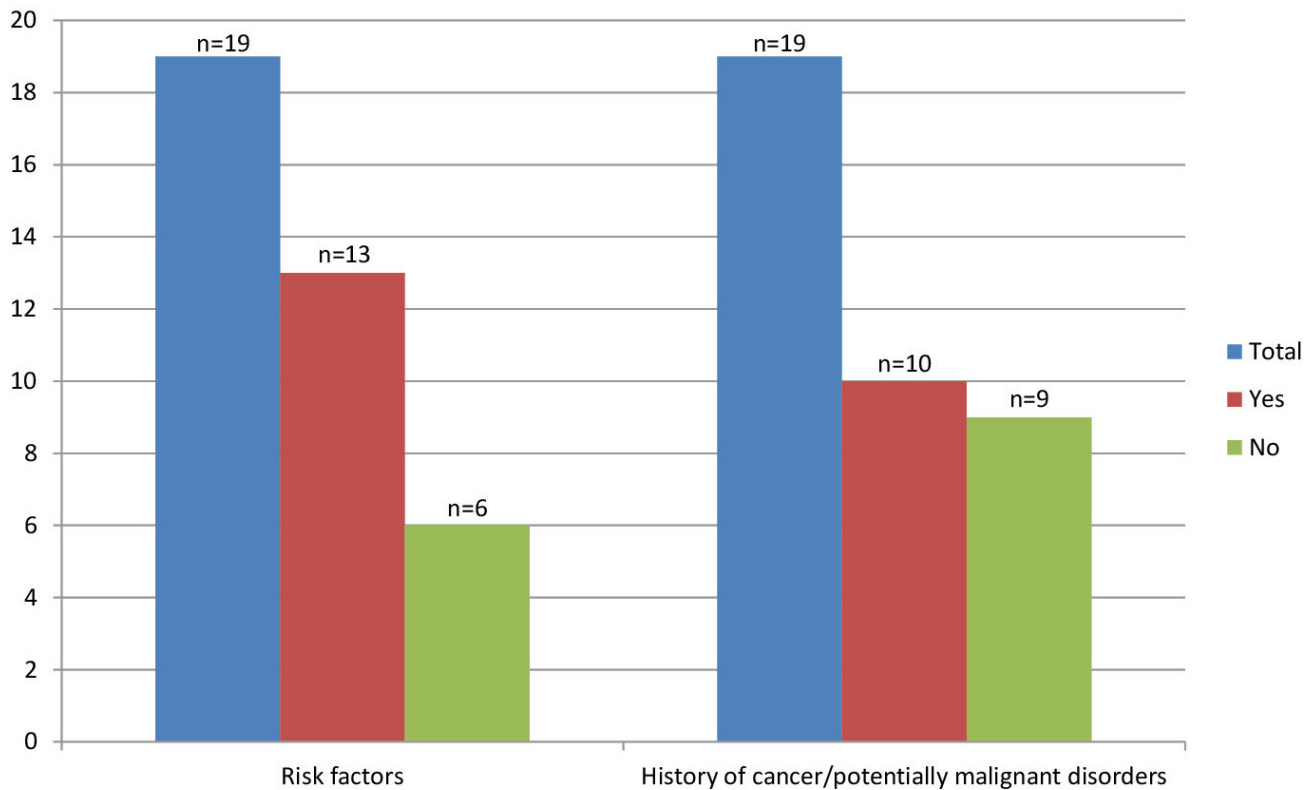


Figure 4. Number of patients rehabilitated with implants presenting risk factors for OSCC or history of cancer/potentially malignant disorders

Raiser *et al.*¹⁶ reported cases of asymptomatic lesions around long-standing implants that resembled peri-implantitis and were subsequently diagnosed as malignant neoplasms. Of 42 malignant tumors associated with implants, between 2000 and 2014, 85.7% were squamous cell carcinomas (69% primary and 9.4% metastatic). Most patients had preexisting risk factors for oral cancer.

Discussion

According to Lang and Berglundh, PID is an inflammatory reaction of microbial etiology caused by the accumulation of bacterial plaque and affecting the peri-implant tissues, subdivided into: peri-implant mucositis and peri-implantitis.¹⁷ As established during the I European Periodontics Workshop, the term peri-implant mucositis refers to a reversible inflammation that affects peri-implant soft tissues, considering peri-implantitis as an inflammatory process that strikes and destroys hard and soft tissues around the implant.¹⁸

Considering the increase of rehabilitated patients with implants, the development of lesions on peri-implant mucosa, in addition to the PID, has been more frequently reported in the literature.³

PG is a reactive lesion of the connective tissue that occurs in response to local irritant factors of low intensity, such as plaque and dental calculus, and is usually developed in pa-

tients with high hormonal levels (pregnant women, for example). Clinically, it is a tumor-like growth of the oral cavity, most often located around the anterior teeth.¹⁹ The study of Dojcinovic *et al.*¹⁰ demonstrated the case of a man who had developed a PG due to the inadequate choice of a healing abutment, thus allowing an accumulation of plaque and chronic inflammation of the peri-implant tissue. Olmedo *et al.*⁴ histologically observed the presence of metal particles in biopsied GPs, suggesting that the etiology of the lesions may be related to the corrosion process of the metallic structure, as shown also by Rodrigues *et al.*⁹ GPCG is a relatively frequent benign reactive lesion of the oral cavity, originating from the periosteum or periodontal membrane, developed in response to local irritation or chronic trauma. Clinically, it presents itself as a red-purple nodule located in the region of the gingiva or edentulous alveolar ridge, occurring with greater prevalence in the fifth and sixth decades of life and presenting a slight predilection for females.²⁰ Bischof *et al.*¹³ described a case of PGCG that evolved due to inadequate angulation of the implants, which hampered the hygiene of the region. This is confirmed by the Ozden *et al.*²¹ study, who described a case of PGCG associated with a poorly adapted implant-supported prosthesis, which provided dental plaque accumulation and lesion development.

Hemangiomas are benign tumors characterized by endothelial cell proliferation. Kang *et al.*¹⁵ reported the devel-

opment of PG and capillary hemangioma on the alveolar ridge of a patient using Warfarin rehabilitated with a dental implant. Therefore, patients with dental implants under antithrombotic therapy should be closely monitored for a possible early detection of this condition.

OSCC is defined as a malignant neoplasm of epithelial origin that usually occurs in men over 60 years old.²² The pathogenesis of OSCC is well established and is largely related to lifestyle, especially excessive alcohol and tobacco consumption.¹ Jané-Salas *et al.*³ study reviewed 19 cases of OSCC associated with dental implants, where 9 of them had no history of neoplasia, neither in the oral cavity nor in another region of the body. Other reports regarding the occurrence of OSCC in patients rehabilitated with dental implants are set out in Table 1.

In addition to OSCC cases, there is a published osteosarcoma in the maxilla case associated with placement of the implant with the use of filling material in the maxillary sinus.²³

The development of OSCC is more frequent in peri-implant mucosa of patients who have risk factors or prior history of cancer. The mechanism by which osseointegrated dental implants may contribute to the development of OSCC is highly debatable, since the association and influence of other risk factors for carcinogenesis, such as smoking and alcoholism, cannot be disregarded. Some studies propose that the development of OSCC may be related to changes in the microbial profile of the oral cavity. Bacterias of the genera *Porphyromonas* and *Fusobacterium*, known as periodontopathogenic bacteria, are known to be found in larger amounts in SCC samples than in healthy adjacent tissues, and high concentrations of *Streptococcus mitis*, *Campylobacterium gingivalis* and *Prevotella melaninogenica* have been reported in the saliva of patients of OSCC when compared to healthy individuals.²⁴ Since several of these species also colonize peri-implant tissues, further investigations are necessary in order for the hypothesis of the influence of bacterial colonization in the peri-implant region to be confirmed or not as the etiological factor for the development of OSCC. Based on this review, it is not possible to establish a direct causal relationship between implant rehabilitation and the development of malignant neoplasia, although, given the large number of cases reported in the literature, implant treatment may possibly be an additional risk factor for OSCC development, with an obvious necessity of studies with better methodological designs, such as case-control studies or cohorts, so that this hypothesis can be confirmed or refuted.

Because it is an aggressive disease with a high rate of

relapse, patients with a history of OSCC should have any lesion in the peri-implant area removed and examined microscopically, to obtain an accurate diagnosis. The cases of Shaw *et al.* demonstrate that the development of a second primary tumor can be masked as benign peri-implant complications, being extremely necessary to have a high degree of vigilance with the periodic removal of fixed prostheses to perform peri-implant mucosa examination.²⁴

This study presented several factors that contribute to and/or are associated with the peri-implant mucosa pathologies, such as poor oral hygiene, history of cancer and the influence of tissue manipulation during surgical procedure. Thus, prior to implant rehabilitation, an accurate history, as well as a thorough physical examination of the patient, should be carried out to detect possible risk factors; and after rehabilitation, a rigorous follow-up protocol should be instituted, where oral hygiene instruction, physical examination and, in specific cases, performance of biopsies play key roles in the prevention and/or diagnosis of peri-implant mucosal diseases.

In terms of treatment, the therapy must be directed to the causal factor of the diagnosed condition. Mucositis treatment involves mechanical debridement to remove the plaque. Regarding peri-implantitis, mechanical debridement should be associated with surgical treatment (open debridement) and treatment with local and/or systemic antibiotics. In general, in the case of reactional lesions (PG, PGCG), irritation factors such as prosthesis, dental calculus, fractured or poorly adapted restorations should be removed, followed by surgical excision of the lesion.^{6,18} Differences exist regarding the need for removal of the implant in these cases.¹⁰ As far as malignant neoplasia, after the histopathological diagnosis the patient should be referred for appropriate oncological treatment.

Conclusion

This study evidenced the relationship between dental implants and various PIDs. Among benign reactive lesions, PG and PGCG are the most commonly associated with implants. The hypothesis that the treatment with dental implants constitute an additional risk factor for the development of OSCC, especially in patients with a history of cancer or who have other associated risk factors, needs additional studies with better methodological designs to be confirmed or refuted. Clinicians should, still, suspect of any changes in the peri-implant mucosa in patients with pre-existing risk factors for a correct diagnosis, which allows establishment of prognosis and definition of appropriate treatment plan for the patient with PID.

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Mini Curriculum and Author's Contribution

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