



## Prevalence and Possible Risk Factors of Peri-implantitis: A Concept Review

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### ABSTRACT

**Aim:** The purpose of this review is to estimate the prevalence of peri-implantitis, as well as to determine possible risk factors associated with its development in patients treated with oral implants.

**Background:** Although implant therapy has been identified as a successful and predictable treatment for partially and fully edentulous patients, complications and failures can occur. Peri-implantitis is considered a biologic complication that results in bone loss around implants and may lead to implant treatment failure.

**Results:** A great variation has been observed in the literature regarding the prevalence of peri-implantitis according to the diagnostic criteria used to define peri-implantitis. The prevalence ranges from 4.7 to 43% at implant level, and from 8.9 to  $\geq 56\%$  at patient level. Many risk factors that may lead to the establishment and progression of peri-implantitis have been suggested. There is strong evidence that presence and history of periodontitis are potential risk factors for peri-implantitis. Cigarette smoking has not yet been conclusively established as a risk factor for peri-implantitis, although extra care should be taken with dental implant in smokers. Other risk factors, such as diabetes, genetic traits, implant surface roughness and presence of keratinized mucosa still require further investigation.

**Conclusion:** Peri-implantitis is not an uncommon complication following implant therapy. A higher prevalence of peri-implantitis has been identified for patients with presence or history of periodontal disease and for smokers. Until now, a true risk factor for peri-implantitis has not been established. Supportive

maintenance program is essential for the long-term success of treatments with oral implants.

**Clinical significance:** The knowledge of the real impact of peri-implantitis on the outcome of treatments with oral implants as well as the identification of risk factors associated to this inflammatory condition are essential for the development of supportive maintenance programs and the establishment of prevention protocols.

**Keywords:** Dental implants, Implant success, Peri-implantitis, Prevalence, Risk factor.

**How to cite this article:** Marcantonio C, Nicoli LG, Junior EM, Zandim-Barcelos DL. Prevalence and Possible Risk Factors of Peri-implantitis: A Concept Review. *J Contemp Dent Pract* 2015;16(9):750-757.

**Source of support:** Nil

**Conflict of interest:** None

### INTRODUCTION

Just as important as osseointegration, which has decidedly been established as a predictable biological process over the past few decades,<sup>1</sup> the behavior of osseointegrated dental implants and the longevity of implant-supported rehabilitation therapies seem to have gained priority in the concern of clinicians and is currently the subject of intense investigation within the academic community. Studying the prevalence of peri-implant disease and investigating the roles played by the vast array of associated risk factors in the onset and progress of peri-implantitis is of crucial importance for the development of dental-implant management programs and the establishment of peri-implantitis prevention and treatment protocols. These protocols should have a major and positive impact on the over-all implant success rate and the predictability of dental implant therapies. Due to the high methodological variability used to establish the parameters of peri-implant disease, interestingly enough, one of the major controversies in studies of peri-implantitis prevalence is

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the characterization of the peri-implant disease itself.<sup>2</sup> Not less significant is the inherent multivariable nature of studies on prevalence and associated risk factors for any particular disease, all of which seem to reflect the wide range of controversy found in implant survival rate studies. Thus, the purpose of the present review is to estimate the prevalence of peri-implantitis, as well as to determine possible risk factors associated with its development in patients treated with oral implants.

## RESULTS

### Definition and Prevalence

Peri-implantitis was defined at the Consensus meeting on Peri-implantitis<sup>3</sup> as an 'infection with suppuration associated with clinically significant progressing marginal bone loss after the adaptive phase, usually restricted to the first year of function'. According to the American Academy of Periodontology,<sup>4</sup> peri-implantitis is 'an inflammatory process around an implant that includes both soft tissue inflammation and loss of supporting bone'. While the definitions currently in use for peri-implantitis do not seem excessively controversial, the wide methodological variability found in the characterization of the peri-implant disease has become subject of concern among many authors. Because of the lack of consistent and definite diagnostic criteria used to describe peri-implantitis, great variation has been observed in the literature regarding the prevalence of this inflammatory condition.

Ferreira et al<sup>5</sup> reported peri-implantitis prevalence of 7.44 and 8.9% at implant and patient levels, respectively. Two hundred and twelve non-smoking Brazilian subjects with 578 implants in function for a period of 6 months to 5 years were evaluated. Peri-implantitis was considered to be installed when implants presented at least one site with PD  $\geq 5$  mm, confirmed by radiographic vertical bone loss, positive BOP and/or suppuration. Roos-Jansåker et al<sup>6</sup> evaluated 218 patients with 999 implants after 9 to 14 years of function. Peri-implantitis was defined as bone loss  $\geq 1.8$  mm compared with 1-year data, combined with BOP and/or pus. Disease was diagnosed among 16% of the patients and 6.6% of the implants.

Zitzmann and Berglundh<sup>7</sup> reviewed the prevalence of peri-implant diseases and verified that only few studies provided data on the prevalence of peri-implant diseases. Only cross-sectional and longitudinal studies including a number higher than or equal to 50 implant-treated subjects exhibiting a function time of at least 5 years were considered. Peri-implantitis was diagnosed in 28 and  $\geq 56\%$  of subjects and in 12 and 43% of implant sites.

Koldslund et al<sup>8</sup> applied different diagnostic thresholds to assess the prevalence of peri-implantitis in 374 osseointegrated dental implants placed in 109 patients

with a mean loading time of 8.4 years. Parameters to assess peri-implantitis included detectable radiographic peri-implant bone loss and the presence of BOP and/or suppuration. Variable parameters were PD and radiographic peri-implant bone loss. When the bone loss threshold was set at  $\geq 2$  mm, peri-implantitis prevalence was found at 20.4 and 15.1%, for PD  $\geq 4$  and  $\geq 6$  mm, respectively. With bone loss threshold set at  $\geq 3.0$  mm, peri-implantitis prevalence was 11.7 and 11.3% for PD  $\geq 4$  and  $\geq 6$  mm, respectively. Their results showed a significant variation for peri-implantitis prevalence as it was assessed at different levels of severity.

A retrospective cross-sectional study was performed to determine the prevalence of peri-implant diseases in 245 patients enrolled in a periodontal maintenance program recruited from private dental practices.<sup>9</sup> The diagnostic criteria for peri-implantitis was bone loss  $\geq 2$  threads with BOP or suppuration. The duration of implant follow-up ranged from 1 to 18 years and 88 implants (9.1%) in 40 patients (16.3%) were diagnosed for peri-implantitis.

Tomasi and Derks<sup>2</sup> verified that eight different thresholds of radiographic bone loss were used as diagnostic criteria of peri-implantitis disease in combination with BOP and/or suppuration in 12 studies. As a result, a variation in the reported prevalence of peri-implantitis around implants was noted. The prevalence varied from 4.7 to 36.6% at implant level and 11.2 to 47.1% at subject level. Recently, Atieh et al<sup>10</sup> performed a systematic review to estimate the overall frequency of peri-implant diseases. Peri-implantitis was defined as the presence of inflamed mucosa with a positive BOP, PD  $\geq 5$  mm and cumulative bone loss of  $\geq 2$  mm and/or  $> 3$  threads of the implant. Among the 504 studies identified, nine studies with 1,497 participants and 6,283 implants were included. The summary estimates for the frequency of peri-implantitis were 18.8% of participants and 9.6% of implants.

### Risk Factors

Associated risk factors found throughout the literature that may lead to the establishment and progression of peri-implantitis may range within a series of conditions, some more consensual or controversial than others, which may include: history of previous periodontal disease, smoking, diabetes, genetic traits, presence of keratinized mucosa and implant characteristics, such as surface roughness.<sup>11-13</sup>

### Presence and History of Periodontitis

In a 10-year follow-up study, Karoussis et al<sup>14</sup> verified that the prevalence of peri-implantitis was significantly higher

for the periodontally compromised patients (PCP) (28.6%) than for periodontally healthy patients (PHP) (5.8%). In addition, patients with implants replacing teeth lost due to chronic periodontitis demonstrated lower survival rates and more biological complications than patients with implants replacing teeth lost due to reasons other than periodontitis.

Renvert and Persson<sup>15</sup> reviewed the literature and concluded based in three studies that subjects with a history of periodontitis may be at greater risk for peri-implant infections. However, considerable variations in study design, different definitions of periodontitis and absence of control of confounding variables were identified in the studies. Simonis et al<sup>16</sup> also verified that PCP were more prone to develop peri-implantitis. The peri-implantitis prevalence for PCP was 37.93% against a rate of 10.53% for PHP.

Pjetursson et al<sup>17</sup> investigated the prevalence of peri-implantitis in periodontitis susceptible patients with 3 to 23 years of follow-up time. For PD  $\geq$  5 mm, peri-implantitis prevalence was registered at 22.2 and 38.6% for implants and patients, respectively. When adopting PD  $\geq$  6 mm, peri-implantitis was present in 8.8 and 17.1% of the implants and patients, respectively. In addition, it was also reported that patients who were enrolled in an effective supportive periodontal therapy program showed a smaller rate of peri-implant disease than patients who did not receive systematic hygiene care; and that peri-implantitis incidence was significantly related to persisting residual pockets (PD  $\geq$  5 mm) after completing of the maintenance program.

Likewise, Costa et al<sup>18</sup> showed that the presence of periodontitis was associated with a higher risk of developing peri-implantitis, and that the absence of preventive maintenance in individuals with pre-existing peri-implant mucositis was also associated with a higher incidence of peri-implantitis. For the global sample, peri-implantitis prevalence was 31.2%. When assessed comparatively, however, figures were 18.0 and 43.9% for groups with and without a periodontal maintenance program, respectively. On the other hand, Swierkot et al<sup>19</sup> demonstrated that, in cases of generalized aggressive periodontitis, long-term implant success rate was highly compromised, even as patients were receiving supportive periodontal therapy. After a follow-up period of 5 to 16 years, peri-implantitis was diagnosed in 26% of the implants placed in patients previously treated for generalized aggressive periodontitis, compared to a presence of 10% of the implants placed in PHP.

In a recent systematic review, Atieh et al<sup>10</sup> verified a small increased frequency of peri-implantitis among participants with a history of periodontal disease. The

summary estimate for the frequency of occurrence of peri-implantitis increased from 18.8 to 21.1% in PCP.

### Smoking

Cigarette smoking has long been associated with poor peri-implant scores and continues to be reported as a potential risk factor for the survival of osseointegrated dental implants.<sup>11-13</sup> Heitz-Mayfield and Huynh-Ba<sup>20</sup> reviewed the literature to evaluate if a history of treated periodontitis and smoking, both alone or combined, could be considered risk factors for adverse dental implant outcomes. Three cohort studies showed a higher risk of peri-implantitis in PCP compared with PHP (OR from 3.1–4.7). Smoking was considered a significant risk for adverse implant outcome in three of four systematic reviews (OR from 3.6–4.6). Although the majority of studies reported high implant survival rates ranging from 80 to 96% in smokers, most studies found survival rates that were statistically and significantly lower for smokers than for non-smokers. The combination of a history of treated periodontitis and smoking increased the risk of implant failure and peri-implant bone loss.

Rinke et al<sup>21</sup> reported an overall patient-level peri-implantitis rate of 11.2%, which was as high as 53% in patients who were smokers with periodontal history, compared to 2.8% for patients who were non-smokers. No peri-implant disease was diagnosed in non-smoking patients without a history of periodontal disease and with a good compliance after treatment. A significant association of peri-implantitis with smoker (or 31.58;  $p < 0.001$ ) and compliance (or 0.09;  $p = 0.011$ ) was identified. Atieh et al<sup>10</sup> also verified a higher frequency of peri-implantitis in smokers. The summary estimate was 18.8% while, for smokers, the estimate was 36.3%.

Despite of the evidence related above, the literature has recently provided rather controversial reports on the influence of cigarette smoking on peri-implant disease. Koldslund et al<sup>22</sup> investigated the association of different risk factors to the occurrence and severity of peri-implant disease. The frequency of peri-implantitis was 20.4 and 11.4% at subjects and implant levels, respectively. Although individuals with a history of periodontitis were considered more prone to developing peri-implantitis, no association was found between smoking and peri-implant disease. More recently, Renvert et al<sup>23</sup> compared the occurrence of risk factors such as systemic disease, periodontitis and cigarette smoking in individuals diagnosed with peri-implantitis to a group who presented healthy or mucositis-affected implants. History of periodontitis and cardiovascular disease were significantly higher in the peri-implantitis group. However, smoking habit was not correlated with a higher



incidence of peri-implantitis. A higher and significant risk of peri-implantitis in smokers (Relative risk 2.1,  $p = 0.001$ ) compared with nonsmokers was revealed by the implant-based meta-analysis performed by Sgolastra et al<sup>24</sup> On the other hand, the patient-based meta-analysis did not reveal any significant differences for risk of peri-implantitis in smokers (Relative risk 1.17,  $p = 0.46$ ).<sup>24</sup>

### Diabetes

The influence of diabetes on the survival of osseointegrated dental implants has been widely investigated. Kotsovilis et al<sup>25</sup> performed a critical review of experimental and clinical studies to determine the effectiveness and predictability of dental implant therapy in diabetic patients. Experimental studies revealed an impaired bone healing response to implant placement in diabetic animals compared with non-diabetic ones, and the majority of clinical studies indicated that diabetes under metabolic control is no contraindication for implant placement.

In a 21-year-long retrospective cohort study, in which 4,680 implants in 1,140 patients were evaluated, Moy et al<sup>26</sup> reported a significantly lower success rate (68.75%) among diabetic patients in comparison with non-diabetic subjects (85%). Ferreira et al<sup>5</sup> reported that diabetes was statistically associated with an increased risk of developing peri-implantitis. Among the 29 diabetic patients, peri-implantitis prevalence was found at 24.13%, against 6.56% in the non-diabetes group.

On the other hand, Salvi et al<sup>27</sup> reviewed the clinical literature related to the association between diabetes and periodontal or peri-implant conditions and concluded that, although poorly controlled diabetes may be considered a risk factor for increased severity of periodontitis, diabetes alone did not represent an absolute contraindication for implant placement in patients with glycemic level control. In fact, the current evidence does not allow a definitive conclusion that diabetic patients have a higher incidence of peri-implantitis.<sup>11,28</sup>

### Genetic Traits

Some genetic variations have been correlated with peri-implantitis. In 2012, a systematic review was performed by Dereka et al<sup>29</sup> to evaluate the relationship between genetic polymorphisms and dental implant biological complications. Based on the results of four studies, there was no evidence to support the association between early implant loss and IL-1, IL-2, IL-6, TNF- $\alpha$  or TGF- $\beta$ 1 genotypes. In two of the three studies which evaluated peri-implantitis in relation to IL-1 genotype, the findings indicate that IL-1RN (intron 2), IL-1A (-899), IL-1B (+3954) gene polymorphisms were correlated to increased peri-

implant tissue infection and destruction. No obvious association between genetic polymorphisms and dental implant failure in terms of biological complications could be observed, although a tendency should be underlined showing the potential link between IL-1 genotype and peri-implantitis.

### Keratinized Tissue

Schrott et al<sup>30</sup> observed that in patients with good hygiene records the presence of at least 2 mm of keratinized mucosa was significant to minimize bleeding and plaque accumulation on the lingual surface and soft tissue recession on the buccal surface of functioning dental implants. Therefore, the authors suggested that, in sites with insufficient keratinized mucosa, special attention should be driven in the maintenance of lingual surfaces and that a higher soft tissue recession should be expected on the buccal surface of dental implants. Conversely, Frisch et al<sup>31</sup> compared sites with a keratinized mucosa gain of approximately 3 mm after mucogingival surgery, with sites with less than 1 mm of keratinized mucosa over a functioning period of approximately 10 years. It was concluded that, at least for patients attending a regular supportive hygiene program, no significant differences were found on the long-term incidence of peri-implant disease, regardless of the presence or absence of keratinized mucosa.

Wennström and Derks<sup>32</sup> reviewed 19 papers and concluded that, at least in patients with proper plaque control, evidence is still limited to support the need for keratinized mucosa around dental implants as a condition to maintain long-term tissue health and stability. However, under a clinical perspective, the authors still recommended that efforts should be maximized to preserve existing keratinized mucosa during implant procedures. Recently, Gobbato et al<sup>33</sup> verified in a systematic review that reduced keratinized mucosa width around implants (<2 mm) was associated with clinical parameters of inflammation and poor oral hygiene.

### Implant Surface

Recent concern over the influence of surface roughness on the long-term success of osseointegrated dental implants has been raised in the literature. Zetterqvist et al<sup>34</sup> compared the incidence of peri-implantitis in fully acid-etched implants with hybrid implants (implants with only the apical and the mid-third portions acid-etched). After a 5-year-follow-up time, overall peri-implantitis prevalence was 0.37% and no significant difference was found for peri-implantitis prevalence between the fully acid-etched group and the hybrid group. Buser et al<sup>35</sup>

evaluated retrospectively 511 sandblasted, large-grit, acid-etched dental implants in function for 10 years. The success and survival rates reported were 97 and 98.8%, respectively. Peri-implantitis prevalence was within 1.8% of the implants. Peri-implantitis was only recorded when implants presented infection, with suppuration and progressive bone loss, regardless of the PD value. Renvert et al<sup>36</sup> after analyzing 13 papers including both human and animal studies, concluded that the reported data was not significant enough to support the evidence that rough-surfaced implants were more prone to presenting peri-implantitis than implants with a smooth surface.

## DISCUSSION

The present paper tries to assess the current status of peri-implantitis investigation, its definition, clinical characterization and the relevance of reported risk factors. Despite of technical variations, most of the definitions for peri-implant disease currently in use are equivalent in the sense that all of them presume marginal soft tissue inflammation and the collapse of the surrounding hard tissue around the implant.<sup>37</sup> One of the main controversies found among researchers in the characterization of peri-implantitis seems to be related to pocket probing depth. It is important to consider that the threads present in most of the commercially available implants seem to make probing on dental implants a much less accurate and a significantly different process than probing on root surfaces.<sup>38</sup> Not less importantly, the nature of soft tissue adherence to titanium implants is also quite different than the one between bone and dental cementum. As previously stated,<sup>8</sup> the considerable variance in the peri-implantitis figures reported in different studies could be related to probing errors. Although it is widely stated that probing depth in peri-implantitis diagnosis should be confirmed by radiographic bone loss,<sup>13</sup> most of the retrospective studies on peri-implantitis prevalence do not present proper initial radiographic data at baseline, which, ideally, would have to be gathered a few weeks after abutment installation and the achievement of tissue homeostasis. Such condition may impair peri-implantitis classification and is certainly another limiting factor in retrospective assessment of peri-implant disease.

Limitations, such as the ones above described have led to significant controversies among researchers regarding the rather alarming figures currently reported in peri-implantitis prevalence. In 2012, Albrektsson et al<sup>3</sup> concluded that, under established protocols, peri-implantitis prevalence figures were under 5% for modern implants, and suggested caution in the interpretation of data in order to avoid an undesirable over-estimation on

the prevalence of peri-implant disease, as results on peri-implantitis prevalence studies can be heavily influenced by substantial methodological limitations. However, Atieh et al<sup>10</sup> verified in a recent systematic review that the summary estimates for the frequency of peri-implantitis were 18.8% of participants and 9.6% of implants.

Although some investigators have previously found correlation between smoking and a higher prevalence of peri-implant diseases<sup>11-13,20,21</sup> controversial evidence on the negative influence of cigarette smoking on the prevalence of peri-implantitis has also been recently reported.<sup>22-24</sup> According to our interpretation of the current literature, while consensus still needs to be reached, patients in such category should definitely be advised about their possible higher risk of experiencing implant failure, particularly, when this habit is associated with a history of previous periodontal disease, as it is many times related.

Several authors have demonstrated that patients with a history of periodontitis are more prone to presenting peri-implant diseases.<sup>13-16</sup> The literature seems to present no controversy over the negative impact of poor periodontal conditions on implant success, although it is also known that supportive periodontal programs can increase the rate of success for dental implants even in patients with a history of periodontal disease,<sup>17,18</sup> as long as no history of aggressive periodontitis is associated.<sup>19</sup>

Lower implant survival rates have been sufficiently reported for diabetes patients.<sup>5,26</sup> On the other hand, it has also been demonstrated that well-controlled diabetes is no contraindication for implant treatment.<sup>27</sup> Thus, for diabetic subjects, it seems undisputed that patient awareness and glycemic level control should be taken into consideration when implant treatment is required, although the current evidence does not allow a definitive conclusion that diabetic patients have a higher prevalence of peri-implantitis.<sup>4</sup> Genetic traits may represent a risk factor for dental implant therapy. However, this association should be investigated in future studies, since no consensus was verified in a systematic review.<sup>29</sup>

Studies on some risk factors, such as the presence of keratinized mucosa or the influence of implant surface on the prevalence of peri-implantitis are not yet abundant in the literature and apparently still require further investigation before reaching significant scientific evidence. Although scientific data are still conflicting and insufficient to demonstrate the role that keratinized mucosa can play on the longevity of osseointegrated dental implants,<sup>32,33,38</sup> the literature seems to support that the type and quality of soft tissue around dental implants play an important role in the achievement of long-term esthetic results for dental implants. Recent publications



have shown that implants used for immediate single-tooth replacements in esthetic areas of individuals with thin gingival phenotypes are more prone to undergo continuing recession of the facial gingival tissue than those placed under the same conditions in individuals with a thick gingival phenotype.<sup>39-41</sup> After 1 year of loading, patients with thin biotypes and not included in supportive maintenance program had a mean bone loss of 0.78 mm while the patients with a thick biotype included in a maintenance program had a mean bone loss of 0.09 mm.<sup>42</sup> In fact, prospective clinical trials are needed to elucidate the role of keratinized mucosa width and mucosal thickness in the maintenance of peri-implant health.

Apparently, many of the dental implant surface treatments proposed so far to favor osseointegration may as well render the implant surface more rough and, therefore, technically more susceptible to bacterial colonization. However, such influence has so far been demonstrated mostly in animal and/or *in vitro* studies.<sup>43,44</sup> Clinical literature has not conclusively yet demonstrated that rough-surfaced implants are more prone to developing peri-implantitis than smooth-surfaced implants.<sup>36</sup>

Implant survival has been used as primary outcome measurement in many studies to provide long-term data on the predictability or validity of osseointegration with respect to different patient characteristics, clinical conditions and medical devices.<sup>45</sup> However, it should be emphasized that a surviving implant may present important mechanical and/or biologic complications. In addition, the presence of the implant in the mouth may not be associated with maintenance or re-establishment of patient well-being.<sup>45</sup> For this reason, implant success rate could be considered a more realistic endpoint.

The prevalence of peri-implantitis has been addressed considering the participant and/or the implant as the unit of analysis. According to Atieh et al,<sup>10</sup> the outcome evaluated is determinant for the choice of the unit of analysis. The implant could be used as the unit of analysis if treatment protocols or morphologic features of implant designs and surfaces will be compared; however, the participant is a more appropriate unit of analysis in studies evaluating demographics, compliance and systemic conditions. The studies reviewed in this manuscript show that prevalence of peri-implantitis assessed at patient level is higher than that evaluated at implant level. In fact, data based on implants could underestimate the true prevalence of peri-implant diseases since each implant cannot be considered an independent unit and intraparticipant correlation among implants needs to be taken into account.<sup>46,47</sup> Hence, it is our understanding that, in order to implement effective prevention protocols

for the clinicians in implant dentistry, the prevalence and the identification of risk factors associated to peri-implantitis must be established.

Considering the increase in number of annual implant replacements, peri-implant diseases have become a challenge. According to a recent review, further studies are required to confirm the efficacy of current therapies proposed for peri-implantitis treatment. However, it is a consensus that long-term and periodical clinical and radiograph evaluations of peri-implant tissues are necessary.<sup>48,49</sup>

## CONCLUSION

Peri-implantitis is not an uncommon complication following implant therapy. The prevalence of this inflammatory condition ranges from 4.7 to 43% at implant level and from 8.9 to  $\geq 56\%$  at patient level, depending on the parameters used to define peri-implantitis. A higher prevalence of peri-implantitis has been identified for patients with history of periodontal disease and for smokers. In fact, the term risk factor has been used to describe factors that are associated with peri-implantitis. Up to date, no true risk factor for peri-implantitis has been established. Prospective longitudinal studies are needed to establish causality of a particular risk factor. Supportive maintenance program is essential to the long-term success of treatments with oral implants.

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