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ORIGINAL ARTICLE

How frequent does peri-implantitis occur? A systematic review and meta-analysis

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Abstract

Objectives The objective of this study is to estimate the overall prevalence of peri-implantitis (PI) and the effect of different study designs, function times, and implant surfaces on prevalence rate reported by the studies adhering to the case definition of Sanz & Chapple 2012.

Material and methods Following electronic and manual searches of the literature published up to February 2016, data were extracted from the studies fitting the study criteria. Meta-analysis was performed for estimation of overall prevalence of PI while the effects of the study design, function time, and implant surface type on prevalence rate were investigated using meta-regression method.

Results Twenty-nine articles were included in this study. The prevalence rate in all subset meta-analyses was always higher at patient level when compared to the prevalence rate at the implant level. Prevalence of PI was 18.5% at the patient level and 12.8% at the implant level. Meta-regression analysis did not identify any association for different study designs and function times while it was demonstrated the significant association between moderately rough surfaces with lower prevalence rate of PI ($p = 0.011$).

Conclusions The prevalence rate of PI remains highly variable even following restriction to the clinical case definition and it seems to be affected by local factors such as implant surface characteristics. The identification of adjuvant diagnostic markers seems necessary for more accurate disease classification.

Clinical relevance The occurrence of PI is affected by local factors such as implant surface characteristics hence the careful assessment of the local factors should be performed within treatment planning.

Keywords Peri-implantitis · Prevalence · Dental implants · Epidemiology

Introduction

Peri-implantitis is a major complication of dental implants and the first cause of implant failure [1, 2]. Briefly stated, the knowledge and clinical protocols were initially simply translated from periodontology to the implant dentistry while the recent implant research reveals different physiopathological features between periodontal and peri-implant tissues. It is proposed that histological specificities and implant-related factors contribute to the more complex physiology and

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pathology around dental implants compared to natural dentition [3, 4]. From a clinical point of view, recent studies indicate that standard clinical parameters provide decreased diagnostic value on implants compared to teeth, while the treatment of peri-implant diseases is considered unpredictable [5, 6]. Regarding peri-implant mucositis considered as a precursor of peri-implantitis and pathological counterpart of gingivitis on implants [7], data have failed to show disease resolution following any of non-surgical protocols applied similarly as for the treatment of peri-implantitis [8]. For these reasons, peri-implant diseases were recently defined as important disease entities as a result of their high prevalence and the lack of a standard treatment protocol [6, 9].

Initial step in assessment of every pathology is evaluation of the epidemiological characteristics of the disease [10] having as goal to estimate how often disease occurs and why. Epidemiological information is further used to evaluate and improve existing preventive strategies for respective disease and is usually implemented in concepts for managing the affected population. Disease prevalence being a fundamental epidemiological parameter was inconsistently reported for peri-implantitis and considerably varied among studies with more than 50% variation [11]. Therefore, the study was performed to assess the quality of reporting on prevalence of peri-implant diseases [12]. The conclusion ensued that quality of reporting needs improvement emphasizing the use of strict case definition as an imperative priority for minimizing inter-study heterogeneity. Related to that, a case definition of peri-implantitis was proposed by Sanz & Chapple on the forthcoming 8th European Workshop of Periodontology (EWOP) [13, 14]. Following that, the same group of authors who provided guidelines for improvement of reporting in epidemiological studies performed a meta-analysis [11] using newly proposed case definition and reported a prevalence of peri-implantitis of 22% at the patient level. The authors also investigated factors in cause of inter-study heterogeneity and demonstrated positive effect of function time on peri-implantitis prevalence [11]. Within implications for the future research, it was proposed the application of consistent case definitions and assessment of additional factors in possible cause of inter-study heterogeneity.

The proposed case definition of peri-implantitis [13, 14] refers to use of clinical endpoints in conjunction with mandatory radiological proof of changes of crestal bone level or bone loss of ≥ 2 mm from the expected marginal bone level following initial remodeling. Such insistence on strict proof of bone loss also indicates the limitation of clinical parameters in implant diagnostics. The numerous host and implant-related factors interfere with periodontal clinical parameters on implants subsequently decreasing their respective diagnostic value [15, 16]. Moreover, the interface between implant surface and peri-implant infection is currently considered an independent factor in pathogenesis of peri-implantitis [16, 17]. In addition to that, the insufficient surface decontamination was proposed as a main culprit for incomplete resolution of peri-implant inflammation following treatment [9] and is considered the leading cause for disease recurrence.

Thus, the objectives of this systematic review and meta-analysis were to estimate the overall prevalence of peri-implantitis and to determine the effect of different study designs, function times, and implant surfaces on reported prevalence of peri-implantitis by assessing the studies using the referent case definition proposed by Sanz & Chapple [13, 14].

Material and methods

Study protocol

This systematic review and meta-analysis comply with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [18] and the MECIR guidelines for Cochrane intervention reviews [19].

Focused questions

- What is the frequency of peri-implantitis according to a case definition previously defined?
- Do certain factors/characteristics (i.e., study design, implant topography or function time) impact upon peri-implantitis frequency?

PECO question (population, exposure, comparison, outcome measures) [20]

- Population: patients wearing dental implants for restoration of oral function in completely or partially edentulous, mandibular or maxillary dental arches.
- Exposure: peri-implant disease diagnosed under a clinical and radiographic examination and adhered to a previously described definition
- Comparison: different implant surfaces, function times, and study designs
- Outcome measures: frequency of peri-implantitis at patient/implant level

Definition of peri-implantitis

Based upon Sanz & Chapple [13, 14], peri-implantitis was defined as the presence of bone loss ≥ 2 mm, positive bleeding on probing and probing depth ≥ 5mm, and/or concomitant probing deepening compared to the radiograph taken at the time of prosthetic placement.

Inclusion criteria were as follows:

- Studies reporting the prevalence of peri-implantitis and adhering to the case definition according to Sanz & Chapple [13, 14]
- Studies reporting on at least 20 participants
- Randomized clinical trials (RCT),
- Prospective and retrospective cohort studies,
- Case-control and
- Cross-sectional studies

In humans, reporting the prevalence of peri-implantitis at implant and/or patient level was considered for this systematic review without language or date of publication restriction reporting ≥ 20 participants were taken included for the qualitative/quantitative analysis.

Exclusion criteria were studies reporting on the outcomes as follows:

- Exclusively from populations with specific biological characteristics (such as periodontally compromised patients or patients with systemic diseases recognized to affect peri-implant condition)
- Exclusively from populations undergoing specific surgical or prosthodontic protocols (such as immediate implant placement, flapless implant placement, etc.)
- Studies with blade and mini (≤ 3 mm diameter) implants.

Search strategy

A search of the Web of Science (Science Citation Index), U.S. National Institutes of Health free digital archives of biomedical and life sciences journal literature (PubMed), The Cochrane Library of the Cochrane Collaboration (CENTRAL) as well as a hand search were conducted to identify articles potentially relevant for the review. Additionally, according to the AMSTAR (http://amstar.ca/index.php) checklist, the Grey Literature Database was screened at the New York Academy of Medicine Grey Literature Report in order to find possible unpublished papers. The search included articles accepted for publication up to February 2016. The following key words were used for that purpose:

(((((TOPIC:(dental implants) OR MeSH HEADING:exp.: (Dental Implantation)OR MeSH HEADING:exp: (Dental Implants)) AND TOPIC:(periimplantitis)) OR (TOPIC: (peri-implantitis) OR MeSH HEADING:(Peri-Implantitis))) OR TOPIC: (peri-implantitis prevalence)) OR TOPIC:(peri-implantitis incidence)) OR((TOPIC: (peri-implantitis) OR MeSH HEADING:exp: (Peri-Implantitis))AND (TOPIC: (epidemiology) ORMeSH HEADING:exp: (Epidemiology)OR MeSH HEADING:exp:(Community Health Services)))

Timespan was not limited although the included papers were published after 2000th.

The manual search was conducted to search the periodontology and implantology-related journals published in the last 5 years (February 2011–February 2016) including the following: *Journal of Dental Research*, *Clinical Oral Investigations*, *Journal of Clinical Periodontology*, *Journal of Periodontology*, *Journal of Oral and Maxillofacial Implants*, *Clinical Oral Implants Research*, *Clinical Implant Dentistry and Related Research*, *The International Journal of Periodontics & Restorative Dentistry and Archives of Oral Biology*. The bibliography of candidate papers was also searched.

Quality assessment

Quality assurance was developed according to Khan et al. [21] via independent screening by two reviewers (M.R and P.G-M.), resolution of disagreement by consensus, discarding of the studies in cases when consensus was not achieved and data extraction in duplicate.

Data extraction and synthesis

Two independent reviewers (M.R. and P.G-M.) performed initial searches and analyzed titles and abstracts in the first stage screening to discard irrelevant articles. Subsequently, the full-texts of the potentially eligible articles were reviewed to assess whether the studies fit the selected inclusion criteria. Any disagreement regarding eligibility of the articles was individually resolved between the reviewers. Data were collected into evidence tables when the following parameters were scored: (1) case definition, (2) study design, (3) function time, (4) sample size, (5) prevalence of peri-implantitis, (6) implant brand, (7) implant surface type, and (8) additional observations related to peri-implantitis prevalence.

Synthesis of the data was performed from evidence tables when the studies reporting on common parameters were identified and selected for meta-analysis and meta-regression analysis.

Data analysis

The OpenMetaAnalyst [22] software was used to estimate the prevalence rate of peri-implantitis and the potential effects of the different function time, study design, and implant surfaces on the prevalence.

The meta-regression analyses (random effects model) with the heterogeneity evaluation obtained from the inverse-variance fixed-effect model [22] was used to estimate the effect of different study designs, implant surfaces, and function times on prevalence of peri-

implantitis while the p value of the covariate coefficient was evaluated using the 0.05 as a level of significance. In brief, the calculation was performed according to DerSimonian-Laird random effects pooling method [23] using the following formula: $Q = \sum_{i=1}^{n} w_i\left(T_i - \overline{T}\right)^2$, while the heterogeneity of effect size (I^2) was calculated using $I^2 = (Q-(k-1))/Q*10$ formula. The heterogeneity of effect size (I^2) represents a measure of inter-study heterogeneity, while < 25%, 25–75%, and 75% indicate low, moderate, or high degree of inter-study heterogeneity, respectively [24, 25].

To assess the effect of different cofactors on prevalence rate, the studies were classified as follows:

- Effect of study design: prospective, retrospective, and cross-sectional study design
- Effect of function time: < 5 years, 5–10 years, and >10 years of function time
- Effect of different implant surface: minimally, moderately, and rough implant surfaces [26]. For this analysis, only the studies reporting exact prevalence by each implant system including the number of initial and affected implants were taken into account.

Due to observed inter-study heterogeneity in reported prevalence rate at the patient and implant level, the meta-analyses were performed at patient and implant level independently, in order to comprehensively examine reported evidence. Results were expressed as Forest plots with weighted mean values and 95% confidence intervals (CI) while the heterogeneity among the studies was expressed using Q statistics and I^2.

Results

Screening process

The flow chart of search process is depicted in the Fig. 1. The initial search yielded 1214 articles using electronic searches. After title screening, 193 articles were considered as potentially eligible while additional 5 articles were identified using hand searches. This resulted in a final number of 198 potentially eligible papers. After abstract reviewing, the full-text analysis of 35 potentially eligible articles was performed. A final review resulted in the selection of 29 articles [27–55] considered as eligible for the purpose of this study (Table 1.). The k value for inter-reviewer agreement for study inclusion was 0.91 for titles and abstracts and 1.00 for full-text articles indicating strong agreement.

General observations

Despite the strict restriction to the case definition, the high rate inconsistency between the studies remained and counted 98.53% for reporting on implant level and 98.3% for reporting at the patient level. In addition to that, the similar high heterogeneity remained following restriction for investigated cofactors as well. Regarding expression of the prevalence rate, it was observed mismatching in number of investigated implants and number of patients in all investigated studies, while the prevalence rate in all meta-analyses was always higher at the patient level when compared to the implant level.

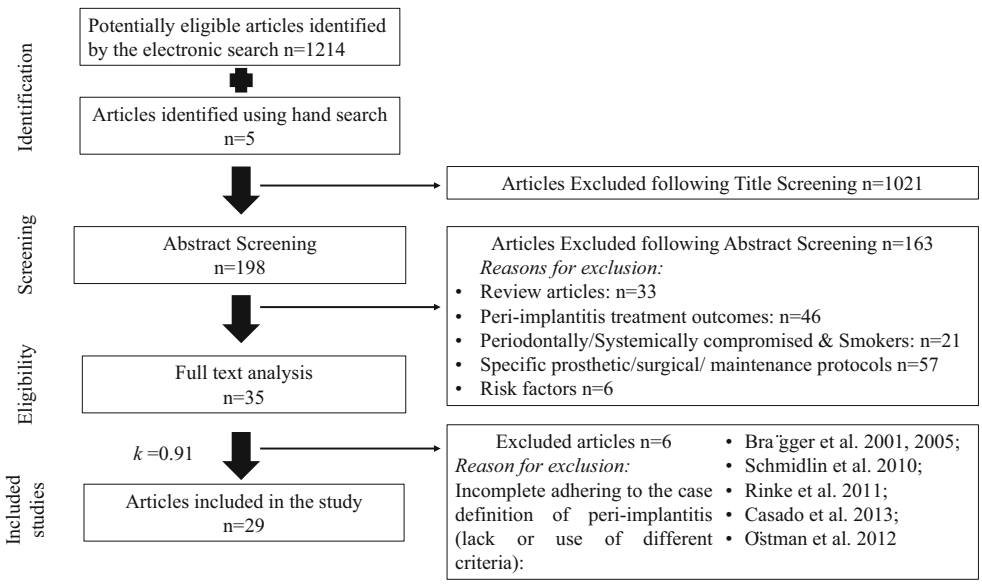

Fig. 1 Flowchart of the search process

Table 1 Description of included studies

Author and year	Case definition	Study design	Function time (years)	Sample size	Prevalence %	Implant brand	Implant surface*	Additional observations
Astrand et al. [27]	SUP plus BL	Prospective	3	P: 28 I: 150	P: ND I: 5%	Straumann	TPS, Machined	25% Smokers 29% Periodontitis+
Becker et al. [28]	PPD > 5 mm, BOP+ and/or suppuration BL > 2.5 mm or > 3 exposed threads	Retrospective	12–23	P:92 I:388	P: ND I:9.7%	Straumann	TPS	
Buser et al. [29]	BOP+ and/or suppuration and progressive bone loss	Retrospective	10	P: 303 I: 511	P: ND I: 1.8%	Straumann	SLA	
Cecchinato et al. [30]	BOP+, PPD ≥6 mm and crater-shaped BL	Prospective	10	P: 133 I: 407	P: 12% I: 5%	Astra Tech	Osseospeed	25% Smokers 41% Periodontitis+
Dalago et al. [31]	PPD > 5 mm, BOP+ and/or suppuration BL > 2 mm	Cross-sectional	1–14	P:183 I:938	P:16.4% I:7.3%	–	–	
Daubert et al. [32]	BOP and/or suppuration, BL ≥2 mm after initial remodeling, PD ≥4 mm	Cross-sectional	≈10.9	P: 96 I: 225	P: 26% I: 16%	3i, Branemark, Nobel, Astra, Straumann, Centerpulse Dental, Sulzer Dental, Steri-Oss	–	7 Smokers
Derks et al. [33]	BoP/suppuration and BL	Retrospective	9	P:588 I: 2277	P:45%	Astra Tech, Nobel Biocare & Straumann	–	Without significant difference in terms of age, sex, systemic disease, and therapy-related parameters
Dierens et al. [34]	BL > 3 threads plus BOP+	Prospective	16–22	P: 50 I: 59	P: 6% I: 5%	Branemark	Machined	
Ferreira et al. [35]	PPD > 4 plus BOP+/ SUP plus	Cross-sectional	5	P: 212 I: 578	P: 8.9% I: 7.44%	Nobel Biocare, 3i & Intra-lock	–	Population: Periodontitis +19.3% The periodontal status was statistically associated with a worse peri-implant condition
Fransson et al. [36]		Retrospective	5–20	P: 662 I: 3413	P: 27.8% I: 12.4%	Branemark	Machined	
Gatti et al. [37]	PPD > 5 mm plus pus or other sign of infection plus BL > 2 mm	Prospective	5	P: 62 I: 227	P: 3% I: 1%	Nobel Biocare, Zimmer, Mathys, Straumann & Friadent	–	53% Periodontitis+
Gruica et al. [38]	SUP plus BL	Prospective	8–15	P: 180 I: 292	P: 19% I: 17%	Straumann	TPS	29% Smokers; implant with complications: heavy smokers: 40%, light smokers: 17%, never/former smokers: 13%
Jemt et al. [39]	BL > 3 mm	Retrospective	8	P:1346 I: ND	P: 182 I: 1029	Branemark	Machined	
Koldsland et al. [40]	PPD > 4 plus BOP+/ SUP plus BL ≥3 threads	Cross-sectional	8.4	P: 109 I: 351	P: 47.1 % I: 36.6%	Astra Tech, Branemark, Straumann, 3i	–	
Konstantinidis et al. [41]	+BOP, PPD > 4 mm; BL > 2 mm	Cross-sectional	≈5.5	P: 186 I: 597	P: 12.9% I: 6.2%	Xive, Frialit2 Straumann	–	11.8% Current smokers, 7.5% ex-smokers, and 80.6% non-smokers 3.2% Patients had radiotherapy at head and neck 8.6% controlled DM 20.4% periodontitis
Marrone et al. [42]	+ BoP, PPD and BL	Cross-sectional	5–18	P: 103 I: 266	P: 37% I: 23%	Straumann, SLA, Cell, CPT	TPS, machined	20 smokers 54 periodontitis+
Maximo et al. [43]	PPD > 4 plus BOP+/ SUP plus BL ≥3 threads	Prospective	–	P 113 I: 374	P: 12% I: 7.5%	Branemark	Machined	19% smokers
		Cross-sectional	1–18	P: 245	P: 16.3	Branemark, 3i, & Nobel Biocare		

Table 1 (continued)

Author and year	Case definition	Study design	Function time (years)	Sample size	Prevalence %	Implant brand	Implant surface*	Additional observations
Mir-Mari et al. [44]	BL ≥ 2 threads with BOP/suppuration			I: 964	% I: 9.1%		Machined, TiUnite & Osseotite	
Renvert et al. [45]	BL ≥ 1 mm after 1st year, BOP+/SUP	Prospective	13	P: 54 I: 234	I: 68%	Astra Tech & Nobel Biocare	Osseospeed, Machined	39% Smokers 24.39% Periodontitis+ peri-implantitis recurrence: 19%
Renvert et al. [46]	PPD > 4 plus BOP+/ SUP plus BL ≥ 2 mm	Retrospective		P: 270 I: 278	P: 172 I: 63.7%	Nobel Biocare, Astra Tech & Straumann	Osseospeed, Machined & SLA	51% Periodontitis Smokers: PI: 46.7%, HI: 32.7%. Periodontitis+: PI: 69.2%, HI: 18.4%.
Rinke et al. [47]	PPD > 4 plus BOP+/ SUP plus BL	Retrospective	2–11	P: 89 I: ND	P: 11% I: ND	Ankylos	Friadent	19% smokers; 72% periodontitis+ PI in non-smokers: 3% PI in smokers + periodontitis: 53%
Rinke et al. [48]	PPD ≥5 mm, BOP, SUP, BL ≥3.5 mm	Retrospective	7	P: 65 I: 112	P: 9.2% I: ND	Ankylos	Friadent	22% smokers; 66% periodontitis+ PI rate in smokers 41.4% and non-smokers: 1.8%
Rodrigo et al. [49]	PPD > 3 plus BOP+ plus BL > 3xSD of repeated measures	Prospective	5	P: 22 I: 68	P: ND I: 6%	Straumann	SLA	36% Smokers 68% Periodontitis+
Roos-Jansaker et al. [50]	BL ≥ 3 threads plus BOP+/SUP	Retrospective	9–14	P: 218 I:999	P: 16% I: 7%	Branemark	Machined	26% Smokers
Rutar et al. [51]	PPD > 4 plus BOP+/ SUP plus BL	Retrospective	5–10	P:45 I: 64	P: ND I: 23%	Straumann	TPS	38% Smokers
Simonis et al. [52]	PPD > 4 plus BOP+ plus BL ≥ 2.5 mm/≥ 3 threads	Retrospective	10–16	P:55 I: 131	P: ND I: 16.9%	Straumann	TPS	16% Smokers; 26% periodontitis+ PI patient level:38% PCP and 11% PHP
van Velzen FJ et al. [53]	BOP+ plus BL > 2 mm	Prospective	10	P: 177 I: 374	P: ND I: 4,2%	Straumann	SLA	
Wahlstrom et al. [54]	PPD > 5 plus BOP+/ SUP plus BL > 5	Prospective	5	P: 112 I: 304	P: 4% I: ND	Astra Tech & Nobel Biocare	–	
Zetterqvist et al. [55]	PPD > 5 mm, BOP/SUP and bone loss >5 mm from loading	Prospective	5	P: 112 I: 304	P: 1% I: 0.4%	3i	Osseotite & Fully DAE**	Non-smokers

P patients; *I* implants; *ND* not defined; *PPD* probing pocket depth; *BOP* bleeding on probing; *SUP* suppuration; *BL* radiological bone loss; *PCP* periodontally compromised patients; *PHP* periodontally healthy patients; *SLA s*andblast acid etching; *TPS* rough titanium plasma spray

*Implant surfaces are specified only for the studies considered for analysis of the effect of different implant surfaces on peri-implantitis prevalence rate

**Fully etched implant with the DAE surface extending to the implant platform

Prevalence of peri-implantitis

The overall prevalence of peri-implantitis was estimated using meta-analysis (Fig. 2.) at the implant (A) and patient level (B) independently. Twenty-four studies reported on prevalence at the implant level [27–32, 34–38, 40–46, 49–53, 55] ranging between 0.2 and 63% with estimated prevalence of peri-12.8% at the implant level. Moreover, 22 studies reported on peri-implantitis prevalence at the patient level [29–44, 46–48, 50, 54, 55] ranging between 1 and 46% with estimated prevalence of 18.5% at the patient level.

Effect of study design on prevalence of peri-implantitis

Meta-analyses were performed to assess peri-implantitis prevalence between 7 cross-sectional, 10 prospective, and 7 retrospective studies at the implant level as well as 6 cross-sectional, 6 prospective, and 10 retrospective studies at the patient level (Fig. 3). There was a common observation at the implant and patient level of lower prevalence rate in prospective studies (7.6 and 9.3%, respectively), a higher prevalence rate in retrospective studies (18.5 and 23.4%, respectively), while reported prevalence rate for cross-sectional studies was in the middle (14.5 and 18.6%, respectively). Despite clear differences, meta-regression analysis did not confirm any significant effect of different study designs on reported prevalence.

Effect of implant function period on prevalence of peri-implantitis

The effect of function time on peri-implantitis prevalence was estimated in the 7 (at the implant level)/9 (at the patient level) studies for the 5–10-year timeframe as well as for the 13 (at the implant level)/11 (at the patient level) studies for function time of 10+ years (Fig. 4.). There was one single study reporting the prevalence rate for the function period less than 5 years [27] regularly listed with other studies but was not considered for quantitative analysis. Prevalence rates at the implant level were relatively similar between investigated periods, while the rates at the patient level were slightly higher for the 10+ period when compared to the mean loading period. Even though, the meta-regression analysis did not demonstrate any significant effect of function time on the prevalence of peri-implantitis.

Effect of the different implant surfaces on prevalence of peri-implantitis

The number of the studies reporting prevalence by implant surfaces was twofold lower at the patient level ($n = 12$) compared to studies reporting at the implant level ($n = 25$) (Fig. 5.). It was observed about threefold lower prevalence for moderately rough when compared to the minimal and rough implant surfaces at both implant and patient level, counting 5.4 and 5.9% prevalence rate, respectively. The meta-regression analysis confirmed the association of moderately rough implant surfaces with lower prevalence of peri-implantitis ($p = 0.011$).

Discussion

The present meta-analysis estimated similar peri-implantitis prevalence of 12.8% at the implant level and 18.5% at the patient level. Despite the strict inclusion criterion regarding proposed case definition of peri-implantitis [13, 14], the high rate inconsistence of about 98% persisted between investigated studies. Meta-regression analyses showed the positive association between implants with moderately rough implant surfaces and lower prevalence of peri-implantitis, while the

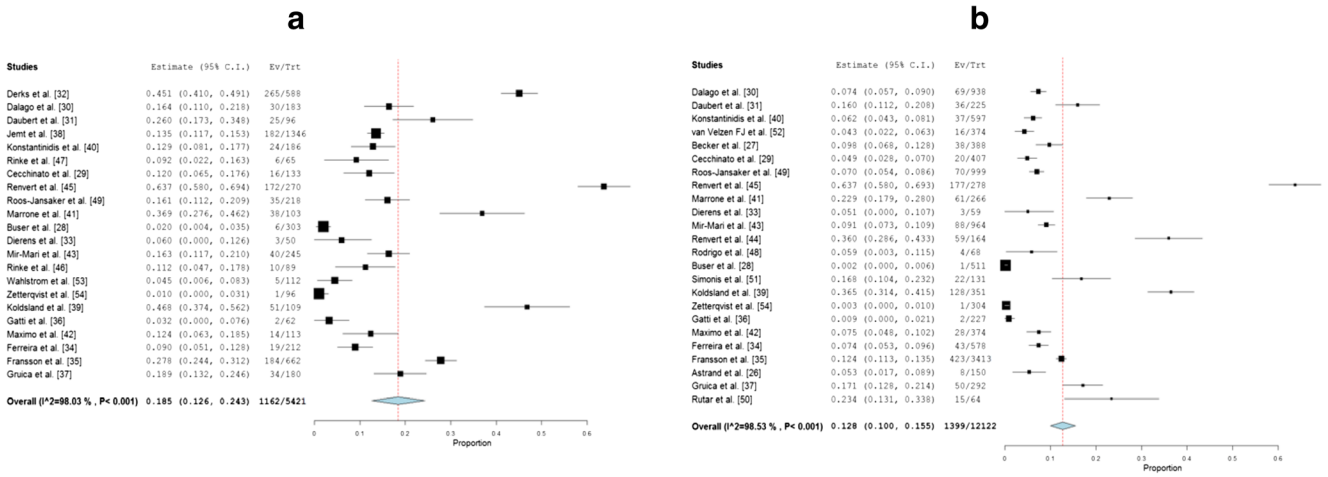

Fig. 2 Overall prevalence of peri-implantitis at patient (**a**) and implant (**b**) level

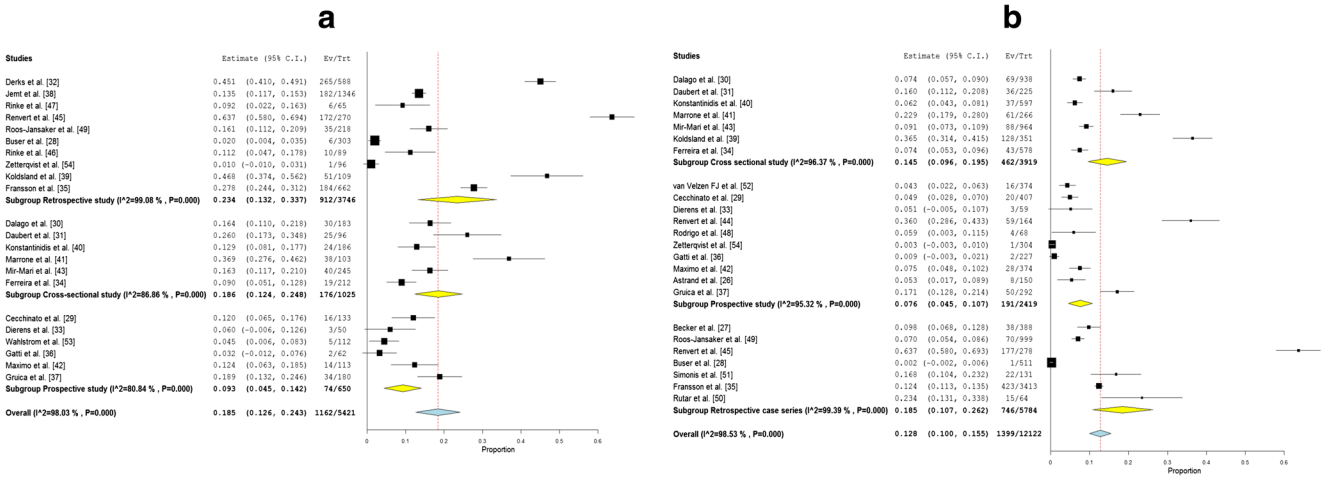

Fig. 3 Prevalence of peri-implantitis in relation to performed study design in reported studies at patient (**a**) and implant (**b**) level

different study designs and function times did not demonstrate any significant effect on prevalence rate of peri-implantitis.

Nowadays, great efforts are invested in dental implant research to systemize reported knowledge and increase the utility of reported finings, frequently decreased due to inter-study heterogeneity. Peri-implantitis represents the typical example for that since discordance in disease definition among published studies makes impossible estimation of the elementary epidemiological parameters such as prevalence.

Motivated by this, the present study was designed to follow the state-of-the-art trends on peri-implantitis regarding both methodological and clinical recommendations, to ensure the quality and reproducibility of the evidence that would contribute in resolution of the increasing peri-implantitis problematics.

To do so, the referent case definition of peri-implantitis by Sanz & Chapple [13, 14] represented the strict inclusion criterion while the meta-analysis reported by Derks & Tomasi [11] was regarded as a state-of-the-art work. Finally, the present research was carefully designed to comprehensively review the published literature and retrieve as much as possible data from the filtered study pool.

Regarding prevalence rate, the estimated prevalence of 18.5% was just slightly lower than previously reported 22% [11], while the positive relation between implant function time and prevalence of peri-implantitis was not confirmed in the here present study.

Although the previously reported [11] and the present study were similar by attempting to estimate the prevalence of peri-implantitis, respective study objectives and experimental designs were differently defined starting with a fact that present study focused strictly on peri-implantitis. The major tendency in the here present study was not only to estimate the prevalence of peri-implantitis, but to comprehensively examine reported literature in order to disclose potential factors in cause of such high inter-study inconsistence. From a clinical standpoint, identification of such factors would facilitate the identification of potentially novel susceptibility factors

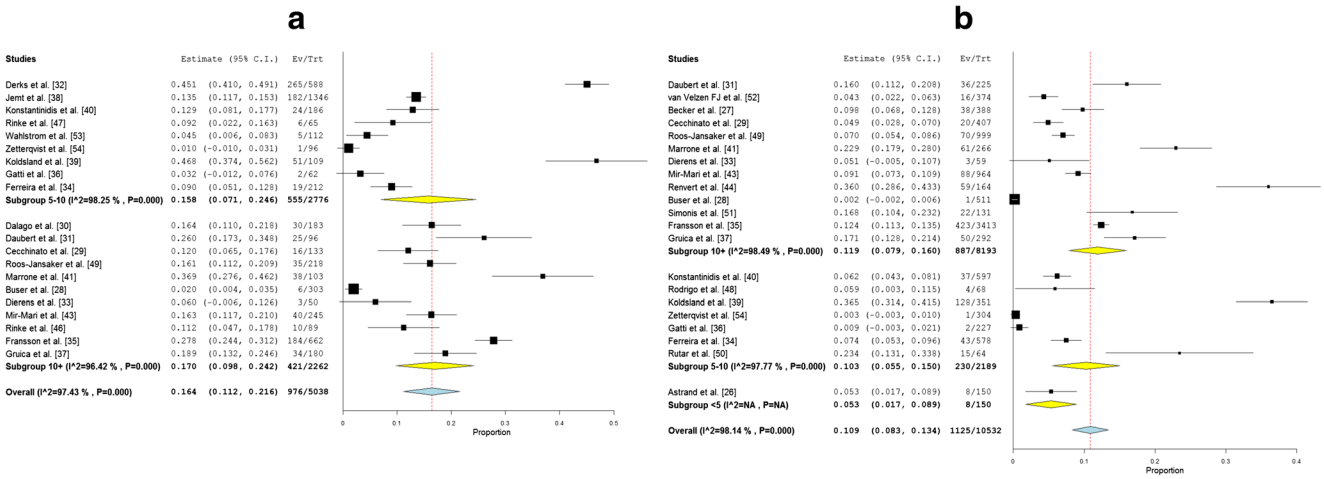

Fig. 4 Prevalence of peri-implantitis in relation to the function period at patient (**a**) and implant (**b**) level

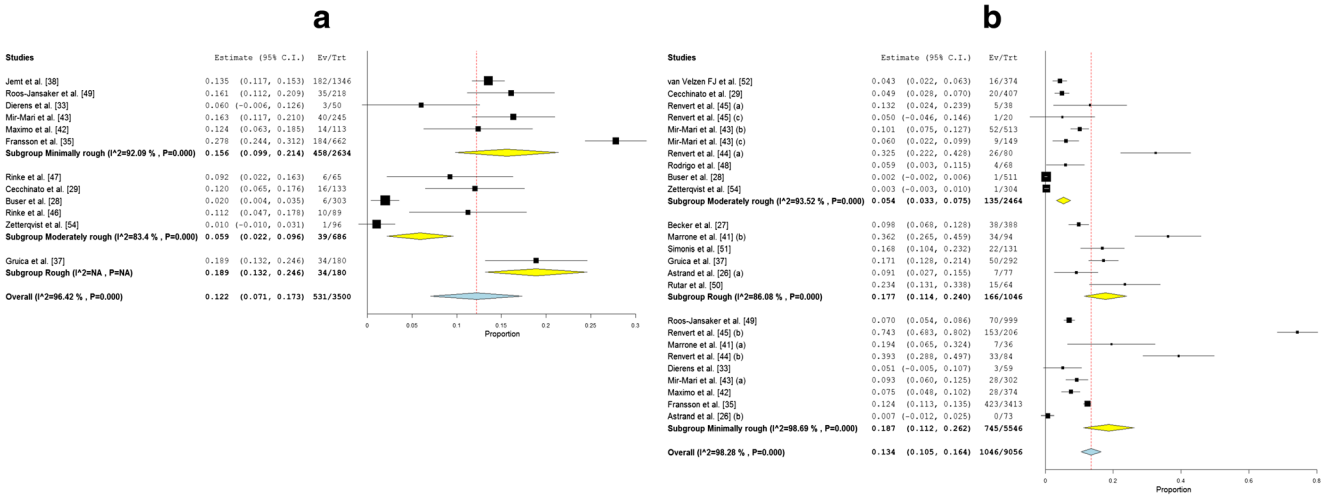

Fig. 5 Prevalence of peri-implantitis in relation to the implant surface at patient (**a**) and implant (**b**) level

associated with insufficiently resolved pathological pattern of peri-implantitis. Moreover, the minimal sample size in the present study was set significantly lower compared to the > 100 subjects required in the previous study, since it is recommended within guidelines for meta-analyses that studies seeking to identify factors of inter-study heterogeneity should be as much inclusive as possible without insisting on great sample size [56]. Such approach has as main advantage the possibility of performing a meta-analysis that enables integration of the findings from independent studies thus increasing the statistical power from the individual studies to compensate for the small sample sizes in the clinical trials. [56] However, 70% of the studies from the study pool reported on more than 100 participants and only three studies reported on less than 50 patients while the estimated prevalence was similar to the prevalence reported in the previous study indicating the comparable results with study applying higher sample size threshold. Furthermore, as peri-implantitis is considered a site-specific pathology, in the present study prevalence rate was additionally estimated at the implant level as it is considered that ratio between prevalence at the patient and implant level might provide important insights [57]. Related to that, only two studies had approximately equal numbers of participants and implants, while a vast majority of the studies had 2–5 times more implants than participants. This finding together with the higher prevalence found at patient level compared to the implant level indicates that not all implants were affected by peri-implantitis and underlines the importance of assessing the outcomes at the implant level as well. Additionally, this finding points out the site-specific nature of peri-implantitis [58] and important role of the local etiological factors in disease pathogenesis.

Regarding different study designs, the lowest prevalence rate was observed in prospective studies that were almost threefold lower when compared to the retrospective studies and two times lower than in cross-sectional studies. A possible explanation for this trend is that patients participating in prospective studies are generally enrolled in well-controlled peri-implant maintenance therapy (PIMT) program. In addition to that, a recent systematic review has demonstrated that strict PIMT every 5–6 months may prevent the incidence of peri-implant diseases by approximately three times [59].

Moreover, the effect of different implant surfaces on peri-implantitis prevalence was investigated since it was proposed that surface topography and chemistry might increase the susceptibility for peri-implantitis [17, 60]. The meta-analysis estimated threefold lower prevalence for moderately rough when compared to the minimal and rough implant surfaces while the meta-regression confirmed the association of moderately rough implant surfaces with lower prevalence of peri-implantitis. Regarding moderately rough implant surfaces, the studies fitting the study criteria reported on “big five” implant systems including TiUnite, Sandblast acid etching (SLA), Osseospeed, Osseotite, and Friadent [26]. However, it should be considered that follow-up period for the implants with rough and minimally rough implant surfaces was generally higher than for the modern implants with moderately rough surface.

Besides estimating the potential impact of three factors on prevalence of peri-implantitis, the studies reporting exclusively on the population affected by the established risk factors for peri-implantitis such as periodontitis, smoking, or diabetes mellitus represented exclusion criteria in the present study in order to avoid a false increase in the prevalence rate. However, it should be considered that exclusion of the studies exclusively reporting on this risk affected population did not disclose exclusion of the individuals affected by the same risk factors within included studies reporting on general population.

Inconsistently reported prevalence rate represents a common finding for the multifactorial diseases and meta-analysis

is an analytical instrument of choice for resolving such problem. The main advantage of meta-analysis is the ability to consolidate the findings from the unlimited number of small clinical trials thus increasing the statistical power of small sample sizes from the individual studies. Such approach simultaneously enables comprehensive assessment of large-scale parameters and identification of the new intrinsic pathogenetical factors in cause of inter-study heterogeneity. However, besides evident advantage in strengthening evidence, data pooling within meta-analyses is susceptible to the numerous biases mostly due to different methodological approaches among studies. Moreover, due to mandatory focusing on the target inclusion criteria, many important specific factors remain disregarded bringing another important bias for this methodological approach. In case of peri-implantitis prevalence, it was already emphasized that random sample would provide the most reliable results [11] while this kind of studies represented minority of the study sample. Additionally, many biological and implant-related factors are reported to affect peri-implant profile in health and disease why appropriate diagnosis of peri-implant conditions and their respective classification are currently challenged. In that regard, consideration of only target group of factors within inclusion criteria might be considered another source of bias and this should be considered when interpreting the outcomes of the meta-analyses. Finally, it should be kept in mind that the most frequently encountered risk when analyzing such a big data pool using meta-analysis method is related to the missing studies and associated data which might substantially influence the study outcomes.

When considering results as a whole, mismatching in prevalence rate at the implant and patient level together with significant effect of implant surface on prevalence rate confirms site-specific nature of peri-implantitis. Future research should attempt to establish critical thresholds for the time and volume of the bone resorption to distinguish physiological bone remodelation and progressive bone loss associated with peri-implantitis. The assessment of adjuvant objectively measurable parameters such as biomarkers might contribute to a faster and more accurate diagnosis of the disease as previously suggested [61–63].

Conclusion

Within limitations of the present study, peri-implantitis affects about 18.5% patients and 12.8% implants while the implants with moderately rough surface seems to be associated with lower prevalence rate.

Persistence of substantial inter-study heterogeneity following restriction to the clinical case definition indicates the necessity for identification of adjuvant diagnostic markers that would enable a more accurate disease diagnosis. Due to site-specific nature of the peri-implantitis, future studies should focus on local cofactors possibly playing in inter-study inconsistence, while the implication of local factors should be carefully considered during treatment planning.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this type of study, formal consent is not required.

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