

Original Article

Risk of peri-implantitis in patients with diabetes mellitus: a meta-analysis

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Received December 9, 2015; Accepted March 19, 2016; Epub August 15, 2016; Published August 30, 2016

Abstract: Background: Diabetes mellitus is one of the most common contraindications to dental implant therapy. This study aimed to analyze the relationship between diabetes and peri-implantitis. Method: A comprehensive search performed by two reviewers using the PUBMED, EMBASE, and OVID search engines as well as a separate manual search extending up to March 2015 yielded 5993 publications. After screening the retrieved literature, five studies were considered eligible and included in the meta-analysis, which was used to pool estimates of odds ratios (ORs) and 95% confidence intervals (CIs). Begg's and Egger's regression tests and visualization of Funnel plots were used to assess publication bias. Results: The meta-analysis revealed a significant relationship between peri-implantitis and diabetes (OR, 1.89; 95% CI, 1.31-2.46) with no evidence of heterogeneity ($P=0.872$; $I^2=0\%$). Publication bias measured using Egger ($P=0.69$) and Begg's test ($P=1.00$) shows no evidence for diabetes bias in peri-implantitis. Conclusion: A significant relationship between diabetes and peri-implantitis was revealed in this meta-analysis. Due to the limited number of published studies included, further investigations are required to confirm the result of this meta-analysis.

Keywords: Peri-implantitis, meta-analysis, diabetes mellitus, hyperglycemia

Introduction

Over the past few decades, oral osseointegrated implants have been widely accepted as a support treatment for removable prostheses and missing teeth and are perceived to provide effective treatment outcomes [1]. Nevertheless, despite the high success and survival rates of dental implants, there are several risk factors and complications that could lead to their ultimate failure, such as poor oral hygiene, history of periodontitis, and smoking status [2]. Moreover, numerous conditions including general systemic diseases (diabetes, osteoporosis, and coronary heart disease) and implant design (length and implant surface) are also considered to affect the treatment outcome for patients with dental implants [3-6].

Peri-implant diseases include peri-implant mucositis and peri-implantitis. While peri-implant mucositis is defined as the presence of in-

flammation in the mucosa at an implant site with no signs of loss of the supporting bone, peri-implantitis is associated with inflammation in the mucosa as well as loss of the supporting bone [7]. A study investigated some immunohistochemical features of peri-implant mucositis and peri-implantitis lesions and discovered that peri-implantitis showed features similar to those of periodontal disease [8]. In addition, the causative pathogens of peri-implantitis and periodontitis have been found to be more similar than different [9]. The prevalence and severity of periodontal disease in patients with type 2 diabetes mellitus is relatively higher than it is in patients without diabetes [10]. Taken together, these factors strongly suggest that diabetes mellitus might be associated with the increasing incidence of peri-implantitis.

Diabetes mellitus is one of the most commonly encountered contraindications to dental im-

plant therapy [11]. A study demonstrated that patients with diabetes were 2.75 times more likely to develop implant failure than other patients [12]. However, not all of the studies that have been conducted in this area are in agreement with the viewpoint. Some studies found no obvious tendency for higher implant failure rates in patients with diabetes [13, 14]. Furthermore, a review of previous implant therapies did not find any relationship between levels of glycemic control and implant failure [15]. It is well known that there is a high percentage of implant failure associated with peri-implantitis. Therefore, we sought to investigate whether diabetes mellitus is associated with an increased risk of peri-implantitis.

The aim of the present study was to assess the evidence reported in epidemiological studies involving patients with diabetes and incidences of peri-implantitis published in the international scientific literature. Our primary focus was to determine if there is indeed an associated risk of peri-implantitis in patients with diabetes.

Material and methods

Protocol

The meta-analysis performed in this study adhered to the recommendations of the Cochrane Collaboration [16] and the principles of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [17].

Search strategy

A number of systematic literature searches were conducted using the Pubmed, Embase, and OVID electronic databases covering the period up to March 2015. The search strategy used in identifying all the relevant studies was medical subject headings (MeSH) or free text words. The outcome and key subjects (peri-implantitis, peri-implantitis, peri-implant disease, and peri-implant) were combined with associated risks (risk, factor, diabetes, diabetic, and diabetes mellitus) or prevalence (prevalence) search terms were in English, but the included study publications had no language restriction). The authors of the relevant studies were contacted by email for additional information when necessary. Furthermore, relevant

reviews were screened for potential missing articles, and no restriction was placed on the year and languages of publication to avoid selection bias.

Inclusion criteria

Two blinded reviewers (K. Tseng and X. Zheng) conducted the search and review of all the studies with relevant titles and abstracts independently. Studies that provided quantitative estimates regarding the relevance between diabetes mellitus and peri-implantitis were selected if they fulfilled the following inclusion criteria: 1) Cohort, case-controlled, and cross-sectional studies. 2) Human study population. 3) The risk estimates such as relative risks (RRs), odds ratios (ORs), or incidence rate with 95% confidence intervals (CIs) of diabetes on peri-implantitis were included.

Exclusion criteria

The exclusion criteria for the study included: 1) Case reports. 2) Animal studies. 3) *In vitro* or experimental studies. 4) Reviews. 5) Studies without qualitative analysis of the risks of diabetes on peri-implantitis.

Data extraction and quality assessment

The data of the included studies were reviewed, and the relevant information was extracted by the two blinded reviewers independently. The final collation of the relevant information from the publications included name of first author, year of publication, study design, country, gender, age, year of function, sample size, the risk estimates with their 95% corresponding CIs, and diagnosis of diabetes. The quality assessments of the included studies were conducted according to the guidelines of the Agency for Healthcare Research and Quality (AHRQ) [18]. The two reviewers independently scored the studies using the quality assessment guide, which consisted of 11 criteria, and the results are shown in **Table 1**. The studies were scored based on the following scale: a maximum of 11 points could be scored, which denoted the highest quality while 0-3, 4-7, and 8-11 were considered as low, moderate, and high quality, respectively. Any inconsistency that occurred after data extraction and quality assessment was completed by discussion or the intervention of another independent reviewer (X. Qu).

Peri-implantitis, diabetes

Table 1. Quality assessment of studies by the Agency for Healthcare Research and Quality

Criteria	Daubert, 2015	Renvert, 2014	Marrone, 2013	Dvorak, 2011	Ferreira, 2006
Defined the source of information	★	★	★	★	★
List inclusion and exclusion criteria for exposed and unexposed subjects or refer to previous publications	★	★	★	★	★
Indicate time period used for identifying patients	★	★	★	★	0
Indicate whether or not subjects were consecutive if not population-based	★	0	0	0	0
Indicate if evaluators of subjective components of study were masked to other aspects of the status of the participants	★	★	★	★	★
Describe any assessments undertaken for quality assurance purposes	★	★	★	★	★
Explain any patient exclusions from analysis	★	★	★	0	★
Describe how confounding was assessed and/or controlled	★	0	0	★	★
If applicable, explain how missing data were handled in the analysis	★	0	★	0	0
Summarize patient response rates and completeness of data collection	★	★	★	0	0
Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained	★	0	0	★	0
Total (11/11)	11/11	7/11	8/11	7/11	6/11

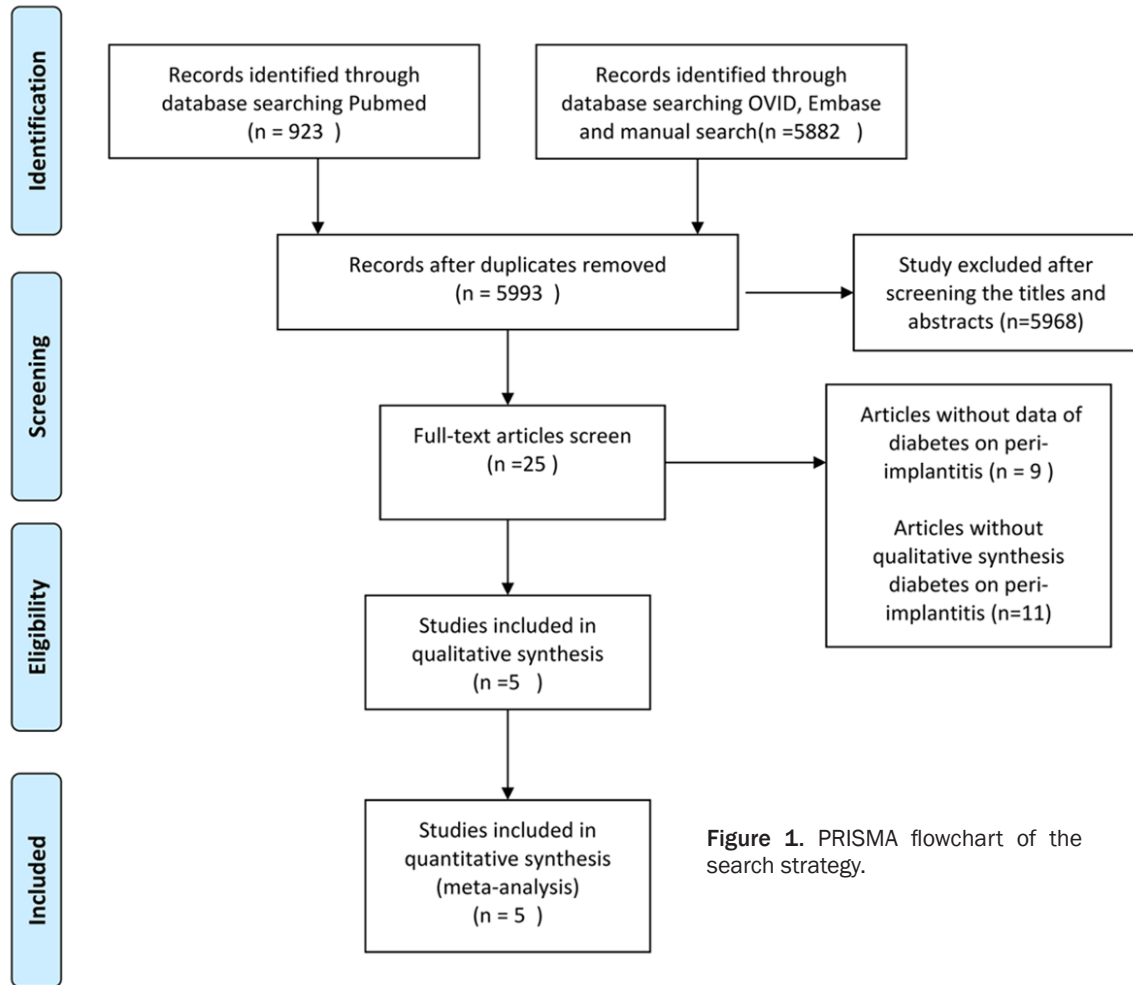


Figure 1. PRISMA flowchart of the search strategy.

Statistical analysis

The primary outcome evaluated in this study was peri-implantitis attributable to diabetes, which was expressed as the ORs, RRs, and 95% CIs. For the studies that reported multifarious association measures, we selected the results of the adjusted measures. In addition, the RRs in one included study were transformed into ORs [19]. The heterogeneity of the inter-study was assessed using the Cochran I^2 statistics where I^2 values greater than 25, 50, 75% are regarded as low, moderate, and high heterogeneity, respectively [20]. Because the p -value of heterogeneity of the inter-study was >0.1 , a fixed-effects model was used to calculate the pooled ORs and 95% CIs. The Begg's and Egger's regression tests and visualization of the Funnel plots were used to assess the publication bias [21]. The "trim and fill" procedure was used to assess the possible publica-

tion bias in this meta-analysis [22]. This procedure estimated the possibility of hypothetical "missing" studies, and then the theoretically pooled ORs that had actually been present were recalculated. All information was pooled and the data analysis was performed using Stata version 11 (StataCorp, College Station, TX, USA), and p -values <0.05 were considered statistically significant.

Results

Literature search

The results of the literature search using the study focus strategy are shown in **Figure 1**. The literature search resulted in 6805 articles being retrieved using the electronic database search engines and manual searches. After excluding duplicates, 5993 articles were found (inter-reviewer agreement, $\kappa=0.82$). The num-

Peri-implantitis, diabetes

Table 2. Characteristics of included studies with relevant information analyzed

Author, year	Study design	Country	Gender (M/F)	Mean age	Year of function	Number of PI, P	Number of PI, Im	Mean follow-up time	OR/RR (95% CI)	Diagnosis of diabetes
Daubert, 2014	Cross-sectional study	America	48/48 at baseline	67.6±10.6 yr	NR	25 at baseline	36 at follow-up	10.9±1.5	Univariate analyses RR=3.0 (1.2-7.7) at baseline, RR=1.2 (0.3-4.5) at follow-up	NR
Marrone, 2013	Cross-sectional study	Belgium	38/65	62±13.4 yr	8.5±3.2 yrs	38	62	NR	Multi-level OR=0.91 (0.16-5.38)	NR
Renvert, 2013	Cross-sectional study	Sweden	109/161	44.7±15.9 yr	PI=11.8±3.3 yrs Imhealth/peri-implant=7.0±3.0 yrs	172	NR	NR	Unadjusted OR=6.1 (0.80-48.10)	NR
Dvorak, 2011	Cross-sectional study	Austria	0/177	63±9 yr	NR	42	110	6.0±4	Adjusted OR=2.81 (0.13-59.33)	NR
Ferreira, 2006	Cross-sectional study	Brazil	115/97	NR	42.5 (SD=17.1) m	19	43	NR	Adjusted OR=1.9 (1.0-2.2)	Fasting blood sugar ≥126 mg/dl or had been taking anti-diabetic medicine over the past 2 weeks

PI=Peri-implantitis; M=Male; F=Female; P=Patients; Im=Implants; yr=Year; m=Month; NR=No report.

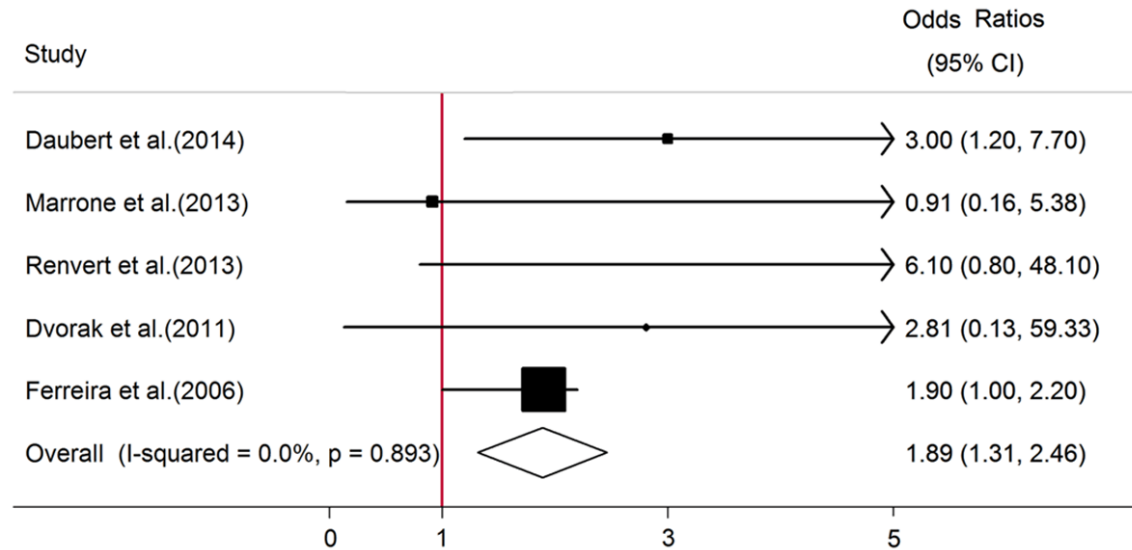


Figure 2. Odds ratios (ORs) of diabetes (95% CI) and peri-implantitis using the fixed-effects mode.

ber of eligible full-text articles was 25 after screening titles and abstracts. Furthermore, nine articles without data for diabetes in peri-implantitis and 11 articles without ORs of diabetes on peri-implantitis were excluded. Finally, five articles were included in the meta-analysis [19, 23-26].

Characteristics of included studies

The detailed analyses of the data from the five included studies are presented in **Table 2**. The number of patients in each study ranged from 80-270. The designs of all the studies selected were cross-sectional. There were 858 participants in this meta-analysis and 296 patients had peri-implantitis. Four of the studies recruited male and female participants while one recruited only postmenopausal women. The five studies were each conducted in different geographical locations including the USA [19], Belgium [23], Sweden [24], Austria [25], and Brazil [26]. While all the studies reported the diagnosis of peri-implantitis, only one reported the diagnosis of diabetes [26]. All the studies analyzed were patient-based. Only three studies adjusted their quantitative synthesis outcomes for known and confounding risk factors [23, 25, 26]. Two studies attained the high score range on quality assessment [19, 23], one of which obtained the maximum score [19].

Results of meta-analysis

Five studies that included a total of 858 individuals were reported in the results of the meta-analysis, and the pooled ORs of peri-implantitis for diabetes using fixed model are presented in **Table 2** and **Figure 2**. For risk of peri-implantitis, the pooled ORs between the patients with and without diabetes on a patient-based analysis were 1.89 (95% CI, 1.31-2.46). Because a limited number of the studies met our inclusion criteria, no subgroup analysis could be performed based on the study characteristics.

Heterogeneity and sensitivity analysis

The association analysis between diabetes and peri-implantitis showed no evidence of heterogeneity ($P_{\text{heterogeneity}}=0.872$, $I^2=0\%$) in the inter-study assessment. In addition, the sensitivity analysis revealed no significant change when any study was excluded from the pooled outcome.

Publication bias

The Egger ($P=0.69$) and Begg's ($P=1.00$) tests and visualization of the funnel plot (**Figure 3**) demonstrated no evidence of publication bias for diabetes on peri-implantitis. In addition, the studies did not lie outside the limits of the 95% CI in the funnel plot and appeared symmetrical. There were three possibly missing

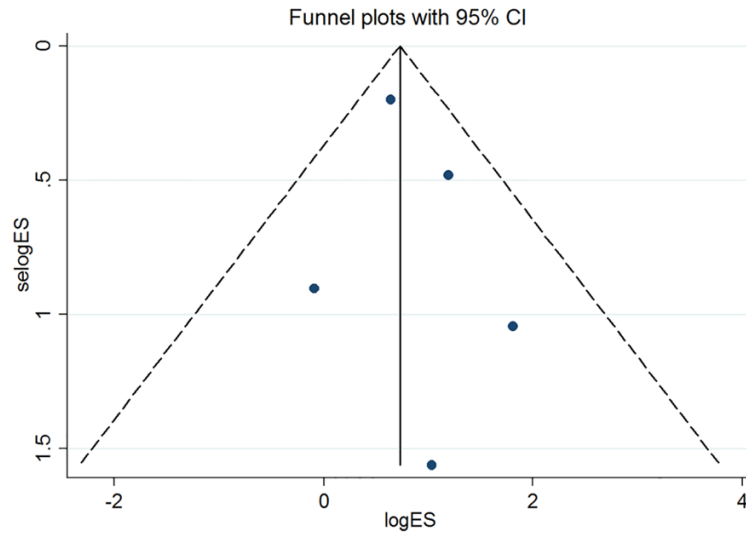


Figure 3. Begg's funnel plot of publication bias for association analysis of diabetes on peri-implantitis. CI, confidence interval. SeLogES, standard error of Log effect size. LogES, log effect size.

studies confirmed by the “trim and fill” method that could alter the pooled estimation of the result. Furthermore, the recalculation of the theoretically pooled ORs was 1.85 (95% CI, 1.28-2.42).

Discussion

Principle findings and limitations

The present meta-analysis aimed to assess the scientific evidence and verify the hypotheses that diabetes mellitus may be a potential risk factor for peri-implantitis. To the best of our knowledge, this is the first meta-analysis to determine this specific risk. Interestingly, a significant relationship was discovered between peri-implantitis and diabetes in this study (ORs, 1.89; 95% CI, 1.31-2.46). Furthermore, the analysis revealed an 89% greater risk of peri-implantitis in patients with diabetes than in those without, following implant placement.

Although there is a statistically significantly higher level of peri-implantitis in patients with diabetes than in those without it in this meta-analysis, some important issues need to be considered.

First, only one of the included studies reported diagnostic criteria for diabetes [26] while the others did not report the duration of diabetes or glycemic control of patients with diabetes. In

addition, none of the studies discussed the status of peri-implantitis associated with diabetes at different levels of severity. Evidence shows that there is a high percentage of implant failure attributable to peri-implantitis. Therefore, the severity of the diabetic condition might be associated with the dental implant success rate. For example, some clinics have reported good dental implant success rates in patients with “well-controlled” type 2 diabetes mellitus [27-29]. However, due to the limited information acquired from the few included studies, we could not perform the meta-regression analysis to deter-

mine the different severity levels of diabetes, which may influence the outcome of peri-implantitis. Another point to consider is that different definitions were used in the depiction of peri-implantitis in the included studies. All the studies reported inflammatory lesions in the peri-implant tissue. However, at sites of probing pocket depth, two studies reported the presence of PPD>5 mm [23, 26], one reported PD≥4 mm [24], and the others did not mention it [19, 25]. In the diagnosis of radiological bone loss, three studies reported the loss of supporting bone of 2 mm [19, 23, 24] while others just reported bone loss without providing precise details [25, 26]. Therefore, different diagnostic criteria may influence the prevalence of peri-implantitis. Because all included studies were cross-sectional, the measures abstracted for this meta-analysis were expressed as ORs. Only three studies adjusted their ORs and RRs of outcomes for known and confounding risk factors [23, 25, 26] while the remaining two did not report this information [19, 24]. The unadjusted results might be influenced by other confounding risk factors and, thereby, could lead to an inaccurate result. One of the included studies provided two RRs [19] including one at baseline and the other at the follow-up. We selected the baseline data to meet our inclusion criteria to analyze whether diabetes may increase the risk of peri-implantitis after implant placement. In addition, other factors

might have exerted an unpredictable influence on the outcome of this meta-analysis such as different characteristics of implants (brand, surface, placement position, etc.), year of function, and time of follow-up.

The underlying mechanisms mediating the association of diabetes with peri-implantitis are currently unknown. However, there is some information that we could be used to correlate these conditions. Both peri-implantitis and periodontitis appear to have similar clinical and microbial characteristics [8, 9, 30]. Previous studies have demonstrated that the prevalence of peri-implantitis was associated with a history of periodontitis [3, 31-34]. In addition, patients with poorly controlled diabetes also have an increased possibility of developing periodontal disease [35, 36]. Therefore, we reasonably inferred and tried to verify whether implant placement in individuals with diabetes increases the risk of peri-implantitis development. Microvascular disease of the gingiva in patients with diabetes may adversely affect blood supply, contribute to delayed oral wound healing, and increase the susceptibility to infection [37]. Tissue hyperglycemia impacts every aspect of wound healing by adversely affecting the immune system including neutrophil and lymphocyte function, chemotaxis, and phagocytosis [38]. An animal study found that bone density around osseointegrated implants in diabetic rats was decreased [39].

There appeared to be some deficiencies as well in the meta-analysis. The statistically significant result was considered to have low power due to the limited number of studies and patients in this review. Furthermore, the search strategy we used did not find any randomized controlled studies conducted in this area. Potential biases are likely to be greater for non-randomized studies than they are for randomized trials and, therefore, our results should be interpreted with caution when they are included in reviews and meta-analyses [16]. Therefore, even though the pooled outcomes revealed no evidence of heterogeneity, the results should be interpreted carefully considering the inherent limitations of this meta-analysis.

Suggestion for future studies

A significant relationship was found between peri-implantitis and diabetes in this study.

However, with the inherent limitations of our meta-analysis, the results should be confirmed in future studies. Furthermore, several questions and limitations need to be addressed when designing and conducting future studies.

First, any future cohort studies should report the diagnostic outcome and well-defined stratification of the diabetic status. Second, further studies should also be required to correlate the implant failure and peri-implantitis with different severity of diabetes and other wound healing problems. Third, the studies we included in this meta-analysis did not involve any prospective studies. Therefore, prospective studies on this topic, which are free from retrospective bias, should be included in future studies. Four, the expected outcome of the studies should be adjusted to prevent other possible confounding factors. Furthermore, one point that should be considered by future studies A high percentage of implant failures resulted from peri-implantitis and one meta-analysis determined there was no direct impact of diabetes on the risk of implant failure [40]. In view of the above outcome, future prospective studies should classify reasons for implant failure and, thereby, confirm the results of this meta-analysis.

Implications for clinical practice

Based on the result of this analysis, we propose that caution should be observed when implants are placed in patients with diabetes. It would be expedient for such patients to reduce or entirely preclude the incidence of peri-implantitis and implant failure before implant placement. This cautionary measure would include ensuring an excellent degree of glycemic control, supportive periodontal treatment, and a well-designed peri-implant plan.

Acknowledgements

Grant support for this project was provided by National Natural Science Foundation of China (Grant No. 81570948) and Shanghai Key Laboratory of Orthopaedic Implant.

Disclosure of conflict of interest

None.

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References

- [1] Schwartz-Arad D, Kidron N and Dolev E. A long-term study of implants supporting overdentures as a model for implant success. *J Periodontol* 2005; 76: 1431-1435.
- [2] Lindhe J, Meyle J; Group D of European Workshop on Periodontology. Peri-implant diseases: Consensus Report of the Sixth European Workshop on Periodontology. *J Clin Periodontol* 2008; 35: 282-285.
- [3] Roos-Jansaker AM, Renvert H, Lindahl C and Renvert S. Nine- to fourteen-year follow-up of implant treatment. Part III: factors associated with peri-implant lesions. *J Clin Periodontol* 2006; 33: 296-301.
- [4] Lee HJ, Kim YK, Park JY, Kim SG, Kim MJ and Yun PY. Short-term clinical retrospective study of implants in geriatric patients older than 70 years. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2010; 110: 442-446.
- [5] Cosyn J, Vandenbulcke E, Browaeys H, Van Maele G and De Bruyn H. Factors associated with failure of surface-modified implants up to four years of function. *Clin Implant Dent Relat Res* 2012; 14: 347-358.
- [6] Barfeie A, Wilson J and Rees J. Implant surface characteristics and their effect on osseointegration. *Br Dent J* 2015; 218: E9.
- [7] Zitzmann NU and Berglundh T. Definition and prevalence of peri-implant diseases. *J Clin Periodontol* 2008; 35: 286-291.
- [8] Gualini F and Berglundh T. Immunohistochemical characteristics of inflammatory lesions at implants. *J Clin Periodontol* 2003; 30: 14-18.
- [9] Heitz-Mayfield LJ and Lang NP. Comparative biology of chronic and aggressive periodontitis vs. peri-implantitis. *Periodontol* 2000 2010; 53: 167-181.
- [10] Mealey BL and Ocampo GL. Diabetes mellitus and periodontal disease. *Periodontol* 2000 2007; 44: 127-153.
- [11] Li KK, Varvares MA and Meara JG. Descending necrotizing mediastinitis: a complication of dental implant surgery. *Head Neck* 1996; 18: 192-196.
- [12] Moy PK, Medina D, Shetty V and Aghaloo TL. Dental implant failure rates and associated risk factors. *Int J Oral Maxillofac Implants* 2005; 20: 569-577.
- [13] Bornstein MM, Cionca N and Mombelli A. Systemic conditions and treatments as risks for implant therapy. *Int J Oral Maxillofac Implants* 2009; 24 Suppl: 12-27.
- [14] Anner R, Grossmann Y, Anner Y and Levin L. Smoking, diabetes mellitus, periodontitis, and supportive periodontal treatment as factors associated with dental implant survival: a long-term retrospective evaluation of patients followed for up to 10 years. *Implant Dent* 2010; 19: 57-64.
- [15] Oates TW, Huynh-Ba G, Vargas A, Alexander P and Feine J. A critical review of diabetes, glyce-mic control, and dental implant therapy. *Clin Oral Implants Res* 2013; 24: 117-127.
- [16] Higgins JP and Green S. *Cochrane handbook for systematic reviews of interventions*. Wiley Online Library; 2008.
- [17] Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg* 2010; 8: 336-341.
- [18] Rostom A, Dubé C, Cranney A. *Celiac Disease*. Rockville (MD): agency for healthcare research and quality (US); 2004 Sep. (evidence reports/technology assessments, No. 104.) 3, Results, 2013.
- [19] Daubert DM, Weinstein BF, Bordin S, Leroux BG and Flemming TF. Prevalence and predictive factors for peri-implant disease and implant failure: a cross-sectional analysis. *J Periodontol* 2015; 86: 337-347.
- [20] Higgins JP, Thompson SG, Deeks JJ and Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; 327: 557-560.
- [21] Egger M, Davey Smith G, Schneider M and Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; 315: 629-634.
- [22] Peters JL, Sutton AJ, Jones DR, Abrams KR and Rushton L. Performance of the trim and fill method in the presence of publication bias and between-study heterogeneity. *Stat Med* 2007; 26: 4544-4562.
- [23] Marrone A, Lasserre J, Bercy P and Brex MC. Prevalence and risk factors for peri-implant disease in Belgian adults. *Clin Oral Implants Res* 2013; 24: 934-940.
- [24] Renvert S, Aghazadeh A, Hallstrom H and Persson GR. Factors related to peri-implantitis - a retrospective study. *Clin Oral Implants Res* 2014; 25: 522-529.
- [25] Dvorak G, Arnhart C, Heuberger S, Huber CD, Watzek G and Gruber R. Peri-implantitis and late implant failures in postmenopausal women: a cross-sectional study. *J Clin Periodontol* 2011; 38: 950-955.

- [26] Ferreira SD, Silva GL, Cortelli JR, Costa JE and Costa FO. Prevalence and risk variables for peri-implant disease in Brazilian subjects. *J Clin Periodontol* 2006; 33: 929-935.
- [27] Abdulwassie H and Dhanrajani PJ. Diabetes mellitus and dental implants: a clinical study. *Implant Dent* 2002; 11: 83-86.
- [28] Farzad P, Andersson L and Nyberg J. Dental implant treatment in diabetic patients. *Implant Dent* 2002; 11: 262-267.
- [29] Alsaadi G, Quirynen M, Komarek A and van Steenberghe D. Impact of local and systemic factors on the incidence of late oral implant loss. *Clin Oral Implants Res* 2008; 19: 670-676.
- [30] Botero JE, Gonzalez AM, Mercado RA, Olave G and Contreras A. Subgingival microbiota in peri-implant mucosa lesions and adjacent teeth in partially edentulous patients. *J Periodontol* 2005; 76: 1490-1495.
- [31] Aguirre-Zorzano LA, Estefania-Fresco R, Telletxea O and Bravo M. Prevalence of peri-implant inflammatory disease in patients with a history of periodontal disease who receive supportive periodontal therapy. *Clin Oral Implants Res* 2015; 26:1338-44.
- [32] Karoussis IK, Salvi GE, Heitz-Mayfield LJ, Bragger U, Hammerle CH and Lang NP. Long-term implant prognosis in patients with and without a history of chronic periodontitis: a 10-year prospective cohort study of the ITI Dental Implant System. *Clin Oral Implants Res* 2003; 14: 329-339.
- [33] Koldslund OC, Scheie AA and Aass AM. The association between selected risk indicators and severity of peri-implantitis using mixed model analyses. *J Clin Periodontol* 2011; 38: 285-292.
- [34] Sgolastra F, Petrucci A, Severino M, Gatto R and Monaco A. Periodontitis, implant loss and peri-implantitis. A meta-analysis. *Clin Oral Implants Res* 2015; 26: e8-16.
- [35] Tervonen T and Oliver RC. Long-term control of diabetes mellitus and periodontitis. *J Clin Periodontol* 1993; 20: 431-435.
- [36] Control CfD and Prevention. National diabetes statistics report: estimates of diabetes and its burden in the United States, 2014. Atlanta, GA: US Department of Health and Human Services; 2014.
- [37] Shernoff AF, Colwell JA and Bingham SF. Implants for type II diabetic patients: interim report. VA Implants in Diabetes Study Group. *Implant Dent* 1994; 3: 183-185.
- [38] Goodson W, Hunt T. Wound-Healing in well-Controlled diabetic men, in surgical forum, amer coll surgeons 54 east erie st. Chicago, IL; 60611, 1984.
- [39] de Moraes JA, Trindade-Suedam IK, Pepato MT, Marcantonio E Jr, Wenzel A and Scaf G. Effect of diabetes mellitus and insulin therapy on bone density around osseointegrated dental implants: a digital subtraction radiography study in rats. *Clin Oral Implants Res* 2009; 20: 796-801.
- [40] Chen H, Liu N, Xu X, Qu X and Lu E. Smoking, radiotherapy, diabetes and osteoporosis as risk factors for dental implant failure: a meta-analysis. *PLoS One* 2013; 8: e71955.