Risk Factors for Peri-Implantitis: Effect of History of Periodontal Disease and Smoking Habits. A Systematic Review and Meta-Analysis

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ABSTRACT

Objectives: The purpose of this review was to evaluate whether history of periodontitis and smoking habits could represent a risk factor for peri-implantitis and implant loss.
Material and Methods: This systematic review followed PRISMA guidelines and was registered at the PROSPERO database [registration numbers CRD42016034160 (effect of history of periodontitis) and CRD42016033676 (effect of smoking)]. Broad electronic (MEDLINE) and manual searches were conducted among articles published from January 1st 1990 up to December 31st 2015, resulting in 49332 records for history of periodontitis and 3199 for smoking habits. Selection criteria included prospective studies comparing two cohorts of patients, with and without the investigated risk factor, with a minimum follow-up period of three years, and reporting data on peri-implantitis and implant loss occurrence. Considering that only prospective studies were included, dichotomous data were expressed as risk ratios and 95% confidence intervals.
Results: Three studies evaluating history of periodontitis (on which quantitative analysis was performed) and one study on smoking effect were included. Both implant and patient-based meta-analyses revealed a significantly higher risk of developing peri-implantitis in patients with a history of periodontitis compared with periodontally healthy subjects, but not a statistically significant increased risk for implant loss.
Conclusions: The outcomes of this systematic review indicate history of periodontitis as a possible risk factor for peri-implantitis, while insufficient data are present in literature to evaluate the role of smoking. However, available evidence is still weak and immature, and sound epidemiological studies are needed to analyse the specific contribution of these potential risk factors.

Keywords: dental implants; peri-implantitis; periodontitis; risk factors; smoking; systematic review.

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INTRODUCTION

Over the last decades, the use of implant-supported dental rehabilitations has known a significant increase [1]. Despite a high overall success rate, various risk factors can negatively affect the predictability of dental implants, leading to peri-implant tissue inflammation, bone resorption and, ultimately, to implant loss. Among them, history of periodontal disease and smoking habits have often been identified as conditions favouring the onset of peri-implant pathologies [2-3]. Even if several longitudinal studies have been conducted on these issues, showing some evidence of a negative impact on implant success [4-6], recent systematic reviews on this topic did not draw definitive conclusions [7-10].

The influence of the different risk factors, together with their specific weight and role in favouring peri-implant disease, needs to be fully clarified to elucidate the health/disease process affecting the marginal tissues surrounding dental implants. Strict disease definitions, accurate stratification of the study groups and control of the confounders are crucial points to design appropriate trials, in order to evaluate the impact of each single risk factor in promoting the development of this multifactorial pathology.

The aim of this systematic review was to assess current scientific evidence regarding history of periodontitis and smoking habits as risk factors for implant loss and incidence of peri-implantitis, applying stringent selection criteria for study inclusion and quality assessment.

MATERIAL AND METHODS

Protocol and search strategy

The present systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [11], and it has been registered at the PROSPERO database (www.crd.york.ac.uk/PROSPERO) with registration numbers CRD42016034160 (effect of history of periodontitis) and CRD42016033676 (effect of smoking).

Focus questions

The following PICO (Patient, Intervention, Comparison and Outcome) questions were aimed to be answered:

1. In patients with osseointegrated dental implants, does a history of periodontal disease influence the occurrence of peri-implantitis and implant loss compared to a history of periodontal health?

Population: patients with osseointegrated dental implants.
Intervention or exposure: patients with a history of periodontal disease.
Comparison: periodontally healthy patients.
Outcome: occurrence of peri-implantitis/implant loss.

2. In patients with osseointegrated dental implants, does the presence of smoking habits influence the occurrence of peri-implantitis and implant loss compared to no smokers?

Population: patients with osseointegrated dental implants.
Intervention or exposure: smoker patients.
Comparison: no smoker patients.
Outcome: occurrence of peri-implantitis/implant loss.

Information sources

A broad electronic search was conducted on MEDLINE (PubMed, www.ncbi.nlm.nih.gov/pubmed) by two independent authors (AF and TL), selecting articles published from January 1st 1990 up to the latest access on December 31st 2015. A manual search among the references of all full text articles and reviews emerging from the electronic search was also performed. No language restriction was applied, in order to limit selection bias.

Search

Search in the selected electronic database was performed by using the following algorithms.

1. Effect of history of periodontitis:

((((((((((“dental implants”) OR “dental implant”) OR “peri-implantitis”) OR “peri-implant bone”) OR “perimplantitis”) AND “periodontitis”) OR “chronic periodontitis”) OR “aggressive periodontitis”) OR “periodontal disease”) OR “periodontal pocket”) OR “attachment loss”) OR “alveolar bone loss”).

2. Effect of smoking:

((((((((((“peri-implantitis”) OR “perimplantitis”) OR “peri-implant disease”) OR “peri-implant inflammat*”) OR “perimplant inflammat*”) OR “peri-implant mucositis”) OR “perimplant mucositis”) OR “dental implant disease”) OR “dental implant inflammation”) OR “oral implant disease”) OR “oral implant inflammation”).

Selection of studies

Two blinded authors (CS and FB) independently performed the eligibility assessment of the studies. Intra-examiner reliability in the study selection

process was assessed through the Cohen k-test assuming a threshold value of 0.61 [12]. Conflicts were resolved by discussion of each article, until consensus was reached. An attempt to contact the corresponding Authors of the included studies was made, in order to retrieve any missing information or to clarify specific items.

Types of publications

This systematic review included prospective studies conducted on human subjects. Systematic reviews and studies of lower quality within the hierarchy of scientific evidence (such as PhD theses, expert opinions, letters, editorials, case reports, case series, and retrospective studies) were excluded.

Types of studies

Only prospective studies with two cohorts of patients (patients with periodontal disease compared to periodontally healthy/smokers compared to no smokers) reporting data on the incidence of peri-implantitis and implant loss in the two groups and complying with inclusion criteria listed below were included.

Types of participants/population

Subjects analysed in the included studies must have had at least one osseointegrated titanium screw-shaped dental implant followed at least for three years.

Inclusion and exclusion criteria

Full texts of the possibly relevant studies were evaluated for selection according to the following inclusion criteria:

- Prospective cohort studies comparing an exposed with a not exposed cohort (patients with periodontal disease compared to periodontally healthy/smokers compared to no smokers);
- Studies reporting the incidence of implant biological complications in the cohorts;
- Studies reporting the incidence of implant loss in the cohorts;
- Studies reporting a clear definition of peri-implantitis;
- Studies reporting a clear definition of periodontal disease (for part a) Effect of history of periodontitis);
- Studies reporting a clear definition of smoking habits (for part b) Effect of history of smoking);
- Minimum follow-up period of three years;
- Minimum of 10 evaluated implants per cohort.

The following exclusion criteria were applied:

- Animal or *in vitro* studies;
- Studies involving patients with systemic conditions potentially influencing dental implants outcome (e.g. immunologic disorders, uncontrolled diabetes mellitus, osteoporosis, HIV positive);
- Studies investigating dental implants manufactured in materials different from titanium;
- Articles published prior to January 1, 1990.

Sequential search strategy

Following the initial literature search, all article titles were screened to eliminate irrelevant publications, *in vitro* and animal studies, case reports, case series, retrospective studies and review articles. Then, studies were further selected basing on data obtained from the screening of the abstracts. In the final stage, the full texts of the selected papers were examined to confirm study eligibility, following inclusion and exclusion criteria.

Data extraction

Data were independently extracted from selected studies in form of variables by two authors (CS and FB), according to the aims and themes of the present review, as listed below.

Data items

The following items were extracted by using pre-defined forms: i) year of publication, ii) study design, iii) sample size, iv) gender distribution, v) mean age or age range, vi) number of implants, vii) smoking habits, viii) definition of peri-implantitis, ix) definition of periodontal disease, and x) other confounding factors. Moreover, primary outcomes included: i) incidence of peri-implantitis: number of events between baseline and end of the follow-up period, evaluated on a patient and implant level, ii) implant loss: number of events between baseline and end of follow-up period in the cohorts, evaluated on a patient and implant level. The corresponding 95% confidence intervals (CIs) were also calculated including continuity correction.

Assessment of risk of bias in individual studies

Risk of bias in individual studies was assessed by two independent blinded examiners (FA and TL) according to the Newcastle-Ottawa scale (NOS) for cohort

studies [13]. The NOS evaluates the study quality on the basis of three major components: selection, comparability, and outcome. It assigns up to four stars for selection, two stars for comparability, three stars for outcome. According to this analysis, a maximum of nine stars/points can be given to an observational study, with this score representing the highest quality, where six or more points are considered associated to a high quality study.

Assessment of risk of bias across studies

Heterogeneity was assessed using the χ^2-based Q-statistic method with a significant P value < 0.1. However, because of the moderate insensitivity of the Q statistic [14], an I^2 index was also reported with values ≥ 50% considered associated to a substantial heterogeneity among the studies [15]. In particular, the I^2 index describes the percentage of total variation across studies due to heterogeneity rather than chance. The τ^2 was also calculated for the heterogeneity assessment. The Review Manager software (version 5.2.6 - http://www.cochrane.org) was used for the assessment of heterogeneity. Due to the limited number of included studies, additional investigations regarding publication bias or sensitivity analysis were not performed.

Statistical analysis

Risk ratios (RRs) were used for statistical pooling of data and results were expressed as mean and 95% CIs. Moreover, to account for any heterogeneity of the studies, a random effect model was used for calculations of all the overall effects [16]. Finally, these analyses were reported both for the implant loss incidence between exposed and not exposed patients, and for the peri-implantitis incidence between exposed and not exposed patients. In particular, the main outcomes were reported and analysed using both implant and patient as statistical unit. The Review Manager software (version 5.2.6 - www.cochrane.org) was used for meta-analysis.

RESULTS

Search results

Effect of history of periodontitis

A total of 58037 articles (in English, German, Chinese, Korean, Russian, Dutch, Italian and French languages) were found through electronic and manual searches (57960 in Medline and 77 manually) and, after removing duplicates, 49332 publications were evaluated (Cohen k-test for inter-reviewer agreement = 0.81). After examination of titles and abstracts, 49312 articles were excluded and twenty papers were examined in full text to assess their eligibility (inter-reviewer agreement = 0.87). Seventeen articles were excluded in the selection process [4-6,17-30] and three studies [31-33] were included in this systematic review (inter-reviewer agreement = 1). The first included study was published in 2003 [31], the last one in 2012 [33]. Median year of publication was 2008.

Effect of smoking

A total of 3719 articles (in English, German, Chinese, Russian, Italian and French languages) were found through electronic and manual searches (3696 in Medline and 23 manually) and, after removing duplicates, 3199 publications were evaluated (Cohen k-test for inter-reviewer agreement = 0.88). After examination of titles and abstracts, 3167 articles were excluded and thirty-two works were examined in full text to assess their eligibility (inter-reviewer agreement = 0.87). Thirty-one articles were excluded in the selection process [6,27,29,30,33-59] and one study [31] was included in this systematic review (inter-reviewer agreement = 1). The included study was published in 2003 [31].

The results of the electronic and manual searches are summarised in Figure 1. The list of the excluded studies and reasons for exclusion are provided in Table 1 and 2.

Study characteristics

Effect of history of periodontitis

The sample size in the single studies ranged from a minimum of 53 [31,33] to a maximum of 62 [32] patients. The total number of treated patients was 168 (68 females, 47 males and 53 not specified). One study [31] did not report the sex distribution. Age range varied from 18 [32] to 85 [32] years old. Overall mean age was 49.7 years. One study [31] did not report the mean age of the patients. On the total of 168 patients, 92 subjects were periodontally healthy (54.8%), while patients with a history of periodontitis were 76 (45.2%). These 76 patients had different histories of periodontal disease: eight patients were affected by chronic periodontitis (10.5%) [31], seven patients by moderate periodontitis (9.2%) [32], 26 patients by severe periodontitis (34.2%) [32] and 35 subjects by generalised aggressive periodontitis (46.1%) [33]. The total number of inserted implants was 518 (193 in periodontally healthy patients, 325 in patients with a history of periodontitis).

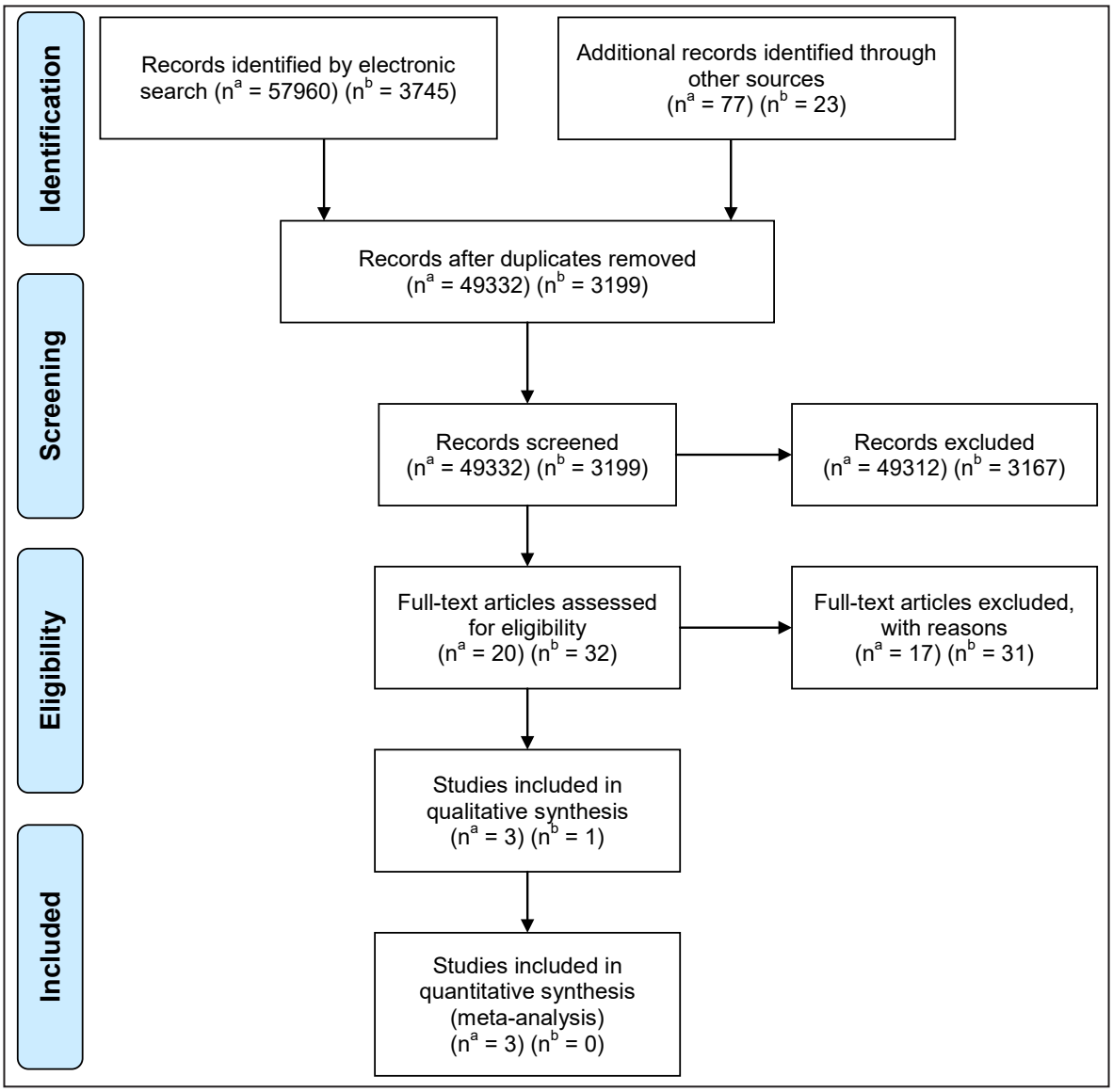

Figure 1. PRISMA flow diagram.
[a]number of records for history of periodontitis.[b]number of records for smoking.

Table 1. List of excluded studies and reasons for exclusion (history of periodontitis)

Study	Year of publication	Type of study	Reason of exclusion
Ferreira et al. [4]	2006	Cross sectional	Not prospective
Roccuzzo et al. [5]	2010	Prospective	Did not report information on peri-implantitis
Kostantinidis et al. [6]	2015	Cross sectional	Not prospective
Sbordone et al. [17]	1999	Prospective	No control group
Mengel et al. [18]	2001	Prospective	No control group
Mengel et al. [19]	2005	Prospective	Did not report information on peri-implantitis
Mengel et al. [20]	2007	Prospective	Did not report information on peri-implantitis
Fardal and Linden [21]	2007	Prospective	No control group
De Boever et al. [22]	2009	Prospective	Peri-implantitis criteria not clearly defined
Koldsland et al. [23]	2009	Cross sectional	Not prospective
Levin et al. [24]	2011	Prospective	Did not report information on peri-implantitis
Horwitz and Machtei [25]	2012	Prospective	No control group
Pjetursson et al. [26]	2012	Prospective	No control group
Casado et al. [27]	2013	Retrospective	Not prospective
Jiang et al. [28]	2013	Prospective	Did not report information on peri-implantitis
Marrone et al. [29]	2013	Cross sectional	Not prospective
Roccuzzo et al. [30]	2014	Prospective	Peri-implantitis criteria not clearly defined

Table 2. List of excluded studies and reasons for exclusion (smoking habits)

Study	Year of publication	Type of study	Reason of exclusion
Kostantinidis et al. [6]	2015	Cross sectional	Not prospective
Casado et al. [27]	2013	Retrospective	Not prospective
Marrone et al. [29]	2013	Cross-sectional	Not prospective
Roccuzzo et al. [30]	2014	Prospective	Did not compare smokers vs. no smokers
Swierkot et al. [33]	2012	Prospective	Did not compare smokers vs. no smokers
Roos-Jansåker [34]	2006	Prospective	Did not compare smokers vs. no smokers
Costa et al. [35]	2012	Follow up study	Did not report information on smoking
Dvorak et al. [36]	2011	Cross sectional	Not prospective
Schropp et al. [37]	2014	Randomized clinical trial	Did not compare smokers vs. no smokers
Göthberg et al. [38]	2014	Randomized clinical trial	Did not report information on peri-implantitis
Sanz et al. [39]	2015	Randomized clinical trial	Did not report information on smoking
Cecchinato et al. [40]	2014	Prospective	Did not compare smokers vs. no smokers
Wang et al. [41]	2014	Cross sectional	Not prospective
Meijer et al. [42]	2014	Prospective	Did not report information on smoking
Canullo et al. [43]	2016	Cross sectional	Not prospective
Aguilar-Salvatierra et al. [44]	2016	Prospective	Did not report information on smoking
Serino et al. [45]	2015	Prospective	Did not compare smokers vs. no smokers
Mangano et al. [46]	2014	Prospective	Did not compare smokers vs. no smokers
Kütan et al. [47]	2015	Randomized clinical trial	Did not report information on smoking
Gomes et al. [48]	2015	Prospective	Did not report information on smoking
Becker et al. [49]	2015	Prospective	Did not report information on smoking
Donati et al. [50]	2015	Prospective	Did not report information on smoking
Pozzi et al. [51]	2015	Prospective	Did not report information on peri-implantitis
Schwarz et al. [52]	2015	Cross sectional	Not prospective
Krennmair et al. [53]	2016	Prospective	Did not compare smokers vs. no smokers
van Velzen et al. [54]	2015	Prospective	Did not compare smokers vs. no smokers
Malchiodi et al. [55]	2015	Prospective	Did not compare smokers vs. no smokers
Hita-Iglesias et al. [56]	2015	Prospective	Did not report information on peri-implantitis
Daubert et al. [57]	2015	Cross sectional	Not prospective
Gherlone et al. [58]	2015	Prospective	Sample not representative of general population
Konermann et al. [59]	2016	Cross sectional	Not prospective

The criteria used to diagnose peri-implantitis and periodontal disease slightly varied among the included studies, one study [31] did not define clear diagnostic criteria for assessing history of chronic periodontitis.

Two studies [32,33] showed a higher and statistically significant implant loss rate in patients with a history of periodontitis both on an implant and patient level; also in the third study [31] the implant loss rate (on an implant level; patient level data were not reported) was greater in periodontal than in healthy patients, but without reaching a statistical significance.

Two studies [32,33] found a higher and statistically significant peri-implantitis incidence in the periodontally compromised patients groups, both on an implant and patient level, while the third study [31] reached the same conclusions on an implant level only (patient level data not reported).

Detailed data of the included studies are listed in Table 3.

Effect of smoking

The total number of treated patients in the selected study was 53 [31]. Sex distribution and age of the sample were not reported. The total number of inserted implants was 112 (28 implants in 12 smoker patients, 84 implants in 41 no smoker patients).

The criteria used to diagnose peri-implantitis was the presence of probing depth ≥ 5 mm, associated to bleeding on probing and radiographic signs of bone loss.

In this study, implant loss rate and peri-implantitis incidence, on an implant level, resulted higher in smoker than in no smoker patients, but without reaching a statistical significance (patient level data not reported).

Detailed data of the included study are listed in Table 4.

Table 3. Characteristics of included studies (history of periodontitis)

Study	Year of publication	Study design	Patients/ implants	Mean Age/Sex (years [M/F])	Implant failures (events/implants; events/patients)	Peri-implantitis (events/implants; events/patients)	Smokers Smokers/Non-smokers	Diagnosis of peri-implantitis	Diagnosis of periodontal disease	Confounders
Karoussis et al. [31]	2003	Prospective cohort	H: 45/91 CP: 8/21	NR	H: 3/91; NR/45 CP: 2/21; NR/8	H: 5/91; NR/45 CP: 8/21; NR/8	28/84	PD ≥ 5 mm + BOP + radiographic signs of BL	NR	Declared: smoking, different prosthetic rehabilitations. Discussed: smoking.
Gatti et al. [32]	2008	Prospective cohort	H: 29/72 MP: 7/26 SP: 26/129	H: 40 (9/20) MP: 56 (4/3) SP: 56 (10/16)	H: 0/72; 0/29 MP: 0/26; 0/7 SP: 2/129; 1/26	H: 0/72; 0/29 MP: 0/26; 0/7 SP: 4/129; 2/26	14/48 H: (6/29) MP: (3/26) SP: (5/26)	PD ≥ 5 mm + suppuration or other signs of infection + BL > 2 mm	Periodontal screening and recording index: 0 - 2 (H) 3 (MP) or 4 (SP)	Declared: age, smoking, regenerative procedures, healing period, prosthetic rehabilitations, implant brands, oral hygiene maintenance. Discussed: age, smoking, implant brands.
Swierkot et al. [33]	2012	Prospective cohort	H: 18/30 GaP: 35/149	GaP: 39.6 (15/20) H: 38.6 (9/9)	H: 0/30; 0/18 GaP: 6/149; 3/35	H: 3/30; 2/18 GaP: 39/149; 15/35	14/39	PD ≥ 5 mm + BOP + BL > 0,2 mm/years	According to AAP criteria	Declared: smoking, sex, age, implant features, prosthetic rehabilitations, bone quality, regenerative procedures. Discussed: smoking, sex, age, implant features, prosthetic rehabilitation, bone quality, regenerative procedures.

M = male; F = female; H = healthy; CP = chronic periodontitis; MP = moderate periodontitis; SP = severe periodontitis; GaP = generalised aggressive periodontitis; PD = probing depth; BOP = bleeding on probing; BL = bone loss; NR = not reported.

Table 4. Characteristics of the included study (smoking habits)

Study	Study design	Patients/ implants	Age/ sex	Implant failures (events/implants)	Peri-implantitis (events/implants)	Diagnosis of peri-implantitis	Definition of smoking	Confounders
Karoussis et al. [31]	Prospective cohort	Smokers = 12/18 Non-smokers = 41/84	NR	Smokers (2/28) Non-smokers (3/84)	Smokers (5/28) Non-smokers (8/84)	PD ≥ 5 mm + BOP + radiographic signs of BL	NR	Declared: history of periodontitis, different prosthetic rehabilitations. Discussed: history of periodontitis.

PD = probing depth; BOP = bleeding on probing; BL = bone loss; NR = not reported.

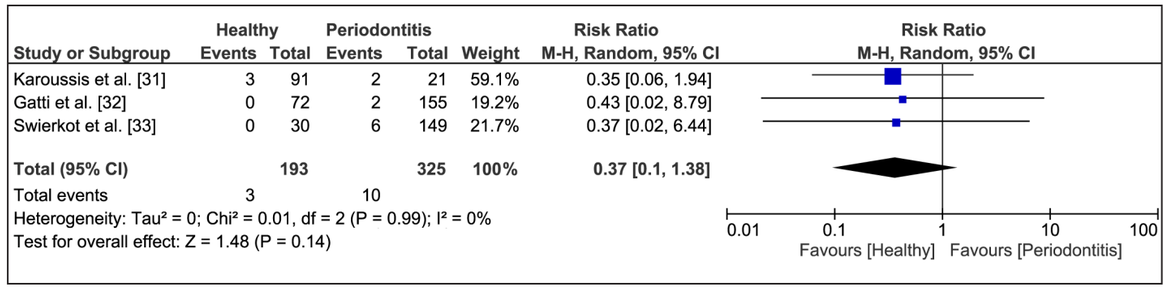

Figure 2. Forest plot for the event 'implant loss' comparing periodontally healthy with periodontally compromised patients (implant as statistical unit).

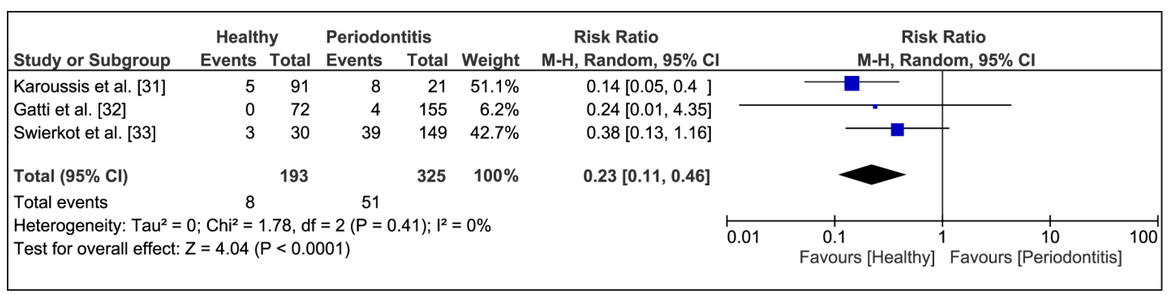

Figure 3. Forest plot for the event 'peri-implantitis' comparing periodontally healthy with periodontally compromised patients (implant as statistical unit).

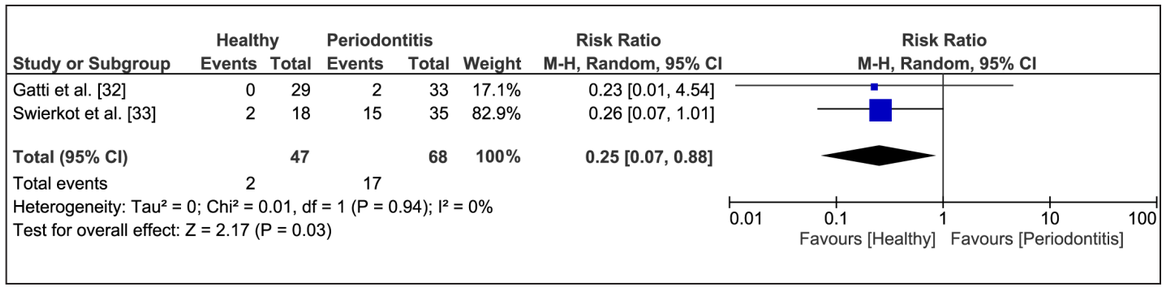

Figure 4. Forest plot for the event 'implant loss' comparing periodontally healthy with periodontally compromised patients (patient as statistical unit).

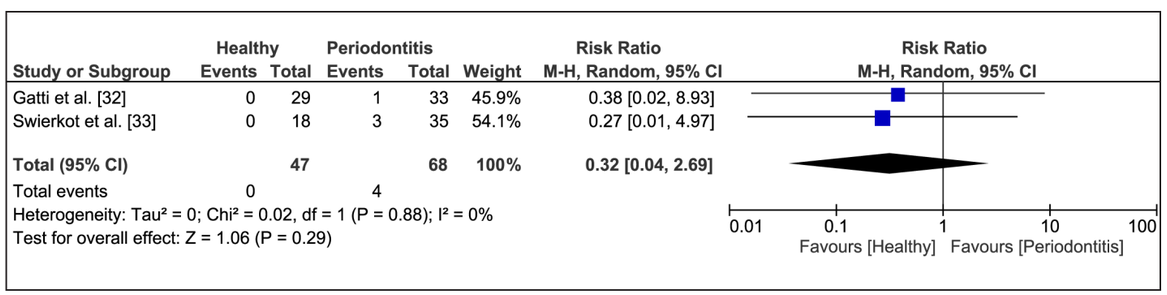

Figure 5. Forest plot for the event 'peri-implantitis' comparing periodontally healthy with periodontally compromised patients (patient as statistical unit).

Results of meta-analysis

Meta-analysis could be performed only for the three studies analysing the influence of history of periodontal disease: detailed results for the primary outcomes are shown in Figures 2 - 5. The RRs are expressed as mean (95% CI).

For the implant loss (considering the implant as the statistical unit) the overall RR was 0.37 (0.1 - 1.38) in favour of the periodontally healthy patients. The overall effect was not significant (P = 0.14) (Figure 2). For the occurrence of peri-implantitis (considering the implant as the statistical unit), the overall RR was 0.23 (0.11 - 0.46) in favour of the periodontally healthy patients. The overall effect was significant (P < 0.0001) (Figure 3). For the implant loss (considering the patient as the statistical unit), the overall RR was 0.32 (0.04 - 2.69) in favour of the periodontally healthy patients. The overall effect was not significant (P = 0.29) (Figure 4). For the occurrence of peri-implantitis (considering the patient as the statistical unit), the overall RR was 0.25 (0.07 - 0.88) in favour of the periodontally healthy patients. The overall effect was significant (P = 0.003) (Figure 5).

In all the comparisons, no heterogeneity was seen with I^2 = 0% and Chi square not significant (P = 0.41, at least).

Risk of bias in individual studies

None of the included studies reached the maximum score of the NOS (Tables 5 and 6). Two studies [31,32] reached the maximum score for the selection item, one study [32] reached the maximum score for the exposure item, and no study had the maximum score for the comparability item.

Additional analysis

Due to the limited number of included studies, additional investigations regarding publication bias or sensitivity analysis were not performed.

DISCUSSION

When analysing the risk factors of a disease, a clear definition of the indagated pathological condition is of paramount importance. Then, especially in multifactorial pathologies, an accurate stratification of the sample and a strict control of the various confounding factors are crucial points to design appropriate trials, in order to evaluate the impact of each single risk factor on the onset of the disease. In literature, a variety of different parameters and diagnostic criteria have been used when studying incidence, prevalence and risk factors of peri-implant diseases: in a recent review on the quality of the clinical research, Tomasi and Derks [60] indicate the absolute need for improved reporting of epidemiological studies on this topic.

We found a confirmation of this statement in our systematic review, whose aim was to verify whether history of periodontitis and smoking habits may act as predisposing factors for implant loss and occurrence of peri-implantitis. In fact, a very limited number of articles could be included in the final analysis, seeming to confirm the influence of the history of periodontal disease as a potentially relevant risk factor for the onset of peri-implantitis, analysed both at implant and at patient level. However, history of periodontitis did not result as a significant risk factor for implant loss. It was impossible to draw general conclusions regarding the impact of smoking in favouring peri-implantitis and implant loss because only one study could be selected for the qualitative analysis.

The results of our meta-analysis are consistent with the conclusions of previous systematic reviews examining the history of periodontal disease as a risk factor for the onset of peri-implantitis, but applying broader inclusion criteria [7-9,61].

Peri-implantitis is actually defined as an inflammatory condition with bleeding on probing and/or purulent exudate, associated with clinically significant progressive crestal bone loss after the adaptive phase [62-64].

Table 5. Risk of bias in the included studies (history of periodontitis)

	Selection				Comparability	Outcome			
	1	2	3	4	1	1	2	3	Total
Karoussis et al. [31]	★b	★	★a	★		★b	★		6★
Gatti et al. [32]	★b	★	★a	★		★b	★	★b	7★

Table 6. Risk of bias in the included study (smoking habits)

	Selection				Comparability	Outcome			
	1	2	3	4	1	1	2	3	Total
Karoussis et al. [31]	★b	★	★a	★		★b	★		6★

The presence of bone loss and probing depth alone may not be enough to formulate a diagnosis of peri-implantitis: bone loss can have a number of non-bacterial causes including surgical technique [65], implant design [66], implant positioning [67], crestal bone thickness [68,69] or occlusal overload [70]. For this reason, we excluded a consistent number of studies (although included in recent reviews [7-9,61,71,72]), which were reporting only data concerning bone loss around implants, without giving a definite diagnosis of peri-implantitis.

According to Lindhe and Meyle [62], who stated that the assessment of incidence and risk factors require longitudinal, prospective or case-control studies, we included in the present review only prospective trials comparing a cohort of individuals presenting the investigated risk factor with a group of not exposed individuals in the format of a longitudinal study. However, it is necessary to evaluate prospective cohort studies for internal validity due to the presence of selection bias and confounding variables. The three publications included in this systematic review [31-33] did not fully address the STROBE checklist for cohort studies, especially in terms of sample size definition, exposures, predictors, potential confounders, and effect modifiers. Also the diagnostic criteria for peri-implantitis were slightly different among the studies and the definition of periodontal disease followed different parameters (one study did not report it at all [31]). Potential confounders (e.g. systemic conditions, age, sex, bone quality, implant features, type of prosthesis, parafunctions) were only partially reported and seldom assessed during outcomes analysis. The quality assessment following NOS (Newcastle-Ottawa Scale) scheme, accordingly, revealed the absence of complete adherence to the different items.

Summary of evidence

This systematic review reported weak evidence supporting the hypothesis that history of periodontal disease could act as a risk factor for peri-implantitis; moreover, no evidence was found to clarify the influence of smoking in the pathogenesis of this disease. History of periodontitis resulted to be a risk factor for the occurrence of peri-implantitis both in patient and in implant-based analyses, but it did not result a significant risk factor for implant loss. However, according to the low number of selected studies and their limitations (for both the analysed issues), no clinical recommendations could be given.

Further prospective trials are needed to confirm the results of the present meta-analysis: future studies should include adjustment of their results for known and potential confounding factors, and should report their results according to a clear and widely accepted definition of peri-implantitis, together with a well-defined stratification of periodontal disease and smoking status.

Limitations

It is worth considering that the narrow inclusion criteria adopted in this review increase studies homogeneity but, at the same time, also the risk to exclude significant data [73]: nevertheless, we think that this strict methodological approach may help readers to understand the real available evidence on this specific topic, with all the limitations and drawbacks, and could be a motivation for researchers in designing appropriate trials.

Hence, the results reported in this review should be interpreted with great caution. The low number of studies, the heterogeneity of case definitions and the substantial lack of control of the confounders represent concrete risks of bias for the correct estimation of the role of smoking habits and history of periodontitis in favouring the onset of peri-implant diseases.

CONCLUSIONS

Based on the results of the present systematic review to assess the influence of smoking habits and history of periodontal disease as risk factors for implant loss and occurrence of peri-implantitis, the following conclusions can be drawn:

1. There is limited evidence to suggest that history of periodontal disease could be a risk factor for peri-implantitis;
2. There are no sufficient data to assess the role of smoking as a risk factor for implant loss and peri-implantitis.

Adequately powered long-term prospective studies are necessary to analyse the role of these potential risk factors using clear and accepted disease definitions, accurate sample selection and strict control of confounders.

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