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Systematic Review
Dental Implants

Systemic risk factors for peri-implant bone loss: a systematic review and meta-analysis

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Abstract. The aim of this study was to determine the influence of patient-related systemic risk factors (systemic disease, genetic traits, chronic drug or alcohol consumption, and smoking status) on peri-implant bone loss at least 1 year after implant installation and prosthetic loading. An electronic search was performed of MEDLINE, EMBASE, and The Cochrane Central Register of Controlled Trials up to January 2012. One thousand seven hundred and sixty-three studies were identified. After applying a three-stage screening process, 17 articles were included in the qualitative analysis, but only 13 in the quantitative analysis, since smoking was a common exposure. The meta-analysis of these 13 studies (478 smokers and 1207 non-smokers) revealed a high level of heterogeneity and that smoking increases the annual rate of bone loss by 0.164 mm/year. Exposure to smoking had a harmful effect on peri-implant bone loss. However, the level of evidence for oral implant therapy in patients with systemic conditions is very low. Future studies should be improved in order to provide more robust data for clinical application.

Keywords: bone loss; risk factors; meta-analysis; systemic diseases; smoking; dental implants.

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The achievement of osseointegration is a biological concept already adopted in implant dentistry.[1] The long-term maintenance of bone around an osseointegrated implant is paramount to clinical success, and peri-implant bone remodelling has commonly been expressed in terms of survival rates.[2,3] It is believed that several factors may affect peri-implant bone resorption: local, surgical, implant, post-restorative, and patient-related risk factors, which include systemic diseases, genetic traits, chronic drug or alcohol consumption, and smoking status. Nevertheless, there is uncertainty around some factors. As an example, the results of a number of in vitro studies that aimed to investigate the association between specific interleukin 1 (IL-1) gene polymorphisms and peri-implant diseases were unclear[4]; this later generated further methodological problems.[5] On the other hand, other factors have been identified as a risk. It has been observed that smokers have a higher risk of dental implant failure than non-smokers,[6–8] with an increased risk for patients with a history of treated periodontitis.[2]

Diabetes is considered a relative contraindication for dental implant treatment. The success rates improve by 85–95% with the eradication of co-morbidities (poor oral hygiene, cigarette smoking, and periodontitis), stabilization of glycaemic control (glycated haemoglobin (HbA1c) around 7%), and preventive measures against infection.[9] Implant failure in patients using oral/intravenous bisphosphonates to treat osteoporosis is a subject that remains controversial. In a recent systematic review, only two out of 10 selected papers demonstrated a negative

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impact of bisphosphonates on implant success.[3] Moreover, no scientific data are available to sufficiently support any specific treatment protocol for the management of bisphosphonate-related osteonecrosis of the jaws (BRONJ).[10] Finally, although the ravages of cancer therapy are well-known, implants can osseointegrate and remain functionally stable in oral cancer patients who have undergone radiotherapy and chemotherapy.[11]

Nevertheless, the current goals of implant therapy include long-term function, the capability to maintain good oral hygiene at home (even in posterior areas of the oral cavity), and overall aesthetics. In cases of implant survival, it is very important to address how much bone is lost over time radiographically. Furthermore, there is a lack of results on peri-implant soft tissue outcomes (bleeding on probing, plaque index, gingival recession, and width of keratinized tissues).

The aim of the present study was to review, in a systematic manner, the influence of systemic risk factors on peri-implant bone loss.

Materials and methods

Study protocol

The recommendations of the PRISMA statement[12] were followed for the review process.

Focused question

The question in focus was 'In patients undergoing dental implant treatment, what is the influence of systemic risk factors (systemic disease, genetic traits, chronic drug or alcohol consumption, and smoking status) on the occurrence of peri-implant bone loss at least 1 year after implant installation and prosthetic loading?'

Eligibility criteria

The following inclusion criteria were applied: (1) English language publications; (2) randomized controlled clinical trials, controlled clinical trials, cohort studies, case–control studies, and case series with at least five patients (in order to include as many studies as possible); (3) human subjects presenting systemic risk factors (systemic disease, genetic traits, chronic drug or alcohol consumption, and smoking status); (4) intervention involving dental implants and/or immediate loading of dental implants; (5) studies reporting on radiographic peri-implant bone level changes assessed by means of intraoral or panoramic X-rays; and (6) follow-up of at least 1 year after implant placement and prosthetic loading (to avoid the risk of false-positive measurements of peri-implant bone loss due to bone remodelling in the first 3–6 months after implant placement, or early implant loss due to surgical procedures).

The following were exclusion criteria: (1) letters, reviews, and unpublished data; (2) patients with acute medical conditions that could contraindicate implant therapy (acute infection, severe bronchitis or emphysema, severe anaemia, uncontrolled diabetes, uncontrolled hypertension, abnormal liver function, nephritis, severe psychiatric disease, conditions with a severe risk of haemorrhage, endocarditis, and myocardial infarction); and (3) studies reporting only implant failure, survival, and/or success rates.

Study selection

Information sources and the search strategy are available in the Supplementary Material, available online.

A three-stage screening process was performed independently by two reviewers (MC and PHOR). Initially, all titles were screened to eliminate non-related publications and reviews. During the second stage, all selected abstracts were analyzed and the full-text articles were consequently retrieved. Then, all reference lists of the selected studies, relevant reviews, and studies from the 'grey literature' were screened for additional papers that might meet the eligibility criteria of this systematic review. In the third stage, selected articles were analyzed. Any disagreements between the two reviewers were resolved after additional discussion with a third reviewer (LC). The inter-reviewer reliability of the data extraction was calculated by determining the percentage of agreement and the correlation coefficient (kappa, 5% level of significance). In addition, study authors were contacted for incomplete or missing data when necessary.

Heterogeneity of the outcome

In order to evaluate the heterogeneity of the outcome between the selected studies, the following factors were recorded: (1) study design; (2) duration of follow-up; (3) number, mean age (range), and gender of subjects; (4) numbers and types of dental implants; (5) type of prosthetic unit; (6) systemic risk factor affecting the study population; (7) measurement of bone level changes (in mm); and (8) peri-implant soft tissue outcomes (bleeding on probing, plaque index, gingival recession, and width of keratinized tissues).

Risk of bias

Two reviewers (MC and PHOR) assessed the methodological quality using the forms 'quality assessment of a cohort study' and 'quality assessment of a randomized clinical trial', combining the proposed criteria of the MOOSE statement,[13] STROBE statement,[14] and PRISMA.[12] These two validity tools consist of eight and nine items, respectively, which have to be scored with a plus, a minus, or a question mark. In accordance with Tellerman et al.,[15] it was decided that studies scoring four or more plusses were methodologically acceptable. The two observers, who were blinded to the author, institute, and journal, independently generated a score for the articles. Any disagreement was resolved with a third reviewer (LC).

Data analysis and synthesis

The meta-analysis was based on the DerSimonian and Laird method. The weighted mean difference (WMD) was expressed for bone loss under a randomized effects model. WMD estimations were accompanied by the 95% confidence interval (95% CI) of the standard error and the *P*-value of the distinction of a null effect of the smoking factor (WMD = 0) for the solution of the meta-analysis, including the statistical value of association Q_A. The statistical Q_H value for heterogeneity and the relative *P*-value for the χ^2 test were both included. At the same time, the index I^2 was also calculated, considered as representative of the total variation due to heterogeneity. A forest plot was obtained for better visualization of the results, and a funnel plot was drawn to assess potential publication bias. The software used to perform this meta-analysis was Sinergy 3.2 (Biometrics Department, GlaxoSmithKline). All analyses were conducted with a 5% level of significance.

Results

Study selection

The search identified 1763 references up to January 2012. A further 160 references were retrieved from other sources and cross-checked references, giving a total 1923 studies. After duplicates were removed, 1824 references were available for screening. Of these, 254 publications