CLINICAL ORAL IMPLANTS RESEARCH

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Occlusal overload and bone/implant loss

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Abstract

Aim: The aim of this search was to assess the *biological* consequences that *overload* might have on already osseointegrated oral implants through a systematic screening of the scientific literature.

Method: Detailed searches through PUBMED, OVID, EMBASE and LILACS databases were made. Articles published up to December 2011 and those reported on the clinical, radiographic and/or histological outcome of oral implants subjected to so-called overload were considered eligible for inclusion. Identified studies were assessed by one non-blinded reviewer according to well-defined inclusion and exclusion criteria. When doubt arose, the co-authors were counselled until final agreement was obtained. The PICO questions formulated was:"what is the effect of overload vs. no overload on bone/implant loss in clinically stable implants?"

Results: The database searches as well as additional hand searching, resulted in 726 potentially relevant titles. Eventually, 16 clinical and 25 animal studies were considered relevant to the topic. After inclusion/exclusion criteria assessment, all clinical studies and all but three animal studies and one systematic review were considered at high risk of bias and excluded. The included animal studies did not reveal an association between overload and peri-implant bone loss in the absence of peri-implant inflammation, whereas in its presence, overload seemed to aggravate the peri-implant tissue breakdown.

Conclusions: The effect of implant overload on bone/implant loss in clinically well-integrated implants is poorly reported and provides little unbiased evidence to support a cause-and-effect relationship. The PICO question remained unanswered. At the animal level, "overload", mimicked by supra-occlusal contacts acting in an uninflamed peri-implant environment, did not negatively affect osseointegration and even was anabolic. In contrast, supra-occlusal contacts in the presence of inflammation significantly increased the plaque-induced bone resorption.

Excessive surgical trauma together with an impaired healing ability, premature loading of not primary stable implants besides infection are likely to be the most common causes of early implant losses (Esposito et al. 1998a; Chiapasco 2004). Peri-implantitis and overload in conjunction with the host characteristics are said to be the major aetiological agents causing late failures (Esposito et al. 1998b).

Peri-implant diseases may affect the peri-implant mucosa only (peri-implant mucositis) or involve the supporting bone as well (peri-implantitis) (Zitzmann & Berglundh 2008). Peri-implant disease following successful integration of an endosseous implant is the result of an imbalance between bacterial load and host defence (Heitz-Mayfield et al. 2004). The proportion of implant patients suffering from peri-implantitis varies from about 6% (Roos-Janåker et al. 2006) to 12% at the implant level (Fransson et al. 2005). Recently, Koldsland et al. (2010) assessed peri-implantitis at different levels of severity and yielded a substantial variance in prevalence (11.3–47.1%) of the investigated study population. Peri-implant inflammation was a common clinical observation that occurred with and without peri-implant bone loss. However, if undiagnosed, peri-implantitis may lead to complete loss of osseointegration (Lang & Berglundh 2011). Thus a cause-and-effect relationship between bacterial load (plaque) and peri-implant bone loss has been observed. Others reported the association of poor oral hygiene with smoking to increase the peri-implant bone loss (Lindquist et al. 1997). Thus the preventive plaque removal and smoking cessation have been shown to be effective measures in the maintenance of peri-implant health comparable to the natural tooth situation (Serino & Ström 2009).

High occlusal load challenges the implants, its components and the prostheses and may eventually lead to mechanical failure. Elasticity analysis of a one-piece 3.3 mm diameter implant showed that, after applying 500 N under 45°, stress exceeded 500 MPa, which is the proof stress of grade four pure titanium (Nagasawa et al. 2008).

The applied occlusal load also results in stress on the bone which eventually results in a deformation of the latter. This deformation is expressed in strain and displayed as the Greek letter ε. Strain is defined as the relative change in the length of a (long) bone, i.e. either lengthening or shortening and is often expressed in micro strain (με). 1000 με equals to a deformation of 0.1%. The magnitude of strain is directly related to the applied stress on the bone, as e.g. through the loading of an implant. However, the same force may affect cortical and spongious bone tissue quite differently, depending on its stiffness (E-mod.). This means that, the same amount of stress can result in a different amount of strain depending on its bone properties. An impact force evoking 25.000 με results in fracture of healthy bone.

Mechanical loading, evoking stress and strain into the load bearing bones, can both have a positive (anabolic) as well as a negative (catabolic) effect for the net bone tissue. This has been supported by correlations between exerted forces and bone response (Duncan & Turner 1995; Hsieh & Turner 2001; Frost 2004). Frost's (2004) mechanostat relates four levels of mechanical strain magnitude to the bone response: (i)disuse atrophpy, resulting in net bone loss (50–100 με), (ii) steady state (100–1.500 με), (iii) mild overload, resulting in net bone gain (1.500–3.000 με) and iv) fatigue failure, resulting in net bone loss (> 3.000 με). If the latter happens, the load can theoretically be classified to what is called overload. Besides force magnitude, other parameters such as frequency (Hsieh & Turner 2001), duration (Farr et al. 2011), rest periods between load bouts (Robling et al. 2002), etc. all play a role in the bone response to loading.

Although stress and strain can well be defined at the outer bone surface e.g. through strain gauge technology, and even at the implant-bone interface through numerical modelling, the stress and strain evoked at the implant-bone interface remain impossible to be quantified today in the animal/clinical settings (Mellal et al. 2004). Because of the latter it remains challenging, if not impossible, to correlate occlusal loading to implant failure. The semantics, for what is mentioned by "overload" remains crucial. The reader should keep in mind that whenever the term overload is used in this review, it only refers to what has been used in the referred papers and does not necessarily imply that real overload (> 3000 με), as coined by Frost (2004), has been measured/quantified at the bone-implant interface.

It is well accepted that some limited bone loss around the neck of the implants, in the months following loading, have to be considered as a remodelling phenomenon (Brånemark et al. 1977, 1999; Manz 2000). It is without saying that overloading will result in the mobilization, and thus failure, of the not-primary stable implant during the healing period (Merli et al. 2008; Esposito et al. 2009). The former observations are out of the scope of this review.

Several have, derived from animal as well as from clinical observations, suggested that occlusal forces on a well-osseointegrated oral implant can result in loss of the marginal bone or even in implant failure (Adell et al. 1981; Esposito et al. 1998b; Isidor 2006).

The aim of this paper is to elucidate the biological consequences overloading might have on already osseointegrated oral implants through a systematic screening of the scientific literature.

Methods

PICO question

A well-structured question in the PICO format was formulated to direct the literature searching where PICO stand for: P: patients with stable implants, I: overloaded implants, C: control implants and O: marginal bone loss. The PICO question was structured as follows: "what is the effect of overload compared to controls on marginal bone loss, in clinically stable implants?"

Study selection

Studies reporting on the outcome of dental/oral implants subjected to so-called overload were considered eligible for inclusion. Clinical as well as animal experimental trials were selected. Studies from the highest level of evidence such as randomized clinical trials (RCT) and systematic reviews of RCT were considered. However, it was anticipated that hardly any RCT has been conducted. Therefore, non-randomized trials downwards till case series were included as well.

Types of interventions: outcome measures: inclusion/exclusion criteria

Interventions: Administration of overload vs. control.

Outcome: Clinical, radiographic and/or histological outcome of implants subjected to overload.

Inclusion/Exclusion criteria: Clinical studies were selected that considered overload of oral/dental implants as the aetiological factor for marginal bone loss/implant loss and in which (occlusal) forces have been quantified. Furthermore, studies in which factors were identified that could be associated with increased leverage (single vs. splinted implants, short vs. long cantilevers, small vs. large crown-implant (C/I) ratios, etc.) were selected as well since, according to finite element analysis, increased stress and strains at the implant-bone interface are anticipated in those situations (Li et al. 2007). For the clinical case series, a follow-up period of at least 6 months was required, with a minimum of 10 patients.

For animal trials, only those with (i) an intra-oral experimental site, (ii) including an appropriate control group and (iii) with an adequate plaque control programme were selected. Concerning the controls, inclusion of a sham-control-group – i.e. with superstructure and with physiological (sub-) occlusal/food bolus loading-was considered a prerequisite for inclusion.

Studies not specifically focusing on overload as the aetiological factor for marginal bone loss, nor including measured or defined parameters that could be associated with increased strains at the bone-implant interface, were excluded. Papers that did not report or were on numerical modelling and photo elastic studies, or in a language other than English were excluded as well. Narrative reviews have only been used for completeness of the search through consulting the reference lists.

Search strategy

The identification of titles considered or included for this review was performed through a detailed search strategy of four databases; MEDLINE (via PubMed), MEDLINE (via Ovid), Excerpta Medica Database (EMBASE), and Latin American and Caribbean Health Sciences Literature (LILACS). Papers published up to and including December 2011 were searched for. Free text-terms, key words, and controlled terms from the Medical Subject Headings (MeSH) were used and Boolean operators (OR, AND, NOT, *, (XX), etc.) were used to combine searches.

The search strategies applied were; via PubMed: oral OR dental AND implant$ AND (load OR overload OR excessive load OR force $ OR bruxism) AND (bone loss OR bone

resorption OR implant failure$); via Ovid: oral OR dental AND implant$ AND (load OR overload OR excessive load OR force$ OR bruxism) AND (bone loss OR bone resorption OR implant failure$) AND [ovid]/lim NOT [pubmed]/lim {Including Limited Related Terms}. Even with the Boolean operator (NOT [Pubmed]/lim) a 30% overlap remained; via Embase: "oral"/exp OR oral OR dental AND ("implant"/exp OR implant$) AND (load OR overload OR excessive AND load OR force$ OR "bruxism"/exp OR bruxism) AND ("bone"/exp OR bone AND loss OR "bone"/exp OR bone AND resorption OR "implant$"/exp OR implant$) AND failure$ and via Lilacs: oral OR dental implant$ AND overload OR force$ OR bruxism AND bone loss OR bone resorption OR failure$.

In addition, as mentioned above, the reference lists of the review papers were hand searched for possible missing titles.

Assessment of validity and quality

The potentially relevant titles identified were examined by one non-blinded reviewer (IN). When any doubt arose from the title, the abstract was retrieved and reviewed. The relevant full papers selected on the basis of the abstract were subsequently read and reviewed. When doubt arose about the selection criteria, counselling with the other authors of this paper was considered until common agreement was found. In case of missing data of relevant papers, the authors of the original reports were contacted for further details.

The methodological quality of the included clinical studies was assessed by considering the following items: method of randomization, controls included, allocation concealment, sample size calculations, completeness of patient reporting and length of the follow-up period, all potentially leading to a high risk assessment of bias. The quality of the methodology used in the included animal trials was appraised such as: the design of the control group, the method of randomization if any, the number of implants (min. required for valid statistical analysis), blinding and the follow-up and reporting of all originally installed implants.

Results

Search results

Table 1 summarizes the potentially relevant titles of each of the search strategies separately. In addition to the 683 potentially relevant titles retrieved from Pubmed, an additional 43 titles were found through the search of the three other databases and hand searching. Table 2 depicts the relevant papers sorted by study design and split into clinical and animal studies.

Table 1. **Potentially relevant titles from the four database searches**

Database	Potentially relevant results
PUBMED	683
OVID	843*
EMBASE	545
LILACS	595

*About 30% overlap with PubMed.

From a total of 726 titles of potentially relevant papers, 685 were excluded after review of the titles and abstracts based on the inclusion/exclusion criteria (Fig. 1). The full text papers of the remaining 41 articles were considered relevant to the topic and reviewed in detail. Sixteen and 25 papers dealt with clinical and animal studies respectively.

The main study characteristics and the reasons for exclusion of some of the clinical trials (with a higher robustness) and of all the animal studies, are depicted in Tables 3–5. The results will separately be dealt with into either clinical or animal studies.

Table 2. **Relevant results sorted by study design and split into clinical and/or animal studies**

PUBMED/OVID/EMBASE/ LILACS Databases + hand searching	Relevant results
Clinical	
Randomized control trial	1
Controlled clinical trial	1
Crossover study	1
Cohort study (prospective (P)/retrospective (R))	4(P)/5(R)
Case-control study	0
Case series/report	4
Subtotal	16
Animal	
Systematic review	1
Controlled trial	16
Crossover study	0
Case series/report	8
Subtotal	25
Clinical + animal	
Total	41

Clinical studies

Study description

Three clinical trials, characterized by high robustness of the study design were found: one randomized controlled trial (Jofré et al. 2010), one controlled clinical trial (Vigolo & Zaccaria 2010), and one crossover study (van Kampen et al. 2005) (Table 3). Jofré et al. (2010) and van Kampen et al. (2005) both dealt with the effect of maximum bite forces on the marginal bone loss in two-implant mandibular overdentures, whereas Vigolo & Zaccaria (2010) compared splinted (single tooth replacement) with unsplinted (partial fixed dental prostheses) implants in the posterior maxilla

Outcome

In none of the above-mentioned studies was bone loss related either to the magnitude of the bite forces or to the splinting or not of the implants.

Quality assessment

In two studies (van Kampen et al. 2005; Jofré et al. 2010) a real effort to quantify forces,

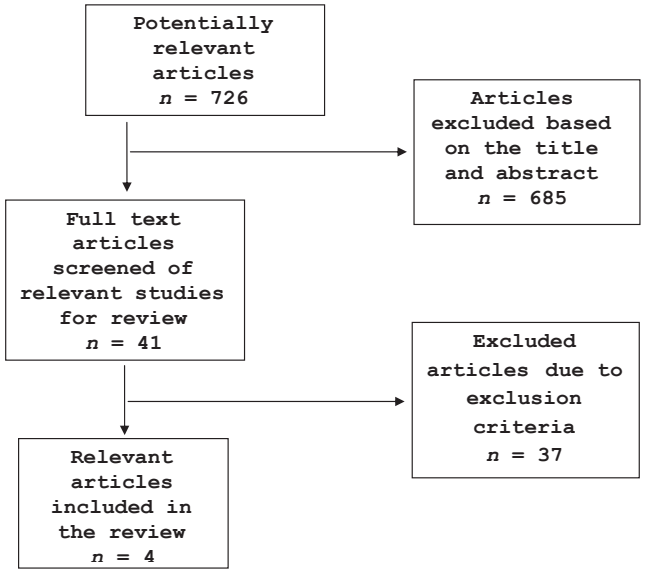

Fig. 1. Flow chart of screened, withdrawn and included articles through the review process.

Table 3. **Study characteristics and quality assessment of the clinical trials with the highest robustness of study design**

Study	Year	Method	Patients/ implants/ prostheses/loading time/ follow-up time	Type of intervention/methods	Outcome	Reason for exclusion
Jofré et al.	2010	RCT	45 (one-piece)/90 two-implant mandibular overdenture Immediately loading 15 m	Two retention systems *ad random* allocated (ball/bar) X-rays were taken at implant installation and after 5, 7, 10 and 15 m. Max. bite force was measured before and 5, 7, 10 and 15 m post-surgery	No relationship ($R = 0.14$) between marginal bone loss and max. bite force	Max. bite force was defined at prosthesis level lack of sample-size calculations
Vigolo et al.	2010	CCT	44 (two-piece)/132 Fixed partial dental prosthesis/single tooth replacement delayed healing 60 m	All part. edentulous in the posterior maxilla at the left side and all ones at the right side got three implants. The former were splinted, the latter remained non-splinted X-rays were taken at abutment connection and every 3 m in the first year and every 6 m thereafter	No implants failed after loading. No sign. difference in MBLoss between splinted vs. non-splinted ones	Two drop-outs, 123 of 132 impl. left Lack of sample-size calculations
van Kampen et al.	2005	Crossover study	18 (two-piece)/36 two-implant mandibular overdenture delayed healing 9 m	Three retention systems *ad random* allocated (ball/magnet/bar) changed 3 m each X-ray and max. bite force measurements after abutment connection and after 3, 6 and 9 m of function	No relationship ($R = 0.02$) between marginal bone loss and max. bite force	Lack of sample-size calculations max. bite force was defined at prosthesis level

Table 4. **Study characteristics and quality assessment of the prospective clinical trials**

Study	Year	Method	Patients/ implants/ prostheses/loading time/ follow-up time	Type of intervention/ methods	Outcome	Reason for exclusion
Rossi et al.	2010	Cohort prospective	35 pat./35(Straumann)/ single teeth/2 years	Single tooth replacement in posterior area X-rays ever year	No impl. failure/stable bone	Lack of sample-size calculations no control bite force not defind
Lindquist et al.	1996	Idem	47 pat./273(Branemark)/ Fixed full dental proth./ delayed 12–15 years	Fixed full dental prostheses in the mandible X-rays ever 3–5 years. Max. bite forces strain gauges	No correlation with cantilever length and max bite force	Lack of sample-size calculations no control bite force at prosthesis level
Akça et al.	2006	Idem	29 pat./3-unit tooth/ implant. sup. fixed partial dental prosth. delayed 2 years	One tooth/1 implant 3-unit prosth. in post. areas X-rays every year Max bite forces strain gauges	No correlation with low/high max bite forces and bone loss	Lack of sample-size calculations no control bite force at prosthesis level
Blanes et al.	2007	Idem	93 pat./192(Straumann) single or FPDP delayed 10 years	Defined clinical C/I ratios annuals X-rays	More bone loss in low vs high C/I ratios ($R = -0.3$)	C/I > only 4.2% and 81% of the implants were splinted

although limited to the prosthesis level was done. Besides, in all studies sample-size calculations were lacking and the lack of allocation concealment was questionable in one study (Vigolo & Zaccaria 2010). This brings these three studies at high risk of bias and for these reasons they were excluded (Table 3).

Nine cohort studies were identified; four pro- and five retrospective studies.

Study description

Of the prospective studies, Rossi et al. (2010) looked at early loaded, 6 mm short, moderately roughened SLA Straumann implants in the posterior regions replacing single tooth in 35 patients after 1 and 2 years. Lindquist et al. (1996) followed 47 fixed full mandiblular prostheses, on machined Brånemark implants, for 12–15 years. Akça et al. (2006) looked at one tooth/one implant supported 3-unit fixed dental prostheses in the posterior area in 29 patients over a 2-year period. Maximum bite forces were obtained through strain-gauged occlusal bite fork measurements in both former studies. Blanes et al. (2007) well defined the clinical crown-implant ratios in 192 single tooth replacements or fixed partial dental prostheses (Straumann®) in 93 patients which were followed for 10 years (Table 4).

Outcome

In the study of Rossi et al. (2010), no implants failed after 2 years of loading and stable bone apposition was found. Lindquist et al. (1996) did not find correlations of loading factors (e.g. cantilever length and maximal bite forces) with marginal bone loss. Akça et al. (2006) could not find a correlation with maximal bite forces, as grouped above or below mean/median values, and marginal bone loss. Blanes et al. (2007) found

statistically significant greater marginal bone loss in low C/I ratios compared to high ones. Correlation analysis also showed a significant inverse relationship between the two variables ($r = -0.3$).

Quality assessment

These studies did not quantify at all or did quantify forces, but at the prostheses level, lacked sample-size calculations and any controls. Such studies were considered to be at high risk of bias and were excluded. The cohort of Blanes et al. (2007) lacked unfavourable clinical situations. Indeed, the number of cases with clinical C/I ratios greater than three was only 4.2%, besides the fact that 81.3% of the implant restorations have been splinted. Consequently, most of the theoretically negative effect of the C/I ratio could have been diminished by the protective scenario provided by splinting the implants. The paper suffered from high risk of bias as well and was excluded.

Study description

Of the five retrospective studies only Urdaneta et al. (2010) identified factors that could be associated with increased leverage such as C/I ratios. In 81 patients, 326 single tooth replacements (locking-taper Bicon®) were followed over a mean period of 70 months. The remainder based their assumptions for overload on: tooth-implant connections (Naert et al. 2001), or occlusal wear (Engel et al. 2001), or the absence of bilateral contact in the posterior area in the maximal intercuspal position and lack of balanced occlusion during excursions (Wennerberg et al. 2001) or the presence of bruxism as reported by the patient (Ekfeldt et al. 2001).

Outcome

Although the increased C/I ratios in the study by Urdaneta et al. (2010)-mean 1.6 (range: 0.8–4.95) and 16.2% $\geq$ 2-led to an increase in mechanical implant failures, these ratios did neither lead to an increased risk for marginal bone loss nor for implant failure. Naert et al. (2001) found significantly more bone loss in rigid tooth-implant supported restorations vs. freestanding ones. Engel et al. (2001) based on occlusal wear did not. Neither Wennerberg et al. (2001) nor Ekfeldt et al. (2001), in which implant failure was the outcome measure, could find any correlation with the type of occlusion or bruxism.

Quality assessment: All these studies suffered from their inherent weaknesses of the retrospective design character such as: missing or incomplete data for all patients, study not originally designed for, no correction for confounding factors, besides lack of sample-size calculations all leading to high selection bias. For all these reasons, these studies were excluded.

Four case series were selected as being relevant to the topic.

Tawil (2008) and Piattelli et al. (1998) reported on three and one implants respectively. Wiskott et al. (2004) reported on seven patients among one on overload. Esposito et al. (2000) histologically reported on 10 late failures of which eight dealt with overload. However, the aetiology of the failures was deduced speculatively. Because the selection criterion of $n \geq 10$ patients was not met in any of these case series, they were excluded from the review.

Animal studies

Table 5 summarizes the animal study characteristics, outcome and reason(s) for exclusion from the review.

Description of included studies

One systematic review (Chambrone et al. 2010) was selected. Three controlled trials (Hürzeler et al. 1998; Gotfredsen et al. 2001a; Kozlovsky et al. 2007), two adopting overload in the dynamic (Hürzeler et al. 1998; Kozlovsky et al. 2007), and one in the static loading mode (Gotfredsen et al. 2001a) were retrieved as well (Table 6).

The systematic review by Chambrone et al. (2010) selected 347 potentially relevant titles. Eleven full articles were reviewed in more detail. Eventually, only two papers were included for analysis (Heitz-Mayfield et al. 2004; Kozlovsky et al. 2007). Only the study by Kozlovsky et al. (2007) was selected for the present review, since a proper sham-control group was lacking in the study of Heitz-Mayfield et al. (2004), which was one of our exclusion criteria. In addition, the report of Hürzeler et al. (1998) – estimated non-potentially relevant by Chambrone et al. (2010) – was included. These two selected studies as well as the trial adopting static overload used a split-mouth design (Gotfredsen et al. 2001a).

All studies were performed in the dog at the same anatomical site. Implants were placed, 12 weeks after extraction of the teeth, in the mandibular premolar region and a strict hygiene protocol was respected. Similar implant types with slightly varying dimensions were used: Hi-Tec screw-type machined (L: 10.0 mm; ø: 3.75 mm; Kozlovsky et al. 2007), Brånemark (L: 7.0 mm; ø: 3.75 mm, Hürzeler et al. 1998), and ITI hollow-screw non-submerged implants (L: 8.0 mm; ø: 3.3 mm, Gotfredsen et al. 2001a). All exhibited delayed loading (12–16 weeks of healing). Dynamic "overload" in the study of Kozlovsky et al. (2007) was performed via a supra-occlusal contact pattern resulting in an increased anterior vertical dimension of at least 3 mm. To do so, the same abutments, but with varying lengths, were used as prosthesis for both physiologically and supra-occlusal loaded implants, thereby offering an acceptable sham-control group. A total of 16 loaded implants for two experimental overload conditions resulted in eight implants/condition. Follow-up was repeated at 3, 6, 9, and 12 months. In the study of Hürzeler et al. (1998), dynamic overload was created through a splint cemented on the antagonistic front teeth and attached to an orthodontic wire construction fixed on the remaining mandibular teeth, resulting in supra-occlusal contacts. The occlusion of the implants not subjected to trauma was maintained physiologically, thereby offering an adequate sham-control group. A total of 20 implants for two experimental load conditions resulted in 10 implants/condition. The experiment lasted 16 months. Moreover, for both referred studies, the experimental set-up was such that the influence of overload could also be tested in ligature-induced peri-implantitis conditions. An equal number of implants as mentioned above, i.e. 16 and 20 implants for Kozlovsky et al. (2007) and for Hürzeler et al. (1998), respectively, installed at the contralateral mandibular side, received plaque retentive ligatures, which remained in place throughout the whole experiment.

Static "overload" (Gotfredsen et al. 2001a) was performed via orthodontic expansion screws. A total of 24 loaded implants for four experimental conditions resulting in six implants per condition were considered. Up to 24 weeks of loading period was set. Control implants were provided with the same prosthetic superstructure and the same occlusal design as the test ones, resulting in an appropriate sham-control group.

Outcomes

Given the heterogeneity of the included studies (dynamic vs. static "overload" with/without peri-implantitis), the clinical, radiographic and histological data were considered individually (Table 7).

Dynamic overload in uninflamed conditions

Kozlovsky et al. (2007) reported no changes for the clinical parameters (PD, PI, GI) from

Table 5. **Study characteristics and quality assessment of the animal studies *excluded* for the review**

Study	Year	Model	Study design	Intention to overload	Load mode	Type of loading	Microbial control	Reason for exclusion
Assenza et al.	2003	Dog mandible	Four dogs, • two dogs: 6 months of loading • two dogs: 12 months of loading 12 implants/dog • six imp. received a prosthetic superstructure • six imp. received a healing screw	No	Occlusion	Dynamic	Yes (3x/week)	No intention to overload No sham control
Berghlundh et al.	2005	Dog mandible	Six dogs, split-mouth design eight implants per dog, two different implant systems Per implant system: • one unloaded control implant • three loaded implants, splinted by a fixed partial prosthesis	No	Physiological occlusal load	Dynamic	Yes (daily)	No intention to overload
Bousdras et al.	2007	Pig mandible	12 pigs: • Six pigs received a hard diet • Six pigs received a soft diet four implants per pig: • one implant with a cover screw • one implant with a healing abutment • one implant with a crown in sub occlusion • one implant with a crown in occlusion	No	Physiological occlusal load	Dynamic	Yes (3x/week)	No intention to overload No osseointegration prior to implant loading
Duyck et al.°	2001	Rabbit tibia	10 rabbits, three implants/rabbit: • Statically loaded implant • Dynamically loaded implant • Unloaded implant	Yes	Static and dynamic loading device	Dynamic and static	No, extra-oral	Extra-oral model No appropriate control for the dynamically loaded implant (subcutaneous)
Gotfredsen et al.	2001b	Dog mandible	Three dogs, four implants per dog: • two implants with a TPS surface • two implants with a machined surface All implants were statically loaded	Yes	Static loading device	Static	Yes (daily)	No unloaded control implant
Gotfredsen et al.	2001c	Dog mandible	Three dogs, six implants per dog: • three implants subjected to 10 weeks of load • three implants subjected to 46 weeks of load	Yes	Static loading device	Static	Yes (daily)	No unloaded control implant
Gotfredsen et al.	2002	Dog mandible	Five dogs, six implants per dog: • three turned implants • three implants with a SLA surface three test conditions: 1. Mucositis + static loading 2. Peri-implantitis 3. Peri-implantitis + static loading	Yes	Static loading device	Static	Yes (depending on test condition)	Inappropriate control (no unloaded implant without peri-implantitis)
Heitz-Mayfield et al.	2004	Dog mandible	Six dogs, eight implants/dog: • two imp. + TPS surface : overloaded • two imp. + SLA surface: overloaded • two imp. + TPS surface : not loaded • two imp. + SLA surface: not loaded 8 months of (un)loading	Yes	Overload through supra-occlusion	Dynamic	Yes (daily)	No sham control (no crowns on unloaded imp.)
Hoshaw et al.	1994	Dog tibia	20 dogs, two implants per dog: 1. Unloaded control implant 2. Implant loaded in axial tension 12 weeks of (un)loading	Yes	Dynamic loading device	Dynamic	No, extra-oral	Extra-oral model

Table 5. *(continued)*

Study	Year	Model	Study design	Intention to overload	Load mode	Type of loading	Microbial control	Reason for exclusion
Isidor°	1996	Monkey mandible	Four monkeys, split-mouth design five implants per monkey: • two impl. in supra occlusion (overload) • three impl. with ligature-induced peri-implantitis (only abutment, no superstructure) Loading/infection for 18 months	Yes	Supra-occlusion	Dynamic	Yes (brushing 1x/week, subgingival cleaning: 1x/month)	No appropriate control (no unloaded implant without peri-implantitis) Limited oral hygiene control
Isidor°	1997a	Monkey mandible	Four monkeys, split-mouth design five implants per monkey: • two impl. in supraocclusion (overload) • three impl. with ligature-induced peri-implantitis (only abutment, no superstructure) Loading/infection for 18 months	Yes	Supra-occlusion	Dynamic	Yes (brushing 1x/week, subgingival cleaning: 1x/month)	No appropriate control (no unloaded implant without peri-implantitis) Limited oral hygiene control
Isidor°	1997b	Monkey mandible	Four monkeys, split-mouth design five implants per monkey: • two impl. in supraocclusion (overload) • three impl. with ligature-induced peri-implantitis (only abutment, no superstructure) Loading/infection for 18 months	Yes	Supra-occlusion	Dynamic	Yes (brushing 1x/week, subgingival cleaning: 1x/month)	No appropriate control (no unloaded implant without peri-implantitis) Limited oral hygiene control
Junker et al.	2010	Dog mandible	Six dogs, split-mouth design eight implants per dog: • four different implant surfaces • four loaded and four unloaded implants	No	Physiological occlusal load	Dynamic	Yes (1x/week)	No intention to overload Limited oral hygiene control
Kim et al.	2008	Dog mandible	Six dogs, split-mouth design two implants per dog: • one implant was immediately loaded • one implant was loaded after 3 months of healing	No	20N at 120° angle from crown axis, 1800 cycles/day	Dynamic	Yes (daily)	No intention to overload No osseointegration prior to implant loading
Ko et al.	2003	Pig mandible	17 pigs (two implants per pig): • 4: 1 month of healing + 5 months of loading • 4: 2 months of healing + 5 months of loading • 4: 4 months of healing + 5 months of loading • 5: external control implants with 6, 7, or 9 months of unloaded healing Internal control implant in the 12 test pigs: equal healing time, no loading	No	intra-oral hydrolic device providing cyclic load (6.5 N, 1 Hz, 10'/d.)	Dynamic	Not clear	No intention to overload No oral hygiene protocol was mentioned
Miyamoto et al.	2008	Dog mandible	12 dogs, three implants per dog (one implant per animal was subjected to (non-) loading and analyses) • four dogs: unloaded implant for 24 weeks • four dogs: 12 weeks healing + 20 weeks of loading • four dogs: 4 weeks healing + 12 weeks of loading	Yes	Loading of cantilever	Static	Yes (3x/week)	No appropriate control

Table 5. (continued)

Study	Year	Model	Study design	Intention to overload	Load mode	Type of loading	Microbial control	Reason for exclusion
Miyata et al.	1998	Monkey mandible	Five monkeys, one implant per monkey: 1. No occlusal load 2. Occlusal load for 1 week 3. Occlusal load for 2 weeks 4. Occlusal load for 3 weeks 5. Occlusal load for 4 weeks	Yes	Supra-occlusion	Dynamic	Yes (1x/week)	Only 1 implant per test condition Control is not clear (submerged? supra-structure?) Limited oral hygiene control
Miyata et al.°	2000	Monkey mandible	Four monkeys, one implant per monkey: 1. No occlusal load 2. 100 μm supra-occlusion 3. 180 μm supra-occlusion 4. 250 μm supra-occlusion 4 weeks of loading	Yes	Supra-occlusion	Dynamic	Yes (1x/week)	Only 1 implant per test condition Control is not clear (submerged? Supra-structure?) Limited oral hygiene control
Miyata et al.	2002	Monkey mandible	Four monkeys, one implant per monkey three test conditions: 1. Overload + no oral hygiene for 8 weeks 2. Overload + no oral hygiene for 4 weeks, followed by no load + oral hygiene for another 4 weeks 3. Physiological load + oral hygiene for 8 weeks	Yes	Supra-occlusion	Dynamic	Yes (1x/week)	Only 1 implant per test condition No appropriate control (overload + oral hygiene) Limited oral hygiene control
Ogiso et al.	1994	Monkey maxilla and mandible	Six monkeys two implants per monkey: • one implant in maxilla • one implant in mandible Loading for 1 (n = 3) or 3 (n = 3) months	yes	Supra-occlusion	dynamic	Yes (1x/week)	No unloaded control implant Limited oral hygiene control
Piatelli et al.	1993	Monkey maxilla	Three monkeys, two non-submerged implants per monkey: • one implant received a crown • one implant was left unloaded 15 months of (non-)loading	No	Physiological occlusal load	dynamic	Oral hygiene was performed 1 month after implantation, and every 6 months thereafter	No overloading Limited oral hygiene control

*these studies showed, but not in accordance with the inclusion criteria set in this review, bone loss/implant loss in their experiments.

baseline for both supra-occluded and physiologically loaded implants. The clinical parameters were not evaluated by Hürzeler et al. (1998).

Radiographs taken at the end of 12 months follow-up revealed crestal bone changes, but confined to the implant neck (Kozlovsky et al. 2007), for both groups. Radiographic outcomes were absent in the report of Hürzeler et al. (1998).

The histological findings of Kozlovsky et al. (2007) revealed that supra-occlusal loading significantly increased the percentage of bone-to-implant contact (BIC). A slightly increased, although insignificant crestal bone resorption in response to supra-occlusion, was noted. This resorption did not progress beyond the implant neck. The study of Hürzeler et al. (1998) did not observe peri-implant bone changes in healthy implant sites in case of supra-occlusion.

Dynamic overload in inflamed conditions

Physiologically as well as supra-occlusally loaded implants with ligature-induced peri-implantitis presented high inflammatory indices throughout the observation period, as displayed by the clinical parameters recorded by Kozlovsky et al. (2007). At the end of 12 months follow-up, radiographs showed marked peri-implant bone loss for both groups, extending onto the implant threads in the inflamed sites. Histological findings from Kozlovsky et al. (2007) unveiled that supra-occlusal loading worsened the plaque-induced bone loss when peri-implant inflammation was present. Under the conditions of the study of Hürzeler et al. (1998), supra-occlusal loading did not have an effect on the peri-implant bone changes in diseased implant sites.

Static overloading

The clinical examinations (inter-implant distance, PD, GI) revealed neither change over time nor between the groups. The radiographs documented neither marginal bone level alterations that had occurred during the lateral static loading period, nor differences between loaded and unloaded implants. Histometric analysis revealed higher BIC and peri-implant bone density for static loaded compared to unloaded implants (Gotfredsen et al. 2001a).

Quality assessment

The three included controlled animal studies were split-mouth designed, but not randomized. All implants healed uneventfully and sufficient data were available for statistical analysis. A properly designed sham-control group was present in all studies.

Table 6. **Study characteristics and quality assessment of the animal studies *included* for the review**

Study	Year	Model	Study design	Load mode	Type of loading	Microbial control	Outcome	Remarks
Kozlovsky et al.	2002	Dog mandible	Four dogs, four implants/dog, one imp./test condition: 1. Peri-implantitis + overloadingNo peri-implantitis + overloading 2. Peri-implantitis + no overloading 3. No peri-implantitis + no overloading 4. 12 months of over- or unloading	Overload through supra-occlusion	Dynamic	Yes (3x/week)	• Significantly more bone loss in case of peri-implantitis • BIC increased significantly in case of overloading • Overloading aggravated bone resorption in case of peri-implantitis	Supra- vs. infra-occlusion (by means of 5- or 8 mm abutments)
Hürzeler et al.	1998	Monkey mandible	Five monkeys, eight implants/monkey: • four impl.: ligature-induced peri-implantitis two impl. overloaded two impl. physiologically loaded • four imp.: no peri-implantits two impl. overloaded two impl. physiologically loaded 16 weeks of (over)loading	Overload through static load device + supra-occlusion	Dynamic load superimposed on a static load	Yes (3x/week)	• All implants remained osseointegrated. • No histological effect of overload. • Significantly less BIC in case of peri-implantitis.	Supra- vs. infra-occlusion
Gotfredsen et al.	2001a	Dog mandible	Three dogs, eight implants per dog 1 static loading device per pair of implants, resulting in four static loading units/animal: 1. No activation 2. 0,2 mm expansion 3. 0,4 mm expansion 4. 0,6 mm expansion 24 weeks of (un)loading	Static loading device	Static	Yes (daily)	• No marginal bone loss for all groups. • BIC and BF were higher for the loaded compared to the unloaded implants	Overload through static load through expansion screw

Discussion

The search on clinical studies focusing on the potential effect of overload on peri-implant tissue response resulted in three clinical studies of higher hierarchical study design; one randomized controlled clinical trial (Jofré et al. 2010), one controlled clinical trial (Vigolo & Zaccaria 2010), and one cross-over study (van Kampen et al. 2005).

When an implant is loaded, the stress will be transferred by the implant to the bone, with the highest stress in the most coronal portion of the latter. This follows a general engineering principle that when two different materials are in contact and one is loaded, the stress will be highest where the materials have their first contact (Kitamura et al. 2004). Independently of the length of the implant, the highest stresses always occur at the neck of the implant. This might explain the nearly equal outcome of short and long implants once they are integrated into the bone. However, in all the clinical studies, when the load magnitude was defined, it was at the prosthesis level, and not at the bone-implant interface. This is not surprising since many practical and ethical obstacles prevent the satisfactory conduct of randomized controlled trials within the clinical field. Indeed, randomized controlled trials are inappropriate and unethical for questions about harm (overload) (Fitzpatrick-Lewis et al. 2009). Thus, the effects of excessive forces can only ethically be ascertained in animal studies. Moreover, the clinical studies, even those with the highest ranked study designs, were at high risk of bias as well. For e.g., was the lack of relationship due to the fact that maximum bite forces or unsplinted implants or large C/I ratios did not lead to real overload at the implant-bone interface, or was it due

Table 7. **Outcome measures of the three included animal studies**

Study	Loading mode	Period	Outcome					
			LU vs. UU (= healthy)			LI vs. UI (= inflamed)		
			Clinical	X-ray	Histology	Clinical	X-ray	Histology
Kozlovsky et al. (2007)	Dynanic	12 m	/	/	+	/	n.r.	–
Hürzeler et al. (1998)	Dynanic	16 m	n.r.	n.r.	/	n.r.	n.r.	/
Gotfredsen et al. (2001)	Static	6 m	/	/	+	n.a	n.a.	n.a.

n.r. = not reported; n.a. = not applicable; LU vs. UU, loaded uninflamed vs. "unloaded" uninflamed; LI vs. UI, loaded inflamed vs. "unloaded" uninflamed; – = catabolic effect of "overload" on peri-implant tissues; / = no effect of "overload" on peri-implant tissues; + = anabolic effect of "overload" on peri-implant tissues.

to the fact that small sample sizes could not detect differences since sample-size calculations were lacking in all these studies? Eventually all these clinical studies could neither evidence nor refute a cause-and-effect relationship between bone loss and the so-called overload.

Despite what the hierarchy of evidence would have us believe, randomized controlled trials do not have a unique ability to determine the effectiveness of treatment interventions (Borgerson 2009). A recent systematic review by Fitzpatrick-Lewis et al. (2009) reported that both randomized controlled trials and studies without control groups could produce similar results. Poor execution of the primary study design rather than the study design itself appeared to be the most important factor influencing the reported results. Well-conducted prospective case series are simpler than randomized controlled trials and may provide valid evidence of the effectiveness of treatment interventions. Vere & Joshi (2011) phrased it as such: prospective case series have greater value than the hierarchies of evidence suggest. This study design should be more widely used in the field of dental implantology.

However, none of the cohort studies, either prospective or retrospective could establish or refute a cause-and-effect relationship between overload and marginal bone loss as they were considered to be prone to high risk of bias. Either they lacked any definition for measuring occlusal overload or wear was used as a surrogate for occlusal overload although wear is not the result of grinding only (quid; erosion, abrasion, material selection, etc.). Alternatively, either deduction for overload was based on the absence of bilateral contact in the posterior area in the maximal intercuspal position and the lack of balanced occlusion during excursions or on the patients' reporting of bruxism. As mentioned earlier, one may wonder if overload as such can ever be applied in clinical studies, because the opportunity to test such a hypothesis in humans remains inappropriate and unethical (Chambrone et al. 2010)

Overall, most clinical studies have rather few patients included and, at the same time, only a small frequency of failed implants or bone resorption was reported. The marked heterogeneity between studies did not allow data to be combined for meta-analyses. Besides all clinical studies were prone to a high risk of bias. All together, this makes it difficult to reveal any correlation between (occlusal) overload and marginal bone loss or implant failures. Most of the knowledge in this field, therefore, is derived from animal experimental studies. This left the PICO question unanswered.

The search for animal studies revealed one systematic review (Chambrone et al. 2010). The authors reported that although application of stringent inclusion and exclusion criteria, the selected studies still were at high risk of bias. The conclusions drawn were as follows: (i) it is not well established if an excessive occlusal load catabolically affects osseointegration when adequate plaque control is performed. Overload seems to increase bone density around dental implants; (ii) overload might play a key role in the development of peri-implant tissue breakdown when plaque accumulation is present; (iii) although studies with a well-designed methodology were selected, few were available for meta-analysis, and no RCTs were conducted. The main reason for exclusion of all but two animal studies in the referred review was the fact that splinted instead of single implants were used. One may wonder if this is a valid exclusion criterion, since overload cannot be the exclusivity of single restorations only.

For the current review, two unburdened exclusion criteria used were as follows: (i) the absence of a strict control hygiene programme (minimum 3x/week) and (ii) the absence of a genuine control condition in the experimental design. The rationale for claiming meticulous plaque control is self-evident: the causal relationship between oral plaque and peri-implant bone loss has repeatedly been demonstrated (see for review; Quirynen et al. 2002; Lang & Berglundh 2011), and bacterial load as a confounding co-variant warrants exclusion when addressing the question of mechanical overload as a trigger for peri-implant bone loss. The second requirement, a genuine control condition, forced us to exclude many studies (Table 5). A control condition was considered genuine or sham when the experimental test (e.g. loading) condition was fully replicated, except for the parameter under investigation (overload). This implies that the control implants must have undergone abutment surgery (submerged implants were excluded), should have been exposed to the same micro flora, should have received the same plaque-control regime, must have been restored with an identical prosthetic supra-structure, and must have been subjected to physiological loading, either through occlusal or food-bolus contact.

In all three selected studies (Hürzeler et al. 1998; Gotfredsen et al. 2001a; Kozlovsky et al. 2007) at least food-bolus contact of the control implants was established. The preservation of the antagonistic teeth in all three studies and the provision of a prosthetic superstructure (either crown or abutment) enabled normal texture food intake and unchanged chewing comfort, resulting in physiological loading of the control implants. The authors gave high importance to this second inclusion/exclusion criterion when selecting the studies, and call attention that not only the selection of a high evidence study design must be encouraged, but that the inclusion of an appropriate sham-control condition in the study design, an aspect which has been neglected in most of the potentially relevant papers of the systematic literature search, is even more important. As mentioned by Borgerson (2009) poor execution of the primary study design rather than the study design itself appears to be the most important factor influencing the results.

Although different exclusion/inclusion criteria were set in this review, the findings corroborate well with those set by Chambrone et al. (2010). Indeed, there is a lack of association between overload and peri-implant tissue loss in healthy conditions. However, here is an inappropriate use of the term overload, since according to the definition by Frost (2004), overload should lead to a catabolic reaction of the bone. As shown by Kozlovsky et al. (2007) and Gotfredsen et al. (2001a) an anabolic rather than a catabolic effect of "overload", in bacterial unchallenged peri-implant bone tissues, was found. Thus, the strains in the peri-implant bone evoked by the so-called "overload", either by dynamic or by static loading, were within the strain window of mild overload and not of catabolic overload, resulting in bone density gain (see mechanostat, Frost 1998). The correct semantics is once again shown to be of crucial importance when communicating results or its interpretations.

However, when the tissues surrounding the bone were exposed to inflammation, the same strain magnitude was shown to be catabolic, as observed by Kozlovsky et al. (2007) where supra-occlusal contacts aggravated the plaque-induced bone resorption. Hürzeler et al. (1998) did neither observe bone gain nor bone loss in uninflamed vs. inflamed peri-implant tissues in response to overloading. The reasons may be related to the small orthodontic spring forces onto the implants. Although initially named as "mechanical trauma forces" in their study objectives, the authors appreciated the forces as physiological when discussing their findings.

An important remark has to be made to the definitions of overload used in the reported

clinical and animal studies. Even when one raises the occlusion with 3–4 mm, increases the C/I ratio's or isolates bruxers from non-bruxers, as long as the stresses and strains are not measured at the bone-implant interface one may only speculate about the real effect of the latter. Clinical indices concerning the magnitude, the direction, the frequency, etc. are not available as they are for plaque accumulation and peri-implant mucositis (Mombelli et al. 1987). This renders it very difficult to correlate occlusal loading and peri-implant tissue reaction. Animal experimental research, however, has this potential and several methodologies with external loading devices enabling well-controlled and well-defined load application to explore the peri-implant tissue response to mechanical stimuli have been proposed (Hoshaw et al. 1994; Duyck et al. 2001, Duyck et al. 2004; Ko et al. 2003; De Smet et al. 2006; Leucht et al. 2007). In particular, loading devices used in extra-oral set-up offer excellent control of the mechanical loading history. However, the latter studies were considered as non-relevant for the present review as the extra-oral implant site does not harbour the oral micro flora. On the other hand, the majority of the searched animal studies with an intra-oral implant location were defectively designed owing to the lack of randomization and the lack of genuine control conditions. This opens perspectives and motivates incentives for establishing guidelines and quality assessment tools for animal experimental research.

It is further worth mentioning that even when an animal study investigating the effect of overload on peri-implant bone tissue would meet all criteria to be classified as low risk bias, it is still impossible to measure the exact strains the peri-implant tissues are exposed to. Strain gauges experiments have tried to do so (Geris et al. 2004; Jaecques et al. 2004; Mellal et al. 2004), although these are *in se* invalid as the measured strains are strains at the bone surface level and not at the bone-implant interface itself. Hence, for a better understanding of the biomechanical conditions validated numerical modelling data can be valuable.

Although bone/implant loss has not been evidenced in the absence of peri-implant inflammation and in the presence of "overload", some animal studies did (see Table 5 indicated by*). However, as mentioned earlier, these studies were not in accordance with the inclusion criteria of this review and thus excluded.

Chvartsaid et al. (2008) proposed besides, the peri-implantitis and the overloading hypothesis, another one to explain implant failure and/or bone loss namely the healing/adaptation theory. They claim that marginal bone loss and implant failure depend on similar mechanisms, with only the magnitude of the trauma deciding whether an implant may fail or/and will result in marginal bone loss. The healing/adaptation theory sees adverse loading or peri-implantitis to be, at best, part of the problem behind marginal bone loss. Other factors are much more common such as: (i) poor surgical techniques, (ii) poor host beds owing to genetical disorders, drug abuse, disease or previous irradiation, (iii) too much strain from implant prosthesis misfit, bone cell adjustment or prosthodontic errors or (iv) smoking, allergies or similar conditions that disturb bone cells or their vascular supply. According to Wennerberg & Albrektsson (2011) if ongoing marginal bone loss does occur, implant micro movements may ensue that in turn develop what may be termed as secondary peri-implantitis. This secondary problem may, of course, need clinical treatment. They hasten to say that this theory is much more generally applicable to the true clinical situation than are hypotheses of isolated peri-implantitis or overloading, the alleged reasons for marginal bone loss in many experimental papers, however, of poorly proven clinical relevance. The current review offers ammunition for this phrasing, at least regarding overloading.

Wennerberg & Albrektsson (2011), continued to say that to focus on peri-implantitis as the primary problem around osseointegrated implants is as misconceived as focusing on overloading; such approaches will lead to incorrect precautions and the treatment of symptoms rather than the actual reason for problems relating to marginal bone loss.

Although some evidence can be found in the literature, this concept has not yet been validated and any proof of concept is lacking.

This systematic review was restricted to studies published in English which may have introduced language bias. However, given that the studies considered in this review emanate from many countries where English is not the first language, we may not have missed too many significant reports. Furthermore, hand searching of popular implant journals may have identified additional studies for this review.

Conclusion

Randomized and/or controlled trials of treatment interventions of oral implants designed to study overload and published till December 2011 are nearly lacking. Indirectly derived from factors identified that could be associated with increased leverage and thus resulting in increased strains at the implant-bone interface a few well-conducted studies, but short term and underpowered, could not reveal any relationship between those factors and marginal bone loss. Thus, the PICO question remains unanswered yet.

The systematic review of included animal experimental data provided evidence for a differential peri-implant bone tissue response to so-called "overload" depending on the mucosal health: supra-occlusal contacts acting in an uninflamed peri-implant environment did not negatively affect osseointegration and are even anabolic. In contrast, supra-occlusal contacts in the presence of inflammation significantly increased the plaque-induced bone resorption.

Overall, the reader should be well aware that the current literature on overload of stable osseointegrated implants is very limited and needs careful interpretation. High risk of bias in many papers and lack of quantification of so-called "overload" at the implant level in the intra-oral setting are the main shortcoming.

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