

PERI-IMPLANTITIS IN IMPLANT DENTISTRY: A REVIEW OF RISK FACTORS

Dr. Jaspreet Singh Badwal*

MDS Oral and Maxillofacial Surgery, Phulkian Enclave, Jail Road, Patiala.



*Corresponding Author: Dr. Jaspreet Singh Badwal

MDS Oral and Maxillofacial Surgery, Phulkian Enclave, Jail Road, Patiala.

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ABSTRACT

Purpose: The aim of this critical review is to investigate into the evidence required in relation to risk factors associated with peri-implantitis in implant dentistry. **Materials and Methods:** An electronic search was conducted across the various databases such as PUBMED, SCOPUS, EMBASE. In addition, a search over the Google search engine was conducted to find related studies. The search terms used were “peri-implantitis”, “peri-implant mucositis”, “peri-implant disease”, “risk factors” and “etiology”. **Results:** About 12 risk factors have been identified that are associated with peri-implantitis. **Conclusion:** The various risk factors associated with peri-implantitis have been discussed in detail in this critical review, based on best possible evidence available, so that the reader may comprehend the subject in an easy, yet comprehensive manner.

KEYWORDS: Peri-implantitis, risk factors, etiology, peri-implant mucositis, peri-implant disease.

INTRODUCTION

Dental implants form a contemporary essential part of any dental practice. This can be attributed to the fact that dental implants have shown a high survival rate in the range of 90-95% for more than 5 years.^[1] However, despite their formidable success, the number of complications associated with dental implants are reported to be progressively increasing^[2,3], as the number of patients receiving dental implants is continually growing.

Peri-implantitis may be considered to be one of the most common biological complications affecting functional implants. Peri-implantitis is defined as an inflammatory reaction with the loss of supporting bone in the tissues surrounding a functional implant.^[4] Due to the large variation in studies regarding the number and type of patients, function time and case definitions used for identification of peri-implantitis, highly variable prevalence rates have been reported for peri-implantitis, ranging from 1% to 47%.⁵ Meta-analyses of various studies reported weighted mean values between 20% and 22%.^[5,6]

The consensus report of Session IV of European Workshop described specific definitions for ‘peri-implant disease’, ‘peri-implant mucositis’, and ‘peri-implantitis’.^[4] The term ‘peri-implant disease’ was described as a collective term for inflammatory reactions in the tissues surrounding an implant. The term ‘peri-implant mucositis’ was used to describe a reversible inflammatory condition in the soft tissues surrounding an

implant. The term ‘peri-implantitis’ was used to describe inflammatory reactions with loss of supporting bone in the tissues surrounding a functioning implant. The 2017 World Workshop on Classification of Periodontal and Peri-implant Diseases and Conditions further modified the definition of peri-implantitis^[7], describing it as a plaque-associated pathological condition occurring in tissues around dental implants, that is characterized by inflammation in peri-implant mucosa and subsequent progressive loss of supporting bone.^[8]

PURPOSE: The aim of this critical review is to investigate into the evidence required in relation to risk factors associated with peri-implantitis in implant dentistry.

MATERIALS AND METHODS: An electronic search was conducted across the various databases such as PUBMED, SCOPUS, EMBASE. In addition, a search over the Google search engine was conducted to find related studies. The search terms used were “peri-implantitis”, “peri-implant mucositis”, “peri-implant disease”, “risk factors” and “etiology”.

RESULTS: About 12 risk factors have been identified that are associated with peri-implantitis. These risk factors may be classified as follows

(A) Site specific risk factors

- 1) Implant material and surface characteristics
- 2) Implant type and prosthetic design
- 3) Peri-implant soft tissue conditions
- 4) Bio-corrosion and presence of titanium particles

- 5) Poor plaque control and peri-implant mucositis
- 6) Iatrogenic factors.

(B) Patient related risk factors

- 1) Periodontal disease and associated microbiological aspects
- 2) Deficiencies in maintenance therapy
- 3) Smoking including cigarettes, Vaping, water pipes, smokeless tobacco and cannabis
- 4) Systemic conditions
- 5) Genetic factors
- 6) Occlusal load and para-functional habits.

DISCUSSION

In order to derive evidence based conclusions for prevention and management of peri-implantitis, it is essential to understand the risk factors associated with peri-implantitis.

IMPLANT MATERIAL AND SURFACE CHARACTERISTICS

Titanium has been the material of choice in implant dentistry. The surface roughness and surface energy of dental implants have an impact on initial biofilm formation but it's long term effect on inflammatory tissue reaction and pattern of bone loss is still controversial.^[9,10,11] A systematic review by Rakic et al^[12] showed that moderately rough implants are three times less affected by peri-implantitis compared with rough or machined ones. However, in another critical review, Doorneward et al^[13] found significantly lower bone loss around minimally rough surfaces compared with moderately rough and rough ones.

IMPLANT TYPE AND PROSTHETIC DESIGN

A poorly designed superstructure such as asymmetric prosthesis with a suboptimal emergence profile, would favour plaque accumulation, contributing to an increase in risk of peri-implantitis 4.3 times.^[14,15] Similarly, a poor marginal fit is also a detrimental risk factor for development of peri-implantitis.^[16] Dalago et al published their results in 2017, stating that cemented implant restorations are 3.6 times more prone to peri-implantitis compared with screw-retained ones.^[17] This is related to the risk of leaving excess cement in the submucosal region, especially when resin luting cements are utilized.^[18] As such deep submucosal margins should be avoided, so as to provide sufficient visibility and access for cement removal.^[19] Also, bone-level implant designs, combined with convex restorations at an angle exceeding 30°, significantly increase the risk of peri-implantitis.^[15] When compared to single crowns, full-mouth implant-supported fixed restorations have been associated with a 16-fold increase in peri-implantitis.^[17] This could be due to poor accessibility for plaque control.

Platform-switching has been recommended to reduce peri-implant bone loss but it's advantages are debatable.^[20] A systematic review by Monje et al.^[21], that

evaluated earlier systematic analyses, favored platform-switching for peri-implant bone preservation. This can be attributed to the relocation of microgap between the implant and the abutment.^[21] As this microgap is wide enough to allow for bacterial colonization, its horizontal offset away from the bone leads to reduced risk of peri-implant inflammation.^[22]

To implement the knowledge of above factors for reducing the risk of peri-implantitis, tissue-level implant designs have been recommended by some authors for non-aesthetic implant restorations due to the supramucosal location of microgap and their accessibility for plaque control. When bone level implants are indicated, platform-switching is advised with screw-retained superstructures and anatomically shaped emergence profiles. Also, screw retained prosthesis is easily retrievable when better visibility and access are required for treatment.

PERI-IMPLANT SOFT TISSUE CONDITIONS

Giovannoli et al^[23] published their results on influence of soft tissue condition around an implant over susceptibility to peri-implant disease. The authors concluded that patients with thin periodontal phenotypes are more vulnerable to peri-implant mucosal recessions. Other authors have also associated peri-implantitis and marginal bone loss with keratinized soft tissue width < 2mm.^[24,25,26] On the contrary, some studies have found that its absolute necessity is controversial.^[8,27]

BIO-CORROSION AND PRESENCE OF TITANIUM PARTICLES

Chemical corrosion, mechanical wear and implant surface treatment have been suggested as sources of titanium in tissues around implants.^[28] Souza et al^[29] used the term 'tribocorrosion' for describing the combination of wear and corrosion processes. In two studies by different groups, greater levels of titanium particles were detected in peri-implant soft tissue biopsies taken from fixtures with peri-implantitis compared with healthy sites.^[30,31]

POOR PLAQUE CONTROL AND PERI-IMPLANT MUCOSITIS

A high plaque index is associated with an eight fold increase in susceptibility to peri-implantitis.^[14] As such, a patient's self-performed plaque control is one of the most important factors influencing the prognosis of dental implants.^[8,24,32] The formation of bacterial biofilm on implant and abutment surfaces leads to peri-implant inflammation known as mucositis.^[33] Such mucositis is a precursor of peri-implantitis and the two share several risk factors including poor oral hygiene, smoking and submucosal presence of excess cement.^[33]

IATROGENIC FACTORS

The number of implants placed has not been associated with risk of peri-implantitis.^[34] However, the position of implants within the dental arch is critical for long term

success.^[35] Malpositioned implants present a significant risk for peri-implantitis.^[35] Crestal bone loss can occur around implants that have been placed too close to natural teeth or other implants.^[36] Fixtures located outside the bony cover or those with thin facial bone (< 1mm) are prone to mucosal recession.^[23] The placing of an implant 6 mm or more apical to cemento-enamel junction of adjacent teeth, increases risk of peri-implantitis by 8.5 times.^[14]

PERIODONTAL DISEASE AND MICROBIOLOGICAL ASPECTS

Hardt et al^[37] (2003) conducted a 5-year retrospective radiographic study to determine the outcome of implant therapy in relation to experience of periodontal tissue destruction in 97 partially edentulous patients. The study concluded that early failures of implants were more frequent in patients with previous history and diagnosis of periodontitis.

Wennstrom et al^[38] (2004) conducted a 5-year prospective randomized controlled trial to study the outcomes of dental implant therapy in periodontitis-susceptible subjects. The study reported few implant losses and relatively small amounts of marginal bone loss in these periodontitis-susceptible patients. The difference in outcomes of study by Wennstrom et al compared with those of Hardt et al could be attributed to differences in maintenance programs, such as frequency of recall visits.

More recently (2018), Ferreira et al^[39] conducted a systematic review and meta-analysis to evaluate periodontitis as a risk factor for peri-implantitis. This meta-analysis showed that patients with periodontitis had 2.29 times higher risk of peri-implantitis than patients without periodontitis (95% CI: 1.34 – 3.24). This association, however, was not observed when only the cohort studies were analyzed.

De Wall et al^[40] (2016) conducted a case-control study on microbial characteristics of peri-implantitis. The study concluded that peri-implantitis was significantly associated with submucosal presence of Porphyromonas gingivalis, Prevotella media, Tannerella forsythia and Fusobacterium nucleatum (odds ratio of 15.1).

LACK OF MAINTENANCE THERAPY

Peri-implant maintenance therapy has been shown to significantly lower the risk of peri-implant biological complications. A minimum recall interval of 5-6 months has been recommended.^[41,42] Factors that are used to assess the risk of peri-implantitis include percentage of BOP (bleeding on probing), prevalence of active residual pockets, oral hygiene level, smoking habits and presence of genetic or systemic conditions.^[43] Individuals with high-risk profile would require 3-4 annual visits^[43,44] and their attendance is a determining factor for prevention and early detection of peri-implantitis.^[45] One out of five non-compliant subjects would be diagnosed with peri-

implantitis within 5 years^[24], while better compliance is associated with 86% fewer peri-implantitis cases.

SMOKING INCLUDING CIGARETTES, VAPING, WATER PIPES, SMOKELESS TOBACCO AND CANNABIS

Several studies have proven smoking as a risk factor for peri-implantitis.^[14,46,47] Smoking has been shown to significantly affect implant's colonization with periodontal pathogens such as Porphyromonas gingivalis and Fusobacterium nucleatum.^[48] As such, smokers are almost twice more at risk of developing peri-implantitis compared with non-smokers.^[49] Furthermore, smoking is associated with increased severity of peri-implantitis lesions^[16] along with a dose dependent relationship between smoking and tissue destruction.

Use of electronic cigarettes (e-cigarettes) or vaping, have become popular in European and American continents. Though they are misconceived as harmless products, various studies have associated vaping with periodontal attachment loss and marginal bone resorption.^[50,51] A cross-sectional study by Al-Aali et al^[52] demonstrated significantly deeper peri-implant probing depths and increased marginal bone loss in vaping patients compared with never smokers.

Use of water pipes, also known as hookah, shisha or narjilah is associated with significantly higher risk of periodontitis compared with cigarette smokers, though the adverse effects were strongly related to duration and quantity of daily use.^[53] Most studies have so far focused on periodontal conditions in general and not peri-implantitis in particular.

Smokeless tobacco exerts adverse effects on periodontal and peri-implant tissues which are comparable to those of cigarette smoking.^[54,55] Akram et al^[55] found deeper probing depths and higher degrees of peri-implant bone loss in cigarette smokers and smokeless tobacco users compared to non-tobacco users.

Smoking of cannabis has been associated with higher prevalence and severity of periodontitis.^[56,57] However, evidence is still lacking regarding peri-implantitis.

SYSTEMIC CONDITIONS

Turri et al have shown that poorly controlled diabetics are at 46% higher risk of developing peri-implantitis, exhibiting deeper peri-implant pockets and higher marginal bone loss, as compared to normoglycaemic controls.^[58] Smokers and poorly controlled diabetics are considered at a similar risk for peri-implantitis. Non-smokers with poor glycaemic control are at 3.39 times higher risk of developing peri-implantitis compared with normoglycaemic subjects. As such, hyperglycaemia, not diabetes per se^[8], is a significant risk factor for peri-implantitis.

Several clinical studies have established obesity as a risk factor for peri-implantitis.^[59,60,61] In comparison to individuals with normal body weight, obese patients exhibit significantly higher percentages of bleeding on probing, deeper peri-implant probing depths and increased marginal bone loss.^[60,61] Also, the severity of peri-implant inflammation is significantly associated with level of obesity.^[59]

With regard to relation between cardiovascular diseases and peri-implantitis, some studies showed a significantly higher risk of peri-implantitis and additional bone loss for patients suffering from heart disease.^[62,63,64] However, the results are believed to be controversial.^[62,65]

Several authors have studied effect of different kinds of autoimmune diseases on peri-implantitis, yet conclusions could not be drawn due to the scarcity of evidence.^[62] Krennmaier et al^[66] showed that rheumatoid arthritis with concomitant connective tissue disease is associated with higher percentages of bleeding on probing and peri-implant bone loss. Korfage et al^[67] evaluated dental implants in patients with Sjogren's syndrome. The results did not show an increased prevalence of peri-implantitis. However, higher prevalence of mucositis in these patients may indicate an increased susceptibility to peri-implantitis.

The effect of osteoporosis and its concomitant medications on peri-implant health has been evaluated in different studies. Though osteoporosis could not be linked to peri-implantitis, Bisphosphonate (BP) therapy was shown to significantly increase marginal bone loss and implant thread exposure with BP intake.^[68] However, a systematic review by Stavropoulos et al^[69] revealed that low-dose BP did not negatively affect peri-implant bone levels. Hormone replacement therapy significantly compromised marginal bone levels.

GENETIC FACTORS

Genetic predisposition has been suspected to have a role in peri-implantitis. However, specific risk factors still need to be established.^[70] The increase in levels of two pro-inflammatory cytokines, IL-1 α and IL-1 β have been shown to be associated with peri-implantitis. Furthermore, their levels were correlated with severity of disease.^[70,71] However, conflicting results have been reported regarding this association.^[70,72,73,74] While some of the studies failed to confirm the association between IL-1 polymorphism and peri-implantitis^[71,73], a more recent study^[74] showed that subjects with IL-1 polymorphisms were 1.9 – 2.47 times more at risk of developing peri-implantitis. Various studies reported TNF- α as a pro-inflammatory cytokine that has been associated with peri-implant inflammation and bone destruction. While some studies^[70,75] have demonstrated that TNF- α polymorphism increased the risk of peri-implantitis by five to eight times, a meta-analysis of

relevant data could not show a significant correlation between the two conditions.^[76]

The role of other genetic polymorphisms, in relation to peri-implantitis, has been evaluated by few studies^[70], whereby no definite conclusions could be drawn, owing to the scarcity of evidence.

OCCLUSAL OVERLOAD AND PARA-FUNCTIONAL HABITS

The effect of occlusal overload on implant-supported prosthesis is a controversy.^[77,78] The underlying mechanism by which occlusal overload causes marginal bone loss around implants, is still debatable.^[77,78] However, several studies have exhibited that overloading of a dental implant beyond a certain limit, leads to increase in marginal bone loss.^[77,79,80] Yet, under similar overload, peri-implantitis affected sites exhibited significantly higher marginal bone loss compared to those with mucositis.^[81] The effect of occlusal overload on marginal bone loss around implants can be enhanced by sub-optimal implant positioning, poorly designed prosthetic reconstructions, inadequate bone quantity or poor quality of bone.^[77] Para-functional habits that lead to increased non-axial occlusal forces, may also cause increase in peri-implant marginal bone loss.

Also, attrition and wear of natural dentition or prosthetic reconstructions may be used as a sign of occlusal overload and para-functional habits. Dalago et al showed that presence of wear facets on implant supported prosthesis was associated with 2.4 times increase in prevalence of peri-implantitis.^[82] Some other studies^[83,84] have concluded that occlusal adjustment may result in peri-implant bone repair.

CONCLUSION

Peri-implantitis is a complex multifactorial disease. The various risk factors associated with peri-implantitis have been discussed in detail in this critical review, based on best possible evidence available, so that the reader may comprehend the subject in an easy, yet comprehensive manner.

FUTURE IMPLICATIONS

As the use of dental implants is continually increasing throughout the world, dental professionals should be aware of the various risk factors associated with peri-implantitis. Clinicians interested in implantology should be prepared for increased demand of supportive peri-implant care, as well as non-surgical and surgical interventions related to peri-implant disease.

CONFLICT OF INTERESTS

The author declares that there is no conflict of interests that could influence this work.

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ETHICAL APPROVAL

This article does not contain any studies with human participants or animals performed by the author.

REFERENCES

- Berglundh T, Persson LG, Klinge B. A systematic review of the incidence of biological and technical complications in implant dentistry reported in prospective longitudinal studies of at least 5 years. *J Clin Periodontol.*, 2008; 3: 197–212.
- Jung RE, Zembic A, Pjetursson BE, Zwahlen M, Thoma DS. Systematic review of the survival rate and the incidence of biological, technical, and aesthetic complications of single crowns on implants reported in longitudinal studies with a mean follow-up of 5 years. *Clin Oral Implant Res.*, 2012; 23(Suppl6): 2–21.
- Pjetursson BE, Thoma D, Jung R, Zwahlen M, Zembic A. A systematic review of the survival and complication rates of implant supported fixed dental prostheses (FDPs) after a mean observation period of at least 5 years. *Clinical Oral Implant Res.*, 2012; 23(Suppl 6): 22–38.
- Albrektsson T, Isidor F. Consensus Report of Session IV Proceedings of the 1st European Workshop on Periodontology. Switzerland. Quintessence Publishing Co., Ltd., 1993.
- Derks J, Tomasi C. Peri-implant health and disease. A systematic review of current epidemiology. *J Clin Periodontol.*, 2015; 42(Suppl 16): S158-S171.
- Mombelli A, Muller N, Cionca N. The epidemiology of peri-implantitis. *Clin Oral Implants Res.*, 2012; 23(Suppl 6): 67-76.
- Berglundh T, Armitage G, Araujo MG, et al. Peri-implant diseases and conditions: consensus report of workgroup 4 of the 2017 world workshop on the classification of periodontal and peri-implant diseases and conditions. *J Clin Periodontol.*, 2018; 45: S286-S291.
- Schwarz F, Derks J, Monje A, Wang HL. Peri-implantitis. *J Clin Periodontol.*, 2018; 45: S246-S266.
- De Bruyn H, Christiaens V, Doornewaard R, Jacobsson M, Cosyn J, Jacquet W, et al. Implant surface roughness and patient factors on long-term peri-implant bone loss. *Periodontol.*, 2017; 73(1): 218–27.
- Rasperini G, Maglione M, Cocconcilli P, Simion M. In vivo early plaque formation on pure titanium and ceramic abutments: a comparative microbiological and SEM analysis. *Clin Oral Implants Res.*, 1998; 9(6): 357–64.
- Albouy JP, Abrahamsson I, Persson LG, Berglundh T. Implant surface characteristics influence the outcome of treatment of periimplantitis: an experimental study in dogs. *J Clin Periodontol.*, 2011; 38(1): 58–64.
- Rakic M, Galindo-Moreno P, Monje A, Radovanovic S, Wang HL, Cochran D, et al. How frequent does peri-implantitis occur? A systematic review and meta-analysis. *Clin Oral Investig.*, 2018; 22(4): 1805–16.
- Doornewaard R, Jacquet W, Cosyn J, De Bruyn H. How do peri-implant biologic parameters correspond with implant survival and peri-implantitis? A critical review. *Clin Oral Implants Res.*, 2018; 29(Suppl 18): 100–23.
- Kumar PS, Dabdoub SM, Hegde R, Ranganathan N, Mariotti A. Site-level risk predictors of peri-implantitis: a retrospective analysis. *J Clin Periodontol.*, 2018; 45(5): 597–604.
- Katafuchi M, Weinstein BF, Leroux BG, Chen YW, Daubert DM. Restoration contour is a risk indicator for peri-implantitis: a cross-sectional radiographic analysis. *J Clin Periodontol.*, 2018; 45(2): 225–32.
- Saaby M, Karring E, Schou S, Isidor F. Factors influencing severity of peri-implantitis. *Clin Oral Implants Res.*, 2016; 27(1): 7–12.
- Dalago HR, Schuldt Filho G, Rodrigues MA, Renvert S, Bianchini MA. Risk indicators for peri-implantitis. A cross-sectional study with 916 implants. *Clin Oral Implants Res.*, 2017; 28(2): 144–50.
- Quaranta A, LimZW, Tang J, Perrotti V, Leichter J. The impact of residual subgingival cement on biological complications around dental implants: a systematic review. *Implant Dent.*, 2017; 26(3): 465–74.
- Staubli N, Walter C, Schmidt JC, Weiger R, Zitzmann NU. Excess cement and the risk of peri-implant disease—a systematic review. *Clin Oral Implants Res.*, 2017; 28(10): 1278–90.
- Hsu YT, Lin GH, Wang HL. Effects of platform-switching on peri-implant soft and hard tissue outcomes: a systematic review and meta-analysis. *Int J Oral Maxillofac Implants.*, 2017; 32(1): e9–e24.
- Monje A, Pommer B. The concept of platform switching to preserve peri-implant bone level: assessment of methodologic quality of systematic reviews. *Int J Oral Maxillofac Implants.*, 2015; 30(5): 1084–92.
- Sasada Y, Cochran DL. Implant-abutment connections: a review of biologic consequences and peri-implantitis implications. *Int J Oral Maxillofac Implants.*, 2017; 32(6): 1296–307.
- Giovannoli JL, Rocuzzo M, Albouy JP, Duffau F, Lin GH, Serino G. Local risk indicators—consensus report of working group 2. *Int Dent J.*, 2019; 69(Suppl 2): 7–11.
- Rokn A, Aslroosta H, Akbari S, Najafi H, Zayeri F, Hashemi K. Prevalence of peri-implantitis in patients not participating in well-designed supportive periodontal treatments: a cross-sectional study. *Clin Oral Implants Res.*, 2017; 28(3): 314–9.

25. Perussolo J, Souza AB, Matarazzo F, Oliveira RP, Araujo MG. Influence of the keratinized mucosa on the stability of peri-implant tissues and brushing discomfort: a 4-year follow-up study. *Clin Oral Implants Res.*, 2018; 29(12): 1177–85.
26. Wada M, Mameno T, Onodera Y, Matsuda H, Daimon K, Ikebe K. Prevalence of peri-implant disease and risk indicators in a Japanese population with at least 3 years in function-a multicentre retrospective study. *Clin Oral Implants Res.*, 2019; 30(2): 111–20.
27. Fiorellini JP, Luan KW, Chang YC, Kim DM, Sarmiento HL. Peri-implant mucosal tissues and inflammation: clinical implications. *Int J Oral Maxillofac Implants.*, 2019; 34: s25–33.
28. Delgado-Ruiz R, Romanos G. Potential causes of titanium particle and ion release in implant dentistry: a systematic review. *Int J Mol Sci.*, 2018; 19(11): 3585.
29. Souza J, Barbosa S, Ariza E, Celis J-P, Rocha L. Simultaneous degradation by corrosion and wear of titanium in artificial saliva containing fluorides. *Wear.*, 2012; 292: 82–8.
30. Pettersson M, Kelk P, Belibasakis GN, Bylund D, Molin Thoren M, Johansson A. Titanium ions form particles that activate and execute interleukin-1beta release from lipopolysaccharide-primed macrophages. *J Periodontal Res.*, 2017; 52(1): 21–32.
31. Fretwurst T, Nelson K, Tarnow DP, Wang HL, Giannobile WV. Is metal particle release associated with peri-implant bone destruction? An emerging concept. *J Dent Res.*, 2018; 97(3): 259–65.
32. Ferreira SD, Silva GL, Cortelli JR, Costa JE, Costa FO. Prevalence and risk variables for peri-implant disease in Brazilian subjects. *J Clin Periodontol.*, 2006; 33(12): 929–35.
33. Heitz-Mayfield LJA, Salvi GE. Peri-implant mucositis. *J Periodontol.*, 2018; 89(Suppl 1): S257–S66.
34. Passoni BB, Dalago HR, Schuldt Filho G, Oliveira de Souza JG, Benfatti CA, Magini RES, et al. Does the number of implants have any relation with peri-implant disease? *J Appl Oral Sci : revista FOB.*, 2014; 22(5): 403–8.
35. Canullo L, Tallarico M, Radovanovic S, Delibasic B, Covani U, Rakic M. Distinguishing predictive profiles for patient-based risk assessment and diagnostics of plaque induced, surgically and prosthetically triggered peri-implantitis. *Clin Oral Implants Res.*, 2016; 27(10): 1243–50.
36. Lindhe J, Lang NP, Berglundh T, Giannobile WV, Sanz M. *Clinical periodontology and implant dentistry*. Sixth edition. ed. Chichester: West Sussex, John Wiley and Sons, Inc., 2015.
37. Hardt CR, Gröndahl K, Lekholm U, Wennström JL. Outcome of implant therapy in relation to experienced loss of periodontal bone support: a retrospective 5- year study. *Clin Oral Implants Res.*, 2002 Oct; 13(5): 488-94. doi: 10.1034/j.1600-0501.2002.130507.x. PMID: 12453125.
38. Wennström JL, Ekestubbe A, Gröndahl K, Karlsson S, Lindhe J. Oral rehabilitation with implant-supported fixed partial dentures in periodontitis-susceptible subjects. A 5-year prospective study. *J Clin Periodontol.*, 2004 Sep; 31(9): 713-24. doi: 10.1111/j.1600-051X.2004.00568.x. PMID: 15312092.
39. Ferreira SD, Martins CC, Amaral SA, Vieira TR, Albuquerque BN, Cota LOM, Esteves Lima RP, Costa FO. Periodontitis as a risk factor for peri-implantitis: Systematic review and meta-analysis of observational studies. *J Dent.*, 2018 Dec; 79: 1-10. doi: 10.1016/j.jdent.2018.09.010. Epub 2018 Nov 2. PMID: 30391683.
40. de Waal YC, Eijsbouts HV, Winkel EG, van Winkelhoff AJ. Microbial Characteristics of Peri-Implantitis: A Case-Control Study. *J Periodontol.*, 2017 Feb; 88(2): 209-217. doi: 10.1902/jop.2016.160231. Epub 2016 Sep 26. PMID: 27666672.
41. Renvert S, Quirynen M. Risk indicators for peri-implantitis. A narrative review. *Clin Oral Implants Res.*, 2015; 26(Suppl 11): 15–44.
42. Monje A, Aranda L, Diaz KT, Alarcon MA, Bagramian RA, Wang HL, et al. Impact of maintenance therapy for the prevention of peri-implant diseases: a systematic review and meta-analysis. *J Dent Res.*, 2016; 95(4): 372–9.
43. Lang NP, Suvan JE, Tonetti MS. Risk factor assessment tools for the prevention of periodontitis progression a systematic review. *J Clin Periodontol.*, 2015; 42(Suppl 16): S59–70.
44. Armitage GC, Xenoudi P. Post-treatment supportive care for the natural dentition and dental implants. *Periodontol.*, 2016; 71(1): 164–84.
45. Monje A, Wang HL, Nart J. Association of preventive maintenance therapy compliance and peri-implant diseases: a cross-sectional study. *J Periodontol.*, 2017; 88(10): 1030–41.
46. Gurlek O, Gumus P, Buduneli N. Smokers have a higher risk of inflammatory peri-implant disease than non-smokers. *Oral Dis.*, 2018; 24(1–2): 30–2.
47. Pham TAV, Kieu TQ, Ngo LTQ. Risk factors of periodontal disease in Vietnamese patients. *J Investig Clin Dent.*, 2018; 9(1).
48. Geisinger ML, Geurs NC, Ogdon D, Reddy MS. Commentary: targeting underlying biologic mechanisms in selecting adjunctive therapies to improve periodontal treatment in smokers: a commentary. *J Periodontol.*, 2017; 88(8): 703–10.
49. Dreyer H, Grischke J, Tiede C, Eberhard J, Schweitzer A, Toikkanen SE, et al. Epidemiology and risk factors of periimplantitis: A systematic review. *J Periodontal Res.*, 2018; 53(5): 657–81.
50. Javed F, Abduljabbar T, Vohra F, Malmstrom H, Rahman I, Romanos GE. Comparison of periodontal parameters and self-perceived oral symptoms among cigarette smokers, individuals vaping electronic

- cigarettes, and never-smokers. *J Periodontol.*, 2017; 88(10): 1059–65.
51. Javed F, Kellesarian SV, Sundar IK, Romanos GE, Rahman I. Recent updates on electronic cigarette aerosol and inhaled nicotine effects on periodontal and pulmonary tissues. *Oral Dis.*, 2017; 23(8): 1052–7.
 52. Al-Aali KA, Alrabiah M, ArRejaie AS, Abduljabbar T, Vohra F, Akram Z. Peri-implant parameters, tumor necrosis factor-alpha, and interleukin-1 beta levels in vaping individuals. *Clin Implant Dent Relat Res.*, 2018; 20(3): 410–5.
 53. Natto S, BaljoonM, BergstromJ. Tobacco smoking and periodontal health in a Saudi Arabian population. *J Periodontol.*, 2005; 76(11): 1919–26.
 54. Kulkarni V, Uttamani JR, Bhatavadekar NB. Comparison of clinical periodontal status among habitual smokeless-tobacco users and cigarette smokers. *Int Dent J.*, 2016; 66(1): 29–35.
 55. Akram Z, Vohra F, Bukhari IA, Sheikh SA, Javed F. Clinical and radiographic peri-implant parameters and proinflammatory cytokine levels among cigarette smokers, smokeless tobacco users, and nontobacco users. *Clin Implant Dent Relat Res.*, 2018; 20(1): 76–81.
 56. Chisini LA, Cademartori MG, Francia A, Mederos M, Grazioli G, Conde MCM, Correa MB. Is the use of Cannabis associated with periodontitis? A systematic review and meta-analysis. *J Periodontal Res.*, 2019 Aug; 54(4): 311–317. doi: 10.1111/jre.12639. Epub 2019 Jan 24. PMID: 30677134.
 57. Hughes FJ, Bartold PM. Periodontal complications of prescription and recreational drugs. *Periodontol.*, 2018; 78(1): 47–58.
 58. Turri A, Rossetti PH, Canullo L, Grusovin MG, Dahlin C. Prevalence of peri-implantitis in medically compromised patients and smokers: a systematic review. *Int J Oral Maxillofac Implants.*, 2016; 31(1): 111–8.
 59. Vohra F, Alkhudairy F, Al-Kheraif AA, Akram Z, Javed F. Peri-implant parameters and C-reactive protein levels among patients with different obesity levels. *Clin Implant Dent Relat Res.*, 2018; 20(2): 130–6.
 60. Abduljabbar T, Al-Sahaly F, Kellesarian SV, Kellesarian TV, Al-Anazi M, Al-Khathami M, et al. Comparison of peri-implant clinical and radiographic inflammatory parameters and whole salivary destructive inflammatory cytokine profile among obese and nonobese men. *Cytokine.*, 2016; 88: 51–6.
 61. Alkhudairy F, Vohra F, Al-Kheraif AA, Akram Z. Comparison of clinical and radiographic peri-implant parameters among obese and non-obese patients: a 5-year study. *Clin Implant Dent Relat Res.*, 2018; 20(5): 756–62.
 62. Guobis Z, Pacauskiene I, Astramskaite I. General diseases influence on peri-implantitis development: a systematic review. *J Oral Maxillofac Res.* 2016; 7(3): e5.
 63. Krennmair S, Weinlander M, Forstner T, Krennmair G, Stimmelmayer M. Factors affecting peri-implant bone resorption in four implant supported mandibular full-arch restorations: a 3-year prospective study. *J Clin Periodontol.*, 2016; 43(1): 92–101.
 64. Ting M, Craig J, Balkin BE, Suzuki JB. Peri-implantitis: a comprehensive overview of systematic reviews. *J Oral Implantol.*, 2018; 44(3): 225–47.
 65. de Souza JG, Neto AR, Filho GS, Dalago HR, de Souza Junior JM, Bianchini MA. Impact of local and systemic factors on additional peri-implant bone loss. *Quintessence Int.*, 2013; 44(5): 415–24.
 66. Krennmair G, Seemann R, Piehslinger E. Dental implants in patients with rheumatoid arthritis: clinical outcome and peri-implant findings. *J Clin Periodontol.*, 2010; 37(10): 928–36.
 67. Korfage A, Raghoobar GM, Arends S, Meiners PM, Visser A, Kroese FG, et al. Dental implants in patients with Sjogren's syndrome. *Clin Implant Dent Relat Res.*, 2016; 18(5): 937–45.
 68. Zahid TM, Wang BY, Cohen RE. Influence of bisphosphonates on alveolar bone loss around osseointegrated implants. *J Oral Implantol.*, 2011; 37(3): 335–46.
 69. Stavropoulos A, Bertl K, Pietschmann P, Pandis N, Schiodt M, Klinge B. The effect of antiresorptive drugs on implant therapy: systematic review and meta-analysis. *Clin Oral Implants Res.*, 2018; 29(Suppl 18): 54–92.
 70. Eguia Del Valle A, Lopez-Vicente J, Martinez-Conde R, Aguirre-Zorzano LA. Current understanding of genetic polymorphisms as biomarkers for risk of biological complications in implantology. *J Clin Exp Dent.*, 2018; 10(10): e1029–e39.
 71. García-Delaney C, Sánchez-Garcés MÁ, Figueiredo R, Sánchez-Torres A, Gay-Escoda C. Clinical significance of interleukin-1 genotype in smoking patients as a predictor of peri-implantitis: a case-control study. *Med Oral Patol Oral Cir Bucal.*, 2015; 20(6): e737–e43.
 72. DerekaX, MardasN, ChinS, PetrieA, DonosN. A systematic review on the association between genetic predisposition and dental implant biological complications. *Clin Oral Implants Res.*, 2012; 23(7): 775–88.
 73. Melo RF, LopesBM, Shibli JA, Marcantonio E, Marcantonio RA, Galli GM. Interleukin-1 β and interleukin-6 expression and gene polymorphisms in subjects with peri-implant disease. *Clin Implant Dent Relat Res.*, 2012; 14(6): 905–14.
 74. He K, Jian F, He T, Tang H, Huang B, Wei N. Analysis of the association of TNF-alpha, IL-1A, and IL-1B polymorphisms with peri-implantitis in a Chinese non-smoking population. *Clin Oral Investig.*, 2019; 24: 693–9.

75. Petkovic-Curcin A, Zeljic K, Cikota-Aleksic B, Dakovic D, Tatic Z, Magic Z. Association of cytokine gene polymorphism with peri-implantitis risk. *Int J Oral Maxillofac Implants.*, 2017; 32(5): e241–e8.
76. Mo YY, Zeng XT, Weng H, Cen Y, Zhao Q, Wen X. Association between tumor necrosis factor- α G-308A polymorphism and dental peri-implant disease risk: a meta-analysis. *Medicine (Baltimore)*, 2016; 95(35): e4425.
77. Fu JH, Hsu YT, Wang HL. Identifying occlusal overload and how to deal with it to avoid marginal bone loss around implants. *Eur J Oral Implantol.*, 2012; 5(Suppl): S91–103.
78. Pellegrini G, Canullo L, Dellavia C. Histological features of peri-implant bone subjected to overload. *Ann Anat.*, 2016; 206: 57–63.
79. Isidor F. Histological evaluation of peri-implant bone at implants subjected to occlusal overload or plaque accumulation. *Clin Oral Implants Res.*, 1997; 8(1): 1–9.
80. Miyata T, Kobayashi Y, Araki H, Ohto T, Shin K. The influence of controlled occlusal overload on peri-implant tissue. Part 4: a histologic study in monkeys. *Int J Oral Maxillofac Implants.*, 2002; 17(3): 384–90.
81. Gottfredsen K, Berglundh T, Lindhe J. Bone reactions at implants subjected to experimental peri-implantitis and static load. A study in the dog. *J Clin Periodontol.*, 2002; 29(2): 144–51.
82. Dalago HR, Schuldt Filho G, Rodrigues MA, Renvert S, Bianchini MA. Risk indicators for peri-implantitis. A cross-sectional study with 916 implants. *Clin Oral Implants Res.*, 2017; 28(2): 144–50.
83. Merin RL. Repair of peri-implant bone loss after occlusal adjustment: a case report. *J Am Dent Assoc.*, 2014; 145(10): 1058–62.
84. Passanezi E, Sant'Ana AC, Damante CA. Occlusal trauma and mucositis or peri-implantitis? *J Am Dent Assoc.*, 2017; 148(2): 106–12.