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Patient-related risk factors for peri-implantitis and pre-implant treatment

Introduction: Peri-implantitis represents a major complication for the long-term preservation of dental implants and is often attributable to the combined effect of risk factors. This review aims to present patient-related risk factors that are linked to peri-implantitis and to discuss possible solutions in terms of a pre-implant therapy.

Material and methods: While implant characteristics and surgical techniques are patient-independent risk factors for peri-implantitis, patient-related factors may also potentially contribute to an increased risk of developing peri-implantitis. The most commonly discussed factors include patient age, medication and other medical treatments, existing periodontitis, plaque and limited oral hygiene, patient compliance related to supportive implant therapy, lack of attached gingiva, smoking, diet, diabetes, and patient genetics.

Conclusion: Whereas patient age was not found to diminish implant survival and the factor genetics is currently considered to be unpredictable, potential influencing measures could be identified for the other risk factors. These include a comprehensive anamnesis and diagnosis, attention to contraindications (e.g. i.v. antiresorptives, patients receiving radiotherapy and smoking simultaneously), treatment of existing periodontitis, smoking cessation, adequate adjustment of HbA_{1c} values in diabetics, dietary counseling, plaque reduction, attention to and creation of attached gingiva and sufficient hard tissue as well as offering a well-structured supportive implant therapy.

Keywords: diabetes; diet; implant aftercare; peri-implantitis; plaque; pre-implant treatment; risk factors; smoking

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Translation from German: Cristian Miron
Citation: Woelber JP, Fretwurst T: Patient-related risk factors for peri-implantitis and pre-implant treatment. Dtsch Zahnärztl Z Int 2022; 4: 36–44
Peer reviewed article: submitted: 02.03.2021, revised version accepted: 14.07.2021
DOI.org/10.53180/dzz-int.2022.0005

Introduction

Dental implant placement is nowadays a routinely and widely used procedure for the replacement of teeth, which has the advantage of conserving the adjacent teeth. It is estimated that around 12 million implants are placed annually worldwide [1]. Implants show survival rates of over 90% in 10-year follow-up studies [29, 44]. However, one of the main complications that limits the long-term success of implants is peri-implantitis. It affects an average 22% of implants and it is not treatable predictably using current methods [7, 14]. For this reason, the prevention of peri-implantitis is of critical importance.

While the choice of implant materials and surgical techniques are two factors that the dental team can directly influence in the prevention of peri-implantitis, patients themselves harbor factors for the development of peri-implantitis, namely the interplay between biofilm and the immunological response (Figure 1). Similar to the "host-mediated dysbiosis" described in the etiology of periodontitis, both the immune system as well as the patient's behavior play significant roles. Furthermore, it is believed that the inflammatory process of peri-implant mucositis is a precursor stage to peri-implantitis, which is then accompanied by irreversible bone resorption [51]. Taking into account the varying influences that can lead to peri-implantitis, it comes as no surprise that a recent study was able to demonstrate strong interindividual differences in the immunohistological response associated with peri-implantitis (at the time of explantation) [12]. The risk factors of peri-implantitis can exert both a strong localized influence (such as plaque and attached gingiva), as well as a strong systemic effect (such as medications, age, smoking).

In order to identify patient-related risk factors that are involved in triggering such individually varying immune responses, it may be helpful to ask how tooth loss occurred in the first place before implants are placed. Apart from trauma and tumor-related reasons, it can be assumed that either genetic and/or behavioral factors (resulting in caries and periodontitis) have resulted in tooth loss. While the development of caries is primarily determined by the increased consumption of processed carbohydrates (such as sugar, sweets, soft drinks, juices), on the one hand, and fluoridation through oral hygiene measures, on the other, other immunomodulatory risk factors play a role in the etiology of periodontitis [31, 47]. Besides the special factor, namely plaque, behaviors such as smoking, pro-inflammatory diets, physical inactivity, and stress augment a possible genetic predisposition [9, 13, 30, 47, 50, 71]. Even though many of these risk factors for periodontitis have been substantiated with robust evidence, they are poorly documented in the context of peri-implant inflammation in the current scientific debate. In this respect, in what follows, the various peri-implant risk factors will be presented in terms of their varying importance and preventive options will then be suggested, where possible.

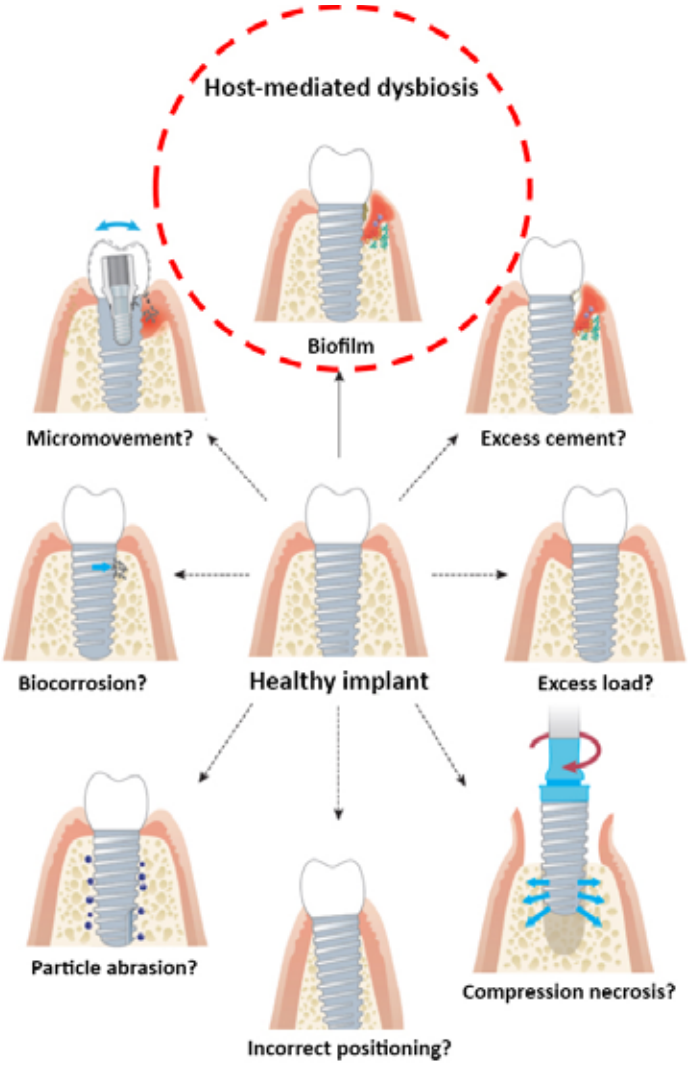

Figure 1 Multifactorial etiology of peri-implant bone resorption. Besides implant-related and surgery-related factors, biofilm is a patient-related risk factor in the interplay between immunology and plaque control ("host-mediated dysbiosis"). Modified according to Fretwurst et al. [19, 21].

Patient-related risk factors and recommended pre-implant treatment measures

Factor age

Aging is associated with many immunomodulatory processes that, collectively, can result in an increased tendency for inflammation. In this con-

text, the term "inflammaging" is also used [18]. Nevertheless, based on a systematic review, chronological age alone does not seem to be a risk factor for implant survival over a period of 1–5 years [57]. However, it must be taken into account that in quite a few studies, a more or less arbitrary age threshold (e.g. definition of "old" at >75 years) was used, and long-term studies regarding an association between age and peri-implant bone resorption or peri-implantitis are still missing [21]. Careful consideration should also be given to the fact that, with advancing age, the number of underlying diseases and prescribed drugs increases, too, and this may likewise have an impact on implant success. Last but not least, genetics, environmental and socioeconomic conditions as well as lifestyle and general health influence the aging process; this can lead to interindividual differences between chronological and biological age [37, 48]. The value of chronological age as a risk factor alone is therefore questionable.
Recommended measures: According to current data, chronological age is not a risk factor for peri-implantitis. For older patients, possible polypharmacy should be carefully considered.

Factor drugs and other medical therapies

The effects of drugs (and their interactions) on implant survival or success are poorly investigated [10, 21]. Antiresorptive drugs are an exception: two systematic reviews have demonstrated that implant survival rates in patients who take low-dose (oral) bisphosphonates (BP) or antiresorptive drugs (denosumab: Prolia®, Xgeva®) are the same as in healthy patients who do not take such drugs [57, 63]. However, the risk of MRONJ (medication-related osteonecrosis of the jaw) must be considered and prophylactic antibiotics are recommended. High-dose BP and antibody therapy lead to the highest incidence of MRONJ, and consequently, implant therapy is not recommended in this patient group at present [54, 64]. For risk evalulation prior to implant treatment, the DGI's plan routing slip "Risiko-Evaluation bei antiresorptiver Therapie vor Implantation" is recommended (https://www.dginet.de/documents/10164/1523441/Laufzettel_Farbe+_+2.pdf/0bee9d86–22d7–4121-ad85-f531ab1d6c9e) or the corresponding guidelines (S3 Guideline "Antiresorptiva-assoziierte Kiefernekrosen"/"Antiresorptive drugs-associated necrosis of the jaw" (AR-ONJ) and the S3 Guideline "Zahnimplantate bei medikamentöser Behandlung mit Knochenantiresorptiva (inkl. Bisphosphonate)"/"Dental implants during drug treatment with bone antiresorptives (incl. bisphosphonates)"). For patients with peri-implantitis who receive antiresorptive drugs, no treatment schemes are available [21, 68].

Furthermore, omeprazole (proton pump inhibitor) and sertraline (selective serotonin reuptake inhibitor) are currently discussed as "potential" risk factors based on a low level of evidence [10]. Levothyroxine and simvastatin, which are also among the 20 most commonly prescribed drugs, cannot be evaluated due to the lack of data. Moreover, it is unclear whether anticoagulants and the new direct oral anticoagulants are a risk factor for implant survival [25]. The increased postoperative bleeding risk should be taken into consideration in this patient group [6, 40].

A systematic review examining immunosuppression and implant survival for 24-month follow-up periods reported a median implant survival of 93.1% in HIV patients, 98.8% in patients receiving chemotherapy, 88.75% in patients with autoimmune diseases, and 100% in patients following organ transplantation [16].

In addition to drugs, other medical treatments such as radiotherapy can influence implant survival. In this regard, it is important to consider the risk of osteonecrosis. Implant survival tends to be lower in patients who have received radiotherapy as compared to healthy patients, but there is no reliable data on peri-implantitis [58]. An absolute contraindication is the condition after radiotherapy in smoking patients. According to the current guideline, the time interval between radiotherapy and implant placement has no effect on implant prognosis [56]. However, a waiting period of 6–12 months after radiotherapy is recommended in order to allow early and delayed radiation effects, especially on the oral soft tissues, to subside. Up to 6 months should be waited for implant healing to occur. Perioperative systemic antiinfective prophylaxis (e.g. amoxicillin, clindamycin) should be given according to the shared statement of the DGZMK and DEGRO.
R**ecommended measures:** Implant treatment in patients who take oral BP and have a low-risk profile is possible under antibiotic prophylaxis (prolonged perioperative systemic antibiotic administration with, for example, 1 g amoxicillin 1–1–1 or 0.6 g clindamycin 1–1–1). The risk of MRONJ should be considered. Implant procedures are contraindicated under i.v. BP therapy. Augmentative procedures should generally be avoided under BP therapy. Immunosuppressed patients usually do not show poorer implant survival than healthy patients during follow-up periods of up to 2 years. However, implant treatment should be carefully considered in these patients. Perioperative antibiotic prophylaxis is strongly recommended in this patient group. No evidence-based statements can be made regarding implant placement in patients who have undergone radiotherapy. Implant placement should be delayed for 6–12 months after irradiation.

Factor periodontitis

Apart from the fact that periodontitis is considered the major cause of tooth loss from advanced adulthood, the presence of periodontitis can be understood as a sign of immune modulation [4]. In this respect, it does not seem surprising that existing periodontitis is likewise a risk factor for the development of peri-implantitis [34, 41]. This is especially true in cases where there is a strong genetic component in the development of periodontitis from a young age (formerly classified as "aggressive periodontitis", now grade C with possibly a molar-incisive pattern). A prospective cohort study which examined 35 patients with "generalized aggressive periodontitis"

found a 5-fold increased risk of early implant loss, a 3-fold increased risk of peri-implant mucositis, and a 14-fold increased risk of peri-implantitis compared to 18 periodontally healthy patients who were treated with implants [66]. This result was also confirmed in a subsequent meta-analysis [67]. Pre-existing periodontitis seems to be a risk factor for the development of peri-implantitis in older patients, too [34]. However, this risk is greatly reduced if patients who are affected by periodontitis receive adequate periodontal treatment in advance and are commited to participate in a recall system [27, 41].

Recommended measures: At least the periodontal screening index (PSI) must be recorded prior to implant treatment. If PSI values 3 are recorded in 2 sextants, systematic periodontal therapy is indicated prior to implant placement [3]. Optimally, as a prerequisitve for implant treatment, increased probing depths (>4 mm) should no longer be recorded in the re-evaluation of the periodontal treatment outcome [27]. Patients with grade C periodontitis should be informed about an increased risk of peri-implantitis.

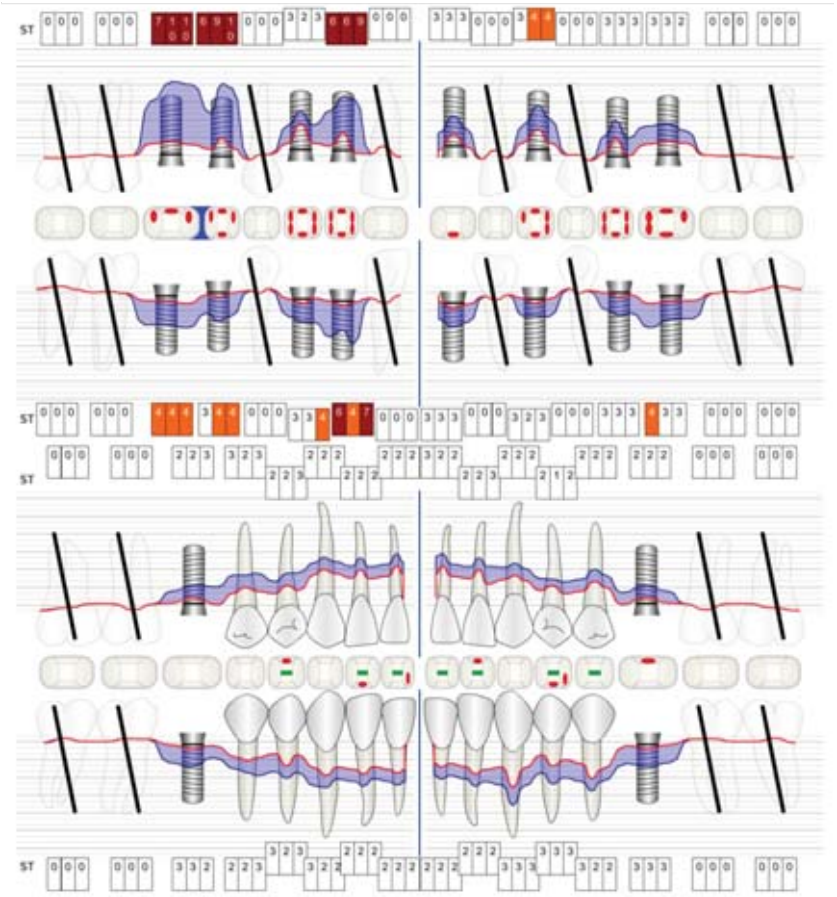

Figure 2 Implant and periodontal status (created using Parostatus.de©) of a 56-year-old smoker with peri-implantitis in regions 16, 15, 12 and peri-implant mucositis in regions 13, 23 and 26.

Factor plaque

Plaque is one of the best-studied factors that is known to promote gingival and mucosal inflammation, not only around teeth, but also around implants [28, 51]. However, owing to the ubiquitous presence of biofilm in the oral cavity, this link has not been unequivocally proven as an etiologic factor [11]. In contrast, plaque control has been established as an evidence-based measure to control peri-implant tissue inflammation [28].

Recommended measures: Professional tooth cleaning and encouraging home-based plaque control. Before implant placement, professional tooth cleaning should be performed and adequate home-based plaque control should be established. This includes the collection of the plaque and bleeding indices and advice regarding which oral hygiene aids are best suited for the patient. Repeated follow-up checks are advisable when lots of plaque and severe gingivitis is present.

Factor compliance/recall behavior

Studies investigating periodontal disease have substantiated the paramount importance of patient compliance to participate in supportive periodontal therapy; similarly, an increasing number of studies have appeared in recent years that support the importance of compliance to participate for long-term implant survival and prevention of peri-implantitis [17, 23]. A retrospective study over a 7-year period was able to determine a 4.25-fold higher incidence of peri-implantitis when only irregular participation in the program of supportive implant therapy was recorded [23]. When a well-structured, supportive implant therapy program was offered, participant compliance was determined at over 60 % [42].

Recommended measures: Patient inclusion in supportive implant therapy. A well-structured therapy program includes regular, repeated clinical examinations of implants, the recording of probing depths and possible bleeding on probing as well as professional mechanical plaque reduction. It also includes patient motivation and instruction on oral hygiene at home and the continuous minimization of possible risk factors.

Factor soft and hard tissue

In principle, soft and hard tissues diagnosis is required prior to implant treatment. In terms of soft tissue, attention should be paid to the quantity of attached gingiva, the gingival phenotype (thin/thick) and the presence of any pathological mucosal changes. Current literature suggests that >2 mm of attached gingiva is needed at the peri-implant site [5, 36]. Although the importance of the attached gingiva with regard to the prevention of peri-implant inflammation

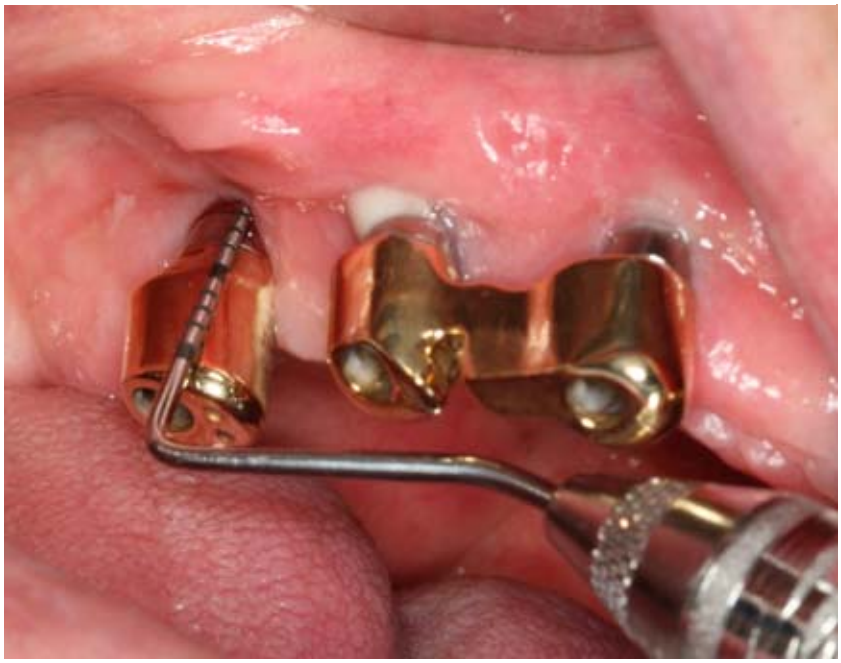

Fig. 1–3: J. P. Wölber

Figure 3 Clinical image showing the outflow of pus at site 15 after probing in the same smoking patient.

has long been discussed [7], its importance has been emphasized in more recent literature [26, 33, 35]. This may also affect the subsequent treatment of peri-implantitis [65].

The position of the adjacent and antagonist teeth (dimension of the subsequent prosthetic superstructure) as well as the jaw relation should be considered during implant planning.

For the assessment of hard tissue, imaging diagnostics are needed prior to implant treatment in order to visualize potential risk structures. Orthopantomograms (OPG) as well as a cone-beam CT (CBCT) represent imaging options for the visualization of hard tissue. With regard to the indication of a CBCT prior to implant treatment, reference is made here to the S2k Guideline [59]. Currently, 1 mm, or preferably 2 mm, of peri-implant bone is required [8].

Recommended measures: Detailed diagnosis of soft and hard tissues prior to implant treatment. In cases of insufficient fixed gingiva, its creation, for example, by means of connective tissue transplantation from the palate is a recommended preventive measure after implant placement. Insufficient fixed gingiva can also be augmented by means of vestibuloplasty with a free mucosa graft. However, it is not clear which dimension (width, thickness) of fixed gingiva leads to a lower prevalence of peri-implantitis. Literature currently states that >2 mm of fixed, peri-implant gingiva is needed [5, 36]. Concerning hard tissue, at least 1–2 mm of peri-implant bone should be present.

Factor smoking

Smoking has been recognized as a risk factor in the new classification of periodontal and peri-implant diseases and conditions [7, 28]. An increased risk (odds ratio 5.89) for the development of peri-implantitis was found in smokers according to a cohort study performed in a practice-based setting [52]. In a long-term study, smoking was correlated with peri-implant mucositis, bone resorption and peri-implantitis [53]. Figure 2 shows periodontal and peri-implant findings in a female smoker with clinical release of pus after probing in regio 15 (Figure 3).

Recommended measures: Smoking cessation and/or smoking withdrawal is advisable. For the prevention of peri-implantitis, a possible smoking status should be recorded in the anamnesis and smokers should be advised to stop smoking [70]. If professional help is not offered for quitting smoking in the practice setting, a third party health psychologist or physician should be consulted. Radiation in the head and neck region in patients who (continue to) smoke is an absolute contraindication for implants due to the increased risk of osteoradionecrosis.

Factor diet

Though the relationship between diet and caries has been scientifically confirmed for a long time, in recent decades, diet has become an increasingly important etiological factor in the development of gingivitis and periodontitis. [47]. The most problematic macronutrients in this context are processed carbohydrates (e.g. sugar, sweets, juices, soft drinks). Whereas these substances are found only in association with anti-inflammatory dietary fibers and antioxidants in nature, they represent an excessively consumed substance in the dietary behavior of Homo sapiens, with approximately 35 kilograms of sugar being consumed per capita per year [15]. The consumption of sugar promotes both caries and gingivitis and it is associated with the presence of periodontitis [30, 31, 39, 71]. In terms of peri-implantitis, initial studies actually show both a plaque-promoting effect of sugar consumption at implant sites as well as an association with peri-implant mucositis and peri-implantitis [62, 69]. Experimental animal studies have also used processed, high-carbohydrate diets to provoke corresponding peri-implant inflammation [61].

Although several anti-inflamatory and pro-inflammatory dietary factors have now been identified in relation to periodontal inflammation [71], hardly any studies exist in the field of implantology. However, the few studies that are available are consistent with evidence deriving from the field of periodontology, e.g. that secondary plant compounds may have an anti-inflammatory effect on peri-implant inflammation [24]. Furthermore, in the field of micronutrients, the regulation of vitamin D is also of interest. According to recent studies, vitamin D levels appear to have an influence on peri-im-

plant osseointegration, and low serum vitamin D levels can also be associated with cases of early implant loss [19, 22, 45]. However, randomized, controlled intervention studies are lacking in this domain in order to provide causal evidence for this relationship. In the field of periodontal therapy, a randomized, controlled intervention study found clinical benefits of adjuvant vitamin D administration in patients with low serum vitamin D levels (<30 ng/ml) [49].

Recommended measures: Dietary counseling. Based on the available evidence, the patient should be advised to reduce or avoid processed carbohydrates (such as sugar, sweets, white flour, juices, soft drinks).

Previous to implant treatment, in cases where tooth loss occurred as a result of periodontitis, a plant-based whole food diet with possible supplementation of vitamin B12, vitamin D, and omega-3 fatty acids may be advisable [71]. This nutritional formula in turn has a positive influence on the whole body. In patients at high risk, serological testing can be considered for a more accurate reflection of their nutritional and micronutrient status. Indicative factors may include cholesterol, HbA_{1c}, and vitamin D. If no dietary counseling is offered in the dental practice, cooperation with appropriate medical colleagues and/or nutritionists is recommended.

Factor diabetes

Although the association between periodontitis and diabetes is well elucidated and considered highly relevant [55], the assoication between diabetes and peri-implant inflammation has not been fully elucidated [28]. It is important to consider the HbA_{1c} level, which reflects the blood glucose level in the last 2 months, because diabetics with well-controlled HbA_{1c} levels do not seem to have an increased risk of peri-implantitis [60]. One study found diabetes to be a stronger influencing factor than smoking in cases where HbA_{1c} values were not well controlled [2]. However, according to systematic reviews, diabetes mellitus does not seem to be a risk factor for short-term (≤5 years) implant survival [44]. But no standardised protocols are available regarding appropriate perioperative treatment (e.g. perioperative antibiotic therapy) and wound closure. Moreover, limited evidence exists in literature relating to bone grafting success and progressive loading protocols in patients with diabetes [21]. Complex surgical procedures should therefore be carefully considered, especially in diabetic patients.

Recommended measures: Serological control of the HbA_{1c} value in diabetics. In cases of abnormal values, the consultation with the general physician and the improvement of medication by the general physician/diabetologist as well as further dietary counseling is advisable prior to implant treatment. Complex surgical interventions should be carefully considered in diabetics, as the data on long-term success is insufficient.

Factor	Recommendation
Factor age	Chronological age is not a risk factor according to current data. Polypharmacy in the age group should be considered.
Drugs and other medical therapies	Implantation under oral BP therapy with a low risk profile is possible under antibiotic shielding. Implantological procedures under i.v. BP therapy are contraindicated. Augmentative procedures should generally be avoided under BP therapy. Implantation in immunocompromised patients should be carefully considered; antibiotic shielding is strongly recommended. Implantation after radiatio in the head and neck region is possible as long as there is no nicotine use.
Periodontitis	When a PSI of ≥3 at ≥2 sextants is detected, systematic periodontal therapy should be initiated prior to implant placement. After periodontal therapy, increased probing depths >4 mm should no longer be present.
Plaque	Professional dental cleaning and promotion of home plaque control.
Adherence	Inclusion in a program of supportive implant therapy (including clinical examination and professional mechanical plaque reduction, motivation and instruction in home oral hygiene, and continuous minimization of possible risk factors).
Hard and soft tissue	Basic clinical and radiological diagnostics. Establishment or creation of sufficient bone supply. Creation of attached gingiva after implantation.
Smoking	Smoking cessation recommendation. Offer of professional smoking cessation (by the practice or professional providers).
Nutrition	Recommendation to avoid processed carbohydrates (such as sugar, sweets, juices, soft drinks). In patients with tooth loss due to periodontitis, a plant-based whole food diet with possible supplementation of vitamin B12, vitamin D and omega-3 fatty acids may be recommended.
Diabetes	Serological control of the HbA_{1c} value in diabetics. In case of an imbalance, consultation with the general practitioner and improvement of the medication pre-implantologically via diabetology and nutritional counseling. Careful consideration of complex surgical procedures in diabetics.
Genetics	Genetic, microbiological or immunological diagnostics are currently not recommended due to lack of informative value.

Table 1 Patient-related risk factors – pre-implant checklist
Table 1: J. P. Wölber, T. Fretwurst

Factor genetics

The genetics of the patient is a fundamental factor that still cannot be influenced in practice, except for findings in epigenetics that suggest the modifiability of the effect of genes [43]. Although various genes have been associated with periodontitis in genome-wide association studies (GWAS) in the field of periodontology, they have not been well documented for peri-implantitis [46]. Interleukin-1 gene polymorphism has long been considered a risk factor for peri-implantitis in scientific literature. However, on the basis of the current heterogeneous study results, no recommended course of action for diagnosis can be derived [32, 38].

Recommended measures: At present, genetic, microbiological or immunological diagnostic tests (e.g. cytokines and biomarkers) in the gingival sulcus fluid of adjacent teeth, or existing implants, cannot be recommended due to a lack of validity with regard to implant success/risk of peri-implantitis [20].

Conclusions

According to the evidence presented, a variety of measures can be implemented to lower the risk of peri-implant inflammation. These include a comprehensive anamnesis and diagnosis, attention to contraindications (e.g., i.v. antiresorptives), treatment of existing periodontitis, cessation of smoking, adequate adjustment of HbA_{1c} values in diabetics, nutritional counseling, plaque reduction, creation of attached gingiva, and offering well-structured aftercare programs.

Table 1 provides a possible workflow checklist for pre-implant treatment.

Conflict of interest

The authors declare that there is no conflict of interest as defined by the guidelines of the International Committee of Medical Journal Editors.

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