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FOUNDATION FOR ORAL REHABILITATION

A FOR consensus conference on

Diagnosis, avoidance and management of complications of implant-based treatments

Catholic University of Leuven, Belgium
November 16th and 17th, 2017

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Editorial

This supplemental issue of *EJOI* is dedicated to the Foundation for Oral Rehabilitation (FOR) consensus conference, 'Diagnosis, avoidance and management of complications of implant-based treatments', which was held on the 16th and 17th November 2017 at the Catholic University of Leuven, Belgium. Scientific associations and other organisations using *EJOI* as their official publication are welcome to publish the outcome of their consensus conferences or working groups in the journal.

It is the policy of *EJOI* that these publications will not be peer reviewed as they are normally. Consequently, readers are encouraged to critically evaluate the findings presented, as they would with all scientific publications. Guidance on how to develop critical skills for research, analysis and the evaluation of scientific publications (an important mission of *EJOI*) can be found in the 'educational articles'[1-4] and on the EQUATOR (Enhancing the QUAlity and Transparency Of health Research) website (http://www.equatornetwork.org/). The EQUATOR Network is aimed at helping authors properly report their health research studies. After selecting the 'Resource Centre', please click on the 'Library for health research reporting' and you will access a comprehensive list of reporting guidelines, organised by study type. More specifically, to evaluate systematic reviews please go to the PRISMA transparency guidelines (http://www.prisma-statement.org/).

The results of consensus conferences or working groups can be interpreted differently, depending on people's perspectives and circumstances. Please consider the conclusions presented carefully. They are the opinions of the review authors, and are not necessarily shared by *EJOI* editors.

We would like to thank all contributors to this supplement for their efforts.

Marco Esposito, Reinhilde Jacobs and Michele Nieri

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The Foundation for Oral Rehabilitation (FOR) as the basis for this consensus conference

It is symptomatic for the FOR to devote a consensus conference to a subject many others try to ignore: "Complications of implant-based treatments". Complications – most of which are reversible –occur regularly when oral endosseous implants are used to carry a dental prosthesis. Although they are mainly reversible, public opinion has still often associated these implants with failure. But complications should not be designated as failures; rather they should be seen as seeds for progress.

Since the deed of foundation of the FOR explicitly mentions: "The purpose of the Foundation is to promote excellence in the fields of oral and maxillofacial rehabilitation… by providing scientifically based knowledge and experience to improve the quality of patients' lives and oral health care effectiveness", it became logical that gathering a group of international scientists and clinicians with different backgrounds known for their expertise in how to deal with complications would benefit the purpose of the Foundation.

To avoid gathering "the usual suspects", the participants in the consensus were selected on the basis of their contributions in the field, their citation index and their willingness to join without receiving financial compensation.

Hippocrates wrote: "There are in fact two things, science and opinion; the former begets knowledge, the latter ignorance". This is particularly true for the subject of complications in this field. Indeed, the verification of certain theories in literature was weak or did not keep pace with recent developments.

The group was nevertheless able to identify a series of factors which contribute to the incidence of complications: improper imaging and planning, local and systemic patient factors, hardware with a special focus on implant surface characteristics, lack of experience of the surgeon and/or restorative dentist, and lack of a team approach.

The use of the term "revision surgery", which is common to several medical specialities, should be adopted in the field of oral rehabilitation to reassure the patient population.

It was a privilege for both of us to coach this happening and interact with so many cooperative colleagues. We are also grateful to Marco Esposito, who as editor-in-chief of this journal hosts us graciously each time.

Reinhilde Jacobs
Daniel van Steenberghe

European Journal of Oral Implantology

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■ Preamble

Using proper semantics (van Steenberghe – page S15) to achieve an efficient doctor-patient communication is a key issue. It is therefore important to use the most appropriate words to ensure a proper message.

Too often has the use of implants to carry a dental prosthesis been associated with the word "failure". Other medical disciplines use different words more focussed on the possible solution and more easily accepted by patients; for instance "revision surgery".

Surgical interventions are associated with sequelae, complications, and failure, and sometimes need revision.

For example, a scar is a sequela as it is an unavoidable result of a surgical procedure. The size and prominence of the scar are the variable consequence, which may or may not require further attention.

A surgical complication is "any undesirable and unexpected result of an operation affecting the patient that occurs as a direct result of the operation and which would not have occurred had the operation gone as well as could reasonably be hoped". Terms within this definition like "unexpected" and "reasonably" illustrate the judgement needed to define what is really a complication. Oedema or haematoma are most certainly not a complication, but are sequelae that are universal consequences of the surgical intervention.

The endpoint for failure of an implant is revision surgery, which is the exchange or extraction of at least part of the implant. Since the placement of oral endosseous implants is definitely elective surgery, which means an operation that is not absolutely medically necessary, the issue of failure is essential, especially from a legal viewpoint. Revision surgery for orthopaedic implants is defined as the removal, exchange, or addition of any implant parts.

Debridement may or may not be an integral part of it. The term revision surgery is also common in neuro- and bariatric surgery. Introducing its use in oral rehabilitation by means of implants may improve the patient's perception of this treatment option.

For intraoral implants, revision surgery may consist of dealing with soft tissue reactions or marginal bone loss or even the replacement of lost implants. The terminology in other languages for revision surgery is "chirurgie de reprise" or "chirurgie de révision", "Chirurgia di revisione", "revisionschirurgie", "cirugía de revisión", "Cirurgia de revisão" etc.

■ Glossary

Semantics: meaning of words
Semiotics: meaning of signs and symbols during communication
Dental implant: foreign body inserted into a tooth. Proper semantics would be oral implants, which carry a dental prosthesis.
Fixation: a persistent or obsessive attachment to something
Sequela: an adverse effect inherent to a surgical procedure (as a scar)
Complication: any undesirable, unintended and direct result of an operation affecting the patient which would not have occurred had the operation gone as well as could reasonably be hoped
Failure: non-performance of something due or expected ending with an unchanged condition
Revision surgery: change of implant (parts). May or may not include debridements.

■ Introductory review papers

Surgical complications (Lutz et al – page S21) can occur during surgery: bleeding and jaw factures are the most dramatic. Postoperatively there are many different complications reported, reaching from neurosensory disturbances – which can persist – peri-implant inflammation of the soft and/or bone tissues, infection of adjacent anatomical structures like the sinus. Neurosensory disturbances can be due to direct surgical trauma or postoperative compression by bleeding or oedema.

Well-documented patient-specific risk factors, which favour the prevalence of complications, are tobacco smoking, radiation therapy, poorly controlled diabetes, untreated periodontitis, and excessive parafunctional habits.

Prosthetic complications (Goodacre et al – page S27) have evolved over time. Comparing the literature from 1981 – 2001 with that of 2001 – 2017, one discovers that some improvements occurred but also some drawbacks. The latter can be due to changes in skills and expertise in today's clinical practice, although most published studies originate from university-based clinics.

For fixed complete dentures, when comparing these two time periods, the risk of framework fractures increased from 3% to 5%, while abutment screw fractures declined from 3% to 2%. For overdentures, the need for retentive mechanisms reactivation increased from 30% to more recently as much as 53%. This high frequency encourages the need to develop retentive mechanisms that can be reactivated or changed by the patients themselves. The increased occurrence of mucosal hyperplasia from 19% to 31% may be due to the increasing aesthetic endeavours of restorative dental clinicians, leading to limited space between the prosthesis and the mucosa. The number of reline procedures also increased between the two time frames from 19% to 26%.

For fixed partial dentures, the reduction of veneer fractures from 14% to 6% was a welcome improvement, while the 4% screw loosening remained unchanged.

For implant single crown restorations, the abutment screw loosening fell from 25% to 8% during the first 20-year period, with a further reduction to 3%.

The ranking of complication rates related to the type of prosthesis remained the same over the two reported time periods.

To allow proper interpretation of data, authors should be encouraged to include a standardised mechanism of reporting of all complications that have been identified in previous clinical studies, including their absence.

■ Systemic patient-related factors

Foreign body reactions (Albrektsson et al – page S37) can be of four different types – from allergic (type I) to delayed hypersensitivity (type IV). Inserting an implant in the jawbone will lead to some inflammatory reaction followed by a steady state, with a close approximation between living, remodelling bone and the implant surface.

Although subsequently marginal bone resorption may occur, the excellent long-term survival rates of oral implants – 10 years and even several decades – renders the concept of peri-implantitis as the etiology of progressive bone loss controversial. Bacteria are not required to cause marginal bone resorption, even if their accumulation may enhance the progression of it. With orthopaedic implants, for example, marginal bone resorption has been coupled with aseptic loosening as the major reason for secondary failures of hip arthroplasties.

Allergic reactions to titanium implants have been documented, but are much more rare than allergies to other metals. Therefore some reported allergies to oral implants might have been due to orthodontic appliances or prosthetic frameworks (Co-Cr, acrylic…), which were not properly excluded in these reports. The diagnostic relevance of the patch tests used to demonstrate titanium allergy is questionable because the specificity is not properly documented. Haematological and newer test methods must be explored.

Movement disorders are associated with changes in muscle function and tone as a result of pathological changes in the neuromuscular system (Packer – page S47). A number of patients exhibit orofacial dyskinesias and dystonias. The most common conditions exhibiting these features are Parkinson's, Down's syndrome, chorea, and epilepsy. Down's

syndrome can be included in movement disorders because of the frequent tongue thrusting and other parafunctional habits. Some medications, such as antidepressants and antipsychotics, may trigger movement disorders as well as negatively impact bone metabolism.

The literature on movement disorders was often anecdotal: 19 patient case reports and 11 patient series. Provision of implant-supported prostheses improves chewing efficiency and quality of life in these patients and thus should be considered. However, prosthetic designs as identified in the paper, which lend themselves to easier long-term maintenance, should be adopted. Increased early implant failure rates have been reported in these patient groups. In addition, prosthesis failure is a likely consequence of occlusal overload.

Patient expectations (Korfage et al – page S65) are often high prior to implant treatment and these expectations may be higher among women. Nevertheless, these expectations are not wholly unrealistic, since they are mostly met. Younger patients have a tendency to be focused on aesthetic expectations, while elderly patients find improved oral function more relevant. It is a concern that patients sometimes expect implants to last for a lifetime and do not perceive the need for special oral hygiene measures. The fear of pain may lead to reluctance for opting for an implant-based rehabilitation.

The variety of applied study designs indicates the need for standardisation.

■ Local factors and imaging

For the past four decades intraoral radiography has been considered to be the standard method for postoperative peri-implant bone evaluation. This method has inherent shortcomings relating to two-dimensional overlap, lack of standardisation of projection geometry, and further limitations to the accuracy of linear measurements.

Implant characteristics and treatment protocols have undergone an important evolution during the same period. They have altered the peri-implant bone remodelling and related bone defects, which led to the need for three-dimensional (3D) assessment. 3D imaging can be achieved by CBCT to depict the peri-implant bone morphology. Yet most machines have shortcomings hampering proper diagnosis: metal artifacts, patient motion, and lack of bone density measurement. Researchers and industry are encouraged to help overcome these limitations.

Until then, there is no evidence to support the routine use of CBCT as the standard postoperative procedure to evaluate peri-implant bone with the presently available hardware and software.

Medication related osteonecrosis of the jaw (MRONJ) has been especially associated with the intake of high doses and the frequent administration of antiresorptive drugs such as bisphosphonates in both adults and child patients with tumours. The complication more frequently arises after several years. Therefore, long-term studies should be encouraged to further evaluate MRONJ. It appears from scrutinising the literature that it is often a combination of drugs that leads to this complication. Intake of antiresorptive drugs such as bisphosphonates in osteoporosis has a low risk of MRONJ.

MRONJ can be implant triggered or implant surgery triggered, but currently it is not possible to differentiate between the incidence and the outcome of the two. Survival rates of oral implants in osteoporotic patients taking antiresorptive drugs are comparable with other patients.

Prior to considering an implant placement it is imperative to take into account all medical conditions and risk factors, as well as the frequency, duration dosage and the managed manner of administration. Implant placement and/or bone augmentation must be avoided in patients with a history of MRONJ when acceptable alternative prosthetic options exist. Further clinical trials with a long-term follow-up are needed for a better risk assessment.

Radiotherapy in the jawbone area can lead to osteoradionecrosis, which is clinically comparable to MRONJ. Here too, the complication may be triggered by the presence of an existing implant or a traumatic event such as a tooth extraction or the insertion of an implant. However, data are still lacking to quantify the risk of osteoradionecrosis when the implant is already in *situ* prior to irradiation.

Asepsia is often pursued during implant surgery, but one should consider it rather clean surgery (Veitz-Keenan – page S113). Aseptic rinses such as chlorhexidine (0.12 to 2 %) are known for their efficiency

and lack of side effects. The benefit of perioperative antibiotics, however, is less well substantiated. Several systematic reviews indicated there was less chance of implant failure when using antibiotics, but the calculated number needed to treat for one additional benefit outcome (NNTB) to prevent one person to have an implant failure was 25. This benefit cannot be ignored, but should be seen against the side effects and risk of causing antibiotic resistance.

It is evident that the use of sterile gloves, gowns and drapes as such, does not guarantee sterility. Breaching the sterility protocol by members of the surgical team occurs, but so far has not been measured in literature. Besides, factors like duration of surgery, traumatic tissue handling, and patients' immune status, are co-variables, which render clear answers difficult. For the time being, no strong recommendations can thus be given based on the literature, but meanwhile local guidelines should be adhered to.

■ Hardware factors

Implant surface characteristics can be associated with the incidence of implant-related surgical complications and revision surgery (Wennerberg et al – page S123). There were 62 studies with a follow-up of 10 years or more. Since the Brånemark turned implant has been so popular and the longest on the market, this type of surface tends to diminish the impact of outcome data concerning other surfaces.

Literature reveals that these turned surface implants have the least peri-implant marginal bone loss. There is no significant difference in survival rates among the implants with moderately rough surfaces. All performed well after 10 years. The plasma-sprayed implants had the highest probability of failure; while an oxidised surface demonstrated the lowest probability for failure.

Ceramic implants have so far been followed for up for 5 years with promising results, but were not included in the paper as they did not meet the 10-year inclusion criteria.

Short and narrow diameter implants (Pommer et al – page S137) are commonly and increasingly used. Their advantage is that they potentially eliminate the need for bone augmentation procedures.

Implants of at least 7.0 mm in length and 3.5 mm in diameter have been used successfully in the past. However, minimum implant dimensions required to ensure a long-term successful outcome have not been determined.

Summing up the results of 82 studies (1997–2017) extra-short and extra-narrow-diameter implants show satisfactory survival rates of over 95% and little marginal bone resorption of around 0.5 mm after a mean follow-up of 3 years. Implant lengths of 5.5 mm to 6.5 mm performed significantly better in the mandible (98%) compared with the maxilla (95%), while lengths of 4.0 mm to 5.4 mm demonstrated similar survival rates in both jaws (95%). Extra-narrow-diameter implants revealed no differences between implant position and jaw location, however, a significantly lower survival rate of diameters between 3.0 mm to 3.25 mm (95%) compared with diameters between 3.3 mm and 3.4 mm (98%) related to a higher rate of early failures. The above results refer to 1-year follow-up data, which means they should be interpreted with caution since bone remodelling has not yet reached a steady state.

Complications can be related to the prosthetic material used (Papia and Larsson – page S147). Most common complications are fracture or chipping of veneer material, loss of retention of cemented restorations and loss of access hole fillings. The latter needs further investigation to allow providing proper instruction. To prevent veneer fractures there are three main factors:

- The shape and dimensions of the substructure to provide proper support;
- Compatibility of properties of substructure and veneer, like coefficient of thermal expansion;
- Manufacturing procedures and laboratory handling variables.

To prevent the loss of retention three main factors have been identified:

- Choice of proper cement;
- Appropriate abutment type and angle of convergence;
- Surface roughness and/or surface treatment.

While achieving their literature search as indicated, some papers known to the authors were not identified. This reveals how important it is to use enough terms and synonyms during the search strategy.

■ Surgeons' experience and learning curve

Surgical experience plays a role in the outcome of implants (Jerjes and Hopper – page S167), but the risk of complications is a multifactorial issue. Since surgery in the oral cavity is confronted with limitation of access and visibility and mostly performed under local anaesthesia in a moving patient, surgical skills and experience can play a role. Available studies are difficult to interpret because experienced surgeons often deal with more complex surgery. Six studies on experience influencing third molar surgery outcome reveal significant differences in the incidence of trismus nerve damage, and osteitis. Curiously, bleeding was more frequent with experienced surgeons, probably because they deal with more complex surgery.

Studies on impacted wisdom teeth comparing dental practitioners with oral surgeons also showed fewer complications for the latter category.

For implant surgery one recent meta-analysis is available based on six studies: four related to sometimes ill-defined specialties and two related to experience, based on a certain number of implants placed. Survival rate of implants related to so-called specialities, but improved after a certain number of implants were inserted. The number of patients is, however, too limited to draw conclusions from this meta-analysis.

Similar reports on the effect of training are available in ENT and general surgery literature: many more complications and longer hospital stays with trainees vs experienced specialists.

The location for surgery also plays a role. Experienced surgeons in either a private practice or a teaching institution treated the two groups of patients. The latter had increased survival rates, however factors such as workload are difficult to evaluate.

There is a need to further investigate the impact of experience on the outcome of implant surgery, but making sure that the experienced surgeons and trainees are treating patients with similar complexities. The impact of gender also merits more interest. Since contrary to other bodily parts surgery in the oral cavity is also accessible to non-surgeons, the need for such data are even more relevant.

■ General conclusions

One can say that sequelae, complications, failures, and revision surgeries with oral implants are due to a large variety of factors involving local and systemic patient factors, proper preoperative planning and radiological follow-up, team approach, the surgeon's experience, avoidance of infections use of implants and the prosthetic components with surface and material characteristics, which have been properly documented. Using positively oriented semantics like revision surgery can help better inform and reassure the patient population.

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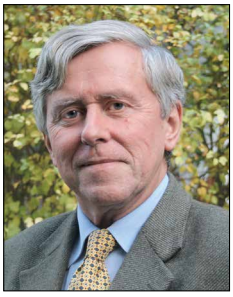
Diagnosis, avoidance and management of complications of implant-based treatments

Semantics: introducing the term revision surgery in oral rehabilitation.



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"If terms be incorrect, then statements do not accord with facts". (Confucius)
"Words form the thread on which we string our experiences". (Aldous Huxley)

Semantics is a term coined by Michel Bréal (1832 to 1915) a Jewish German-French linguist referring to the Greek semantikos (= meaning) in his 1897 book, "Essai de sémantique". He was a very gifted man: for example, he was the one who suggested to Pierre de Coubertin to include the marathon in the Olympic Games and who also, with the help of a Francophile American dental practitioner, Thomas William Evans, created the "Doctorat d'Université", finally allowing American students to pursue their doctorate at a French university.

Semantics is the linguistic and philosophical study of the meaning of words, while semiotics investigates the meaning of signs and symbols during communication. The Oxford English Dictionary defines semantics as: *"The branch of linguistics and logic concerned with meaning"*. The relevance of this science is illustrated each day in political speeches and in diplomacy, but also in medicine. Properly expressed thoughts remain as famous quotations for centuries, such as those of Hippocrates*: "The chief virtue that language can have is clearness, and nothing detracts from it so much as unfamiliar words"*.

In communication, the sender and the receiver may attribute different meanings to the same word because of different backgrounds, education, culture, etc. The words "liberal" or "socialist" have very different connotations according to the country. Therefore, using proper semantics to achieve an efficient doctor-patient communication is also a key issue.

■ Specificity of semantics in oral health care

Each science or art or profession has its own nomenclature which can even impact on the professional conduct. In the field of oral health care and, in particular, the specialities involved in oral rehabilitation, it is striking to see semantics deviate strongly from what is common in all other medical disciplines. It almost seems as if the oral cavity is not part of the human body.

Firstly, there is an obsession with teeth. Dental practitioners constantly use the word "dental" in oral health care, even when there are no teeth at all in the case of the edentulous patient! The latter are encouraged to maintain a proper "dental hygiene" – a surreal approach. Even soft tissue adhesives for intraoral use, e.g. those utilised in mucosal grafting, are regularly termed "dental glue". The expression "dental implant" is another misnomer. Endodontic (diadontic) implants inserted into the root of a tooth are more of

a historical technique, or their performance can be considered as rare as "hen's teeth", so to speak.

Proper semantics would be to use an "oral" or an "endosseous implant", which aims to carry a dental prosthesis. But in a Google search, "dental implant" provides more than 10 million quotes, while "oral implant" only some 140,000. It seems to be a losing battle.

In orthopaedics and ear, nose and throat (ENT) healthcare, the term "bone-anchored prosthesis" is commonly used, but not in oral rehabilitation. This is a consequence of the well-established "fixation to teeth" by many professionals involved: dental practitioners, specialists, auxiliaries, and technicians. Fixation derives from the term "fixierung", coined by Sigmund Freud to denote a persistent or even obsessive attachment to people or things. Fixation can be compared to a psychological imprinting. A possible explanation for this might be the first steps of the university curriculum for future dental clinicians. In most countries they are very much devoted to the anatomy of teeth, hardly including the oral cavity. Consequences are the not-uncommon finding of practitioners who use a tooth as a logo for their professional letterheads, an office entrance, a website, or even display a molar tooth as an ashtray. Such signs create negative meanings and emotions in people's minds. One can only feel relieved that such professionals are not in gynaecology!

Another example of semantics specific to the dental profession is "implant dentistry" (more than 400,000 hits on Google). Nobody would think about "implant orthopaedics" or "implant ophthalmology", although implants are used much more in orthopaedics than in oral health care; but, of course, this neologism never arose. An orthopaedic surgeon would even feel offended if called an "implantologist", while a number of dental practitioners favour this term, which creates the impression of a speciality for the ignorant layperson hiding the fact they are general practitioners. Although implants are a very useful means in several medical disciplines, they should never become an aim as such to promote someone's clinical practice.

Unified semantics is so important for database or web searches concerning health issues by the general population. There is an urgent need to control the medical terminology and nomeclature at a global level so that laypeople from different cultural backgrounds can easily find the proper information. The Unified Medical Language System (UMLS) effort, supported by the US National Library of Medicine[1], is a step in the right direction. The Foundation for Oral Rehabilitation (FOR) can also play an important role in this because of the worldwide dimension of its website and (associate) fellows.

When, after 10 years of clinical testing, osseointegrated implants were proposed in 1977 by P-I Brånemark[2] as a predictable procedure to anchor dental prostheses to the jawbone, the incidence of complications and loss of implants at once became major research themes. This was logical, since historically, endosseous oral implants had led to mistrust by the medical profession because of frequent failures associated with infections and even mutilation of the jawbones. Furthermore, industries or individuals were quick to introduce several "lookalike" products and the surgical principles, as defined by Professor Brånemark, were not always faithfully applied, resulting in less reliable outcomes. It has been demonstrated that a change of hardware can have a negative impact on the outcome. Thus, while communicating with a patient, one should not refer to the data from one implant system while using another[3]. The impact of surgeons' skills and judgements can also be significant[4]. Therefore, complications – sometimes leading to the loss of oral implants – were regularly reported, yet again creating scepticism towards oral implants. The field of osseointegration in oral rehabilitation became a forum for antagonism because the scientific concept was still in its infancy and also because of industrial interests and, especially, personal egos.

■ Negative outcomes after surgery

Negative outcomes after surgical treatment should be differentiated from complications, failure to cure, and sequelae[5,6]. These are three different issues that should be addressed when assessing the outcome of oral implants.

One should definitely distinguish between a sequela, which is an adverse accompaniment inherent to a surgical procedure, and a real complication. A postoperative scar or some gingival recession is evidently sequelae.

A complication means a deviation from the expected postoperative course that is not inherent and does not comprise a failure to cure. Sokol and Wilson[7] defined surgical complication in an iterative approach as to reach "any undesirable, unintended and direct result of an operation affecting the patient that would not have occurred had the operation gone as well as could reasonably be hoped".

Failure to cure means that the condition remains unchanged after treatment. A typical example is implants inserted to anchor a removable complete denture, which are subsequently lost, bringing the patient back to the presurgical situation. It is recommended that such distinctions be made in future clinical evaluations of oral implants and their prosthetic superstructures.

One should definitely distinguish between a sequela, which is an adverse accompaniment inherent to a surgical procedure, and a real complication. Evidently, a postoperative scar or some gingival recession is a sequela.

Since permucosal implants are exposed to the oral environment with its rich and varied microbiota, easily adhering to the implant surfaces, chronic inflammatory reactions of the surrounding gingival and mucosal tissues were often induced. Sometimes the underlying marginal bone resorbed and both animal experiments and clinical observations led to the concept of peri-implantitis, referring to a well-documented chronic periodontal disease: periodontitis. The similarity of symptoms even led many to believe the aetiologies were identical. Specific semantics were soon proposed, such as "ailing", "failing", and "failed" implants. Meta-analysis of the literature available on the clinical outcome of oral implants was thus rendered impossible because of the confusion in defining these concepts.

Although many long-term – 10 years or more – clinical observations reported ≥ 95% successful oral rehabilitations, at least in well-controlled and often university-based studies, the issue of possible failures has been associated with intraoral implants for decades. The expectations of the public are, on the other hand, often too optimistic, presuming properly functioning implant for life. Slogans such as "designing for life" are understood as a formal promise of survival of the inserted implants to one's life end, while systemic, behavioural, or local factors may jeopardise their expected longevity.

One must also question when the word failure is appropriate when oral implants become associated with complications or are even lost. A failure means the non-performance of something due or expected. When an implant functions for an expected time period it needs to be replaced and should not be called a failure. The impact of the treatment outcome on patients' function and health must always be considered when defining success or failure. According to a prospective cohort study of patient satisfaction following oral implant therapy after 10 years, more than 90% of patients were completely satisfied with implant therapy[8], although typically, for the field "expectations relating to aesthetics and function" was primarily considered, rather than "health impact" or "time of survival".

■ Revision surgery

There is a general consensus in orthopaedics that femoral implants, which carry a hip prosthesis, are expected to last between 10 and 15 years: "*The typical life of an artificial hip joint is 10 – 15 years, depending on the patient's daily use of the joint*". (https://my.clevelandclinic.org/health/articles/hip-revision).

More than 90% of total hip arthroplasty procedures are still successful at 10- to 15-year follow-ups, but the annual revision rate is estimated to be 1% to 3%[9].

Thus, from the time of insertion of a femoral implant, the concept of revision surgery is already envisaged. Revision surgery is often defined as the removal, exchange, or addition of any implant parts. Therefore, debridement may or may not play an integral part. The rate of revision surgery is mostly synonymous with the survival rate.

Websites of reputable institutions and orthopaedic surgeons commonly announce: "*When a replacement joint wears out, loosens or develops a problem, it can be resurfaced or replaced in a joint revision operation. Using regular x-ray examinations, the orthopaedic surgeon can detect and monitor any changes, and plan for revision surgery before a major problem develops*". (https://www.cedars-sinai.edu/Patients).

Patients are even informed that: "*Hip revision surgery has less favourable outcomes than first-time*

replacement surgery" (http://www.surgeryencyclopedia.com).

In orthopaedics, open access national registries were established in several countries to quickly identify poorly performing prostheses available on the market to warn the public or eventually sue a manufacturer[10]. As revealed in the Swedish register: *"The idea is to provide feedback to the community … this way of achieving high-quality hip replacement surgery as reflected by a low revision rate has obviously been successful. Over the years, the revision rate in Sweden has been decreasing continuously"*.

The overall revision rate following primary hip replacement in England and Wales calculated using the Kaplan-Meier survival analysis method, was 0.7% at 1 year and 1.4% at 3 years, while for primary knee replacement in the same study the revision rate was 0.4% at 1 year and 1.4% at 3 years[11].

It is estimated that about 22,000 knee revision surgeries are performed annually in the US, out of a total of 600,000 total knee replacements. Half of them are done within 2 years of the patient's first total knee prosthesis. The Unicompartmental Knee Arthroplasty (UKA) reaches annual revision rates of 2.59% according to the joint national register of England and Wales[12]. The latter paper suggests that the benchmark revision rate set by the National Institute for Health and Clinical Excellence (NICE) for hip prostheses should be adjusted downwards.

Multinational databases are now available, allowing an even more elaborate analysis of the outcome of implants. For example, the collective register for the Scandinavian countries – NARA –reports on more than 400,000 total hip replacements[13]. The total hip replacement survival rates varied considerably among the four Nordic countries, which the authors feel may reflect different implant brand choices. They admit that the revision rates are optimistic because they only include revision surgery with a change of implant parts, while debridements as such are not included.

In Australia, the Department of Therapeutic Goods Administration publishes annual reports providing an insight into the performance of orthopaedic implants. "Eight implants with higher-than-expected revision rates were identified in 2015 … and has contacted the sponsors" (https://www.tga.gov.au/publication-issue/medical-devices-safety-update-volume-3-number-6-november-2015).

One can only dream that one day the same will apply to oral implants!

Shoulder joint replacement is less frequently applied, but still totals about 50,000 annually in the US, while the revision rate reaches 11%[14].

The concept of revision surgery is not limited to the use of implants. There are other examples, such as in neurosurgery: *"Reoperation or revision surgery for patients with Chiari malformations is common and may not be due to technical error or inadequate decompression"*[15]*; and in bariatric surgery: "The overall incidence of surgical revision after a primary obesity operation ranges from 5% (biliary pancreatic diversion) up to 50% (laparoscopic gastric band) with intermediate rates for Roux-en-Y gastric bypass and laparoscopic sleeve gastrectomy"*[16].

Oral implants regularly need revision surgery, although the term is not yet used in the field. Several publications deal with the reinsertion of implants in the same site as an implant that was lost or subject to complications, but most are limited case reports[17,18,19,20,21]. Using a more interactive implant surface or a larger implant may improve the outcome of the revision surgery.

When the outcome was compared between a machined and a TiUnite surface of the 29 machined-surface implants replaced by implants with the same surface[17], six failed, while for the 19 machined-surface implants replaced by TiUnite surface implants, only one failed. Of the 10 TiUnite-surface implants replaced by implants with the same surface, none failed. The difference in failure rates between machined-surface and TiUnite replacement implants was statistically significant. In a study on 49 patients (60 implants)[20] who experienced implant loss and underwent a second implantation, the survival rate of the second implant after removal of the failed implant was 88.3%. In another study[21] of 56 patients with a total of 79 failed implants that had to be replaced, 13 failed at between 7 and 78 months of observation, resulting in an overall survival rate of 83.5%.

The limited data available indicate that revision surgery is a predictable treatment in oral rehabilitation, although with a lower survival rate than for implant placements in pristine jawbone sites.

Unhappily the term "revision" was never used while this nomenclature could easily be introduced.

Elective surgery and warranties

Oral rehabilitation by means of implants belongs evidently to the elective surgery category. The latter is defined, according to Collins Dictionary, as *"when someone chooses to have an operation which is not absolutely medically necessary"*. It means surgery that is subject to choice (election). The choice may be made by the patient and/or the doctor and should be discussed between them thoroughly using proper semantics prior to surgery. Thus, since not essential for the patient's health, one should take all necessary precautions before going ahead with such surgery and treatment. Nevertheless, it does not mean payment is due before the procedure as some have posted on their website for elective surgery.

Liability is rarely shared by the implant manufacturing companies. In orthopaedics there has been some recent changes.

For example, in 2015 Biomet announced a Lifetime Oxford Knee Implant Replacement warranty in the US, which involves the cost of the replacement implant only, but not hospital costs, etc. The chief executive of Aesculap Implant Systems, a company that offers some warranty since 2017, declared: "In the consumer market, if a product does not meet expectations, the purchaser expects a money-back type of guarantee. This has not been the norm in the device market".

A warranty can apply to a device when a manufacturer makes the warranty to a consumer, the doctor or the patient, with whom the manufacturer has no direct contractual relationship. Regularly it implies following the protocol that accompanies the insertion of the device. Warranty demands are easier to deal with than proving negligence, which means the manufacturer has shown lack of reasonable care in the production, design, or assembly of the device.

For oral implants, warranties have become common, often even for a lifetime, but regularly with limitations such as: *"This limited warranty does not cover the cost of the surgical procedures and materials or tools and accessories used with the implant"*.

On the other hand, in most countries the cost of oral implants is not covered by social security. This is logical since they are not necessarily inserted by specialist surgeons and since this kind of surgery is definitely elective. Furthermore, the health benefit seems less relevant than for other amputations or orthopaedic devices.

Since in oral rehabilitation there is an increasing tendency for medico-legal litigation, a properly managed informed consent – a permission granted in full knowledge of the possible consequences such as possible risks and benefits – becomes a key issue prior to any elective surgery. It means when implants are considered as a treatment option, avoiding unrealistic expectations concerning the benefit to the patient, for instance a life-long lasting result, unless patients themselves have a predictably definable lifespan. Doctors should be trained in appropriate communication skills, employing proper semantics to optimise patient information and avoid liabilities.

Conclusions

Semantics is unpopular among medical doctors, although it helps to avoid misunderstandings during interaction with patients. Using terms such as "revision surgery", "complications" and "to be expected surgical consequences", when discussing treatment plans, will make the treatment modality more acceptable for public opinion and encourage more patient trust.

Revision surgery, which means to correct undesirable sequelae of previous surgery, is a term that needs to become popular in oral rehabilitation, thus replacing terms associated with failure. Oral implants sometimes have to be removed, or can be lost. The replacement by another implant allows a return to the previous stage or even maintenance of the achieved rehabilitation.

The terminology in other languages for revision surgery is *« chirurgie de reprise"* or *"chirurgie de révision"*, *« Chirurgia di revisione" « revisionschirurgie » « cirugía de revisión » «Cirurgia de revisão"* etc.

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Diagnosis, avoidance and management of complications of implant-based treatments

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Key words *dental implants, oral implants, surgical complications*

This review provides an overview of review and consensus articles of the past 5 years regarding surgical complications in implant dentistry. The focus in this article is on surgical complications occurring after implant insertion and on risk factors that compromise oral implant osseointegration.

■ Surgical complications

The intention of this narrative review paper is to give a synoptic overview about review and consensus papers of the previous 5 years concerning surgical complications in implant dentistry.

■ Search strategy

A Medline search (http://www.ncbi.nlm.nih.gov/pubmed) was performed for articles published in English between January 1, 2012, and March 31, 2017. The following search terms were used: bleeding dental implant, diabetes dental implant, oedema dental implant, flap dehiscence dental implant, hematoma dental implant, infection dental implant, mandible fracture dental implant, periodontitis dental implant, sensory disorders dental implant, sinusitis dental implant, smoking dental implant, surgical complications dental implants, intraoperative complications dental implant surgery and complications zygoma implants. Additional evidence from consensus conferences over the past 5 years, regarding oral implant complications was also evaluated. Therefore, the papers of the 3rd EAO Consensus Conference, February 15 to 18, 2012, Pfäffikon, Schwyz, Switzerland, and the 4th Consensus Conference of the European Association for Osseointegration (EAO), February 11 to 14, 2015, Pfäffikon, Schwyz, Switzerland, were evaluated. Additionally the paper by Albrektsson et al from the consensus meeting on "peri-implantitis" in Rome, Italy, from January 8 to 10, 2016, was also considered[1].

■ Complications arising from oral implant surgery

■ Intraoperative complications

Oral implant complications are defined as pathological conditions occurring after implant insertion[2]. To be differentiated from this are intraoperative complications or accidents that occur during the surgical procedure[2]. There is only limited evidence on the number of intraoperative surgical complications in oral implantology, because these complications are rarely reported in literature[3]. The existing literature describes classifications and possible intraoperative complications[4]. To our knowledge, during the past 5 years there are no reviews displaying the incidence of intraoperative complications in oral implant surgery.

■ Bleeding

Bleeding complications can arise after insertion of oral implants in the anterior and posterior mandible.

Especially when long implants are inserted, there is a danger of perforating the lingual cortical bone and damaging the sublingual artery[5]. In particular, in anti-coagulated patients, haematoma of the floor of the mouth may present a life-threatening complication[6]. In literature, the haematoma of the floor of the mouth was described as unusual, but a life-threatening complication after implant surgery[7,8]. Its rare occurrence makes it even more dangerous, as the procedures of airway management, e.g. intubation or cricothyrotomy, do not regularly form part of most implant surgeons' training programmes[9], which makes it necessary to immediately refer a patient to a specialised clinic in case of a suspicious injury to the vessels of the floor of the mouth[10]. Bleeding complications are described as rare in maxillary sinus augmentation procedures; most bleeding complications result from damaging the anastomosis of the posterior superior alveolar artery and the infraorbital artery in the facial wall of the maxillary sinus[11].

Sensory disorders

Sensory disorders are a relevant complication after mandibular implant surgery. A meta-analysis including 28 studies showed incidence of sensory disorders in 13% (95 % CI: 6% to 25%) of all cases 10 days after implant surgery and 3% (95 % CI: 1% to 7%) persisting disorders after 1 year[12]. Furthermore, the meta-analysis found no influence of the alveolar bone height or the age of the patient in sensory disorders after implant placement in the mandible. Other factors or treatment options were not evaluated.

Peri-implant infection

Due to the bacterial load of the oral cavity and the endo-exo character of oral implants, infections of the peri-implant soft- and hard tissues can occur in oral implant surgery. The key factor may be the modified bacterial composition or the quantity of the microbiological environment in peri-implant infections[13]. The mean prevalence for peri-implant mucositis is higher compared with peri-implantitis (43% vs 22%)[14]. Early infections after implant insertion have an incidence of 6.5% (95% CI: 4.4% to 9.7%) of the patients and 1.7% (9 % CI: 1.2% to 2.6%) of the implants[15]. These implants show a failure rate of about 55% before prosthetic loading. After prosthetic loading, the survival and success rate are reduced to 80% and 50% after a follow-up period of 42.9 ± 10.2 months[15]. A systematic review by Lund et al showed that antibiotic prophylaxis during implant placement could reduce the risk of an implant loss by 2%[16]. The progression of hard-tissue destruction is more extensive in peri-implant as opposed to periodontal infections[17]. Risk factors favouring peri-implant infections are lack of supportive therapy, poor oral hygiene, diabetes, smoking, excess cement in the peri-implant soft tissues and occlusal overload[14,18]. Romeo et al reported a biological complication rate in the sense of peri-implantitis of 5.7% (95% CI: 4.2 to 7.6 %) after 5 years[19]. Mombelli et al found an incidence of peri-implantitis in the order of 10% implants and 20% patients between 5 and 10 years after implant placement, with a high variation rate of the reported data[20]. In a systematic review of Jung et al, the 5-year cumulative soft tissue complication rate, including signs of inflammation, mucosal inflammation, mucositis, bleeding, suppuration and soft tissue dehiscence, was 7.1% (95% CI: 4.4 to 11.3%)[21].

Infection of adjacent structures

Infections of adjacent structures can be associated with implant insertion. Maxillary sinus augmentation is a common procedure that aims to increase bone volume in the posterior maxilla by elevating the sinus membrane and interposing autogenous bone or bone substitute materials. Lateral or transalveolar approaches are used to access the maxillary sinus. The most common complications are perforation of the sinus membrane (prevalence rate between 7% and 44%), bleeding (no information on prevalence) and postoperative maxillary sinusitis (prevalence rate between 1% and 4%)[11,22]. When the sinus membrane is perforated, the risk of maxillary sinusitis is increased[23].

Pathological fractures of the mandible can occur during implant placement or after implant insertion. The latter most frequently occur due to implant failure, with consequent periimplant bone loss[24]. The highest incidence of pathological mandibular fractures after implant insertion was found in edentulous patients in the region of the mandibular symphysis[11].

Risk factors compromising osseointegration

Smoking, excess cement, plaque accumulation and the lack of adjuvant periodontal supportive therapy are risk factors for developing peri-implant infections[25]. Occlusal overload of oral implants was solely investigated in animal experiments, revealing that overload may induce a specific mechanism for the loss of osseointegration[26]. However, there is a lack of data from clinical investigations.

Smoking

In smokers, implant survival rate is decreased, while the rate of postoperative infections, peri-implantitis and marginal bone loss increases[27-29]. There is a tendency, that the higher rate of peri-implant diseases in smokers can be reduced by supportive periodontal therapy[30]. Regarding the effect of smoking on implants inserted after maxillary sinus augmentation, there is a statistically significant increased failure rate in smokers compared with non-smokers (RR: 1.87 (95% CI: 1.35, 2.58), $P = 0.0001$)[31]. In the same study, the subgroup analysis regarding only the prospective studies, found no significant difference [RR: 1.55 (95% CI: 0.91 to 2.65), $P = 0.11$] between the two groups[31]. A meta-analysis of 13 studies displayed an increased annual bone loss rate of 0.164 mm/year in smokers compared with non-smokers[32]. Another meta-analysis displayed a statistically higher bone loss in the smoking group compared with the non-smoking group; this bone loss was statistically significant higher in the maxilla than in the mandible[33]. The implant failure rate was also statistically significantly higher for smokers (OR 1.96, 95% CI: 1.68 to 2.30; $P < 0.00001$)[33]. Regarding the effect of smoking on implants inserted after maxillary sinus augmentation, there was a statistically significant increase in the failure rate in smokers compared with non-smokers [RR: 1.87 (95% CI: 1.35 to 2.58), $P = 0.0001$][31]. In the same study, the subgroup analysis of only the prospective studies found no significant difference [R: 1.55 (95% CI: 0.91 to 2.65), $P = 0.11$] between the two groups[31].

Radiation therapy

Radiation therapy has a negative effect on implant survival, with a statistically significant decrease if the implants were inserted prior to radiotherapy or 12 months after radiotherapy. Higher radiation doses tended to lower implant survival rates, but the difference was not statistically significant (RR: 1.40; 95% CI: 0.73 to 2.68; $P = 0.31$)[34]. The location of the implants (maxilla vs mandible) in irradiated patients showed no significant difference on implant failure (RR: 0.81; 95% CI: 0.09 to 7.27; $P = 0.85$)[34]. Analysis of the data from two studies showed that marginal bone loss was statically significantly higher in irradiated patients compared with non-irradiated patients (mean difference: 0.62; 95% CI: 0.21 to 1.03; $P = 0.003$; heterogeneity: I2 = 92%; $P < 0.00001$, random-effects model).

Diabetes mellitus

A meta-analysis (14 studies) found no significant difference in implant failure between diabetic and non-diabetic patients ($P = 0.65$), while there was statistically significant difference for marginal bone loss (based on two studies), which was higher in the diabetic group ($P = 0.01$)[35]. Another review found influence of poorly controlled type 2 diabetes (one study) on pocket depth and marginal bone loss[28]. In a meta-analysis Monje et al found a higher risk for peri-implantitis (RR = 1.46; 95% CI: 1.21 to 1.77 and OR = 1.89; 95% CI: 1.31 to 2.46; z = 5.98; $P < 0.001$), but not for mucositis (RR = 0.92; 95% CI: 0.72 to 1.16 and OR = 1.06; 95% CI: 0.84 to 1.27; z = 1.06, $P = 0.29$) in patients with diabetes vs non-diabetic patients[36]. Annibali et al showed that diabetes mellitus had a negative effect during the process of osseointegration and in the first year in function. After this period however, during a 6-year follow-up period, there were no negative effects on implant survival observed due to the diabetic metabolic state[37]. In a review by Moraschini et al comparing the failure rates of oral implants in diabetic vs non-diabetic patients there were no statistically significant differences (type 1 diabetes (RR of 3.65; 95% CI: 0.33 to 40.52; $P = 0.29$) and type 2 diabetes (RR = 1.43; 95% CI: 0.54 to 3.82; $P = 0.47$). However, marginal bone loss was significantly higher

($P < 0.00001$) in the diabetic group[38]. In a systematic review, Naujokat et al found that poorly controlled diabetes had a negative effect on osseointegration and a higher rate of peri-implantitis, which resulted in higher failure rates. In patients with well-controlled diabetes the complication rates were similar to healthy patients[39]. A meta-analysis undertaken by Shi et al did not show a direct association between glycaemic control and implant failure rate[40].

Periodontitis

A history of periodontitis may have a marginal effect on implant failure and peri-implantitis; in addition, peri-implant bone loss rate was found to be higher[41]. However, several uncontrolled confounding factors and a lack of randomisation in the studies may indicate limited validity of the data.

Peri-implant bone loss

Hard and soft tissue integration of oral implants results in the formation of scar tissue in the peri-implant soft tissues and an immunologically and inflammatory-mediated foreign body reaction called osseointegration[42,43]. While peri-implant bone resorption, taking place in the first year after implant insertion, occurs due to a disequilibrium resulting from a foreign body reaction of the implant components. Bone loss resulting from peri-implant infections is a late complication caused by bacteria and subsequent immunological reactions[42,44,45]. According to recent reviews, only 1% to 2% of all implants show peri-implantitis when inserted by experienced surgeons[45]. Albrektsson et al questioned the high incidence reported for peri-implantitis and attributed the great majority of peri-implant bone loss to osteolytic reactions induced by the immune system[1]. When peri-implant bone loss has occured, current literature shows that foreign body equilibrium should be regained as fast as possible, even at the cost of bone loss due to surgical therapy[42]. Further knowledge is needed to fully understand the immunologic processes taking place in peri-implantitis induced bone loss[43].

Besides marginal bone loss around oral implants, hard tissue defects may occur as a complication of oral implant surgery causing periapical implant lesions[46]. The aetiology of periapical implant lesions include infection, overheating, pre-existing peri-apical lesions, bacterial contamination, and poor bone quality[47,48]. Vertical and horizontal bone resorption of 0.5 mm to 1.0 mm were described 4 to 12 months after implant surgery following immediate implant placement in extraction sockets[49]. There was no difference between flapped and flapless techniques[49]. In a meta-analysis, Jung et al demonstrated a cumulative hard tissue complication rate (defined as bone loss exceeding 2 mm) of 5.2% (95% CI: 3.1% to 8.6%). Bone loss was higher for cemented reconstructions (2.8%; 95% CI: 2.1% to 3.7%) compared to screwed reconstructions (1.1%; 95% CI: 0.2% to 7.1%)[21].

Complications related to zygomatic implants

A systematic review by Chrcanovic et al with 4556 zygomatic implants in 2161 patients, displayed a cumulative survival rate of 95.2% after 12 years[50]. A negative effect on implant survival was found in irradiated patients. The most common complications reported were: sinusitis: 2.4% (95% CI: 1.8 to 3.0), soft tissue infection: 2.0% (95% CI: 1.2 to 2.8), paresthesia: 1.0% (95% CI: 0.5 to 1.4) and oroantral fistulas: 0.4% (95% CI: 0.1 to 0.6)[50].

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Prosthetic complications with implant prostheses (2001–2017)

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Aim: To present recent data regarding prosthetic complications with implant prostheses and crowns as well as compare this data with data presented in a 2003 publication.
Material and methods: An electronic Medline (PubMed) with MeSH terms search was performed, focussing on clinical studies that reported data on prosthetic complications associated with implant fixed complete dentures, implant overdentures, implant fixed partial dentures, and implant single crowns.
Results: There were nine prosthetic complications reported with implant fixed complete dentures, 17 with implant overdentures, four with implant fixed partial dentures, and six with implant single crowns. The greatest number of complications and the largest incidence of percentages occurred with implant overdentures. The lowest incidence percentages were recorded for implant single crowns. These findings are in agreement with the previous 2003 publication. It is of interest to note that some of the complications reported previously were not reported in this review, and some complications reported in this review were not listed in the 2003 publication, thereby limiting the number of direct comparisons between this paper and the earlier report. A surprising finding was that some complications associated with implant overdentures from the current data exceeded the incidence in 2003 (reactivation of the retentive attachment; mucosal hyperplasia; and the need for overdenture relines).
Conclusions: Implant overdentures are associated with more complications than implant fixed complete dentures, implant fixed partial dentures, and implant single crowns. The lowest incidence of complications was reported with implant single crowns. The most common complication reported with implant fixed complete dentures was denture tooth fracture. The most common complication associated with implant overdentures was the need for adjustments. Porcelain veneer fracture/chipping was the most common complication identified in the studies of implant fixed partial dentures. The most common complication reported with implant single crowns was abutment screw loosening.

Introduction

In 2003, a literature review[1] was published that presented data regarding clinical complications with implants and implant prostheses between 1981 and 2001. A portion of this article provided incidence data regarding prosthetic complications as they related to the following four types of implant prostheses: 1) implant fixed complete dentures; 2) implant overdentures; 3) implant fixed partial dentures; and 4) implant single crowns. The reported data was derived by combining the raw data from included studies so a mean incidence could be calculated. The purpose of the mean incidence was to suggest complication trends with each of the four types of prostheses rather than provide absolute incidence

values. It is important to note that this publication was a literature review and not a systematic review with meta-analysis.

The complications reported in this 2003 publication[1] occurred more commonly with implant overdentures than the other types of prostheses. Complications included loss of overdenture retention/adjustment with a mean incidence of 30%, overdenture relines (19%), overdenture clip/attachment fracture (17%), and overdenture fractures (12%). Fractures of the opposing complete dentures were combined for both fixed complete dentures and overdentures with an incidence of 12%. Acrylic resin base fracture of the fixed complete denture and overdenture had a combined incidence of 7%. There were only three publications that reported porcelain veneer fracture with fixed partial dentures, resulting in a 14% incidence. Abutment screw loosening was high, at 25% for single crowns due to early screw designs and lack of defined methods for tightening the screws, but this reduced to 8% in later studies. Prosthesis screw fractures occurred in 3% of fixed complete dentures and in 5% of fixed partial dentures. There was a 3% mean incidence of framework fractures with fixed complete dentures. The abutment screw fracture incidence was reported as 3% with fixed complete dentures and 1% with fixed partial dentures. Implant fracture was reported as a mean of 1% from studies that were almost exclusively found within fixed complete dentures and fixed partial dentures.

Some of the reported complication incidences in this 2003 publication[1] were based on relatively large numbers of studies, whereas others were calculated on the limited number of studies reporting such a complication between 1981 and 2001. Additionally, little data was provided relative to single crowns on implants because of their less frequent use during the review time period compared with other types of prostheses.

Therefore, the purpose of this article was to review the literature from January 1, 2001 to July 25, 2017, that related only to prosthetic complications for the purpose of presenting data regarding the types of prosthetic complications that have occurred with different implant prostheses and their incidences. An additional purpose was to compare the 2001 to 2017 prosthetic complications data with the previously published data covering the period from 1981 to 2001, to determine if there have been changes in prosthetic complications between the two time periods.

Materials and methods

This current literature review was based on a Medline search of the following MeSH categories: dental prosthesis; dental prosthesis, implant supported; dental implants/adverse effects; dental prosthesis, single-tooth; dental implants/complications. After filtering for articles published in English that had an available abstract relating to implant prostheses, the search resulted in 5851 articles. After searching the abstracts, there were 269 articles selected for comprehensive review. Of these reviewed articles, 74 were included in this literature review based on the inclusion/exclusion criteria described below.

The inclusion criteria included only those studies that reported a follow-up time of at least 1 year, provided data on at least 25 crowns/prostheses, and identified the number of patients, number of implants, number of crowns/prostheses, and the types and number of complications that occurred with each type of prosthesis. For overdentures, only those studies with two or more implants per prosthesis were included. For a specific complication to be included in this review, at least three clinical studies had to have reported that complication.

Exclusion criteria included systematic reviews and literature reviews, as the purpose of this paper was to present a review of prosthetic complications presented in individual clinical studies. For fixed complete dentures, studies reporting on prostheses supported by zygomatic implants were excluded. For fixed partial dentures, studies reporting on cantilever prostheses were excluded, as were those reporting on prostheses attached to implants and natural teeth. For single crowns, studies reporting on one-piece implants were excluded. Some articles examined multiple types of prostheses and reported complications, but did not indicate the specific number of complications that occurred with each type of prosthesis. These were therefore excluded from this review.

The incidence percentages in this literature review were calculated by combining the raw data from multiple studies so a mean incidence could be

determined. This was the procedure used in the 2003 publication[1] and therefore the data presented in this publication only suggests complication trends, as in the previous publication.

Results

The complications were grouped according to the following four types of implant prostheses: 1) implant fixed complete dentures; 2) implant overdentures; 3) implant fixed partial dentures; and 4) implant single crowns.

The complications reported with each type of prosthesis are limited to those identified in the included studies and does not necessarily represent every type of prosthetic complications that could occur.

Implant fixed complete denture complications

The following types of complications and their incidences were reported for fixed complete dentures, (as shown in Table 1):

1. Denture tooth fracture: 226 of 814 prostheses (28%), as reported in 11 studies[2-12];
2. Screw access filling material lost: 38 of 154 prostheses (25%), as reported in three studies[2,7,9];
3. Denture tooth wear: 40 of 266 prostheses (15%), as reported in five studies[4,8-10,13];
4. Fracture of porcelain veneer: 16 of 129 prostheses (12%) as reported in three studies[12-14];
5. Mucosal hyperplasia: 15 of 145 prostheses (10%), as reported in three studies[7-9];
6. Prosthesis remake: 21 of 227 prostheses (9%), as reported in five studies[6-10];
7. Framework fracture: 31 of 658 prostheses (5%), as reported in eight studies[3,5-7,9-11,13];
8. Abutment screw fracture: 7 of 325 prostheses (2%), as reported in three studies[5,7,8];
9. Prosthesis screw loosening: 4 of 369 prostheses (1%), as reported in three studies[5,7,9].

Implant overdenture complications

The following types of complications and their incidences were reported for overdentures, (as shown in Table 2):

1. Overdenture adjustment: 194 of 122 prostheses (159%), as reported in three studies[15-17];
2. Change of attachment: 355 of 394 prostheses (90%), as reported in nine studies[16-24];
3. Reactivation of attachment: 177 of 335 prostheses (53%), as reported in four studies[20,23,25,26];
4. Mucosal hyperplasia: 113 of 361 prostheses (31%), as reported in five studies[15,23,26-28];
5. Overdenture reline: 192 of 737 prostheses (26%), as reported in 12 studies[15-20.24-26,28-30];
6. Opposing prosthesis reline: 49 of 193 prostheses (25%), as reported in four studies[16,18,24,30];
7. Loose attachment: 104 of 568 prostheses (18%), as reported in eight studies[15-17,22,27,31-33];
8. Occlusal adjustment: 42 of 238 prostheses (18%), as reported in four studies[15,18,26,28];
9. Overdenture repair: 22 of 156 prostheses (14%), as reported in three studies[18,30,33];
10. Overdenture remake: 37 of 305 prostheses (12%), as reported in six studies[15,17,18,28-30];
11. Denture tooth fracture: 94 of 793 prostheses (12%), as reported in 12 studies[15,16,19,20,24-26,28,29,32-34];
12. Extension bar fractures: 36 of 353 prostheses (10%), as reported in four studies[15,20,24,25];
13. Overdenture fracture: 84 of 934 prostheses (9%), as reported in 14 studies[17,19,21-29,32,35,36];
14. Bar screw loosening: 25 of 388 prostheses (6%), as reported in three studies[15,25,27];
15. Bar fracture: 44 of 757 prostheses (6%), as reported in 12 studies[15,18,21,24,26-29,32-34,37];
16. Attachment fracture/loss: 33 of 614 prostheses (5%), as reported in eight studies[16,22,23,25,26,32,33,37];
17. Excessive wear of denture teeth: 16 of 401 prostheses (4%), as reported in four studies[15,25,28,29].

Implant fixed partial denture complications

The following types of complications and their incidences were reported for fixed partial dentures, (as shown in Table 3):

1. Porcelain veneer fracture/chipping: 68 of 1,205 prostheses (6%), as reported in 12 studies[38-49];
2. Loss of retention (decementation of cemented prostheses): 41 of 738 (6%), as reported in nine studies[38,39,42,43,45-49,53];

3. Screw loosening with screw-retained prostheses: 37 of 896 prostheses (4%), as reported in seven studies[38,40,46,47,50-52];
4. Screw loosening with cement-retained prostheses: 25 of 756 prostheses (3%), as reported in five studies[38,47,48,51,52].

Implant single crown complications

The following types of complications and their incidences were reported for single crowns:

1. Abutment screw loosening (both screw and cement-retained crowns): 262 of 7,648 crowns (3%), as reported in 22 studies[38,39,41,43,48,49,54-69];
2. Implant fracture: 13 of 438 implants (3%), as reported in three studies[60,61,70];
3. Porcelain veneer fracture/chipping: 177 of 7,245 crowns (2%), as reported in 21 studies[38,39,44,47-49,53,54,57-59,62-65,70-75];
4. Loss of retention (decementation of cemented crowns): 161 of 7,683 crowns (2%), as reported in 17 studies[39,43,47,48,53,54,56,58,59,62,63,65,66,70,72-74];
5. Open proximal contacts: 94 of 4,846 crowns (2%) as reported in three studies[47,50,55];
6. Crown remakes: 38 of 5,471 crowns (0.7%), as reported in six studies[47,58,62,65,73,74].

Comparison with previous complications literature review

In the previous literature review[1], there were more prosthetic complications associated with implant overdentures than implant fixed complete dentures, implant fixed partial dentures, and implant single crowns. Likewise, in this review there were more complications with implant overdentures than the other types of prostheses. However, it was surprising that the studies included in this current review reported higher complication rates for reactivation of the retentive mechanism, mucosal hyperplasia, and overdenture relines than were determined in the 2003 publication. In fact, the difference was quite substantial, with a rate of 30% reported for reactivation of attachments in 2003 and 53% in the current review. The rate for mucosal hyperplasia was 19% in 2003, but was 31% in this review. Likewise, the need for overdenture relines was 19% previously and 26% in this review. No reasons could be determined for this increased incidence. In contrast with the increased incidence found in the current review, the occurrence of fractured retentive mechanisms was reported to be 17% in 2003 and was reduced to 5% in this review. Additionally, it was interesting to note that fractures of the opposing prosthesis were reported with implant overdentures in 2003, but were not reported in the articles included in this current review.

In the 2003 publication[1], fixed complete dentures were associated with the second greatest number of complications and that same ranking was present in this current review. There were two complications reported in both literature reviews (framework fracture and abutment screw fracture) with comparable incidences. Framework fracture in the 2003 publication was 3% and it was 5% in the current review. Likewise, abutment screw fracture was 3% in 2003 and 2% in this review. As for implant fixed complete dentures and implant overdentures, it was interesting to note that opposing prosthesis fracture was a reported complication in 2003 with an incidence of 12%, but it was not reported in this review.

With implant fixed partial dentures, there were only four complications reported in this review; similarly there were only a few complications reported in 2003. The mean incidence of porcelain veneer fracture was 14% in the 2003 publication, whereas it was 6% in this review, an advantageous reduction in a complication that can consist of minor chipping or could be extensive enough to require prosthesis replacement. Screw loosening occurred with a 4% incidence in 2003; in the current analysis it was 4% with screw-retained prostheses and 3% with cement-retained prostheses. Of interest is the 1% abutment screw fracture identified in 2003 whereas there was no reporting of abutment screw fracture in the papers included in this review. Similarly, there was no report of implant fractures in this review, whereas the 2003 publication reported a 1% overall implant fracture rate for all types of prostheses. When the specific studies from 2003 that presented data on implant fractures associated with implant fixed partial dentures were reviewed, the number of fractures was small. For instance, in one study[76] there were five fractures associated with 509 implants that supported fixed partial dentures. The authors indicated the fractures were associated with situations of high

stress and non-axial loading. In another study from the 2003 review[77], there were three fractures among 521 implants. A third study[78] from the 2003 paper reported a 7.2% implant fracture rate associated with 168 mandibular posterior fixed partial dentures; all but one fracture occurred with prostheses that had a cantilever load.

With implant single crowns, mechanical complication data was limited in the 2003 review and focused primarily on abutment screw loosening. The mean incidence of abutment screw loosening was high in the early years of placing single implants (25%), but was reduced to 8% in the most recent studies included in the 2003 review[1]. In this current review, the mean abutment screw loosening was further reduced to 3% based on the 22 included studies. In fact, all the single crown complication incidences reported in this review were low, with values ranging from a maximum of 3% to a minimum of 0.7%.

Discussion

There were three complications presented in the results section that, at first glance, may not appear to be prosthetic complications.

One complication is the incidence of mucosal hyperplasia associated with fixed complete dentures and implant overdentures. The reason for this complication being included relates to the relationship between prosthesis design and the space between the prosthesis and mucosa, since "limited space" or "no space" affects oral hygiene access and increases the likelihood that mucosal hyperplasia can occur. This space restriction was first identified by Adell et al[79] in their classic 1981 publication where hyperplasia was recorded at about 6.7% of the implants due to approximation of the mucosa and prosthesis that "created unfavourable conditions for local tissue hygiene". The second complication is implant fracture associated with single implant crowns. This data is included because non-optimal placement of single implants, particularly in the molar region[80], can lead to crowns with horizontal cantilevers increasing the torque applied to the crown and implant[81]. These torque factors increase the potential for mechanical complications to occur, such as implant fracture.

The third complication is the open proximal contacts that were observed over time with oral implants[82-85]. There are multiple potential causes for such proximal contact opening, one of which is the occlusal relationship established between the implant crown and the natural teeth, and therefore this complication was included in the review.

Data limitation complications

When reviewing the above results, it becomes apparent that the number of studies reporting certain complications was quite limited in the recent literature, as evidenced by the number of complications where the mean incidence was based on just three or four studies. Therefore, drawing conclusions or inferring complication trends related to these complications is tenuous. Other complication incidences were based on calculations from a larger number of clinical studies, which allows one to establish a more realistic trend regarding the potential for such complications to occur.

Implant fixed complete denture complications

With implant fixed complete dentures, denture tooth fracture (28%) and denture tooth wear (15%) occurred at a relatively high incidence level, indicating the need for further improvements in denture tooth materials. Also, the use of occlusal night guards worn over the prosthesis is another means of protecting the prosthetic teeth and reducing wear. Porcelain veneer fracture (12%) is relatively high and also supports the value of occlusal night guards to help protect the teeth from heavy forces that can occur during sleep. The loss of screw access filling material (25%) is indicative of the need for optimal retention for the material that seals screw access channels. Remaking of the prostheses (9%) and framework fracture (5%) are higher than desirable given the consequences of these complications to both the patient and practitioner.

Mucosal hyperplasia was included in the list of prosthetic complications since prosthesis design can reduce or eliminate space between the cervical aspect of the prosthesis and the residual ridge, thereby compromising oral hygiene access[79].

Implant overdenture complications

From the above data, it is apparent that implant overdentures continue to have the greatest number of prosthetic complications. For instance, the percentage of adjustments made to overdentures exceeded 100%, indicating that many overdentures required multiple adjustments. While the need for multiple adjustments is relatively common with traditional complete dentures, one would think that the presence of attachments that help orient an overdenture and provide retention and stability would reduce the incidence of overdentures requiring adjustment. Additionally, many of the studies were not specific enough to identify the types of adjustments required.

Most of the overdenture complications were associated with the retentive mechanisms, supporting the need for more durable attachments. The high mucosal hyperplasia incidence (31%) indicates the importance of meticulous oral hygiene, as well as designing bars with adequate oral hygiene access.

Implant fixed partial denture complications

In the included studies from the 2001 to 2017 data, only four complications were reported (porcelain veneer fracture/chipping, loss of retention (decementation of cemented prostheses), and screw loosening). It was interesting to note that there was a considerably lower incidence of porcelain veneer fracture (6%) in this review than in the 2003 publication that reported an incidence of 14%. This decreased incidence likely indicates that improvements have been made in design, materials, and occlusal relationships. In addition, the 2003 data reported a 1% abutment screw fracture – a complication that was not reported in the studies included in this paper. The lack of abutment screw fracture may be an indication of improved prosthesis fit or design that eliminated this complication in the included studies.

It was not always possible to separate prosthetic screw loosening from abutment screw loosening in the studies where screw-retained prostheses were used, as well as in the studies where cement retained prostheses were used. Therefore, the presented data on screw loosening combines both prosthetic and abutment screw loosening. Similarly, not all of the studies reporting loss of retention (decementation) indicated whether a provisional or a definitive cement was used. Some of those reporting the type of cement used did not specify the type of cement associated with the loss of retention.

Relative to porcelain veneer fracture/chipping, not all of the included studies separated catastrophic fracture from minor chipping that could be smoothed; therefore the two complications were combined.

Implant single crown complications

While the single crown data available at the time of the 2003 study was very limited, the data available today are more substantial in terms of the number of crowns that have been placed and studied. From this more robust database it is encouraging to note that the total number of reported complications (six) is relatively small.

Abutment screw loosening was not a common occurrence, but it was the most commonly reported complication (3%). Unfortunately, the data in some studies was not specific enough to accurately separate the overall screw loosening between screw-retained crowns and cement-retained crowns.

One surprising finding in this literature review was the 3% incidence of implant fracture with single crowns. However, this incidence rate was based on only three studies[60,61,70], with one of the three studies[61] accounting for almost all of the fractures. Therefore, the percentage would be much lower (0.6%) if this study was excluded and the incidence was based on the two remaining studies[60,70]. It seems logical to assume that the lack of reporting of implant fractures indicates that it did not occur, since a catastrophic complication such as this would most likely be reported. In addition, when it does occur, the studies should identify the specific arch location since early data on single implant fractures indicated they occurred primarily in the molar region[77]. As mentioned previously, there are also biomechanical design characteristics[78] that increase the loads applied to implants (such as horizontal offset, vertical offset (crown-to-implant ratio), long axis implant angulation relative to the occlusal plane, and occlusal habits such as bruxism. The potential effect of these

characteristics should be included in the reporting of implant fractures. A further recommendation is that all future studies of single implants provide information about implant fracture, even when it does not occur. By reporting presence, or absence, of implant fracture in future studies, more thorough and accurate calculations can be established.

The complication incidence was low for all other single crown complications, ranging from 0.7% to 2%. Even the 3% screw loosening was much lower than the incidence reported in the 2003 data where a 25% loosening occurred during the very early years, which was subsequently reduced to 8%. This initial decrease was presumably due to newer screw designs, torque devices, and routine use of recommended torque values. One long-term single crown study[86] was not included in this literature review because it included data on screw loosening from both the early years of placing implants on single crowns, as well as in more recent years. However, the study documents more abutment screw loosening in the early years, as well as a lower incidence following the introduction of new screw materials and a standardised torquing of screws.

Limitations of existing complications incidence data

One of the challenges with presenting data regarding complications is that most of the included studies only reported data on the prosthetic complications that occurred in their study. Therefore, it was impossible to know if unmentioned complications did not occur, or were not examined in the study. As a result, the data presented in this literature review only include those studies where specific complications were reported and does not include studies that identified prosthetic complications that did not occur. For instance, one study[87] identified multiple complications that did not occur in the study and therefore the authors reported a "zero incidence" for those complications. However, because many studies did not provide such zero incidence data, a decision was made not to include the "zero incidence data" in this paper since it was not available in most of the included studies.

There is another interesting factor related to the lack of reporting potential complications that did not occur. It is likely that the reported incidence of complications in literature review papers such as this, as well as in systematic reviews, is higher than the actual incidence because the reported complication rates do not include all of the studies where the complication did not occur. Therefore, if all of the reported incidence data included studies with a "zero incidence", the overall incidence of that complication would be reduced, and thereby provide a better representation of the actual incidence. For example, if five studies collectively reported that 10 out of 100 dental implants had single crown abutment screw loosening, the reported incidence rate would be 10% (i.e. 10/100). However, if there were five additional studies that also involved 100 total dental implants and they all reported no screw loosening, the sample size would increase to 200. Thus, the incidence rate would decrease from 10% to 5% (i.e. 10/200).

As a result of the above factors, it is proposed that all future clinical studies provide data specific to each type of implant prosthesis and also include information about each of the mechanical complications that have been identified in previous clinical studies. Even if a complication did not occur in a particular clinical study, it would be helpful for that study to state the fact that the complication did not occur. In that way, the calculation of the complications incidence would include both the studies that encountered a particular complication and those where the complication incidence was zero. Having such information will provide more realistic incidence data and produce a stronger basis for making design/material changes so complications can be further minimised. Therefore, it is recommended that all future complications studies provide data related to the complications listed in Table 5, even when the complication did not occur. The complications listed in this table represent those that were reported in this literature review where at least three studies had reported the occurrence of the complication.

Another factor that limits the accuracy of complications incidence data is the total number of crowns placed in the different studies. As an example, the loss of retention (decementation) of single crowns in this literature review was based on 17 studies with a reported incidence of 2.1% (161 of 7683 crowns loosened). However, when the specific studies

are examined, it is noted that one of the studies[47] involved 4760 crowns, a number substantially larger than the other included studies. If that one study were eliminated from the data pool, there would have been 150 of 2923 crowns that loosened for an incidence percentage of 5.1%. Therefore, one approach to reporting incidence data would be to eliminate any studies where the number of crowns/prostheses/implants placed in the study was much larger than the number present in the other included studies. Additionally, the sample size between the different prostheses groups (i.e. implant single crowns, implant fixed partial dentures, implant overdentures, and implant fixed complete dentures) as well as follow-up times varied considerably between the included studies, and therefore the incidence percentages could be different if these variations were not present. For example, veneer fracture for single crowns includes 7245 crowns, while the same complication for fixed complete dentures only includes 129 prostheses.

Conclusions

1. Implant overdentures are associated with more complications than implant fixed complete dentures, implant fixed partial dentures, and implant single crowns.
2. The lowest incidence of complications was reported with implant single crowns.
3. The most common complication reported with implant fixed complete dentures was denture tooth fracture.
4. The most common complication associated with implant overdentures was the need for adjustments.
5. Porcelain veneer fracture/chipping was the most common complication identified in the studies of implant fixed partial dentures.
6. The most common complication reported with implant single crowns was abutment screw loosening.

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Foreign body reactions, marginal bone loss and allergies in relation to titanium implants

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Key words *foreign body reactions, marginal bone loss, titanium allergy*

Aim: To describe general observations of immunological reactions to foreign materials and to realize that CP titanium gives rise to a foreign body reaction with subsequent bone embedment when placed as oral implants. To analyse the possibility of titanium allergy.
Materials and methods: The present paper is of a narrative review type. Hand and Medline searches were performed to evaluate marginal bone loss of oral implants and the potential of titanium allergy.
Results: Immunological reactions to foreign substances include Type I hypersensitivity reactions such as allergy, Type II hypersensitivity reactions characterised by IgM or IgG antibodies that may react with blood group antigens at transfusion, and Type III hypersensitivity caused by antigen-antibody immune complexes exemplified by acute serum sickness. There is also Type IV hypersensitivity, or delayed hypersensitivity, which is typically found in drug and foreign body reactions. It proved very difficult to find a universally acceptable definition of reasons for marginal bone loss around oral implants, which lead to most varying figures of so-called peri-implantitis being 1% to 2% in some 10-year follow-up papers to between 28% and 56% of all placed implants in other papers. It was recognised that bone resorption to oral as well as orthopaedic implants may be due to immunological reactions. Today, osseointegration is seen as an immune-modulated inflammatory process where the immune system is locally either up- or downregulated. Titanium implant allergy is a rare condition, if it exists. The authors found only two papers presenting strong evidence of allergy to CP titanium, but with the lack of universally accepted and tested patch tests, the precise diagnosis is difficult.
Conclusions: CP titanium acts as a foreign body when placed in live tissues. There may be immunological reasons behind marginal bone loss. Titanium allergy may exist in rare cases, but there is a lack of properly designed and analysed patch tests at present.

Introduction

General observations on immunological reactions to foreign substances

These reactions have traditionally been called type I to IV reactions, but can also be classified as acute, allergic or chronic inflammation.

Type I hypersensitivity is characterised by allergic reactions, including anaphylactic reactions. A typical example is a sensitised patient who has developed IgE antibodies to an allergen (a Th2 driven process). When the allergen is encountered, it is taken up on mucus membranes and exposed to mast cells. Mast cells have bound IgE on their surface and when the antigen crosslink IgE antibodies, several substances – most importantly histamine – are released. Histamine dilates and permeabilises capillaries and small veins, resulting in fluid leakage and reddening of the area. An example of this is conjunctivitis. There is also a later phase when other mediators mobilise cells, particularly eosinophils and

T-cells, leading to a prolonged diseased state and resulting in asthma in susceptible individuals. The normal protective reaction in the body using this reaction is the defence against extracellular parasites.

Type II hypersensitivity is characterised by IgM or IgG antibodies binding to cells or the extracellular matrix. A typical example is antibodies reacting with blood group antigens in transfusion or transplantation, leading to destruction of red blood cells or the transplanted organ. Antibodies can also be directed at self-antigens in autoimmune diseases such as vasculitis, cased by ANCA, or autoimmune haemolytic anaemia. In other situations the

Autoantibodies can block or stimulate receptors without causing inflammation, such as in myasthenia gravis and Graves' disease, respectively.

Type III hypersensitivity is caused by antigen-antibody (immune) complexes formed in the circulation and deposited in the microvasculature. Normally, this reaction is broken up by the complement system and pure type III hypersensitivity is uncommon. Immune complexes are instead formed where antigens are trapped in the circulation in small vessels, typically in the glomeruli, joints or small cutaneous blood vessels, resulting in vasculitis. The classical example of type III hypersensitivity is acute serum sickness caused by administration of large amounts of foreign serum from horses to treat diphtheria, a treatment that is no longer used.

Type IV hypersensitivity is also called delayed type hypersensitivity (DTH) by immunologists, since this reaction typically takes several days to develop, in contrast to type I hypersensitivity. This reaction involves cells, mainly T-helper cells (Th1) and macrophages and cytokines. When a pathogen, such as tuberculosis, is difficult to destroy due to bacterial defence mechanisms, the macrophage needs help from T-cells to augment its functions. Antigens are presented on MHC-class II molecules to T-helper cells, together with amplifying signals (co-stimulatory molecules) stimulating the T-cells to produce cytokines, mainly IL-2 and interferon gamma (IFN-γ). IL-2 is an autocrine growth factor for T-cells multiplying antigen specific T-cells, while IFN-γ changes macrophage functions and phenotype. IFN-γ stimulated macrophages produce more NO, bactericidal enzymes, upregulate MHC-class II, produce matrix degrading enzymes (metalloproteinases) and cytokines, including IL-12. In turn, IL-12 stimulates the T-cells. The macrophage phenotypic change is called epithelioid cells since the macrophages become larger with abundant, granular cytoplasm simulating epithelial cells. This reaction can be seen in autoimmune diseases such as rheumatoid arthritis, drug and foreign body reactions, inflammatory bowel diseases and organ transplantation.

Gell and Coombs[1] introduced the hypersensitivity classification in 1963 and it focuses on the negative, host-destructive effects of immunity and inflammation. Today, it is evident that these reactions partly overlap and further that they are mainly protective, but that tissues can be destroyed in uncontrolled inflammation or in allergy and autoimmune processes. Furthermore, the type III reaction is uncommon and the main function of immune complexes might be to immobilise circulating viral particles in viremia. A more straightforward view is the classification used by pathologists. Allergy is a type I reaction and is driven by allergens, such as pollen. Acute inflammation is a process driven by danger or alarm signals from invading extracellular microorganisms, resulting in vascular dilatation and leakage in order to accumulate mediators from the blood, including complement and neutrophils that will ingest and destruct the invading organisms. IgM and IgG antibodies will help the neutrophils to ingest the microorganism via specific Ig-receptors on their surface (type II reaction). Chronic inflammation is an equivalent of the type IV reaction and driven by antigens on either microorganisms or other foreign particles, including transplanted organs or cells. This reaction is normally aimed at intracellular organisms including bacteria and viruses, where infected cells are destroyed by cytotoxic, CD8+ T-cells.

Materials and methods

Type of review chosen

The initial ambition of the present authors was to present a systematic review of foreign body reactions to titanium (type IV hypersensitivity or chronic inflammation, marginal bone loss/peri-implantitis (= acute inflammation) and titanium allergy (type I or allergic inflammation).

However, our initial ambition had to be abandoned due to lack of universally acceptable standards in the case of marginal bone loss (MBL) and its possible relation to a disease entitled peri-implantitis. It would, of course, have been tempting to use the definition of peri-implantitis presented by Lindhe and Meyle[2] and apply those criteria to long-term reports in the literature. However, whereas Smeets et al[3] based on the Lindhe and Meyle criteria, reported an incidence of peri-implantitis of somewhere between 28% and 56%, these figures are very far away; indeed from 14 recent 10-year reports of modern implants (i.e. implants with moderate surface roughness) where the average rate of peri-implantitis was in the range of 1% to 2%[4-5].

Whatever definitions of peri-implantitis preferred by the authors of those 14 papers, it was certainly not the one suggested by Lindhe and Meyle (2008). In addition, modern research points to the fact that implants are foreign bodies and thereby potential victims of immunological adverse reactions[6], a fact seldom discussed in the older literature.

We perceived another problem in the case of titanium allergy, another topic of our review. Here, we found a plethora of papers claiming enormously, if unrealistically, high figures of this ailment based on a particular test of allergy that has not been scientifically accepted. If, on the other hand, we limited the diagnosis of allergy to CP (commercially pure) titanium to studies with positive patch tests there were only two papers, whereas another four papers with positive patch tests were related to titanium alloys. In other words, we had too few papers with evidence of allergy to CP titanium to make it meaningful with authoring a systemic review.

Results

The frequent use of titanium or titanium alloys in oral, craniofacial and orthopaedic implants and for fracture plate fixation

Titanium is a commonly used material for different types of implants. It is estimated that between 15 million and 20 million oral implants are produced annually. About 95% of all oral implants are manufactured from CP titanium. Most of the remaining 5% of oral implants are made from titanium alloys, particularly Ti6Al4V. Extraoral, craniofacial implants are generally made from CP titanium. Several hundred thousand of such implants have been manufactured and used on indications such as congenital malformations, acquired facial bone deficiencies or as a fixation of directly bone-anchored hearing aids. By contrast, titanium alloys, rather than CP titanium, are preferred for orthopaedic implants and screw-fixation devices, such as plates for fracture healing. The reason for selecting CP titanium or the alloy in different clinical situations seems mainly empirical; as an example may be mentioned that P I Brånemark, the pioneering researcher in oral implantology[7,8], preferred CP titanium and others simply followed his example. However, in the case of major arthroplasties, only one-third of hip and knee implants would actually be manufactured from titanium alloy; remaining joint replacements are made from cobalt chrome alloys or stainless steels. The number of major arthroplasties placed annually is considerable. For example, 13,000 hips are used every year in Sweden based on a population of about 10 million individuals. Since Sweden represents about 1% of the world's trade, this would point to an annual use of somewhere between 1 million and 1.5 million hip replacements worldwide.

Interfacial reactions to titanium and long-term clinical results

When clinical titanium implants are placed in the jaws or the craniofacial skeleton, a bony envelope is developed in direct (light microscopic resolution level) contact with the metal. This bone reaction was termed osseointegration by Brånemark[8]. The general reasoning behind osseointegration was that it depends on very controlled surgery and that implants placed in this way may even establish some sort of chemical interaction with the anchoring bone[9]. The reason for orthopaedic implants generally not displaying direct bone-to-implant contact was hypothesised to be dependent on the relatively blunt surgery used when placing hip and knee implants, which necessitated surgical reaming of the marrow space. This said, orthopaedic implants do display interfacial bone formation, if not in direct contact with the implant.

The first investigator to question that titanium must be an inert material capable of wound-healing reactions in the surrounding tissues was Karl Donath[10,11]. Donath[10] demonstrated that even shrapnel from grenades could be directly anchored to bone and questioned whether titanium behaved similarly to other metals and is not an inert material at all. By clear contrast, every time a titanium implant was placed, Donath claimed that body defence mechanisms were activated; a bony shield developed that separated the foreign material from the tissues. Donath's theories[10-11] have been supported by many papers published this millennium[4,12-15]. This means that osseointegration is but a foreign body response[16], therefore a type IV hypersensitivity reaction. From a clinical standpoint, implants show high survival rates over long terms of follow up.

Orthopaedic implants have demonstrated survival rates of more than 90% at 10 years or more of follow up (Scan Hip registry), even if it must be pointed out that most long term analyses of hip or knee implant outcome are based on reoperation statistics and not on the actual survival of individual implants. Oral implants have been clinically documented with survival rates of clearly more than 90% in 10-year follow-up studies[4,5] (for review). In addition, 20- to 25-year reports with high survival rates of oral implants have been published[17,18], as well as case reports of individual implants spanning between 40 and 50 years[5].

The remaining part of this paper will mainly deal with oral implants, since our knowledge of their tissue reactions over short and long-term observation periods are much more thoroughly reported than is the case in orthopaedic sites. Furthermore, oral implants are more easily radiographed, with the possibility to evaluate the level of anchoring bone, and oral implants are placed in very great numbers every year.

Clinical threats to oral implant function

Even if oral implants work very well over long follow-up times, some implants still fail. One reason for implant failure is marginal bone loss that may prove difficult to treat clinically. The traditional approach to evaluate such secondary implant failures has been inspired from teeth that suffer from a disease called periodontitis that includes infection, inflammation and marginal bone loss.

In the case of oral implants, a disease called peri-implantitis was suggested to explain why bone loss threatened oral implants[19]. The peri-implantitis disease theory is controversial today, at least as the only explanation for marginal bone loss around oral implants. Furthermore, this theory was launched prior to new knowledge indicative of the implant being a foreign body and, thereby, capable of causing immunological (type IV) reactions.

A critical analysis of the notion of disease behind all bone loss after the implant's first year *in situ*

During the first year of clinical function, it seems as if most researchers expect bone remodelling to result in either loss or even – in some cases – gain of marginal bone around an implant. After the first year *in situ*, peri-implantitis has been the assumed reason for any marginal bone loss around the oral implant. Peri-implantitis has been defined as progressive inflammation and loss of supporting bone around an implant, whereas mucositis is a bacteria-induced, reversible inflammation of the soft tissues[2]. This is a very general definition that, not surprisingly, results in very high figures of the alleged disease; mucositis would have an incidence of 80% and peri-implantitis an incidence of between 28% and 56% of all placed implants[2,3]. Recent research criticises the technique of evaluating inflammation based on bleeding on probing or probing depth[20]. Furthermore, implants continue to display very good clinical long-term results, despite the alleged disease, and their bone status seems instead to be in a steady state than being the victim of a progressive ailment[21].

One implant that fulfilled the criteria for progressive disease in the first few years after placement was found in excellent function at a 50-year follow up[5]. In addition, the disease-related theory does not seem concerned with the reason for marginal bone loss. Certain implant designs, despite original osseointegration, continue losing bone thereafter[22]. Implants placed by certain surgeons or restored by certain individuals continue losing bone at an annual rate (Figs 1 and 2), which is very difficult to explain against the notion of a disease affecting them. In

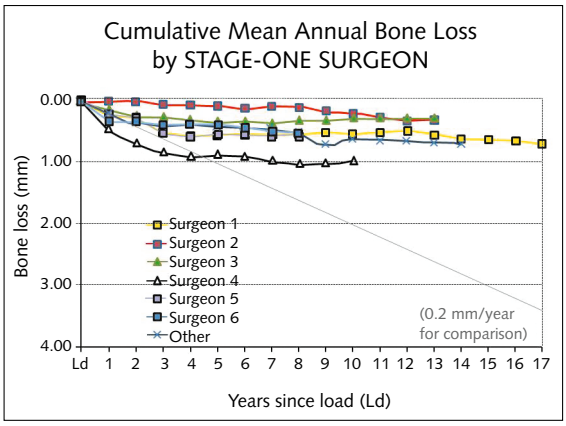

Fig 1 Cumulative MBL related to the surgeon who placed the implant. It is notable that some surgeons see very little annual bone loss whereas others lose bone continuously. Modified from Ross Bryant PhD thesis, University of Toronto, Canada, 2001.

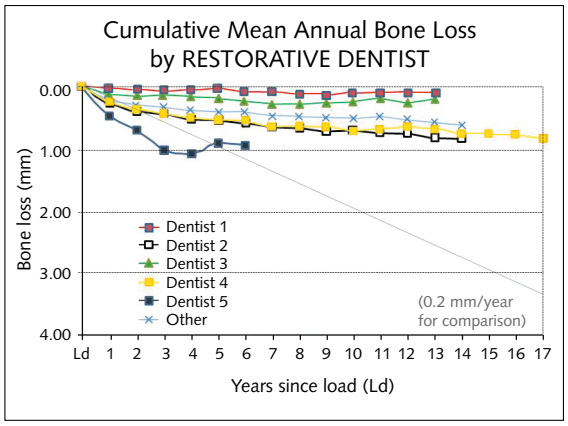

Fig 2 Annual MBL around implants related to the initial restorative dental practitioner who placed them. The same implant type was used in Figures 1 and 2 and the only reason for differing bone loss patterns seems to be the individual restorative dental practitioner. Modified from Ross Bryant, PhD thesis, University of Toronto, Canada 2001.

fact, a common reason for MBL is a complication to treatment. Patients with a poor bone stock will see more marginal bone loss around their implants than ordinary patients[22]. Bone resorption may be related to patient age alone; the older patient may lose bone around implants with no evidence of other pathology[5]. "To date, there is no evidence in the literature that a specific peri-implant "disease" exists as a unique entity with a specific etiology and pathogenesis[5]".

Marginal bone loss and its relation to immunological reactions and to bacteria

Osseointegration is an immune-modulated inflammatory process, where the immune system is locally either up- or down-regulated[23] (Fig 3). Titanium implants have been demonstrated to activate the immune system experimentally[15]. Macrophages may be regarded as effector cells of the immune system[24,25], but at the same time bone cells such as osteoblasts and osteoclasts are considered parts of the immune system as well[26,27]. With these couplings between cells routinely observed in the implant interface and the immune system, it is evident that the balance between bone formation and bone resorption may be influenced, one hitherto commonly ignored reason for MBL. This, coupled inflammatory/immune process regulating the foreign body reaction is present for the *in vivo* lifetime of the implant[14]. Interfacial bone cement around

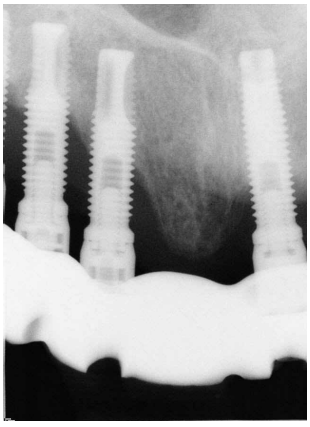

Fig 3 Implants with marginal bone loss. Modern research has identified osseointegration to be an immunological reaction establishing a bony layer to protect the tissues from the foreign titanium material. Marginal bone loss and secondary failures of osseointegration may depend on the sum of the trauma to the implant that may subsequently be finally rejected by the immune system in analogy to what happens in so called aseptic loosening of major joint replacements. Courtesy of Dr Jenö Kisch, Malmö, Sweden.

oral implants causes bone loss due to a foreign body reaction that is coupled to the foreign body reaction to the implants[28]. These observations point to the fact that bacteria are not needed to trigger bone resorption around oral implants, but whether bacteria will worsen the bone resorption or not is another issue[23]. In the case of orthopaedic implants that do not penetrate the tissues in open communication with the outside world, like oral implants, marginal bone resorption has been linked to aseptic loosening as the major reason for secondary failures of hip arthroplasties[29,30].

Christiansen[6] was able to demonstrate that behind aseptic loosening were indeed innate and acquired immunological reactions. More research is certainly needed to learn more about the immunological reactions to implants.

Returning to oral implants, where bacteria are frequently present in the surroundings, we also certainly need more research to learn more about possible bacterial actions. However, the mere presence of interfacial bacteria presents little evidence with respect to possible bone resorption patterns[19]. There are clear differences between periodontitis reactions around teeth and what has been termed peri-implantitis around implants[32,33]. We remain critical to evidence from so-called ligature studies, theoretically assumed to mimic "peri-implantitis" in implant patients, since the ligature itself is a foreign body and, as such, may very well trigger bone resorption when combined with another foreign body, the implant. That said, it is certainly possible that bacteria may act as an additional factor promoting bone resorption due to an acute inflammatory reaction.

Titanium implant allergy

General comments

Titanium leaks from implants, particularly during the first few weeks after implantation[35] and metal particles and ionic leakage may also occur later. This fact forms the background to the possibility of a titanium allergy that would be more likely to be initiated around titanium remnants in the tissues than the bulk metal itself[36]. Most of the relevant literature on what is assumed to be titanium allergy represents a number of case reports and numerous reviews on the topic. In a recent paper, it was suggested that even if titanium sensitivity does occur, its clinical relevance is not yet clear[37]. Other metal allergies seem to be much more common than titanium hypersensitivity. Nickel allergy (a type IV hypersensitivity reaction) may be as common as 10% to 15%[38], at least in the female population who may wear jewellery containing nickel more then men and have therefore become more sensitised. In this context, there were major problems for metal on metal orthopaedic implants in particular. However, It has been assumed that where the patient has a verified metal allergy to other metals, the risk is also greater with a titanium allergy, which motivated Kanyama et al[39] to perform a patch test on such a metal allergic patient prior to placing oral implants. The patch test was negative and the patient was able to receive successful oral implants. Different types of titanium materials were analysed in respect to impurities and it was reported that all tested titanium samples contained traceable amounts of Be, Cd and Co, up to a maximum of 0.001 weight per cent, Cr up to a maximum of 0.33% weight, Cu up to a maximum of 0.007%, Hf up to a maximum of 0.035% weight, Mn up to 0.007% weight, Ni up to 0.031% weight, and Pd up to a maximum of 0.001% weight. This means that a potential allergy to titanium may, in reality, represent an allergy to one or two constituents of titanium[40]. In this paper we have tried to solve this dilemma by referring to "titanium implant allergy" rather than "titanium allergy", since uncertainty exists as to which allergen prompts a reaction.

There was no noticed hypersensitivity reaction to titanium containing endovascular stents reported in an overview[41]. Diagnostic criteria for metal-induced allergic reactions include eczema, which is most severe close to the site of the implant, and positive patch tests to the suspected allergen. Furthermore, complete recovery from symptoms will appear when the allergen is removed[42,43]. A number of references to allergy to "dental implants"[43] were demonstrated to be problems with orthodontic appliances or dental implants bridge materials.

Anecdotal evidence of titanium implant allergy

Searching for evidence of titanium allergy in the literature is not an easy task since search procedures present clear reminiscence of the old amalgam debate; at times you get the notion that every patient will display symptoms of allergy to titanium, but the evidence thereof is lacking. The task is not made easier by a series of publications published in a journal entitled "Neuroendocrinology Letters", where frequency of titanium allergy allegedly is somewhere between 4% and 37.5% of patients and heavy advertising is performed around the so-called Melisa test, allegedly to verify titanium allergy[44]. However, from a strict scientific standpoint we have

been unable to learn much about the relevance of the Melisa testing[45], and as there may be a lack of specificity in lymphocyte proliferations[46] we have, therefore, decided to ignore these publications in the present review.

Furthermore, standing very clearly against the notion that titanium allergy is a most common diagnosis is the fact that most people brush their teeth at least twice daily seemingly without major problems; toothpaste regularly contains titanium white as a colour agent. If any allergies to toothpastes do occur, the incriminating agents are predominantly the flavours and preservatives used[47].

The presence of so many questionable reports of an assumed titanium allergy resulted in our decision to write this part of the paper as a narrative review only. We have differentiated between "weak" or "strong" evidence of titanium allergy based on whether or not a patch test incriminating titanium has been used in the respective studies.

Case histories that present relatively weak evidence of titanium implant allergy

A study of nickel sensitivity in an orthopaedic patient noticed that the patient had an expensive titanium watch with Velcro protecting the skin and assumed this indicated titanium hypersensitivity[48].

One study[49] reported that six titanium mandibular implants of CP titanium grade IV were placed in a female patient. Clinical and radiological complications followed and the implants were removed. Histology of adjacent tissues demonstrated fibrosis around all implants, a chronic inflammatory condition and, in two cases, foreign body giant cells were observed. After implant removal the patient healed without problems and the condition was put down as an example of "a possible true titanium allergy", even if it seemed as if no particular clinical tests verified this suggestion.

A patient with two titanium implants developed a rash that disappeared after implant removal[50]. Titanium allergy is one possible reason for the rash, but for a reliable diagnosis we would need more specific tests.

Several papers have reported of pacemaker allergies[51-53] and Ti6Al4V alloys may be incriminated here. The reason for putting pacemaker allergies in the category of "weak evidence" is the fact that the actual allergy may be to components of the pacemaker other than the metal itself, such as epoxy resins, to mention just one. Having said this, Yamamuchi et al[53] actually had a positive patch test to titanium alloy in one case of pacemaker allergy.

Orthopaedic implants have been incriminated to demonstrate titanium alloy allergy, although the evidence pointing to a particular titanium allergy may be weak[54]. Apart from titanium in Ti6Al4V, there are indications of allergy to vanadium as well[55,56]. Thomas[57] described a case of impaired fracture healing and eczema to a titanium based osteosynthesis plate, with indications of T-cell hyper-responsiveness, but the patch test to titanium was negative.

Case histories that present relatively strong evidence of titanium implant allergy

In a large test-control study of 1500 patients in need of oral implants, patients with general allergic symptoms after implant surgery or having had unexplained implant failures were included in one test group. Another group entitled "predisposing factors", included patients with known severe allergic reactions or extensive surgical internal exposure to titanium. Finally 35 patients were selected for the test group and 35 other patients were selected for the control group and cutaneous and epicutaneous patch testing was performed. Nine out of the original 1500 patients (0.6%) displayed a positive reaction to titanium. Control patients saw no positive patch tests[58].

Hosoki et al[59] reported on a patient who had successfully received two CP titanium oral implants in 2008. In 2010, the patient was treated with "titanium" screws for treatment of lower limb fracture. The type of "titanium" was not mentioned, but the great majority of titanium screws used in orthopaedics are made from Ti6Al4V alloy. The patient noticed eczema developing over the skin surface 6 months later. A patch test demonstrated allergic reactions to cobalt, tin, palladium, indium and iridium, but also demonstrated a "false positive" reaction to copper and titanium. In 2011, orthopaedic screws and adjacent metal was removed, but about 30% of the

eczema still remained. The dental implants remained in function, there were no adverse soft tissue reactions around the implants and no marginal bone loss was recorded.

Another patch testing was performed revealing a positive reaction against cobalt, tin, palladium, indium and iridium, as previously, but also against titanium, gold, platinum, zinc and iron. The dental implants were removed in 2014 and the skin problems disappeared. The patch test used to detect titanium allergy by these very thorough clinicians was based on 0.1% titanium tetrachloride.

A particular problem is the quality of patch tests. The diagnostic relevance of patch tests used to demonstrate titanium allergy may be questionable because of poor documentation of the specificity of such tests. Newer test methods, including haematological analyses, may have to be developed for increased specificity.

A medial displacement calcaneal osteotomy and first metatarsal arthrodesis was conducted in one patient who displayed what was seen as allergic symptoms that were later verified as such by a patch test[60]. All hardware was removed and the patient recovered. The type of titanium was not mentioned in this paper, but must be assumed to be Ti6Al4V, since this grade 5 titanium is preferred in orthopaedic surgery. Likewise, Olsen et al[61] reported of a positive patch test to what probably was Ti6Al4V alloyed screws used for ankle fixation. The patient developed a rash that disappeared after the screws were removed. Granchi et al[62] found positive patch tests to titanium and vanadium in titanium alloy knee arthroplasties, but did not see a difference in the frequency of allergy whether implants were stable or loosened. Lhotka et al[63] found positive patch tests to titanium dioxide in cases with reactions to surgical skin clips. A general drawback of patch tests used to prove titanium allergy is that their specificity has not been properly documented.

Conclusions

1. CP titaniumw acts as a foreign body when placed in live tissues
2. The reason for marginal bone loss around oral and orthopaedic implants is immunologically based, even if additional complications of infection remain a possibility
3. The frequency of oral implant threatening marginal bone loss has been exaggerated in the literature
4. Titanium implant allergy may exist as a clinical reality in rare cases, but the titanium specificity of used patch tests is not known in detail. It is, therefore, possible that the noticed allergy to titanium implants may reflect allergy to microelements of CP titanium implants or bridge elements rather than to titanium itself, at least in some cases.

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A review of the outcome of dental implant provision in individuals with movement disorders

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Movement disorders encompass a wide range of medical conditions that demonstrate changes to muscle function and tone which present with orofacial dyskinesia and dystonia. The most common conditions exhibiting these features are Parkinson's disease, Down syndrome, chorea and epilepsy.

Aim: To establish whether implant success in patients suffering from movement disorders is similar to the general population, identifying risk factors and noting recommendations that may aid maintenance programmes.

Method: PubMed and Medline searches, combined with a manual search of the reference lists of identified full text studies. In total, 19 patient case reports and 11 patient case series were identified for inclusion in the review.

Results: Implant survival in patients may be less than expected in patients with movement disorders, but evidence points to early rather than late failures. Oral hygiene control was widely reported as an issue, although there was insufficient evidence to imply that a lack of oral care will cause more rapid deterioration in implant patients with movement disorders. Maintenance requirements were low for fixed restorations, but more frequently reported in patients treated with overdentures, with the attachment mechanism and the prostheses requiring replacement. Chewing and quality of life in relation to prosthesis wear were improved.

Conclusion: Provision of implant-supported prostheses improves chewing and quality of life for patients with movement disorders and should be considered as an option in the treatment planning for tooth loss in this group of patients. However, straightforward designs that lend themselves to easier long-term maintenance should be adopted.

■ Introduction

Movement disorders encompass a wide range of medical conditions that demonstrate changes to muscle function and tone and, as a result, pathological changes in the neuromuscular system. The movement disorder may be precipitated by an acquired or congenital neurodegenerative disease process, an acquired birth defect, or be the result of pharmacological intervention to treat other aspects of a medical condition. Broadly speaking, movement disorders manifest as dyskinesia and dystonia, and both hyperkinetic and hypokinetic disorders pose challenges to the provision of dental care and oral health maintenance.

Dyskinesia manifests as an involuntary movement and depending upon the severity of the condition can be anything from a mild tremor or tic to more extreme involuntary movements. The severity of the dyskinesia will present a corresponding oral health challenge. Blanchet[1] described oral dyskinesia as "abnormal, involuntary, uncontrollable movements

predominately affecting the tongue, lips and jaw". Dystonia exhibits involuntary sustained or repeated muscle contraction, which may result in an abnormal fixed posture frequently causing twisting movements of the body. Raoofi et al[2] described oromandibular dystonia, as "repetitive or sustained involuntary prolonged spastic movements of the tongue, facial and masticator muscles". Dystonic movements of the face and tongue, which may be combined with abnormal jaw opening or closing movements, present a considerable challenge to the provision of dental treatment and the provision of routine oral health procedures either by the patient or their carer.

As a consequence of compromised oral health and high risk of oral trauma, patients with movement disorders are highly likely to lose teeth and seek a prosthetic solution. Removable prostheses and conventional and resin-bonded fixed-prostheses will, of course, form part of any treatment options, but in this group of patients, the consideration of a shortened-dental-arch approach[3] should be a priority. Nevertheless, implants will also be considered and it is essential to be able to appreciate the risks involved and the potential long-term outcome of such treatments.

It should also be considered that many of these neurological conditions are associated with epilepsy, which is characterised by epileptic seizures that may result in oral trauma[4,5]. In addition, patients with conditions, such as Down syndrome or intellectual disabilities, may have associated habits, including tongue protrusion or digit sucking, as well as clenching and bruxism that risk damaging both the teeth and restorations[6,7]. Therefore, it is important that these conditions are considered in such a review of risks and outcomes.

It is not surprising that movement disorders, in particular Parkinson's disease, have been implicated in the past in reviews of dental implants for medically compromised patients as conditions that may compromise osseointegration and implant survival[8-11]. However, at the time these reviews concluded that supporting evidence was lacking.

The aim of this review was to establish whether implant success in patients suffering from this diverse group of conditions is on a par with the general population. In addition, it was to identify any risk factors that must be considered in the treatment planning process, as well as to note any recommendations to help in any maintenance programme for this group of individuals.

Materials and methods

Electronic Medline and PubMed searches were undertaken in combination with a manual search of the reference lists of identified full text studies. All texts were considered for inclusion provided they were full-text English language publications or where an English language abstract was available. The search terms employed were combinations of the following: {"dental" AND "implant" OR "dental implant"} AND {"movement disorder (35)" OR "Parkinson's disease (9)" OR "dystonia (5)" OR "dyskinesia (9)" OR "Down syndrome (18) OR "epilepsy (8)" OR "epileptic (13) OR "neurodegenerative disease OR Huntington disease(3)"}. In addition {"dental" AND "implant" OR "dental implant"} AND {"neurological (28)"} was searched although this principally returned articles relating to nerve damage.

Results

The most common publication type was the patient case report, with the majority being 2 years or less post-loading. The remaining publications were patient case series observational studies, only one of which compared the outcome to a control group in a retrospective study[12].

Patient case reports (Table 2)

The range of conditions for patients with movement disorders and who had received implant treatment were athetoid cerebral palsy[13], Down syndrome[6,14-17], epilepsy and intellectual disability[4], Huntington's disease[18,19], idiopathic torsion dystonia[20], "'involuntary mandibular movements"'[21], orofacial dyskinesia[22], oromandibular dystonia[23,24], oromandibular dystonia with blepharospasm (Brueghel's syndrome)[25], Parkinson's disease[26,27], maple syrup urine disease[28] (a progressive neurodegenerative disorder) and Tardive dyskinesia[29].

There was a wide age range of patients treated (19 to 83 years) and a variety of implant systems used (Table 2). The majority of implants had usually been placed by a two-stage-process, or at least delayed loading was employed. Although not always reported, a large proportion of the implants were placed under general anaesthetic, usually to override the movement disorder or because of behavioural issues with the patient. One report highlighted the challenges of the provision of sedation for patients with Down syndrome[17,30] due to low blood oxygen saturation and risk of sleep apnoea.

Twelve of the studies followed up the patients for 2 years or less. However, one paper[15] followed-up a 1-year report[14] after 15 years for a patient with Down syndrome who had received three single tooth implants, and reported a successful outcome with no oral health issues, despite the early loss of one implant prior to loading.

The patient case reports in Table 2 described implants restored with single tooth restorations, fixed prostheses/bridges, and removable overdentures. The majority of reports had a 100% prosthesis survival rate during the observation period. One reported a successful implant-stabilised overdenture provided after the initial failure of an immediate fixed bridge and three implants[21]. Maintenance requirements of the overdentures were not reported as being high, with only one report indicating that the Teflon attachment inserts had been changed[22], another the loss of magnetism of the attachment[13], and another the loosening of a magnet keeper[26,27]. In one report an initial resin denture was replaced with a Cobalt-Chromium (Co-Cr) strengthened design and the author made this a recommendation for such treatment[13]. In many of the patient case reports the authors had selected a Co-Cr strengthened design (Table 2). Several studies reported oral hygiene issues and mucositis, but peri-implantitis was not recorded as being an issue, with all implant failures being due to early failures of integration rather than mechanical failures (Table 2).

Observational studies – patient case series

Considering the data presented in Table 3, the patient case studies again reflect the range of movement disorders, with the larger studies incorporating data from a number of different conditions, which nevertheless present with similar clinical challenges. A wide age range of patients (12 to 84 years) was treated, although the Parkinson's disease studies treated a predominately older age group (54 to 81 years). There were a wide variety of implant manufacturers and implant types, predominantly using a two-stage technique, with a high proportion being treated under general anaesthesia. Some studies indicated that additional implants had been inserted to act as "sleepers" in case of early or late integration failures[31].

The data for implant survival demonstrated considerable variance in outcome, with some studies reporting 90% to 100% implant survival in patients with an intellectual disability, cerebral palsy, Down syndrome, dementia and epilepsy[5,32,33] (Table 4). However, other studies reported implant survival of 77% to 86% in patients with Parkinson's disease[31,34], Down syndrome[35], an intellectual disability[36], and orofacial dysfunction[37,38]. Follow-up periods varied from 1 year to 16 years, but most studies reported on patients followed up for at least 4 years, while those reporting data at 1 year and 2 years reported data at 5 years to 10 years[31,34,37,38]. The majority of implant failures happened prior to loading, although

Table 1 Conditions characterised by dyskinesia and dystonia

Conditions characterised by dyskinesia[1] and/or dystonia	Medications Precipitating Dyskinesia
Alzheimer's disease	Anticonvulsants
Autism	Antidepressants
Basal ganglia lesions	Antiparkinsonian (Levadopa induced)
Cerebral Palsy	Antipsychotics (inc Lithium)
Down syndrome	
Encephalitis	
Epilepsy	
Huntington's disease	
Intellectual disability	
Metabolic and endochrine conditions	
Parkinson's disease	
Schizophrenia	
Syphilis	
Tardive dyskinesia	
Tourette's syndrome	
Wilson's disease	

Table 2 Movement Disorders – Patient Case Reports

Author (Year of publication)	Format	Condition/s	Age	Number of implant fixtures	System	Mandibular	Maxillary	GA/LA/Sed	Loading protocol	Early Failure – before loading	Fixture failures – Total	Post-loading follow-up period	Prosthesis	Comment
Rogers JO (1995)[13]	Case report	Athetoid Cerebral Palsy	64	2	Astra	2		GA	2 stage			2 years	Overdenture - Magnet	Improved speech and chewing. Early prosthesis failure and loss of magnetism after 2 years. "The incorporation of a cast metal strengthener is advisable if the denture structure is already weak or further weakened by the inclusion of magnets". 2 sleeper implants placed.
Lustig et al (2002)[14]	Case report	Down syndrome	16	4	MIS	2	2	GA	2 stage	1	1	1 year	Single Tooth	Early loss of narrower implant 3.75 mm others 4.2 mm. Oral hygiene issues and gingival inflammation prior to loading led to delay in prosthesis provision.
Zilberman (2016)[15]	Case report	Down syndrome	{16}	4	MIS	2	2	GA	2 stage	1	1	15 years	Single Tooth	Patient reported by Lustig et al observed 3 monthly for 15 years for plaque and calculus control. Reported no changes in bone height and control of gingival health.
Saponaro et al (2016)[6]	Case report	Down syndrome	27	3	TSV-Zimmer	3		LA	2 stage			21 months	Fixed Bridge	Down syndrome with macroglosia and tongue thrusting, however outcome successful.
Alqahtani et al (2017)[16]	Case report	Down syndrome	44		Straumann SLActive		1		2 stage			less than 6 months	Overdenture - Locator	Stressed need for maintenance of good oral hygiene and long-term maintenance are essential to the overall success in moderately intellectually disabled patients with Down syndrome.
Altintas et al (2017)[17]	Case report	Down syndrome	37		Zimmer	3	2	LA	2 stage	1	1	2 year	Overdenture - Locator	Restored optimal function. CoCr strengtheners recommended for removable prostheses. Noted Sedation risk due to low blood oxygen saturation associated with sleep apnoea and upper airway obstruction.
Károly-házy et al (2014)[4]	Case report	Epilepsy and Intellectual disability										1 year	Overdenture - Locator	The bone volume of the maxilla allowed the placement of only two implants it the region of the canines, compared with the generally required four. On long time recall, after one year, patient's chewing ability was satisfactory.
Jackowski et al (2001)[18]	Case report	Huntington's disease - hyperkinesia and dyskinesia	56	2	ITI - TPS	2		GA noted medn issues	Delayed			1 year	Overdenture - Bar and sleeve	Patient with orofacial hyperkinesia and dyskinesia including bruxism combined with xerostomia due to anticholinergic medication. Nevertheless implant overdenture resulted in improved chewing function, but oral hygiene issues were noted as well as the bar unscrewed at 2 months.
Deniz et al (2009)[19]	Case report	Huntington's disease - hyperkinesia and dyskinesia	67	2	Straumann SLActive	2 (4)		LA/ Sed	Delayed			1 year	Overdenture - Ball	Noted implant fixtures placed in first premolar region and restored with ball abutments, to avoid involuntary tongue protrusion. Plaque detectable by probe and slight inflammation but no bleeding.

Peñarrocha et al (2001) (20)	Case report	Idiopathic torsion dystonia	52	3	ITI	3		Delayed		3 years	Overdenture - Bar	"The lingual and masticatory dystonic movements were not improved by treatment, although chewing function and occlusion improved markedly. Despite poor oral hygiene, both the implants and overdenture satisfied the criteria for success after 3 years of follow-up." Prosthesis provided with a CoCr strengthener.
Shek et al (2012)[21]	Case report	Involuntary mandibular movements	79	6	Nobel Groovy	6		Immediate	3	less than 1-year estimated	Fixed Bridge failed/Overdenture - Locator	The involuntary mandibular movements were not observed by the patient or treating dentists until after the mandibular dentition had been removed. Implant failure attributed to mandibular dystonia, but were they a precipitating factor? Interim mandibular denture fractured and replacement made with CoCr strengthener.
Payne and Carr (1996)[22]	Case report	Orofacial dyskinesia	30	5	Nobel like					17 months	Overdenture - Complex bar with ball retainers	Only issue reported was the need to change the Teflon inserts.
Chung et al (2013)[23]	Case report	Oromandibular dystonia	56								Not reported	Task-specific oromandibular dystonia attributed to implant placement 6 months prior to condition developed, diagnosed at 1 year post symptoms. Followed for 6 months medications including procyclidine, metoclopropamide and dantrolene sodium, resulting in mild-to-moderate improvement without progression.
Sibley (2013)[24]	Case report	Oromandibular dystonia	45	8		4	4	LA/Sed			Overdenture - Bar Maxilla Locators Mandible	Mandibular fixed prosthesis on 4-fixtures failed, replaced by 4-fixtures with Locator attachments and an overdenture. Spastic jaw movements and tongue thrusting attributed to the failure of the initial mandibular implant bridge. The patient reported that their parafunctional habits improved after Botox therapy. Maxillary prosthesis successful bar prosthesis was replaced.
Peñarrocha et al (2001)[25]	Case report	Oromandibular dystonia (with blepharospasm (Brueghel's syndrome))	67	2	3I	2		delayed		5 years	Overdenture - Bar	In the 5 years of follow-up, the patient slowly stabilized their oromandibular dystonic movements, with improved function and aesthetic results. In contrast, the blepharospasm worsened.
Applebaum et al (1997) (26)	Case report	Parkinson's disease	72	2	Dentsply HA coated microvent			2 stage			Overdenture - Bar Hadar clips and ERA	Principally a description of the technique, no apparent follow-up time.
Chu et al (2004)[27]	Case report	Parkinson's disease	83	4	Nobel TiUnite	4		LA/Sed	2 stage	12 months	Overdenture - Magnet	Magnetic keeper loosened, no other issues reported.
Oelgiesser et al (2006) (28)	Case report	Maple Syrup Urine Disease - progressive neurodegenerative disorder	19	1	Micro-Vent Zimmer		1	LA/Sed	2 stage	10 years	Single Tooth	Alternating hypotonia, hypertonia, dystonia and seizures. No problems or signs of mucosal inflammation after 10 years
Kelleher et al (1998)[29]	Case report	Tardive dyskinesia	69	3	Nobel			GA	2 stage	2 years	Overdenture - Bar	Reported trauma to operative site during healing phase, but subsequently no issues.

Table 3 Movement Disorders – Observational Studies – Patient Case Series Implant Placement Data

Study Authors	Number of Patients	Condition/s	Age range (Mean age)	Number of implant fixtures	Implant system	Mandi-bular	Maxillary	GA/LA/Sed	Loading protocol
Ekfeldt (2005)[37]	14	(Orofacial dysfunction) Different disabilities, specifically neurologic disorders causing various orofacial dysfunction problems. Includes 2 with Down syndrome.	19-55 (44)	35	Nobel	8	23	GA	2-stage
Ekfeldt et al (2013)[38]	27	(Orofacial dysfunction) Acquired Neurological Disabilities. Includes 4 with Down syndrome.	19-80 (46)	88	Nobel (TiUnite/ Machined/ Replace/Tap Groovy)	8	20	Stage 1 GA21 LA6 {Stage 2 21/ GA 1/LA}	21 - 2-stage protocol, 5 - single-stage delayed loading, 1 - Immediately loaded
Limeres Posse et al (2016) (35)	25	Down syndrome.	19-60 (34)	73		43 (15 patients)	30 (15 patients)	GA predom	2-stage
Corcuera-Flores et al (2017)[12]	19 (22 control group)	Down syndrome and Cerebral Palsy.		102 (71 cerebral plasy, 31 Down) Control (70 in 22 pat)	Microdent	46 (C39)	56 (C 31)		
López-Jiménez et al (2003)[33]	18	Cerebral Palsy (6 cases), head injuries (3 cases), Down syndrome (4 cases), pyknodysostosis (1 case), Rieger's syndrome (1 case), early-stage senile dementia (3 cases). Not all cases are movement disorders.	12-71 (34.7)	67				GA9 LA/IVSed6 LA/Oral sed 3	2-stage
Durham at al (2006)[36]	6	Intellectual/Cognitive disability due to a variety of conditions (Intellectual disability).		62	Nobel	32	30	GA	2-stage
Oczakir et al (2005)[32]	25 (6 with reported movement disorders)	Medically compromised patients - variety of conditions. Movement Disorders (MD) - 2 with Intellectual/Cognitive disability 5-implants; 1 with Cerebral Palsy 2-implants; 3 with Down syndrome 8-implants. (Intellectual disability, Cerebral Palsy & Down syndrome).	19-89 (56) MD {39-61 (53)}	103 (15 in patients with MD)		13	2	LA and GA	
Heckmann et al (2000)[41]	3	Parkinson's disease	71-81 (76)	9	ITI	9		?	1-stage
Packer et al (2009) (31)	9	Parkinson's disease	54-77 (63)	34 (+4 sleepers)	Astra-Tech	17	11	LA/Sed	2-stage
Packer (2015)[34]	4	Parkinson's disease	54-77 (63)	15 (+1 sleeper) + 3 replacement after 1 year	Astra-Tech				
Cune et al (2009)[5]	61	Severe refractory epilepsy and multiple disabilities (Epilepsy).	(43±15)	134				33 LA/Sed 12 GA	

Table 4 Movement disorders – Observational studies – Patient case series – Implant outcome

Study Authors	Number of Patients	Condition/s	Number of implant fixtures	Post loading follow-up period	Implant failure	Early failure before loading	Late failure after loading	Implant survival in implant movement patients
Ekfeldt (2005)[37]	14	(Orofacial dysfunction)	35	1 to 2 years	5	3	2	81% 2 years
Ekfeldt et al (2013)[38]	27	(Orofacial dysfunction)	88	5 to 10 years	12	3	9	86% cummulative none lost after 6 years
Limeres Posse et al (2016)[35]	25	Down syndrome	73	1 to 10 years (mean 43 months)	17	14	3	77%
Corcuera-Flores et al (2017)[12]	19 (22 control group)	Down syndrome & Cerebral Palsy	102 (71 Cerebral Palsy, 31 Down) (70 Control)	4 years	9			91% (Control 100%)
López-Jiménez et al (2003)[33]	18	Down syndrome, Cerebral Palsy & Dementia	67	3 to 113 months (66.5 mean)	4 (1 replaced)	4		94% (not all movement disorders)
Durham at al (2006)[36]	6	(Intellectual disability)	62	Unclear	4			84.6% MX 100% MN
Oczakir et al (2005)[32]	6 with MD	(Intellectual disability, Cerebral Palsy & Down syndrome)	15 in patients with MD	2-12 years (2-11)	No fixtures lost in the MD patients (3 lost-1 replaced in study)	{3 in study}		100% (97% overall study)
Heckmann et al (2000) (41)	3	Parkinson's disease	9	28, 35 & 42 months				100%
Packer et al (2009)[31]	9	Parkinson's disease	34 (+4 sleepers)	1 year	6	6		82% (85%MX 81%MN)
Packer (2015)[34]	4	Parkinson's disease	15 (+1 sleeper) + 3 replacement after 1 year	8 years	4	3	1	78% (late failure fractured fixture)
Cune et al (2009)[5]	61	(Epilepsy)	134	1-16 years	3			98% after 16 years
								(rounded percentages)

late failures were noted in the Parkinson's disease, Down syndrome and orofacial dysfunction studies[34,35,38]. In some of the larger studies it was difficult to determine whether patients were affected by movement disorders (Table 3), but the majority of those treated will have had an element of either a movement disorder, abnormal oral habits, or a risk of seizure affecting the oral region.

Issues with oral hygiene were reported in many studies (Table 5). There did not appear to be concerns with peri-implantitis or marginal bone loss, although these parameters were largely underreported in the observational studies. Documented prosthesis failures appeared to be limited to fixed bridges and overdentures. In the study reporting the outcome of patients with severe epilepsy and multiple disabilities[5], abutments had been modified to fail in preference to the prosthesis or implant and were easily replaced as screw retention had been employed.

■ Discussion

The key question to be answered was whether implants placed in patients with movement disorders have the same outcome as the general population. Only one study in the patient case series compared the outcome with a control group[12] and reported a 91% implant survival rate after 4 years, whereas the control group had a 100% survival. The control group inclusion criteria ensured that these patients had no medical conditions or oral risk factors. Both groups had been treated at the same faculty, but it was unclear whether the same surgical team placed the implants. In addition, the paper does not report on patient age and whether the groups were age matched. The paper's focus was on marginal bone loss as assessed by panoral radiography, and it was not clear whether the implant failures were post-loading. Nevertheless, these groups were fairly well matched, as attendance at regular review was one of the inclusion criteria, indicating that the groups were similarly committed to the strategy for follow-up and maintenance. Therefore, we can conclude that in an ideal situation; implants placed in patients with movement disorders who regularly attend for review will have favourable outcomes. The authors

Table 5 Movement Disorders – Observational Studies – Patient Case Series – Prosthesis Outcome Data

Study Authors	Number of Patients	Condition/s	Bone Loss/Soft Tissue Complications	Fixed Bridge	Single Tooth	Removable	Prosthesis & attachment complications and comments
Ekfeldt (2005)[37]	14	(Orofacial dysfunction)		6	9		2 implants failed pre-loading in 1 patient with Down syndrome, but prosthesis functional. 2 patients no bruxism, 9 some bruxism, 3 strong bruxism.
Ekfeldt et al (2013)[38]	27	(Orofacial dysfunction)	Perimucositis in 45% of patients 10/22; Of measurable cases 20% Perimplantitis in 20% (3/15); 52% of the measurable fixture no bone loss (27/52).	18	13	1	90% prosthesis survival; 3 bridges replaced due to implant loss; Minor reparable fractures to fixed prostheses. Overdenture fracture. Inadequate retention: 1 treatment failure due to trauma-self harm. OH required help from carers half had perimucositis. 20% patients with peri-implantitis (8% of implants). 2 implants failed pre-loading in 1 patient with Down syndrome, but prosthesis functional, the other 3 Down syndrome patients had no issues reported.
Limeres Posse et al (2016)[35]	25	Down syndrome		(10 patients)	(13 patients)	(2 patients)	1 in 3 patients lost at least 1 implant. Majority lost prior to loading. 17 implants (23.2%) failed in 8 patients (32%). Noted general risks for implant failure periodontitis, osteoporosis immune system dysfunction.

Corcuera-Flores et al (2017)[12]	19 (22 control group)	Down syndrome & Cerebral Palsy	31 Down 29% lost all had MBL. Cerebral Palsy 36% no MBL.	Yes 71.6% (C=21.4%)	Yes 20.6% (C=78.6%)	Yes 7.8% (C=0)	Implant loss higher in the study group compared with (cf) the control group. Study group had higher marginal bone loss (MBL). Significant levels of implant loss and MBL in maxialla (MX) cf mandible (MN). Down patients 31 implants, 29% lost at 4 years. All showed some degree of MBL.
López-Jiménez et al (2003)[33]	18	Down syndrome, Cerebral Palsy & dementia	Noted challenge of oral hygiene and maintenance but no parameters recorded. Did note need for carers involvement and that intermiittent attendance at all follow-up appointments had occured.	Yes	Yes		All cases restored with fixed prostheses. Implant failures in MX of 2 patients with Down syndrome and 1 patient with Rieger's syndrome.
Durham at al (2006)[36]	6	(Intellectual disability)		Yes		Yes	Fractured(#) MN Post stage 1 - altercation; Abutment fractures MN; MX implant failures; MN framework # and abutment # prosthetic-tooth # post altercation.
Oczakir et al (2005)[32]	6 with MD	(Intellectual disability, Cerebral Palsy & Down syndrome)	Oral hygiene issues.			6 with MD	Possible to extract data for patients with potential movement disorders, only issue were OH. All overdentures with bars except 1 ball case.
Heckmann et al (2000)[41]	3	Parkinson's disease	None.			3	Customised telescopic copings used. Slight improvement in weight and reduction in adverse gastrointestinal (GI) symptoms. General deterioration in Parkinson's disease scores.
Packer et al (2009)[31]	9	Parkinson's disease	Oral hygiene problems and 100% hyperplasia under bar 6/6.	3	3	7	Difficulty in removing prosthesis; Bar and clip; two fractured overdentures. Deterioration in natural dentition requiring extractions and MX RPDs. Incomplete elimination of the movement disorder during implant placement may be a factor in early implant failures.
Packer (2015)[34]	4	Parkinson's disease	Hyperplasia and poor oral hygiene.	1	2	3	3 fractured overdentures, bar and clip; Bridge replaced due to natural tooth extraction; Bar fracture; Fixture Fracture; Clip fracture. One patient decoronated crowns of natural teeth against bar. One patient fractured bar then a fixture. 1 patient experienced severe bone loss and fibrous replacement in the opposing maxillary arch managed by rebase then by "spring stabilisation". Evidence of medication induced dystonia. Two bar and clip cases - changed to Locators. Discussed issues of Locator nylon-male attachment wear.
Cune et al (2009)[5]	61	(Epilepsy)		10/45 patients	14/45	2¼5	45 of the 61 patients recalled for follow-up. Fixed prosthesis abutments modified to fail rather than a catastrophic fixture failure. All damaged prostheses were repairable as they were screw retained. Prostheses designed to accommodate patients habits. Ball attachments recommended as easier to maintain. Commonly used antiepileptic drugs have been linked with decreased bone density and fracture risk. No apparent impact on bone levels in this study.

do, however, caution that outcomes for Down syndrome patients may not be as favourable.

At this stage it is pertinent to consider the issue of patients with Down syndrome, as implant outcome varied in the other patient case series studies in this group of patients. Limeres Posse et al reported an implant survival outcome of 77% in 25 subjects[35], whereas 100% outcomes were reported in three cases[32] and 94% in four cases[33]. Ekfeldt et al reported a 86% success rate after 5 years to 10 years[38], which included four patients with Down syndrome. Interestingly, one of these patients lost two implants preloading, but was successfully treated with a fixed prosthesis and followed for 6 years[37,38]. It should also be noted that all the studies, apart from Limeres Posse et al[35], reported on multiple conditions and not all of them can be considered to involve movement disorders; nevertheless they are relevant to the treatment of medically and intellectually compromised groups.

Down syndrome poses several issues to be considered when planning implant placement. Limeres Posse et al[35] discussed how these patients were more at risk of implant failure due to an immune system dysfunction and a higher incidence of osteoporosis. They also considered that the higher incidence of periodontal disease in these patients placed them at a higher risk of implant failure and marginal bone loss than other groups. Nevertheless, it appears from the outcome of the patient case reports and patient case series (Tables 1, 2 and 3) for patients with Down syndrome, that implant failures are more likely to occur before the implants are loaded, indicating a potential that these implants may not integrate, but once integrated we cannot assume that implant survival will be any less favourable than for the general population.

It should also be considered whether patients with Down syndrome should be included in a review of movement disorders? The case for the inclusion of this group of patients is supported by the tongue-thrusting habits and orofacial dyskinesia that have been reported in patients with Down syndrome[6,7]. Faulks et al[7] considered that orofacial dyskinesia may be precipitated or made worse by facial dysmorphology, as well as occlusal instability as a result of tooth loss for these patients. They suggested that restoration of a functional occlusion may reduce the severity of orofacial dyskinesia[7], and as this group of patients is more likely to have missing teeth due to a higher caries and periodontal disease risk[6,7], implant treatment may be considered to aid prosthesis retention. This is especially the case as reduced salivary flow has been noted as one of the dentofacial manifestations of Down syndrome[16], which will compromise the success of conventional prostheses.

Durham et al[36] reported issues with implant loss in a group of patients with intellectual impairment and other disabilities. The study's findings are not transparent, but issues with patient cooperation and behavioural problems, which might compromise implant and prosthesis outcome, should be noted. In the long-term these issues will affect both the maintenance of oral hygiene and prosthesis function. Behavioural problems, either mental or physical, will place a burden on the surgical team, and it is clear from the patient case reports and patient case series that many of the implants were placed under general anaesthesia (Tables 1 and 2). This contrasts with the findings of Smith et al[39], who reported on the outcome of a comparison of healthy and medically compromised patients; 42% of the patients had their implants placed with local anaesthesia (LA) alone and 52% had them placed with LA and sedation. While their patients were medically compromised, none had the conditions under consideration in this review. However, there are issues with anaesthesia with more medically vulnerable patients with conditions where movement disorders are manifest.

Altintas et al[17], citing Yoshikawa et al[30], indicated that patients with Down syndrome posed a risk when undergoing sedation due to low blood oxygen saturation, and that this was associated with sleep apnoea and upper airway obstruction. In patients with Parkinson's disease IV-sedation, midazolam may be beneficial, as this will reduce the risk of the cardiovascular effects of endogenous catecholamines[40]. By contrast, incomplete elimination of the movement disorder was noted in another case series of patients with Parkinson's disease[31], which may have contributed to early implant failures. It is interesting to note that in the case series detailing patients with Parkinson's disease, an 82% success rate was achieved in one study of nine patients[31], while 100% was recorded in another study of three patients[41]. The study of nine patients[31] was followed

up in a review of four of the patients from the original study[34] reporting a late implant failure possibly linked with issues of parafunction that resulted in an implant fracture after 5 years.

Therefore, it may be wise to place an additional central "sleeper" implant when providing two mandibular implants to stabilise a mandibular overdenture[31]. When planning implant-retained fixed bridges, it may be sensible to place as many implants as practical, so that patients can still be successfully restored. Due consideration should be made not to compromise maintenance by providing insufficient space for cleaning. Placement of a "sleeper implant" may avoid the need for additional surgical procedures in these medically compromised patients[31].

Parafunction and risk of implant failure due to bruxism may also affect long-term survival of implants. However, Cune et al[5] reported a 98% success rate after 16 years in patients with severe refractory epilepsy and multiple disabilities. It was surprising that only one observational study in patients with epilepsy was identified, although in many reviews[8,11,42] epilepsy is cited as a risk factor. Karolyhazy et al[4] concluded that patients with epilepsy have a greater risk of losing their teeth, as well as suffering seizure-related injuries to any prostheses used to restore the dentition. However, they felt that the majority of patients suffering from epilepsy should be managed prosthodontically in the same manner as any other patient, but that patients suffering from frequent generalised tonic-clonic seizures should be carefully managed to avoid seizure-related complications. The restorative strategy proposed by Cune et al[5] should be adopted, where components are modified to preferentially fail, to avoid catastrophic damage to key elements of the restorations, e.g. the abutments were modified preferentially fracture to avoid damage to the implants.

Detailed reporting of soft tissue parameters, such as pocket depths and bleeding on probing, are limited in both the patient case reports (Table 2) and the patient case series (Table 5). This is understandable in this group of patients where precision measurements may be challenging due to the movement disorder and the fact that there are behavioural management issues in some of the patient groups. Nevertheless, issues with oral hygiene are widely reported and these have been discussed and addressed by patient and carer education and, in many cases, regular recall and support[12,15]. Ideally, such support should be provided in a primary care environment, but access and engagement have been identified as challenges for implant maintenance in this group of patients[12,34]. There is a recognised association between peri-implant disease, implant failure and active periodontal disease[43,44]. In view of the possible association between both Down syndrome[35] and Parkinson's disease[45,46] with periodontal disease, this should be taken into consideration when planning long-term maintenance for these patients, but should not be seen as a contraindication for treatment in this vulnerable group of patients.

The patient case reports and patient case studies reported on single tooth restorations, complete and partial fixed bridges and implant-retained overdentures (Tables 2 and 5). The predominant restorations in the younger age groups were fixed and in the older Parkinson's disease patients, removable. While early studies utilised bar-retained overdentures, rather than magnets or bars, later studies tended to use the Locator attachment. This is undoubtedly because the Locator attachment has become more popular since its introduction in 2001[47], and gradually more widespread use during that decade. The studies reported a remarkably low incidence of complications and maintenance requirements for the fixed restorations (Tables 2 and 4), which contrasts with the findings of implant studies in patients without reported movement disorders provided with overdentures[48], single tooth restorations[49] and fixed bridges[50]. This may reflect the focus of these studies, in contrast, Durham et al[36] painted a very different picture of patients with an intellectual disability, with damage to fixed prostheses as a result of behavioural issues. Ekfeldt at al[38] reported minor reparable fractures to fixed prostheses. In contrast, studies reported more maintenance requirements for those patients treated with implant-retained overdentures. Packer et al[31] reported prosthesis fractures, clip retainer fractures and bar fractures in the initial study group and the smaller group of patients with Parkinson's disease followed for up to 8 years[34]. This level of maintenance in overdenture patients is not unusual in patients who are not medically compromised[51-53]. The recommendation that a cobalt chromium insert is incorporated into the prosthesis[13] appears to be

common practice in many of the patient case reports and patient case series (Tables 1 and 5). Only one of the patient case series reports on issues with poor oral hygiene and soft tissue inflammation and mucosal enlargement beneath and around the bar attachments[31], whereas this appears to be a common finding in studies of long-term outcomes with overdentures[52,54-56]. Cune et al's[5] use of ball attachments as opposed to bars may have reduced the likelihood of gingival enlargement in patients with epilepsy; this was in spite of the risk of medication-induced gingival enlargement. They also reported that this group required regular oral hygiene support from professionals and from patients' carers. The popularity of Locator abutments in more recent times will also have a similar benefit for soft tissue maintenance, as these are a similar simple design.

It is interesting to note that issues with the attachments were relatively under-reported. The patient case studies reported the need to change magnet attachments[13] and Teflon inserts[22] and replace fractured clip attachments in the patient case series[31,34]. This contradicts the findings of a systematic review of maintenance requirements for the attachments of implant-supported overdentures by Cehreli et al[57]. In addition, many more maintenance episodes were reported in several studies[51,52,58-61]. It should also be noted that patients with Parkinson's disease required frequent replacement of the Locator nylon-male-attachment/insert[34], which is supported by findings in patients with no medical complications[61]. This also reflects the laboratory study of Stergiou et al[62], where Locator male attachment retention rapidly reduced during 3 months simulated wear. Patients struggled to insert the denture with the more retentive nylon-male-attachments, but the less retentive attachments rapidly became ineffective[34]. Non-parallel nylon male attachments had been used, because the author had experienced food packing into the recess of the Locator abutment head in patients with Parkinson's disease. This was a consequence of the patient being unable to cope with more retentive conventional attachments and the lighter attachments had become ineffective. Food-packing into the abutment head occurred when the denture displaced in function. This lack of reporting of Locator nylon male attachment replacement in other reports and studies may reflect the fact that they are easy to replace; we can speculate that this may be seen as part of the routine denture care by patients and carers and not seen as a complication.

It must be said that notwithstanding the potential damage to both fixed and removable prostheses, the outcome of the patient case reports and patient case studies (Tables 2 and 5) present a favourable outcome. This is despite the obvious risk of parafunction due to dystonic clenching and the observation that bruxism is prevalent in patients with orofacial dysfunction[37,38] or Parkinson's disease[34]. It should be noted that in the Parkinson's disease group, rapid resorption of the anterior maxillary alveolus, fracture of teeth against the overdenture bar, fracture of a bar and then an implant fracture was reported[34] (although it should be noted that implant design for the system used has subsequently changed to feature narrower internal abutment screws).

Nevertheless, this points to a potential risk of damage to any implant with a movement disorder over time, which was not necessarily seen in the short-term reports (Table 2). Goldstein[63] considered that bruxism and movement disorders are intimately related and that bruxism should be considered as a movement disorder. Lobbezoo et al[64] concluded, however, that there was insufficient evidence to support the idea that bruxism leads to implant failure. Naert et al[65] were unable to attribute overloading an implant as a risk factor in the absence of gingival inflammation, but occlusal interferences increased bone resorption in the presence of plaque induced inflammation. This is more worrying for the long-term outcome in patients with movement disorders, as low levels of plaque and gingival inflammation are very difficult to achieve without frequent recall and support of carers in maintaining oral health[12,15].

Abnormal mandibular and facial movements are potential causes of soft tissue trauma against implant components. Visser et al[66] reported on a patient with dementia who was no longer able to wear their mandibular overdenture and, as a result, the lower lip had pressed against the ball abutment and punctured a hole in the mucosal tissues of the lower lip. Removal of the abutments had solved the problem, as the patient was no longer capable of wearing their prostheses due to their level of debilitation. The author experienced a similar problem with a patient with Parkinson's disease, where contraction of the

lower lip onto a Locator abutment had punctured a similar hole into the mucosa of the lower lip. This was compounded by their inability to cope with higher retention nylon male attachments and the rapid wear of the lighter retentive nylon male attachment had resulted in the patient abandoning the lower denture. This was made worse as the patient wore their upper denture at night, and this pressed down on the lower lip. Replacing the abutment with the shortest possible Locator abutment and instructing the patient to leave their maxillary denture out at night finally resolved the situation.

Rehabilitation with implants may present considerable challenges for patients and clinicians when patients become more dependant[66], and should prompt clinicians to consider simpler restorative solutions that are easier for carers and clinicians to maintain when patients reach the extremes of life or suffer from degenerative movement disorders, e.g. Parkinson's disease.

Poorly fitting dentures have been proposed as a precipitating factor for oral dyskinesia in elderly patients[1]. Myers et al indicated that the severity of tardive dyskinesia might be increased following tooth loss[67]. In addition, it has been proposed that oromandibular dystonia can be instigated by dental treatment[2]. In contrast, dental treatment can offer relief for these symptoms and restoration of the occlusion may reduce the incidence of oral dyskinesia in patients with Down syndrome[7]. Chung et al[23] reported task-specific oromandibular dystonia being precipitated by the placement of dental implants and Shek et al[21]reported a patient where involuntary mandibular movements were triggered by dental extractions and subsequent implant provision. It does appear that a number of the implants and the original fixed bridge failed, which was then replaced by a Locator abutment-retained overdenture. Sibley[24] reported a patient where oromandibular dystonia was precipitated by the provision of an implant overdenture that subsequently failed, but where some reduction of the dystonia was achieved subsequent to provision of more implants and a Locator abutment-retained overdenture, the oromandibular dystonia was reduced with botulinum toxin. Botulinum toxin may help to reduce dystonias, but evidence is currently sparse[68,69]. Whether the precipitation of oral dyskinesia and oromandibular dystonia should be seen as a rare risk factor in the treatment of any elderly individual is debatable, as we cannot exclude these as coincidental findings that would have developed whether or not this treatment had been provided, as there is contrary evidence to support the reduction in oral dyskinesia after treatment.

One should not neglect the potential risk factor posed by the multiple medications this group of patients may be taking. We know very little about their effect upon bone metabolism and the consequences for osseointegration and long-term implant survival. Serotonin uptake inhibitors have been identified as a potential risk of implant failure[70], but the results are equivocal, with one retrospective cohort study concluding there was a risk[71] and another retrospective cohort study concluding there was no risk[72]. This does not mean we should ignore the influence of medication upon bone metabolism, rather that we should be vigilant and aware of research in this field.

Table 6 lists the main conclusions from the patient case series studies. Similar themes are identified:

- A need for support to maintain oral hygiene, especially by carers who themselves need to be encouraged and supported.
- Rehabilitation will improve aesthetics, masticatory ability and quality of life in relation to chewing function and satisfaction with their prostheses.
- There should be an expectation that maintenance will include repairing and replacing the prostheses.
- There may be a higher incidence of implant loss, especially in patients with Down syndrome. Marginal bone loss may be greater in patients with neuropsychiatric disorders than patients without these conditions;
- Parafunction may lead to damage due to overloading and wear of the prostheses in patients with Parkinson's disease.

While the quality of the movement disorder publications could be criticised regarding study design and the over-reliance on expert opinion and patient case reports, it must be acknowledged that this is an extremely challenging group of patients to treat and maintain. Clinicians must rely heavily on other members of the dental team, as well as professional carers and family carers. The conditions suffered by

Table 6 Movement Disorders – Observational Studies – Patient Case Series Findings.

Study Authors	Condition/s	Conclusions
Ekfeldt (2005)[37]	(Orofacial dysfunction)	Strict adherence to a surgical protocol is needed for the management of patients with neurological disabilities. It is important to inform the patient's caregiver about maintenance of good oral hygiene and the increased risk of complications caused by finger or oral habits.
Ekfeldt et al (2013)[38]	(Orofacial dysfunction)	Patients with different neurological disabilities present more problems during implant treatment and maintenance compared with healthy patients. Nevertheless, it was possible to carry out treatment, and outcomes were relatively favourable.
Limeres Posse et al (2016)[35]	Down syndrome	The success rate for dental implants in individuals with Down syndorme is lower than that observed in the general population.
Corcuera-Flores et al (2017)[12]	Down syndrome & Cerebral Palsy	Marginal Bone Loss (MBL) and loss of implants after 4 years is higher in patients with neuropsychiatric disorders than in patients without systemic pathologies. Patients with Down syndrome are the only patients to lose implants, and these patients had a higher MBL than patients with Cerebral Palsy.
López-Jiménez et al (2003)[33]	Down syndrome, Cerebral Palsy & dementia	In all cases aesthetic rehabilitation and improved masticatory function was achieved. In the clinical cases involving implant failure, rehabilitation proved possible in all patients.
Durham at al (2006)[36]	(Intellectual disability)	Osseointegration appears to be as successful as in the general population. Although fixed prostheses were successful in both arches, the complexity of fixed prostheses suggests that simplified designs with anteriorly placed fixtures, such as overdenture designs, are most favourable in this patient population. A patient's aggressive social behaviour, seizure activity or parafunctional habits that increase the risk of oral trauma and prosthetic stress, also influence prosthetic design. Caregivers must be knowledgeable about the patients' oral prostheses and the importance of thorough oral hygiene practices. Complications with general anesthesia or sedation procedures may be contraindications for implant reconstruction. Provided there is an absence of systemic health risks or poorly controlled behavioural disorders, patients with mild to moderate cognitive impairment appear to have the most favourable prognosis with construction and maintenance of implant prostheses.
Oczakir et al (2005)[32]	(Intellectual disability, Cerebral Palsy & Down syndrome)	Recommend a strict maintenance care programme provided by the caregivers and to a high compliance of the patients who participated in this programme to perform good oral hygiene.
Heckmann et al (2000)[41]	Parkinson's disease	Improved chewing capacity, a moderate gain in body weight and an improved gastrointestinal smptoms GI score as signs of improved predigestion were observed. Using a non-rigid (resilient) telescopic system for overdenture anchorage, the patients had no problems with the handling and maintenance of the prostheses and the implants.
Packer et al (2009)[31]	Parkinson's disease	The quality of life of people with Parkinson's diseases (PD) in the study was improved by the use of dental implants to stabilise an overdenture or to support a fixed prosthesis, in the domains of satisfaction with the prosthesis, eating, and oral well-being. Implant retained/supported prostheses should be considered as a first line of treatment for people with PD to mitigate future denture problems as their PD progresses.
Packer (2015)[34]	Parkinson's disease	Complications as a result of an inability to maintain adequate levels of oral health as well as overloading from mandibular parafunction must be expected. An unexpected high level of alveolar resorption or fibrous replacement of the alveolar ridge may be seen where a dentate arch opposes an edentulous arch as a result of overload due to dystonic-induced clenching. In certain circumstances dental implants will play a role in our patient management. However, high levels of maintenance with its attendant costs should be expected in patients with Parkinson's disease in the form of prosthesis failure, retentive component failure and implant failure.
Cune et al (2009)[5]	(Epilepsy)	Dental implant treatment in a population of patients with severe epilepsy and additional disabilities seems to be a viable treatment option. Implant loss is rare. Although adequate plaque control was not feasible in all patients, marginal bone levels remained stable.

these patients are not homogenous and we should be careful to avoid generalisations, however there are common themes of oral health and prosthesis maintenance that should be taken into consideration when planning treatment for patients with movement disorders. This will also affect health economic considerations for these patients as they are least likely to be above to fund their own treatment and will inevitably have to rely upon government funding. Funding is by no means universal[73], even in the same country, and in the UK this even prompted the use of titanium fixation screws to stabilise complete dentures in a patient with Parkinson's disease[74].

Conclusions

Implant survival in patients may be less than expected in patients with movement disorders, but the evidence points to early rather than late failures. Placement of additional implants if space allows may be wise to avoid repeated surgical intervention.

Reported maintenance requirements were low for fixed restorations, but higher for patients treated with overdentures.

Oral hygiene control was widely reported as an issue, but there is insufficient evidence to imply that a lack of oral care will cause more rapid deterioration in patients with movement disorders than in patients without movement disorders. Nevertheless, the consequence to the quality of life for these patients following the loss of a beneficial restoration should not be underestimated. It is therefore essential that these patients be provided with professional support for their oral care, which must also include education and support for their carers.

Straightforward designs that lend themselves to easier long-term maintenance should be adopted. In addition, it may be prudent to consider the modification of more easily repaired components such as abutments, which in the event of trauma strategically fail, rather than the actual implants.

The provision of implant-supported prostheses improves chewing and quality of life in patients with movement disorders and should be considered as an option in the treatment planning for tooth loss in this group of patients.

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Patients' expectations of oral implants: a systematic review

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Key words *dental implants, patients' expectations, systematic review*

Aim: Nowadays, oral implants are a leading concept in oral rehabilitation. Patient satisfaction with this treatment is high, but are the expectations of the patients met? The aim of this review was to systematically screen the literature on patients' expectations of implant-based therapy before treatment and to assess whether these expectations were being met.

Materials and methods: A search strategy was developed for manuscripts dealing with patients' expectations of implant-based therapy to support different types of prosthodontics. Patients had an indication for implants, were seeking implants or had received implants. PubMed/MEDLINE, Ovid/EMBASE and Cochrane/CENTRAL were searched to identify eligible studies. Two reviewers independently assessed the articles.

Results: In total, 16 out of 3312 studies assessing patients' expectations of patients before implant-based therapy matched the inclusion criteria. A variety of methods were used in the studies. Patients had high expectations, with function followed by aesthetics being the most important expected improvements. Women had higher expectations than men. Costs were a major factor against implant-based therapy. The expectations that implants will last a lifetime and require no special needs of oral hygiene were of concern.

Conclusion: Prior to treatment, patients have high expectations of implant therapy. In general, these expectations are met. Most studies revealed that women have higher expectations than men. The variety of applied study designs impaired comparability of results. Thus, standardised methods for measuring expectations of implant-based therapy are eagerly needed.

■ Introduction

Today, implant-supported prosthodontics is a major treatment concept in oral rehabilitation. A variety of implant-borne dental prosthetic designs are currently available, commonly resulting in an improved chewing ability and, high patient satisfaction, also on the long run[1-5]. Perceived final satisfaction is higher when the treatment outcome meets baseline expectations and perceptions[6].

Disagreements between patients and health care providers are often due to a misunderstanding of what can be or what is to be expected. Expectations of satisfactory outcomes with implant-based oral rehabilitation are presumed to depend on, among others, awareness, patient information, personality traits, previous experiences, implant position and the type of dental prosthetisis[7]. Personality traits, e.g. neuroticism, may have a negative effect on patient satisfaction[8-12].

Expectations are defined as beliefs about future consequences that may contribute to the individual's psychological and physiological change. As such, health expectations are a cyclical and longitudinal

Table 1 Search strategy.

Search strategy		
#1	Dental implants	„Dental Implants"[Mesh] OR „Dental Prosthesis, Implant-Supported"[Mesh] OR „Denture, Overlay"[Mesh] OR overdentur*[tiab] OR „implant-support*" OR implant-retain*[tiab] OR dental implant*[tiab]
#2	Expectations/ personality	„Personality"[Mesh] OR „Health Knowledge, Attitudes, Practice"[Mesh] OR „Patient Satisfaction"[Mesh] OR „Quality of Life"[Mesh] OR percept*[tiab] OR demand*[tiab] OR perspect*[tiab] OR personal*[tiab] OR expectat*[tiab] OR expectan*[tiab] OR expect[tiab] OR expected[tiab] OR expecting[tiab] OR quality of life[tiab] OR qol[tiab] OR hrqol[tiab] OR satisf*[tiab] OR attitud*[tiab] OR patient knowledge[tiab] OR belief*[tiab] OR comfort*[tiab]
#3	Study type	„Epidemiologic Studies"[Mesh] OR „Controlled Clinical Trial"[Publication Type] OR „Surveys and Questionnaires"[Mesh] OR prospective[tiab] OR longitudinal[tiab] OR follow-up[tiab] OR cohort[tiab] OR random*[tiab] OR questionnair*[tiab] OR measur*[tiab] OR assess*[tiab] OR survey*[tiab] OR scale*[tiab]) NOT „Review"[Publication Type] NOT („Animals"[Mesh] NOT „Humans"[Mesh]
Search #1 AND #2 AND #3		

process, including a precipitating phenomenon, a prior understanding, cognitive processing, expectancy formulation, outcome and post-outcome cognitive processing[13]. The term "expectations" is used next to terms such as "preferences", "knowledge", "perceptions", "acceptance", "needs" and "demands".

The systematic review of Yao et al[14] on patients' expectations of treatments using implants concluded that the measurement instruments used to assess expectations are diverse and not validated. Since that review, a growing number of studies on patients' expectations have been published. Yao et al assessed expectations, both before and after oral rehabilitation by means of implants, increasing the risk of a biased result. Moreover, patient samples selected from the general population were included. This will result in an inclusion bias, since patients searching for implant treatment are better informed than the general public[15]. To also reduce the influence of any bias as to including more recent studies on patient expectations (published up to September 1 2017), we aimed to review the literature concerning patients' expectations of implant-based therapy recorded before implants were placed, as well as to assess whether these expectations were met.

Materials and methods

Search strategy

A thorough search of the literature in three online databases (Pubmed/MEDLINE, Ovid/EMBASE and Cochrane/CENTRAL) was conducted (last search September 1 2017). The search was supplemented by hand searching (checking references of the relevant review articles and eligible studies for useful publications). The strategy applied for PubMed is depicted in Table 1. For Embase and Cochrane the same strategy was used. The search strategy was a combination of MeSH terms and free text words. Since patients' expectations represent a rather new area in dental research, no suitable MeSH term was available. No language restriction was applied. Checking references of the relevant review articles and eligible studies completed the search.

Selection criteria

The studies had to meet the following inclusion criteria:

- Type of participants: patients with (possible) indication for implants (missing teeth, edentulous patients), patients seeking implant-based therapy (either by referral or self-administered) or who received implants to carry a dental prosthesis.

Patients should not have previously been treated with implants;
- Type of (proposed, planned or executed) intervention: insertion of implants to support overdentures (IOD), fixed full-arch complete dentures (FFD), fixed partial dentures (FPD) or single crowns (SC);
- Type of data collection: semi-structured interviews, questionnaires and visual analogue scale (VAS)-scores on expectations before treatment was all eligible, measured before, or before and after treatment;

Exclusion criteria:

- Studies not about patients' expectations;
- Studies performed in a general population;
- Studies including patients who had previously been treated with implants;
- Studies only measuring expectations after treatment;
- Retrospective studies.

One reviewer (AK) carried out initial screening of the titles and abstracts, based on the above criteria. Full-text documents were obtained for all articles that met the inclusion criteria. Two reviewers (AK, GR) performed the full-text analysis. Disagreements were resolved through a discussion between the reviewers.

Results

Study selection

The results for the primary search for the period until 1 September 2017, was 1981 hits for the PubMed search, 2201 hits for the Embase search and 303 hits for the Cochrane search. One study was selected by hand search (Fig 1). Using this strategy, 4486 papers were initially identified, of which 1174 articles appeared to be duplicates. After scanning titles and abstracts, a further 3270 papers were excluded because they did not meet the inclusion criteria. One recent study had a small percentage of patients with previously inserted implants[15]. These authors supplied their raw data and the patients who had received implant treatment beforehand were excluded for our analysis.

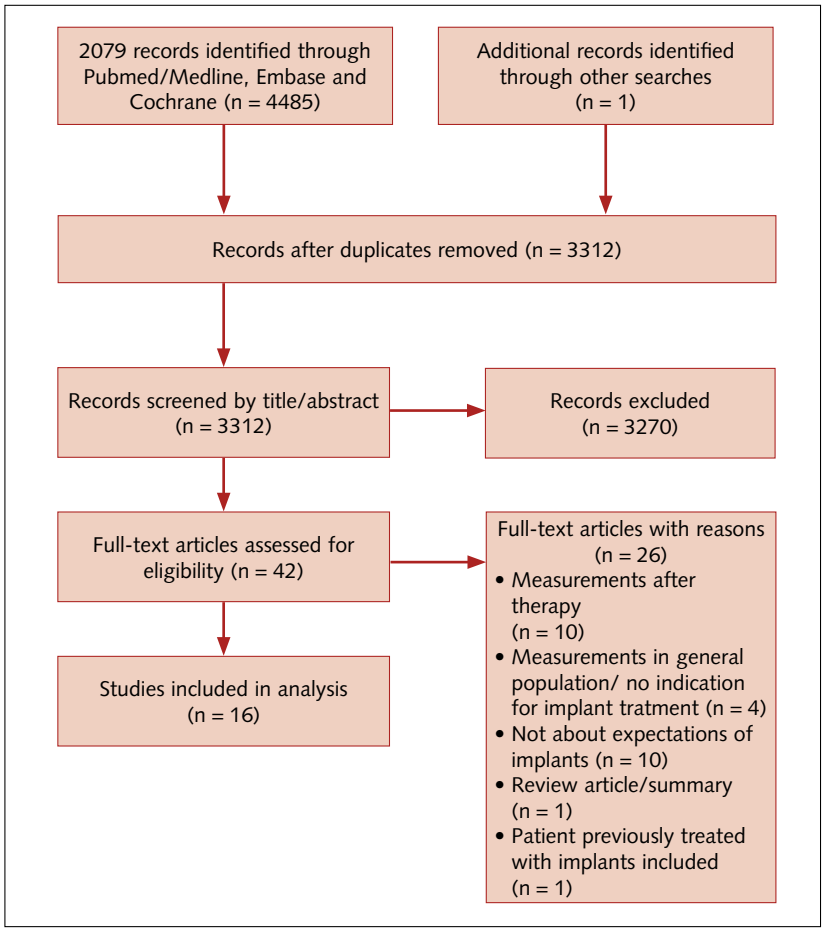

Fig 1 Flow chart showing the results of searches and study selection.

In total, 16 studies were included for review[7,16-30]. Data are summarised in Table 2. Sample sizes varied from between 18 and 300 patients. Different study designs were used for measuring patient expectations on oral rehabilitation by means of implant therapy. One study was a qualitative study using semi-structured interviews[30]. Six studies used visual analogue scales (VAS) on expectations before and satisfaction after oral rehabilitation by implants to assess whether expectations were met[7,19-21,23,26]. Nine studies used different questionnaires[16-18,22,24,25,27-29].

The following parameters of expectation were analysed: outcome improvements (aesthetics and function), speech, oral hygiene maintenance, costs and longevity of the implants (survival time). Some studies separately mentioned expectations and reasons or motivations for choosing implant treatment; some studies merely mentioned one of these.

Table 2 Characteristics of included articles in this systematic review.

Trial number	First author	Year	Country	Sample size	Sample character	Design	Method	Not previously treated with dental implants?	(Planned) prosthetic design on implants
	Al-Dwairi	2013	Jordan	300	150 patients with complete denture, 150 patients with partial removable or fixed denture with prosthetic demands	Before	QT: questionnaire	NS	IOD, FFD, FDP
	Allen	1999	United Kingdom	27	27 patients receiving implants and implant-borne full prosthesis, control group 34 patients receiving new complete dentures	Before	QT: questionnaire	No	IOD
	Baracat	2011	Brasil	50	Patients seeking implants and patients receiving implants	Before and after	QT: VAS	NS	IOD, FFD, FDP, SC
	de Cunha	2015	Brasil	28	Patients receiving implants and full-arch fixed prosthesis	Before and after	QT: VAS	NS	FFD
	de Lima	2012	Brasil	52	Patients reveiving implants	Before and after	QT: VAS	NS	FPD, SC
	Heydecke	2008	Canada	160	Patients seeking prothetic treatment received either new complete denture or implant-borne denture	Before and after	QT: VAS	No	IOD
	Hof	2014	Austria	150	Patients seeking implants	Before	QT: questionnaire	NS	IOD, FFD, FDP, SC
	Jensen	2016	Netherlands	30	Patients receiving implants and implant-supported removale partial denture	Before and after	QT: VAS	No	ISRPD
	Leles	2009	Brasil	165	Partially dentate patients with prosthetic treatment need	Before	QT: questionnaire	NS	FPD
	Leles	2011	Brasil	112	Edentulous patients in clinic with prosthetic treatment need	before	QT: questionnaire	No	IOD, FFD
	Menassa	2016	Canada	18	Patients receiving implants, complete full implant-borne dentures, immediate loading	Before and after	QT: VAS	No	IOD
	Rustemeijer	2007	Germany	315	Patients seeking implants	Before	QT: questionnaire	No	IOD, FFD, FPD, SC
	Simensen	2015	Norway	117	Patient seeking implants	Before	QT: questionnaire	NS	FPD, SC
	Walton	2005	Canada	101	Edentulous patients offered free implant treatment	Before	QT: questionnaires	No	IOD
	Wang	2015	China	28	Patients with at least one missing tooth	Before	QL: semi-structured interview	No	NS
	Yao	2017	China	277	Patients seeking implants with at least one missing tooth	Before	QT: questionnaire	Yes: 14 out of 277 were excluded	NS

QT = quantitative; QL = qualitative; VAS: visual analogue scale; NS = not specified; IOD = Implant overdenture; FFD = fixed full-arch denture; FDP = fixed partial denture; SC = single crown; ISRPD = implant-supported removable partial denture

Analysis

Quantitative studies using VAS

In six studies, VAS-scores were used to report outcomes before and after treatment[7,19-21,23,26]. Several outcome variables were used in these studies, such as aesthetics, function, comfort and phonetics (Table 3). In the majority of studies, no statistical difference was found between pre-treatment expectations and actual post-treatment satisfaction[7,21,23,25], meaning that patients' expectations were met. However, in the study by Baracat et al[19] the post-treatment scores exceeded the expectation scores, mainly due to low expectation scores. In contrast, the study by de Lima[20] showed a tendency towards higher expectation scores and lower satisfaction scores, which was only significant for the aesthetic scores for patients with FPD. Correlation between expectations and satisfaction was mentioned and significant in four out of six studies, meaning the more expected from the benefits of implant treatment, the higher the actual benefits were, suggesting that expectation influences satisfaction[17,19-21]. Studies by Jensen et al[23] and Menassa et al[27] did not report on correlations.

Two out of five studies mentioned a difference between genders, with women having higher expectations than men[7,20]. One study did not observe this difference[19]. The other three studies did not report on this issue[21,23,25].

Qualitative study and quantitative studies using questionnaires

One study used a semi-structured interview to understand participants' expectations regarding implant-based therapy[30]. A variety of questionnaires was used to measure expectation of and attitudes towards this therapy in nine studies[16-18,22,24,25,27-29]. Also, a variety of parameters to rate expectations or motivations to choose implant-based therapy were used (Table 4).

Function

Improved function was mentioned as the main reason for choosing implants in the studies of Al-Dwairi et al[17], Simensen et al[28] and Walton et al[29], while major improvements in oral function were expected in the studies of Yao et al[16] and Allen et al[18]. Leles et al[24] mentioned the desire for a fixed prosthesis being an important motivation for choosing implants.

Aesthetics

Aesthetics was rated as the most important reason for choosing implants by 32% of the participants in the study of Al-Dwairi et al[17]. This was slightly lower in the study of Simensen et al (19.5%)[28]. In the latter study aesthetic outcome was rated as very important or important by 86.1% of the participants. Rustemeyer et al[27] reported that 68% of the women vs 41% of the man rated aesthetics as very important. Yao et al[16], Allen et al[18] and Wang et al[30] found that the majority of patients expected a better appearance after implant-based treatment. In general, patients rated aesthetics as important, but secondary to function. However, patients did expect a better aesthetic outcome after treatment.

Costs

In the study of Al-Dwairi et al[17], 61% of the patients were not aware of the high costs involved. Hof et al[22] found that 67% of patients would accept the additional costs associated with computed tomography, software-based treatment planning and guided implant placement to avoid bone graft surgery. Students were significantly less motivated to spend additional money. Leles et al[24,25] noted that high costs were the most important reason to decline rehabilitation by means of implant treatment. Patients who did choose implants instead of conventional prosthodontics declared that costs were more relevant compared to patients that choose conventional prosthodontics. Costs were also of major concern in the study by Wang et al[30]. In contrast, costs were not decisive or a critical factor for 57.4% of the correspondents in the study of Simensen et al[28].

Table 3 Outcomes of quantitative studies on patients' expectations of implant treatment.

First author	Measuring method	Prosthetic design on implants	Main conclusion	Expectations vs. general satisfaction	Function (not specified)	Aesthetics
Baracat	VAS	IOD, FFD, FDP, SC	Patients' satisfaction exceeded expectations	NS	Posttreatment > pre-treatment	Posttreatment > pre-treatment
de Cunha	VAS	FFD	Expectations were met	NS	No difference pre- and post-treatment	No difference pre- and post-treatment
de Lima	VAS	FPD, SC	Not all expectations met, patients' evaluation of clinician conduct important factor	NS	No difference pre- and post-treatment	No difference pre- and post-treatment, except for patients with FPDs: post-treatment < pre-treatment
Heydecke	VAS	IOD	Patients' expectations of satisfaction were largely met	No difference pre- and post-treatment	NS	NS
Jensen	VAS	ISRPD	Expectations were met	No difference pre- and post-treatment	NS	NS
Menassa	VAS	IOD	Expectations were met	NS	NS	No difference pre- and post-treatment after 2 weeks, 1 and 4 months

VAS = visual analogue scale; NS = not specified; IOD = Implant overdenture; FFD = fixed full-arch denture; FDP = fixed partial denture; SC = single crown; ISRPD = implant-supported removable partial denture

Hygiene maintenance

Most patients believed that implants would require the same level of hygiene as natural teeth[17,27,28]. By contrast, in the study of Yao et al[16] 65.3% disagreed with the statement that implants require less care than natural teeth, while 31.8% agreed.

Longevity

Expectations on longevity of oral endosseous implants varied among the different studies. In the study of Al-Dwairi et al[17], most patients were not aware how long an implant would last, but only 15% of the participants thought implants would last a lifetime. In contrast, in the studies of Hof et al[22] and Simensen et al[28] most patients expected the implants to last the rest of their lives. With their semi-structured interview, Wang et al[30] found that some patients overestimated the potential longevity of implants. The study by Rustemeijer et al[27] showed that most patients expected the implants to last between 11 and 20 years. Longevity was mentioned as an important factor in choosing implants for the treatment[25]. In the study of Yao et al[16], 62.7% of the patients disagreed with the statement that implants last longer than natural teeth, while 31.4% of the patients agreed.

Age-related differences

A lower age was associated with more likelihood of choosing implant therapy in the studies of Leles et al[24] and Walton et al[29] Simensen et al[28] found that younger patients rated aesthetics as more important than older patients, whereas older patients favoured chewing and function. In line with this observation, Yao et al[16] found that younger patients had more realistic perceptions of implant-based therapy and lower outcome expectations.

Chewing/mastication	Comfort	Phonetics/speech	Cleaning	Impact on social life	Gender difference	Correlation expectations/ post-treatment ratings	Educational level difference
NS	NS	NS	NS	NS	No	Yes	No
No difference pre- and post-treatment	No difference pre- and post-treatment	No difference pre- and post-treatment	NS	NS	Yes: on expectation scores of esthetics, phonetics, comfort: female > male	Yes, for aesthetics	No
No difference pre- and post-treatment	No difference pre- and post-treatment	No difference pre- and post-treatment	NS	NS	Yes, on expectation scores of esthetics in patients with SCs: female > male	Yes, for phonetics and comfort in patients with SC's	NS
NS	NS	NS	NS	NS	NS	Yes, only in group of patients between 35-65 years old	NS
NS	NS	NS	NS	NS	NS		NS
No difference pre- and post-treatment after 2 weeks, 1 and 4 months	No difference pre- and post-treatment after 2 weeks, 1 and 4 months	No difference pre- and post-treatment after 2 weeks 1 and 4 months	No difference pre- and post-treatment after 2 weeks, 1 and 4 months	No difference pre- and post-treatment after 2 weeks, 1 and 4 months	NS	NS	NS

Motivations to decline implant provision

Major reasons for declining implant treatment were the high cost, the need for surgery, and fear of pain[17,24,25,29,30]. Other variables that predicted the rejection of implant-based therapy were the desire for removability, the complexity of the treatment and the long treatment time[24].

■ Discussion

A variety of methods have been used in studies to assess patients' expectations of oral rehabilitation by means of implants. Notwithstanding the variety of methods applied, patient' expectations of implant-based therapy were high. Commonly, major improvements in function are expected from implant-based therapy, followed by aesthetic improvement. Although these expectations are high, most studies report that expectations were met. It is with some concern that it is noted that many patients perceive that implants will last a lifetime and require no special oral hygiene requirements.

In the literature, very few studies are available on patients' expectations of implant-based therapy prior to treatment. In this systematic review 16 articles were included, with a variety of methodologies used. Only six studies compared expectations before implant-based therapy, as well as satisfaction after therapy. These studies used VAS-scores on different aspects of expectations, prohibiting the use of a meta-analysis on this subject.

Patient expectations of treatment outcomes are generally high. These high expectations are not unrealistic, since most studies show that their expectations can be met. Improvements in function and aesthetics were the most common expectations. Patients who had lost their anterior teeth have higher expectations of improving aesthetics than patients

Table 4 Outcomes of qualitative studies on patients' expectations of implant treatment.

	Prosthetic treatment	General outcome	Aesthetics	Function	Speech	Psychological welfare/health-related quality of life/social
Al-Dwairi	IOD, FFD, FDP	Majority of patients aware of dental implant therapy as treatment option, however, low level of information	32% of participants preferred implants because of esthetics	56% of participants preferred implants for functional reasons	NS	NS
Allen	IOD	High expectations of dental implant treatment compared to current prosthesis	Patients expect better appearance of IOD	Major improvement expected in oral function	Major improvement expected in ability to speak	NS
Hof	IOD, FFD, FDP, SC	Predictability of treatment success was ranked in 59% as first priority to have dental implants, avoidance of removable dentures second (30%).	NS	NS	NS	NS
Leles 2009	FPD	Choosing dental implants: desire for individualised teeth and fixed prosthesis. Cost, desire for removability, complexity, time of treatment and risk of problems during surgery procedures: refusing implants. Higher educational level and lower age were associated with choosing dental implant treatment	NS	NS	NS	NS
Leles 2011	IOD, FFD	Fixed and removable implant-borne dentures were preferred for the mandible	NS	NS	NS	NS
Rustemeijer	IOD, FFD, FPD, SC	Expectations are in high contrast with willingness to make additional payments	Women and men sign difference, 68% vs. 41% very important	84% women, 74% of men functionality most important (ns)	NS	NS
Simensen	FPD, SC	Improved chewing/function and improved appearance rated very important by 96.5% and 86.1% patients respectively	19.5% most important	46.0% most important, combination aesthetics and function 18.6%	NS	NS
Walton	IOD	Poor chewing function, poor speech, pain, dissatisfaction with appearance of dentures best prediction for accepting implants		Improved stability or security of the mandibular denture (73%) most important reason	NS	NS
Wang	NS	Main motivation for implants: dissatisfaction with prostheses. Expected advantages	Restoration of appearance is expected	Improved function is expected	Improved pronounciation reported motive	Patients expected dental implants to improve quality of life
Yao	NS	Majority of patients had relatively realistic perceptions, with younger subjects and higher education related with more realistic perceptions and lower outcome expectations	Patients had an extend of agreement of 74.6% that implants improved their appearance	Patients had an extend of agreement of 82.4% that dental implants make it easier to chew	NS	Patients had an extend of agreement of 80.9% that implants improved their general QoL and 77.6% of improved social confidence

NS = not specified; IOD = Implant overdenture; FFD = fixed full-arch denture; FDP = fixed partial denture; SC = single crown; CT = computed tomography

Costs	Oral hygiene	Longevity	Age-related differences	Gender-related differences
61% not aware of high costs	78% not aware of special care, 4% related implant loss to poor oral hygiene	81% no idea, 15% a lifetime	NS	NS
NS	NS	NS	NS	NS
67% accept additional costs of CT, software-based treatment planning and guided implant placement to avoid bone graft surgery. Students less motivated to spend additional money	NS	59% a lifetime, 31% for > 10 yrs, 9% < 10 yrs. Estimation 10-year implant success rate 84%.	NS	NS
Cost was most important reason to refuse implants	NS	NS	Lower age was associated with choosing dental implants	NS
Technical and financial concerns more relevant for patients choosing dental implants	NS	Longevity was an important factor for choosing implants	NS	NS
Willingness to pay widely spread, depending on how many implants and prosthetics	31% more care expected, 58% similar, 7% less care	66% expected 11-20 yrs, 3% less than 10 yrs, 3% <10 yrs, 5% 21-25 yrs, 7% >25 yrs	NS	Yes, women had higher expectations than man
Cost was not decisive or a critical factor for 57.4%	67.0% same level of hygiene as natural teeth, 11.3% greater hygiene	10-20 years (33.6%), rest of their life (54.9%)	Yes, younger patients favoured aesthetics, older patients favoured chewing/ function	Yes, women more ambiguous in responses
NS	NS	NS	Yes, younger patients more likely to accept implants	NS
Major concern against implants	NS	Some patients overestimated longevity	NS	NS
NS	65.3% disagreed with the statement that dental implants require less care than natural teeth, 31.8% agreed	62.7% disagreed with the statement that dental implants last longer than natural teeth, 31.4% agreed	Yes, younger patients disagree more on the statement ,dental implants last longer than natural teeth' and lower outcome expectations	Yes, women disagree more on the statement: 'Dental implants are as functional as natural teeth'

with missing posterior teeth or edentulous patients. Patients who were missing posterior teeth or were edentulous found restoration of function most important. This might also explain the age-related differences observed, as younger patients are more likely to be supplied with implant-based prostheses to replace lost or failing anterior teeth, while elderly people were more likely to be missing teeth in the posterior region. Younger patients rated aesthetics as more important than older patients, whereas older patients favoured chewing and function[28]. A reverse relationship between age and functional expectations was found, meaning the older a patient, the less was expected from the functional benefits of implant-based therapy and *vice versa*[16,19]. Younger patients will profit for a longer time frame from this therapy, another potential factor explaining the more likely they are to opt for this treatment. Most studies show that female patients generally have higher expectations than men, especially in aesthetic outcome. However, female patients were not less satisfied with the outcome, in spite of their higher expectations.

In most studies, costs are a major factor for patients not opting for implant-based therapy. However, when removing this factor, there still remain a substantial proportion of patients who will decline implant-based therapy[29]. Evidently, surgical risks or fear of pain are also factors that contribute to not choosing implant-based therapy, even though pain associated with implant placement is generally mild[31-32]. In some studies, costs were considered not as influential in the decision process as expected, perhaps because the patients had already decided to choose implant-based therapy.

The perception that implants were like natural teeth, and did not require a special need for oral hygiene measures[17,27,28,33-35] is a cause for considerable concern. However, the need for maintenance depends largely on the type of prosthesis supported by the implants. A single crown is easier to clean and might not require special methods compared with those used to maintain natural teeth, whereas a fixed full-arch prosthesis might need additional and more complex hygiene measures. Even though many patients recognise the need for regular maintenance, this does not imply that their knowledge or understanding of what implant care means is sufficient[6].

It is quite concerning that there is a wide variation reported in patients' understanding of the potential life expectancy of their implants[6,15,17,22,28,36,37]. Often patients expected that their implants would last a lifetime. Patients searching for implant treatment are better informed on the longevity of implants than the general population, probably due to accessing better information sources[15], but this does not necessarily equate to a better understanding of implant longevity.

Higher educational attainment level was associated with a preference for choosing implant treatment[16,24]. However, the studies of Baracat et al[19] and de Cunha et al[7] did not confirm this finding. Levels of education were a significant predictor of patients' expectations in the study of Yao et al[16], where better educated patients maintained lower expectations and more realistic perceptions. This could be down to better information via the media or information from their social circle (friends/family) resulting from a higher educational level and possible concurrent higher income.

No retrospective studies were included in this review, the rationale being that the longer patients had been functioning with their implant-borne prosthesis the more they were biased in their memory of the expectations prior to having implants.

To reduce differences in treatment needs, our review only looked at studies on patients with a possible treatment need (missing teeth), or those actively seeking prosthetic treatment were included, reducing the risk of bias. Patients not interested in implants or without a treatment need might have different expectations and level of information about this treatment. Other risks of bias included the diversity or absence of definitions for expectations and the different methodologies used. A new standardised and validated questionnaire is mentioned by Yao et al[16], which might be a step forward in standardised research on expectations and assessments in clinic.

In order to predict patient satisfaction, the dental professional should understand their patients' expectations. Patients should be provided with comprehensible and evidence-based information and possible misperceptions need to be recognised early and dealt with to establish realistic expectations from treatment outcomes. As patient' expectation

is a major predictor of patient' satisfaction, the final outcome it is essential to identify and manage those patients with unrealistic expectations. A questionnaire completed before treatment would indicate those patients with unrealistic expectations and these patients could then receive further counselling and, if appropriate, psychiatric evaluation prior to commencing implant therapy[18].

Conclusions

Patients have high expectations of the successful outcome of implant rehabilitation and, in general, these expectations are met. Most studies show that women have higher expectations than men, but this did not appear to affect overall satisfaction between the groups. As a variety of study designs were identified, thus impairing the generalisation of the results, a standardised method for measuring expectations of oral rehabilitation is required.

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CBCT vs other imaging modalities to assess peri-implant bone and diagnose complications: a systematic review

Key words *bone defects, CBCT, imaging, implant dentistry, peri-implantitis*

Aim: The objective of this systematic review was to evaluate the diagnostic value of CBCT compared with 2D imaging and clinical gold standard techniques in peri-implant bone defect detection and measurement.

Materials and methods: Literature search was performed using MEDLINE, Embase and Web of Science databases up to July 2017. Clinical, *ex vivo*, *in vitro* and animal studies that assessed and measured peri-implant bone defects using different imaging modalities were included in this review. Two reviewers performed data extraction and qualitative analysis. The methodological quality of each study was reviewed using the QUADAS-2 tool.

Results: The initial search revealed 2849 unique papers. Full-text analysis was performed on 60 articles. For the present review, nine studies were considered eligible to be included for qualitative analysis. CBCT performed similar to intraoral radiography in mesiodistal defect detection and measurements. Additional buccolingual visualisation and volumetric and morphological assessment of peri-implant bone defects are major advantages of 3D visualisation with CBCT. Nevertheless, one must be aware of metal artefacts masking osseointegration, shallow bony defects and other peri-implant radiolucencies, thus impeding early diagnosis of intrabony lesions.

Conclusions: The present review did not provide evidence to support the use of CBCT as standard postoperative procedure to evaluate peri-implant bone. Up to date, we are clinically forced to remain with intraoral radiography, notwithstanding the inherent limitations related to restricted field of view and two-dimensional overlap. A 3D imaging approach for postoperative implant evaluation is crucial, making further development of an optimised and artefact-free CBCT protocol indispensable.

■ Introduction

For several decades, implants have been widely used to replace missing teeth and restore impaired oral situations. Despite the remarkably high implant survival rates (ranging from 95% to 98%) reported in literature over past decades[1], recent epidemiological meta-analyses state that in the past decade the prevalence of peri-implant diseases could rise to more than 20%[2–4]. This relatively new pathological entity adds to a collective awareness regarding the significant risk factors of oral implant placement and the development of appropriate diagnostic and therapeutic approaches. The inflammatory conditions, affecting both soft and hard tissues around the intraoral implants, may in the long run cause implant failure, with consequent loss of the implant and the surrounding bone. In the current context of heterogeneity of definition[5] and considering the lack of consensus regarding the definition of peri-implantitis[6,7], imaging of the peri-implant bone is of paramount importance to further develop

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diagnostic and therapeutic strategies for peri-implant structures. Routinely taken radiographs offer a non-invasive technique for longitudinal follow-up of the peri-implant status. However, when diagnosis arrives too late and marginal bone loss is advanced, treatment options become scarce, often resulting in explantation, meanwhile compromising bone quality and quantity and eventual oral rehabilitation. Nearly every consensus report states that intraoral radiography (IO) remains the ultimate diagnostic tool in the follow-up of peri-implant conditions[8–10]. Intraoral radiography units are widely accessible in private dental practices. Somewhat less present is panoramic radiography (PR), while cone beam computed tomography (CBCT) and multi-slice computed tomography (MSCT) imaging techniques remain mostly restricted to secondary care. Despite the variant techniques and methods for reproducible and standardised IO images, inter- and intra-observer reliability of measurements on IO radiographs vary significantly, with superimposition of anatomical structures leading to underestimation of the actual bone defect dimensions[11,12]. Moreover, minor variations in x-ray beam orientation may compromise a reliable follow-up and decrease the accuracy of peri-implant bone level measurements[13]. These drawbacks render the 2D intraoral radiographic outcome measures for peri-implant bone assessments unreliable and clinically meaningless below 0.3 mm.

Since two-dimensional imaging techniques offer merely mesiodistal and vertical detection of bone defects, three-dimensional (3D) imaging techniques can enhance the diagnosis with valuable additional spatial information. As clinicians focus increasingly on esthetics, depending on the preservation of the vestibular tissues, 3D CBCT imaging offers complementary buccolingual visualisation of the peri-implant bone[14,15]. Accurate evaluation of the full dimensions and morphology of the peri-implant bone defects benefits treatment decision-making and a patient's rehabilitation outcomes. Nonetheless, 3D imaging techniques are less cost-efficient, increase exposure to radiation and struggle with imaging artefacts around metal objects[11,19].

With regard to proper visualisation of peri-implant bone structure and osseointegration, micro-computed tomography (μCT) offers excellent 3D reconstruction of the implant and surrounding bone morphology, allowing analysis of cortical and trabecular bone structures, without the need for histological sections[20,21]. Nevertheless, this imaging technique is restricted mainly to research projects in the secondary care environment due to the restricted availability of the equipment for clinical practice.

Furthermore, researchers are experimenting with non-ionising imaging, such as ultrasound, magnetic resonance imaging (MRI) and optical coherence tomography (OCT), yet currently the clinical practicality of such applications remains questionable in the short-term until further developed[19–22]. Although these imaging modalities are excluding the hazards of electromagnetic radiation, peri-implant bone defect diagnosis – and certainly measurements of defects – needs further refinement before entering routine clinical practice[23].

The purpose of this systematic review was to evaluate the diagnostic value of the above-mentioned 2D and 3D imaging techniques in peri-implant bone defect detection and measurement.

Materials and methods

Protocol and registration

This review was conducted following the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) guidelines to ensure comprehensiveness[24]. Methods of analysis and inclusion criteria were specified in advance and registered at PROSPERO (Prospective Register of Systematic Reviews) with protocol number CRD42017078625.

Objective and PICO question

To evaluate the diagnostic (and predictive) value of different 2D and 3D imaging techniques in detection and measurements of peri-implant bone level changes and defects. The PICO question consisted of the following components: (P) implant fixtures with peri-implant bone defects, (I) CBCT imaging, (C) other imaging modalities or clinical gold standards, (O) assessment and measurement of peri-implant bone loss and bone defects.

Information sources and search strategy

The search strategy was developed for MEDLINE and adapted for Embase and Web of Science. The electronic databases were searched in July 2017. The search strategy consisted of a combination of controlled terms (MeSH and EMTREE terms, respectively) and keywords. The full search strategy can be consulted in Appendix 1. No language restrictions were applied when searching the electronic databases. Moreover, reference lists of relevant articles and former systematic reviews in the field were manually screened for additional relevant publications. Duplicated hits were manually checked and removed.

Eligibility criteria

Clinical, *ex vivo*, *in vitro* and animal studies that assessed and measured peri-implant bone defects by use of different imaging modalities were included in this review. Exclusion criteria consisted of reviews, letters to the editor, guideline reports, case reports, clinical follow-up studies, case control studies, studies that did not evaluate imaging techniques, and studies comparing clinical diagnostic parameters or different treatment options.

Study selection

Two reviewers (MV and TV) independently reviewed the titles and abstracts of all records. Subsequently, all full-text papers of the studies deemed eligible for inclusion were obtained and full-text reading analysis was performed. In both title/abstract reading phase and full-text reading phase, disagreements were resolved by discussion between the two reviewers. When consensus could not be reached, an experienced third author (RJ) was consulted.

Data extraction

Data were extracted by both reviewers (MV and TV) and discussed. Data recorded for qualitative analysis were:

- Study characteristics: authors, year of publication and level of evidence;
- Methods: study design (clinical, *ex vivo, in vitro*, animal), number of samples, and number of implants;
- Intervention characteristics: induction of bone defect, directions of detection, imaging modality, reference technique, and number of observers;
- Outcomes: type of measurements, intra- and interrater reliability, clinical applicability, results and conclusion.

Risk of bias assessment

The methodological quality of each study was critically reviewed using the QUADAS-2 tool (Quality Assessment of Diagnostic Accuracy Studies 2)[25]. This tool evaluates the risk of bias in four domains: patient selection, index test, reference standard and flow and timing. Moreover, the clinical applicability of the patient selection, index test and reference standard was assessed. The qualitative evaluation of the methodology was carried out by one reviewer, (MV), in duplicate. Discrepancies were resolved by discussion with a second reviewer (RJ).

Results

Search results

In total, searching the MEDLINE, Embase and Web of Science databases, respectively, identified 1199, 575 and 2071 records. Additionally, 27 articles were identified through a hand search and the screening of reference lists. Duplicates were manually removed, resulting in 2849 unique papers. Publication dates of these articles ranged from 1975 to 2017. Figure 1 shows the PRISMA flow diagram describing the selection process. According to the title screening of all 2849 records, 104 papers were deemed eligible for inclusion in the review. Based on the abstract reading, another 18 records were excluded. Finally, 86 articles were selected for full text reading. A total of 26 articles turned out not to meet the strict inclusion criteria and were subsequently excluded for further analysis. Reasons for exclusion are listed in Table 1. From the remaining 60 articles, 43 described the detection and measurements of peri-implant bone levels and defects with the use of different 2D and 3D imaging

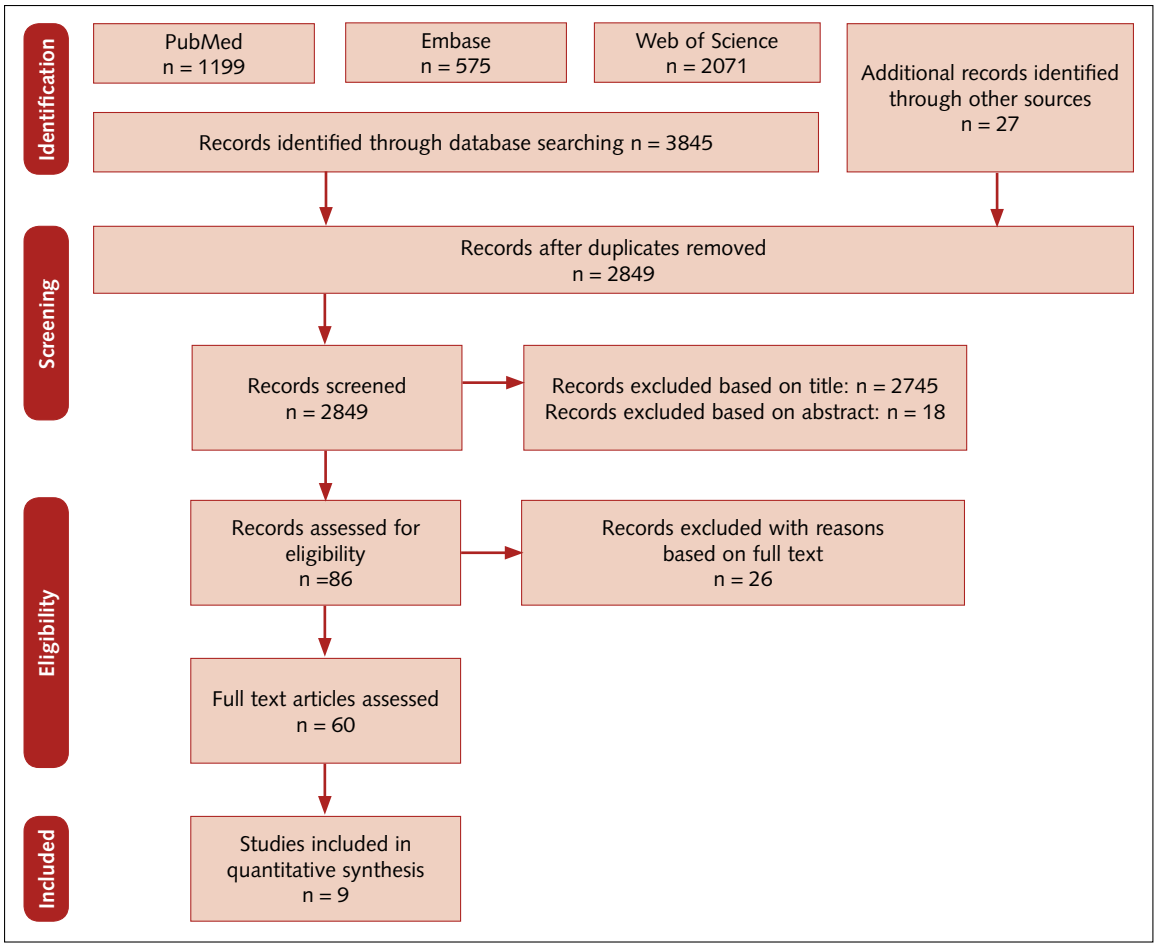

Fig 1 Flow diagram of the selection process (PRISMA 2009 format)[24].

modalities (Table 2 and Fig 2). Additionally, 17 records presented a technique to create reproducible IO radiographs to ensure proper follow-up evaluation of the peri-implant hard tissues and allow comparison of serial radiographs (Table 3). Finally, nine studies were considered eligible to include in the qualitative analysis of this review, as they reported the use of CBCT vs other imaging modalities or gold standard clinical techniques for the assessment of peri-implant bone loss (Table 4).

Study characteristics

A total of 43 papers compared bone defect detection and/or measurements on different kinds of radiographic images with a reference measurement technique. Only 14 authors used a clinical sample of patients presenting with peri-implant bone loss[12,19,26–36]. The majority of studies was conducted with the use of animal bone specimens[15,37–52] or human cadavers[13,53–61]. One study used acrylic blocks simulating alveolar ridges[62]. Above all, IO radiography was the most studied diagnostic imaging technique for intraoral implant follow-up. Four papers added PR to the methodology[31–34], and another four papers tested the detection capability of 2D tomography[35,36,56,60]. One paper explored the possibilities of ultrasonography, which is not widely used in implant dentistry[19]. The diagnostic potential of CBCT, whether or not compared with conventional MSCT and/or 2D techniques, was investigated 16 times[15,38,40,41,43–50,57–59,63].

As displayed in Table 2, 19 papers assessed the presence or absence of a peri-implant radiolucent space[26–28,36,38,38,40,41,43–46,53–57,59,60], whereof only one measured the volume of the detected defect[58]. A total of 21 papers described linear measurements executed in mesial, distal and/or buccal and lingual directions from the implant's vertical axis[12,13,15,19,29–31,33,34,37,39,42,47–51,61–64]. The number of threads to determine bone level

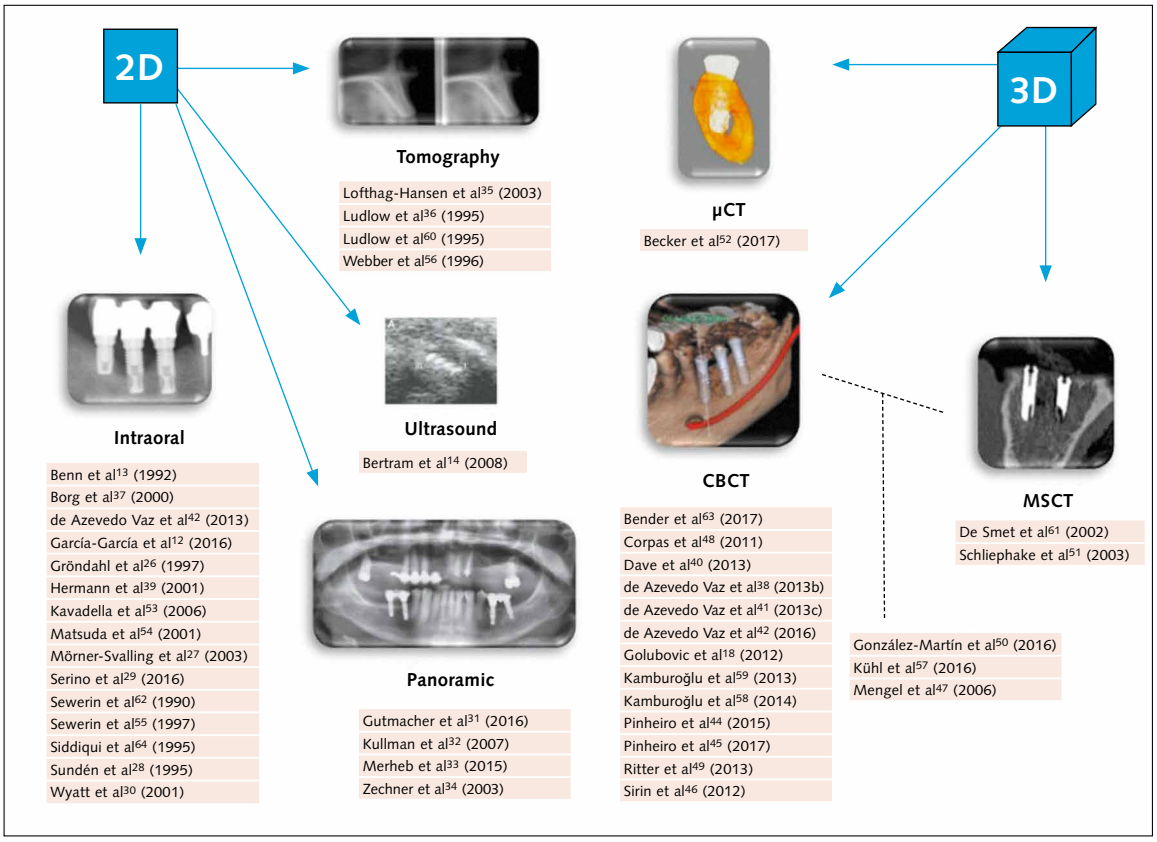

Fig 2 2D and 3D imaging modalities to assess and measure peri-implant bone changes. Intraoral, tomography, panoramic and CBCT images from own collection; µCT image by courtesy of Huang Yan; ultrasound image from Bertram et al (2008).

Table 1 Excluded articles with reasons.

Author (year)	Reason
Becker et al (2015)	3
Benic et al (2015)	1
Brägger et al (1994)	1
Butz et al (2006)	3
Chan et al (2017)	3
Chopra et al (2016)	3
Daubert et al (2015)	2
De Bruyn et al (2013)	1
Esposito et al (1993)	2
Fienitz et al (2012)	3
Harris et al (2002)	1
Harris et al (2012)	1
Huang et al (2014)	3

Author (year)	Reason
Korn et al (2015)	3
Lang et al (2011)	2
Pan et al (2013)	2
Papantonopoulos et al (2017)	3
Raes et al (2013)	2
Salvi et al (2004)	1
Sanda et al (2016)	3
Slagter et al (2015)	3
Truhlar et al (1993)	1
Vera et al (2012)	2
Wang et al (2013a)	3
Wang et al (2013b)	3
Yepes et al (2015)	3

1) Reviews, letters to the editor, EAO guideline reports; 2) no evaluation of imaging techniques; 3) irrelevant outcome measures for this review (e.g. bone structure analysis, osseointegration, morphology, bone thickness measurements).

was used in two papers[32,35]. Becker et al (2017) reported a promising volumetric dehiscence profile through microCT scanning of the implant and surrounding bone[52]. However, this technique is currently not clinically applicable.

Since IO radiography remains the imaging technique of choice in daily clinical practice, 17 papers covered the widely clinically used paralleling technique to take reproducible IO radiographs and additional methods to evaluate serial images over

Table 2 Measurements of marginal bone levels and peri-implant bone defects with the use of 2D and 3D imaging modalities.

Imaging technique		Author (year)		Type of measurements	Measured distances	Directions	Reference	Clinical applicability
2D	Periapical radiography	Gröndahl et al[26] (1997)		Presence/absence of radiolucency	-	M & D	None	✓
		Kavadella et al[53] (2006)		Presence /absence of radiolucency on five-point scale	-	M & D	None	✓
		Matsuda et al[54] (2001)		Presence /absence of radiolucency on five-point scale	-	M & D	Periodontal probe	✓
		Mörner-Svalling et al[27] (2003)		Presence /absence of radiolucency	-	M & D	None	✓
		Sewerin et al[55] (1997)		Presence /absence of radiolucency on five-point scale	-	M & D	Known dimensions	✓
		Sundén et al[28] (1995)		Presence /absence of radiolucency on five-point scale	-	M & D	Radiographs of clinically stable implants	✓
		Borg et al[37] (2000)		Linear (mm)	Defect height	M & D	Histology	✓
		De Azevedo Vaz et al42 (2013)		Linear	Defect height	M & D	None	✓
		Hermann et al[39] (2001)		Linear (mm)	Defect height	M & D	Histomorphometry	✓
		Serino et al[29] (2016)		Linear (mm)	Defect height	M & D	Surgical re-entry	✓
		Wyatt et al[30] (2001)		Linear (mm)	Defect height	M & D	Direct measurements	✓
		Siddiqui et al[64] (1995)		Linear (mm)	Defect width	M & D	Known dimensions	✓
		Benn et al[13] (1992)		Linear (mm)	Inter-thread distance	M & D	None	✓
		Sewerin et al[62] (1990)		Linear (mm)	Inter-thread distance	M & D	None	✓
		García-García et al[12] (2016)		Linear (mm)	Intrabony height Supracrestal part Defect width	M & D	Surgical re-entry	✓
	Panoramic radiography	Gutmacher et al[31] (2016)		Linear (mm)	Supracrestal part	M & D	IO	✓
		Merheb et al[33] (2015)		Linear (mm)	Defect width	M & D	Clinical data and IO	✓
		Zechner et al[34] (2003)		Linear (mm)	Defect height	M & D	Pocket depth, Periotest, bleeding on probing and IO	✓
		Kullman et al[32] (2007)		Number of threads	Supracrestal part	M & D	IO	✓
	Tomography	Lofthag-Hansen et al[35] (2003)		Number of threads	Supracrestal part	M & D	IO	✓
		Ludlow et al[36] (1995)		Presence/absence of radiolucency on five-point scale	-	B & L	IO	✓
		Ludlow et al[60] (1995)		Presence/absence of radiolucency on five-point scale	-	M D B L	IO	✓
		Webber et al[56] (1996)		P resence/absence of radiolucency on five-point scale	-	M D B L MB ML DB DL	IO	✓

2D	Ultrasound	Bertram et al[14] (2008)		linear (mm)	Defect height	B	Surgical re-entry (probe)	✓
3D	CBCT	Dave et al[40] (2013)		Presence/absence of radiolucency on five-point scale	-	M & D	Known dimensions and IO	✓
		De Azevedo Vaz et al[38] (2013)		Presence/absence of radiolucency on five-point scale	-	B & L	None	✓
		De Azevedo Vaz et al[41] (2013)		Presence/absence of radiolucency	-	B & L	None	✓
		De Azevedo Vaz et al[42] (2016)		Presence/absence of radiolucency on five-point scale	-	B & L	None	✓
		Kamburoğlu et al[59] (2013)		Presence/absence of radiolucency on five-point scale	-	B & L	None	✓
		Pinheiro et al[44] (2015)		Presence/absence of radiolucency on five-point scale	-	M D B L MB ML DB DL	None	✓
		Pinheiro et al[45] (2017)		Presence/absence of radiolucency on five-point scale	-	M D B L MB ML DB DL	None	✓
		Sirin et al[46] (2012)		Presence/absence of radiolucency on five-point scale	-	M D B L	IO, PR, MSCT, clinical picture	✓
		Kühl et al[57] (2016)		Presence/absence and type of defect	(i) No defect visible (ii) Defect present, but not classifiable (iii) Defect C (2-wall) (iv) Defect B (3- wall) (v) Defect A (4-wall)	M D B L	IO, PR, MSCT, direct measurements (calliper)	✓
		Kamburoğlu et al[58] (2014)		Presence/absence of radiolucency, linear (mm) and volumetric measurements	Defect height Defect width Defect volume	M D B L	Direct measurements	✓
		Bender et al[63] (2017)		Linear (mm)	Defect height; intrabony height; supracrestal part; defect width morphology	M D B L MB ML DB DL	None	✓
		Mengel et al[47] (2006)		Linear (mm)	Defect height; supracrestal part defect width	M D B L	IO, PR, MSCT, direct measurements	✓
		Corpas et al[48] (2011)		Linear (mm) percentage of bone % density (mmAleq)	Intrabony height; bone fraction bone structure	M D B L	IO and histology	✓
		Ritter et al[49] (2013)		Linear (mm)	Supracrestal part	M D B L	IO and histology	✓
		González-Martín et al[50] (2016)		Linear (mm)	Supracrestal part buccal bone thickness	B & L	MSCT and direct measurements (calliper)	✓
		Golubovic et al[18] (2012)		Linear (mm)	Supracrestal part intrabony height	B & L	Histology	✓
	MSCT	De Smet et al[61] (2002)		Linear (mm)	Supracrestal part	M D B L	IO, PR, direct measurements (calliper)	✓
		Schliephake et al[51] (2003)		Linear (mm)	Supracrestal part	M D B L	IO with and without magnification and histology	✓
	µCT	Becker et al[52] (2017)		Volumetric dehiscence profile	Defect height	Vector rotated in 5-degree steps around implant	Histology	✓

Five-point scale for assessment of peri-implant radiolucent space: 1 radiolucency definitely not present, 2 probably not present, 3 uncertain, 4 probably present, 5 definitely present; Abbreviations: M, mesial; D, distal; B, buccal; L, lingual; IO, intraoral periapical radiography; PR, panoramic radiography; CBCT; cone-beam computed tomography; MSCT, multislice computed tomography; µCT, microcomputed tomography; GS, gold standard. Colour code study types: green, clinical sample; light green, *ex vivo*; yellow, *in vitro*; red, animal bone specimen.

Table 3 Reproducibility of intraoral radiography for assessment of peri-implant bone changes.

Technique	Method	Author (year)	Assessment of peri-implant bone changes	Specification of measuring technique
Parallelling technique	Stepwedge	Jeffcoat[65] (1992)	Bone density	Digital subtraction
		Jeffcoat et al[66] (1993)	Bone density	Digital subtraction
	Occlusal key	Naser et al[67] (2011)	Bone density	Semi-automated digital measures
		Meijer et al[68] (1992)	Bone level	Linear measures with sliding calliper
		Meijndert et al[17] (2004)	Bone level	Linear measures with sliding calliper
		Malloy et al[69] (2017)	Bone level	Linear measures with digital ruler
		Larheim et al[70] (1979)	Bone level	Measuring grid
		Larheim et al[71] (1982)	Bone level	Measuring grid
		Galasso[72] (2000)	Bone level	Linear measures with sliding calliper
		Nicopoulou-Karayianni et al[73] (1997)	Bone density	Digital subtraction
		Cunha et al[74] (2013)	Bone level	Semi-automated digital measures
		Meijer et al[75] (1993)	Bone level	Semi-automated digital measures
		Wakoh et al[76] (2006)	Bone density	Digital subtraction
	Unstandardised	Bittar-Cortez[77] (2006)	Bone density	Digital subtraction
		Geraets et al[78] (2012)	Bone density	Digital subtraction on panoramic radiographs
		Reddy et al[79] (1992)	Bone level	Semi-automated digital measures
		Patil et al[80] (2015)	Bone level	Semi-automated digital measures

Colour code study types: Green: Clinical sample, light green: *ex vivo*, yellow: *in vitro*, red: Animal bone specimen

time[14,65–80]. Both changes in bone level and bone density are important to assess in follow-up evaluations. Therefore, Table 3 differentiates authors describing a digital subtraction technique using a reference step wedge and/or occlusal key, and authors describing methods for consecutive bone level measurements, whether or not with the use of semi-automated digital measurements.

Qualitative analysis of the methodology

The methodological quality analysis included nine papers comparing CBCT to other diagnostic techniques[15,40,46–50,57,58]. The publication dates of these papers ranged from 2011 to 2016, confirming the relatively recent nature of CBCT as a diagnostic tool for peri-implant complications. One study was performed in Belgium, one in the United Kingdom, three in Germany, two in Turkey and one in Switzerland. None of the papers in the qualitative analysis studied a clinical sample of patients presenting with peri-implantitis (Table 4). Animal or cadaver bone specimens were the samples of choice. Bender et al[63] investigated a clinical sample of patients with CBCT; however, the authors did not compare CBCT with a 2D imaging technique or clinical gold standard, so the study was not included in Table 4. The mean number of implants used in the selected papers was 49 (± 29). Mechanical induction of the defects was performed in seven out of nine studies. The number of observers diverged from one to nine, with varying intra- and interrater reliability values, as shown in Table 4.

Taking all findings into account, CBCT performed similar to IO and gold standard techniques in mesiodistal detection and measurement of defects[40,46,48,49,58,81]. Additional buccolingual visualisation of the defects is the main added value in the diagnosis of peri-implant bone defects with CBCT. Nevertheless, one must be aware of the occurrence of metal and potential motion artefacts, as well as the limited feasibility of CBCT to evaluate bone density, as shown by Corpas et al[48].

Risk of bias within studies

All studies in the qualitative analysis were considered low level of evidence in evidence-based medicine

Table 4 Analysis of studies comparing CBCT with other imaging modalities or clinical gold standard in the measurement of peri-implant bone defects.

Study characteristics	Sample characteristics			Intervention characteristics					Outcome characteristics		
Author (year)	Study design	Samples (n =)	Implants (n =)	Induction of defect	Test group	Reference		Observers (n=)	Intrarater reliability	Interrater reliability	Results and conclusion
					3D imaging	2D imaging	Gold standard				
Corpas et al[48] (2011)	Minipig	10	80	N	CBCT	IO	Histology	?	×	×	Defect depth: CBCT ≈ IO bone density changes: CBCT << IO & GS
Dave et al[40] (2013)	Bovine	4	15	Y Mechanical	2 CBCT machines: 3D Accuitomo 80 i-CAT NG	IO	-	9	IO ✓ CBCT✓	IO ✓ CBCT✓	Small defects: CBCT << IO larger defects: CBCT ≈ IO
Golubovic et al[18] (2012)	Dog	6	48	Y Ligature	CBCT	-	Histology	1	✓	×	CBCT << GS
González-Martín et al[50] (2016)	Bovine	10	60	N	2 CBCT machines: i-CAT NG Newtom VGi MSCT	-	Direct measurement (calliper)	2	×	×	MSCT << CBCT << GS
Kamburoğlu et al[58] (2014)		5	69	Y Mechanical	CBCT	-	Direct measurement (calliper)	3	✓	✓	CBCT ≈ GS
Kühl et al[57] (2016)		1	6	Y Mechanical	CBCT MSCT	IO PR	Direct measurement (calliper)	7	×	✓	CBCT << PR << IO CBCT >> MSCT
Mengel et al[47] (2006)	pig	19	19-38	Y Mechanical	CBCT MSCT	IO PR	Direct readings with reflecting stereomicroscope with measuring ocular	1	×	×	MD: CBCT ≈ MSCT ≈ GS >> IO ≈ PR BL: CBCT ≈ MSCT ≈ GS >> IO ≈ PR CC: CBCT ≈ MSCT (IO & PR: depth not measurable)
Ritter et al[49] (2014)	dog	12	26	Y	CBCT	IO	Histology	RX 2 histo 1	✓	✓	MD: CBCT ≈ IO << GS BL: CBCT ≈ GS >> IO
Sirin et al[46] (2012)	bovine	?	100	Y Mechanical	CBCT MSCT	IO PR	Clinical picture	7	✓	✓	Small defects: CBCT ≈ IO >> MSCT ≈ PR Larger defects: CBCT ≈ IO ≈ MSCT ≈ PR

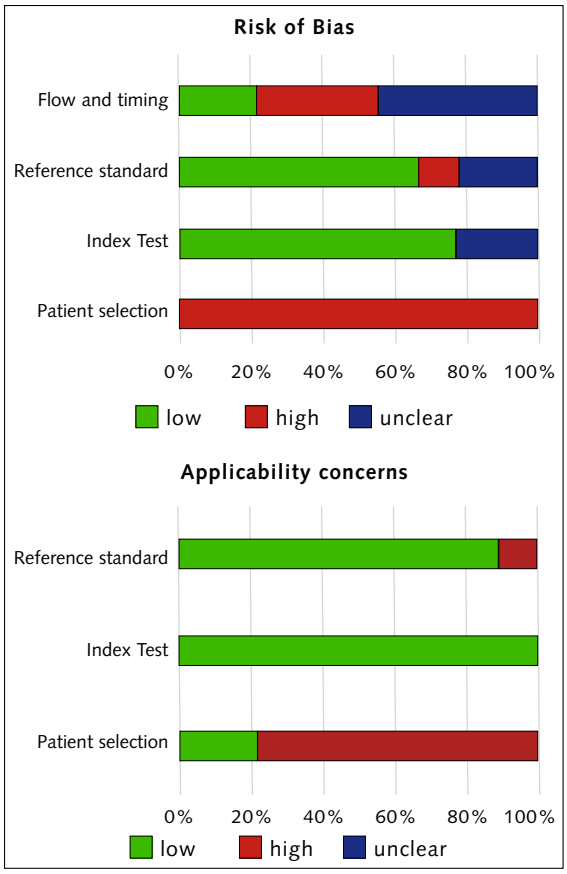

Fig 3 Summary of QUADAS-2 risk of bias assessment and applicability concerns.

(EBM), since they were conducted using animal or cadaver specimens. The methodological quality of the included papers was assessed using the QUADAS-2 tool and corresponding signalling questions[25]. Table 5 and Figure 3 show the overview of outcomes and summarising plots of the risk of bias assessment and applicability concerns. The variety of specimens (non-randomised) and sample preparation techniques, as well as the different imaging machines and settings, can have introduced bias. In three papers, concerns arose with regard to flow and timing, as the authors did not clarify the process of detection of defects with the index test and the reference standard[49,58], and the uniformity of the reference standards used[48]. In general, clinical applicability of the analysed papers was low, except for patient selection. This originates from discrepancies in the severity of the target condition. The mechanical induction of peri-implant defects in the study populations hampered evaluation of the clinical relevance of CBCT in detection of the actual pathogenesis of peri-implant marginal bone loss, while this is the aim of this review.

Discussion

CBCT shows promising results in peri-implant bone defect detection (Table 4) and allows measurements in three planes. In six out of nine studies, CBCT equated IO and gold standard clinical techniques in the detection of advanced bone loss defects[46–49,58]. However, CBCT images, and the implant-related metal artefacts (e.g. blooming, streaks and scattering, as well as black bands) can hide narrow peri-implant radiolucencies and impede early diagnosis of these starting intrabony lesions[11,15,40,50,57,82]. Clinicians should be aware of image distortions and artefacts caused by high-density materials, such as zirconium or titanium implants. Typical artefacts hampering peri-implant diagnosis on CBCT images are streaks, black bands and blooming. Blooming may cause a clinically relevant implant perimeter increase, directly affecting peri-implant diagnosis[16]. Unfortunately, metal artefact reduction algorithms are inefficient to significantly correct the images[43,59]. Motion artefacts due to patient movement during the scanning process can reduce the diagnostic image quality even more, especially when expressed in combination with metal artefacts. MSCT is even worse in artefact expression compared with CBCT, making assessment of peri-implant bone levels and trabecular bone structure almost impossible. Moreover, as MSCT yields higher dose levels, more costs, and reduced accessibility, it is not advocated when it comes to surgical follow-up of implant placement.

Highly accurate and detailed imaging of the peri-implant bone without scattering or blooming caused by the implant would obviously be the desired diagnostic technique. The volumetric dehiscence profile, shown by Becker et al, used microCT to approach this goal[52]. They placed implants in foxhound jaws and, after sacrificing the animals, performed microCT and histomorphometric analysis of the specimens. This microCT technique allows the evaluation of differences in bone level changes as a function of insertion depth and abutment type, yielding complementary 3D information, which is not possible with histology alone[52]. By almost eliminating all scattering and blooming, authors managed to visualise the peri-implant bone on a 360-degree plot. In this way, very detailed information on peri-implant bone can be obtained,

Table 5 Risk of bias assessment using the QUADAS-2 tool.

Author (year)	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Corpas et al[48] (2011)	↑	↓	↓	↑	↓	↓	↓
Dave et al[40] (2013)	↑	↓	↓	↓	↑	↓	↓
Golubovic et al[18] (2012)	↑	?	?	?	↑	↓	↓
González-Martín et al[50] (2016)	↑	↓	↓	?	↓	↓	↓
Kamburoğlu et al[58] (2014)	↑	↓	↑	↑	↑	↓	↑
Kühl et al[57] (2016)	↑	↓	↓	?	↑	↓	↓
Mengel et al[47] (2006)	↑	?	?	?	↑	↓	↓
Ritter et al[49] (2014)	↑	↓	↓	↑	↑	↓	↓
Sirin et al[46] (2012)	↑	↓	↓	↓	↑	↓	↓

Legend: ↓ low risk of bias, ↑ high risk of bias, ? unclear risk of bias
Abbreviations: Y, yes; N, no; M, mesial; D, distal; B, buccal; L, lingual; CC, craniocaudal; IO, intraoral periapical radiography; PR, panoramic radiography; CBCT; cone-beam computed tomography; MSCT, multi-slice computed tomography; µCT, microcomputed tomography; GS, gold standard.
Colour code study types same as Table 2.

opening potential new diagnostic gateways. Nevertheless, in order to achieve comparable 360-degree volumetric outcomes with CBCT, the imaging technique still has to be improved in terms of accuracy and artefact suppression.

As long as imaging techniques do not offer a 100% accurate reflection of the actual peri-implant bone conditions, the obtained radiographic images should always be combined with clinical information. Probing depth, bleeding on probing and suppuration, together with radiographic data, increase the odds of early detection of peri-implant disease, offering a possibility to adequately intervene, treat and prevent further complications[83]. In this context, the volumetric and morphological characterisation of the 3D bone defect may be far more relevant as a diagnostic staging tool for early clinical management, yet further development of optimised, low dose and artefact-free CBCT imaging protocols are required to reach this goal.

Considering the above, and in line with the basic ALARA-principle (As Low As Reasonably Achievable) and the more clinically applicable ALADIP principle, CBCT imaging devices and protocols should strive to develop as low as diagnostically acceptable CBCT protocols that are indication-oriented and patient-specific[84]. Until further advances occur, CBCT imaging should rather be considered for specific indications in complex clinical cases. Meanwhile, IO radiography will remain the standard imaging technique for the long-term follow-up of peri-implant conditions[9,57]. But when doing so, one should realise that superimposition of implant and bone creates a lack of information of true buccal and lingual bone levels, obstructing a realistic visualisation of the potential defect, hampering detailed diagnosis such as in the aesthetic zone[14]. In the same light, this review revealed the lack of clinical samples involving CBCT assessments. Only Bender et al studied a limited cohort of patients affected by peri-implantitis[63]. Meanwhile, the *in vitro* nature of the included studies and the (mechanical) induction of peri-implant defects detract from the clinical relevance of the capacity of CBCT to detect the effects of peri-implantitis.

Recently, Bohner et al conducted a meta-analysis of IO and CBCT imaging for diagnosis of peri-implant bone loss[85]. The authors screened literature from 1991 to 2016 and concluded that both techniques showed similar sensitivity, specificity and AUC values. However, they state that voxel size, field of view and image detection system play a major role in the image efficacy of CBCT, thus influencing the detection threshold. The use of filters can improve the visualisation of peri-implant radiolucencies, enhancing the detection of true-positive and true-negative cases[41]. Furthermore, peri-implant defect size plays a significant role in the accurate detection of bone loss. Similar to our findings in the qualitative analysis, Pinheiro et al showed that smaller peri-implant

bone defects are identified less frequently with CBCT compared with larger defects[44]. Overall, heterogeneity of CBCT protocols induces drastic differences in terms of image quality, thus leading to important variation of diagnostic performances[41,44,45,58].

This review was limited to the use of CBCT vs other imaging modalities in the detection and measurement of peri-implant bone defects. Therefore, bone thickness measurements, bone morphology, bone quality/density and other subjects are not discussed. However, besides linear measurements, Corpas et al[48] demonstrated that CBCT is inferior to IO radiography and histology when it comes to bone density evaluation. In this light, it is crucial to emphasise that CBCT should not be used for this purpose. Pauwels et al[86,87] showed that large errors can occur when using CBCT grey values in a quantitative way. Pseudo-Hounsfield units from CBCTs are not reliable, and alternative methods of assessing bone quality and density on CBCT should be further investigated[88].

Conclusions

The present review did not provide evidence to support the use of CBCT as standard procedure to evaluate peri-implant marginal bone. Nevertheless, a 3D imaging approach for postoperative implant diagnosis is surely crucial when dealing with pathological entities, such as peri-implantitis. Yet, the currently available methods for 3D imaging assessment suffer from artefacts and inaccuracies in visualisation and quantitative assessment of the peri-implant hard tissues. Therefore, in clinical practice, intraoral radiography remains the most commonly used technique for diagnosis and monitoring. However, when applying this technique for postoperative assessment and bony defect evaluation, we should be very aware that the true dimensions and morphology of the defect remain masked.

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Appendix 1

MEDLINE:

((((((((("Dental Implants"[Mesh] OR "dental implantation"[Mesh] OR "peri-implantitis"[Mesh] OR "Dental Implant" [tiab] OR "Dental Implants" [tiab] OR "endosseous implant" [tiab] OR "endosseous implants" [tiab] OR "dental implantation" [tiab] OR "oral implant" [tiab] OR "oral implants" [tiab] OR "oral implantation" [tiab] OR periimplant [tiab] OR peri-implant [tiab] OR peri-implantitis [tiab] OR periimplantitis [tiab] OR "peri-implant conditions" [tiab] OR "periimplant conditions" [tiab])))) AND ("Alveolar Bone Loss"[Mesh] OR approximal bone[tiab] OR "implant complications"[tiab] OR "crestal bone"[tiab] OR "bone change"[tiab] OR "bone defect"[tiab] OR "bone level"[tiab] OR "bone levels" [tiab] OR "bone loss"[tiab] OR "bone contour"[tiab] OR "bone contouring"[tiab] OR "bone-to-implant contact"[tiab] OR "supracrestal bone"[tiab] OR "marginal bone"[tiab] OR "bone measurement"[tiab] OR "bone measurements"[tiab] OR "bone height"[tiab] OR osseointegration[tiab] OR pocket[tiab] OR "pocket depth"[tiab] OR "hard tissue"[tiab] OR "alveolar bone"[tiab] OR "bone evaluation"[tiab])) AND (("Diagnostic Imaging"[Mesh] OR "Radiography, Dental"[Mesh] OR "Imaging, Three-Dimensional"[Mesh] OR "Cone-Beam Computed Tomography"[Mesh] OR radiography [ti] OR radiographs [ti] OR radiographic [ti] OR radiographic data [ti] OR dental radiography [ti] OR radiologic [ti] OR radiologic data [ti] OR ultrasonography [ti] OR ultrasound [ti] OR two dimensional imaging [ti] OR two-dimensional imaging [ti] OR panoramic radiograph [ti] OR panoramic radiographs [ti] OR pantomography [ti] OR orthopantomography [ti] OR intraoral radiograph [ti] OR intraoral radiographs [ti] OR intra-oral radiograph [ti] OR intra-oral radiographs [ti] OR three dimensional imaging [ti] OR three-dimensional imaging [ti] OR "cone-beam computed tomography" [ti] OR "cone beam computed tomography" [ti] OR "Cone-Beam CT" [ti] OR "Cone Beam CT" [ti] OR "computed tomography" [ti] OR CBCT [ti]))) AND ((Assessment [tiab] OR evaluation [tiab] OR accuracy [tiab] OR prediction [tiab] OR accuracy [tiab] OR detection [tiab] OR monitoring [tiab] OR methodology [tiab] OR methodological [tiab] OR method [tiab] OR "postoperative evaluation" [tiab] OR "golden standard" [tiab] OR evaluation technique [tiab] OR reproducibility [tiab] OR diagnostics [tiab] OR diagnostic [tiab] OR "radiographic techniques" [tiab])))))))

Embase:

('dental implant':ti,ab OR 'dental implants':ti,ab OR 'endosseous implant':ti,ab OR 'endosseous implants':ti,ab OR 'dental implantation':ti,ab OR 'oral implant':ti,ab OR 'oral implants':ti,ab OR 'oral implantation':ti,ab OR 'periimplant':ti,ab OR 'peri-implant':ti,ab OR 'peri-implantitis':ti,ab OR 'periimplantitis':ti,ab OR 'peri-implant conditions':ti,ab OR 'periimplant conditions':ti,ab) AND ('alveolar bone loss':ti,ab OR 'approximal

bone':ti,ab OR 'implant complication':ti,ab OR 'crestal bone':ti,ab OR 'bone change':ti,ab OR 'bone defect':ti,ab OR 'bone level':ti,ab OR 'bone levels':ti,ab OR 'bone loss':ti,ab OR 'bone contour':ti,ab OR 'bone contouring':ti,ab OR 'bone-to-implant contact':ti,ab OR 'supracrestal bone':ti,ab OR 'marginal bone':ti,ab OR 'bone measurement':ti,ab OR 'bone measurements':ti,ab OR 'bone height':ti,ab OR 'osseointegration':ti,ab OR 'pocket':ti,ab OR 'pocket depth':ti,ab OR 'hard tissue':ti,ab OR 'alveolar bone':ti,ab OR 'bone evaluation':ti,ab) AND ('assessment':ti,ab OR 'evaluation':ti,ab OR 'prediction':ti,ab OR 'accuracy':ti,ab OR 'detection':ti,ab OR 'monitoring':ti,ab OR 'methodology':ti,ab OR 'methodological':ti,ab OR 'method':ti,ab OR 'postoperative evaluation':ti,ab OR 'golden standard':ti,ab OR 'evaluation technique':ti,ab OR 'reproducibility':ti,ab OR 'diagnostics':ti,ab OR 'diagnostic':ti,ab OR 'radiographic techniques':ti,ab) AND (radiography OR 'cone beam computed tomography' OR 'diagnostic imaging' OR 'dental radiology' OR 'three dimensional imaging' OR radiodiagnosis OR echography OR 'two-dimensional imaging' OR 'panoramic radiography')

Web of Science:

TS = (Dental Implant OR Dental Implants OR endosseous implant OR endosseous implants OR "dental implantation" OR "oral implant" OR "oral implants" OR "oral implantation" OR periimplant OR peri-implant OR peri-implantitis OR peri-implantitis OR peri-implant conditions OR periimplant conditions) AND TS=(approximal bone OR "implant complications" OR "crestal bone" OR "bone change" OR "bone defect" OR "bone level" OR "bone levels" OR "bone loss" OR "bone contour" OR "bone contouring" OR "bone-to-implant contact" OR "supracrestal bone" OR "marginal bone" OR "bone measurement" OR "bone measurements" OR "bone height" OR osseointegration OR pocket OR "pocket depth" OR "hard tissue" OR "alveolar bone" OR "bone evaluation") AND TS=(radiography OR radiographs OR radiographic OR radiographic data OR dental radiography OR radiologic OR radiologic data OR ultrasonography OR ultrasound OR two dimensional imaging OR two-dimensional imaging OR panoramic radiograph OR panoramic radiographs OR pantomography OR orthopantomography OR intraoral radiograph OR intraoral radiographs OR intra-oral radiograph OR intra-oral radiographs OR three dimensional imaging OR three-dimensional imaging OR cone-beam computed tomography OR cone beam computed tomography OR Cone-Beam CT OR Cone Beam CT OR computed tomography OR CBCT) AND TS=(assessment OR evaluation OR accuracy OR prediction OR accuracy OR detection OR monitoring OR methodology OR methodological OR method OR postoperative evaluation OR golden standard OR evaluation technique OR reproducibility OR diagnostics OR diagnostic OR radiographic techniques)

Christian M Schmitt, Mayte Buchbender, Rainer Lutz, Friedrich-Wilhelm Neukam

Oral implant survival in patients with bisphosphonate (BP)/antiresorptive and radiation therapy and their impact on osteonecrosis of the jaws. A systematic review

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Key words *bisphosphonates, dental implant, implant loss, implant survival, implant success, irradiation, necrosis of the jaw, osteonecrosis, radiation therapy, radiotherapy systematic review*

Aim: In this systematic review, we aimed to assess the impact of endosseous implants on the formation of an osteonecrosis of the jaw, as well as implant survival rates for patients under bisphosphonate (BP), antiresorptive and radiation therapy.

Materials and methods: An electronic search was performed using PubMed, Embase, and Medline databases with the logical operators: "dental implant", "antiresorptive", "bisphosphonate", "irradiation", "radiotherapy", "radiation", "necrosis" and "survival". The search was limited to articles published up to 15 December 2016. Recent publications were also searched manually to find any relevant studies that might have been missed using the search criteria noted above. The outcome variables were the implant survival rate and the frequency of osteonecrosis of the jaws.

Results: In total, 18 studies addressing oral implants in patients with BP or antiresorptive therapy and 23 with radiation therapy met the inclusion criteria and were included in this systematic review. Most of the studies had a retrospective design with a level of evidence (LoE) of III (moderately high risk of bias). Implant survival rate ranged from 92.86% to 100% in patients with BP/antiresorptive therapy (all due to osteoporosis) and 38.5% to 97.9% in patients with radiation therapy. For BP patients, osteonecrosis in relation to oral implants more frequently occurred in patients taking BPs due to malignant diseases. In patients with radiation therapy, an "implant triggered" necrosis is also a potential complication. The lack of data in the current literature concerning this issue does not allow a proper risk assessment to date.

Conclusions: Within the limits of this systematic review, implant treatment concepts seem to be a valuable approach in patients with radiation therapy and patients with BP therapy due to an osteoporosis. In patients taking BPs due to a malignant disease, implant treatments are not recommended due to the high number of reported implant-related necrosis in this patient cohort. Outcomes of this review should, however, be regarded with caution due to the low level of evidence of the currently existing data.

■ Introduction

According to the current literature, long-term survival of oral implants, commonly called "dental implants", can be specified as high, with survival rates > 90% after 10 years[1-3]. However, most of the studies reporting relatively high implant survival and success rates are based on strict study inclusion criteria in terms of the treated region, as well as the medical status of the patient. This cannot be characterised as everyday clinical practice, since many patients are not comparable with such selective patient groups. There are conditions and factors that are known to influence the treatment outcome and can therefore make the difference between success, complication and failure. Overall, these factors can be divided into:

1. Local factors (treatment site specific factors);
2. Systemic factors (concerning the medical and physical status of the patient);
3. Individual factors (relating to the patient's behaviour).

In spite of high implant survival rates, complications do still occur and these are very much dependent on the onset and accumulation of one or more of these factors. The successful management of these untoward events presupposes that the practitioner comprehends, identifies and can rate the risk of the specific factor and properly deals with the individual situation that might arise.

Fortunately, most of the potential complications are minor issues that may easily be solved without a severe adverse event or overt harm to the patient. This mostly relates to local, site-specific factors, which in the worst case leads to the loss of the implant. Some complications – and these are mainly due to the systemic factors – can lead to serious effects for the patient.

One severe complication is the occurrence of a necrosis of the jaw, which can be associated with a loss of bone locally or over a more extensive area in the affected jaw segment, which may warrant jaw resection. This not only results in a total loss of function but also pronounced aesthetic complications[4-8].

The osteonecrosis of the jaw is mainly associated with patients under bisphosphonates or antiresorptive therapy, as well as patients with head and neck cancer who are treated with a definitive or adjuvant radiation therapy where the jaws are mostly in the irradiated field.

So-called Medication-Related Osteonecrosis of the Jaw (MRONJ) is clinically characterised by exposed bone or bone that can be probed through a fistula in the maxillofacial complex that has persisted for more than 8 weeks in patients who have received current or previous treatment with antiresorptive or antiangiogenic agents[9,10]. The osteoradionecrosis of the jaw (ORN) is clinically also characterised by exposed non-vital bone as a result of the effects of radiation on the bone[10].

In both cases, the initial trigger is mainly an injury of the mucosa due to tooth extraction or other surgical treatments in the oral cavity that expose the bone. Furthermore, extensive pressure due to removable dentures seems a relative risk, resulting in the exposure of bone and eventually the formation of an osteonecrosis in such patients. Therefore, an implant-retained denture has been recommended to avoid these complications.[11,12]

However, the insertion of implants in the jawbone can also be regarded as a potential trigger for the formation of a necrosis[7,11,12].

The literature is controversial in terms of the recommendations for implant treatments in patients after radiation therapy and antiresorptive therapy[4-7,11,12]. In patients with malignant diseases who are prescribed bisphosphonates (BP), implant treatment was especially described as being a high risk for the formation of a necrosis and has not been recommended[4-7]. On the other hand, implant treatment of patients under oral BPs due to a primary osteoporosis has been rated as a safe procedure[13-16].

Therefore, the overall aim of the systematic literature review was to analyse the current literature regarding:

1. The overall survival/success rate of implants placed in patients under antiresorptive or irradiation therapy;
2. The frequency of a necrosis of the jaw that is related to implants in patients with antiresorptive or irradiation therapy.

Materials and methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and the recommendations of the Cochrane Handbook for Systematic Reviews[17-20].

Bisphosphonate and antiresorptive therapy (Group 1)

Articles related to oral implants and patients under bisphosphonates (BP) or antiresorptive therapy or dealing with established osteonecrosis of the jaws that are related to BPs or antiresorptive therapy and dental implants were reviewed.

The central review questions were as follows ("PICO" format; P = Patient/Problem/Population, I = Intervention, C = Comparison, O = Outcome):

1. In patients with antiresorptive therapy (P, test group), compared with patients without antiresorptive therapy (C, control group), receiving oral implants (I) what is the frequency of the formation of an implant related osteonecrosis (O)?
2. In patients with antiresorptive therapy (P, test group), compared with patients without antiresorptive therapy (C, control group), receiving oral implants (I), what is the implant survival rate (0)?

The following additional question in terms of an established osteonecrosis of the jaw related to implants was addressed:

3. In patients with an established osteonecrosis of the jaw in relation to oral implants, what are the influencing factors, i.e. antiresorptive medication, region of the necrosis etc?

Inclusion criteria

Studies were included according to the following general inclusion criteria:

1. Publication in an international peer-reviewed journal;
2. Study published in English;
3. Publication not older than 10 years;
4. Only clinical studies dealing with at least 10 patients in terms of:
   a) Antiresorptive therapy and oral implants (review question 1 and 2), or
   b) An osteonecrosis of the jaw related to BPs or an antiresorptive therapy and oral implants (review question 3);
5. Retrospective and prospective studies.

Exclusion criteria

1. Studies dealing with osseous metastases of the jaws;
2. Articles published in another language;
3. Experimental or *ex vivo* studies;
4. Narrative or systematic reviews;
5. Letters to the editor commentaries or abstracts;
6. Case reports/series with fewer than 10 patients, as mentioned above.

Publications not meeting all mentioned inclusion criteria were excluded from this systematic review. In the presence of duplicate publications, only the study with the most inclusive data was selected.

Radiation therapy (Group 2)

Articles related to oral implants and patients prior to or after radiation therapy of the head and neck were reviewed. The central review questions were as follows ("PICO" format; P = Patient/Problem/Population, I = Intervention, C = Comparison, O = Outcome):

1. In patients with radiation therapy (P, test group), compared with patients without radiation therapy (C, control group), receiving oral implants (I) what is the frequency of the formation of an osteonecrosis (O)?
2. In patients with radiation therapy (P, test group), compared with patients without radiation therapy (C, control group), receiving oral implants (I), what is the implant survival rate (0)?

Inclusion criteria

Studies were included according to the following general inclusion criteria:

1. Publication in an international peer-reviewed journal;
2. Study published in English;

3. Publication not older than 10 years;
4. Only clinical studies dealing with at least 10 patients in terms of radiation therapy and oral implants;
5. Retrospective and prospective studies.

Exclusion criteria

1. Articles published in another language;
2. Experimental or *ex vivo* studies;
3. Narrative or systematic reviews;
4. Letters to the editor commentaries or abstracts;
5. Case reports/series with fewer than 10 patients, as mentioned above.

Publications not meeting all mentioned inclusion criteria were excluded from this systematic review. In the presence of duplicate publications, only the study with the most inclusive data was selected.

Search strategy

The following electronic databases were searched:

1. The Cochrane Library (up to 15 December 2016)
   - CDSR (Cochrane Database of Systematic Review)
   - The Cochrane Central Register of Controlled Trials (CENTRAL)
   - The Cochran Review Groups.
2. MEDLINE (up to 15 December 2016);
3. EMBASE (up to 15 December 2016).

BP and antiresorptive therapy

An electronic search was carried out using the logical operators: "dental implant", "antiresorptive", "bisphosphonate", "necrosis" and "survival" combined with AND or OR. In addition a hand search was carried out for the past 6 months in the following journals: Australian Dental Journal, British Dental Journal, British Journal of Oral and Maxillofacial surgery, Clinical Implant Dentistry and Related Research, Clinical Oral Implants Research, Clinical Oral Investigations, European Journal of Oral Implantology, International Dental Journal, Implant Dentistry, International Journal of Oral & Maxillofacial Surgery, Journal of Cranio-Maxillo-Facial Surgery, Journal of Dental Research, Journal of Clinical Periodontology, Journal of Dentistry, Journal of Oral and Maxillofacial Surgery, Journal of Oral Implantology, Journal of Oral Rehabilitation, Journal of Periodontology, Journal of Periodontal & Implant Science, Journal of Periodontal Research, Journal of the Canadian Dental Association, oral and maxillofacial surgery clinics of North America, oral surgery, oral medicine, oral pathology and oral radiology, Periodontology 2000, Quintessence international, the International Journal of Oral & Maxillofacial implants, The Journal of the American Dental Association and the International Journal of Periodontics & Restorative Dentistry.

Radiation therapy

Electronic search was carried out using the logical operators: "dental implant", "irradiation", "radiotherapy", "radiation", "necrosis" and "survival" combined with AND or OR. In addition, a hand search was carried out for the past six months in the following journals: Australian Dental Journal, British Dental Journal, British Journal of Oral and Maxillofacial surgery, Clinical Implant Dentistry and Related Research, Clinical Oral Implants Research, Clinical Oral Investigations, European Journal of Oral Implantology, Head & Neck, International Dental Journal, Implant dentistry, International Journal of Oral & Maxillofacial surgery, Journal of Cranio-Maxillo-Facial Surgery, Journal of Dental Research, Journal of Clinical Periodontology, Journal of Dentistry, Journal of Oral and Maxillofacial Surgery, Journal of Oral Implantology, Journal of Oral Rehabilitation, Journal of Periodontology, Journal of Periodontal & Implant Science, Journal of Periodontal Research, Journal of the Canadian Dental Association, oral and maxillofacial surgery clinics of North America, oral oncology, oral surgery, oral medicine, oral pathology and oral radiology, Periodontology 2000, Quintessence international, The International Journal of Oral & Maxillofacial Implants, The Journal of the American Dental Association and the International Journal of Periodontics & Restorative dentistry.

Study selection

Two independent examiners (CS, NFW) carried out the search and screening process to minimise the potential for reviewer bias. After electronic search, all titles, key words and abstracts were screened. Studies not meeting the inclusion criteria were excluded. All full texts of the remaining articles were acquired for the second screening. The references of all selected publications were additionally checked for further relevant data. In cases of missing or insufficient data the corresponding authors were contacted via e-mail. After detailed full text examination and agreement between examiners, further articles were excluded. All remaining studies were included in this systematic review. The references were managed with specific bibliographic software (EndNoteX7, ThomsonReuters, New York, NY, USA).

Data extraction

The two reviewers (CS, NFW) used data extraction tables to perform independent data extractions. In case of disagreement, the data were double checked with the original. The following data were extracted from the selected articles concerning the BP and antiresorptive therapy: 1) authors and year of publication; 2) study design; 3) level of evidence (LoE); 4) primary and secondary outcomes; 5) medical reason for BP or antiresorptive therapy, as well as the used BP; 6) number of participants/implants/ necrosis; 7) Implant survival rate; 8) follow- up; 9) region of necrosis; 10) risk factors; 11) outcomes.

The following data were extracted from the selected articles concerning radiation therapy: 1) authors and year of publication; 2) study design; 3) level of evidence (LoE); 4) primary and secondary outcomes; 5) medical reason for radiation therapy as well as radiation dosage; 6) time of implant placement; 7) number of participants/ implants/necrosis; 8) implant survival rate; 9) follow-up.

Level of evidence (LoE) assessment

The included studies were judged according to the definition of levels of evidence (LoE) and overall strength of evidence (SoE)[21]. This was carried out by two independent reviewers (CS, NFW).

Results

Systematic literature search

The pattern of available literature led to the formation of two groups as follows:

1. Group 1: Data dealing with patients under BP or antiresorptive therapy, in combination with oral implants. This included the evaluation of implant loss or survival rates in this collective, as well as the relative risk/frequency of the formation of an osteonecrosis of the jaw triggered by an implant treatment in such patients.
2. Group 2: Data analysing the implant loss and survival rates of inserted implants in patients prior or after radiation therapy as well as the relative risk/ frequency of the formation of an osteonecrosis of the jaw triggered by an implant treatment in such patients.

The study selection process for BP and antiresorptive therapy (Group 1) is summarised in Figure 1, and radiation therapy (Group 2) in Figure 2. The initial electronic literature search identified 423 publications for BP and antiresorptive therapy and 543 publications for radiation therapy (Figs 1 and 2). Hand search did not provide any additional studies for either group. Review of all titles, key words and abstracts led to the exclusion of 371 studies in Group 1 and 454 in Group 2. After a more detailed screening of potential studies and screening of their references, 18 studies were included in Group 1[4-7,13-16,22-31] and 23 in Group 2[32-54].

Description of included studies

Since the included and available literature was so inhomogeneous in both groups, statistical measures were not applied and data were solely depicted descriptively.

In general, the quality and the level of evidence of the included studies were low. Almost all the studies were retrospective analyses. LoE ranged from II (moderately low risk of bias) to III (moderately high risk of bias), with a clear majority of level III studies.

Since at least one of the following study conditions existed in most of the included studies: 1) insufficient allocation concealment of the participants;

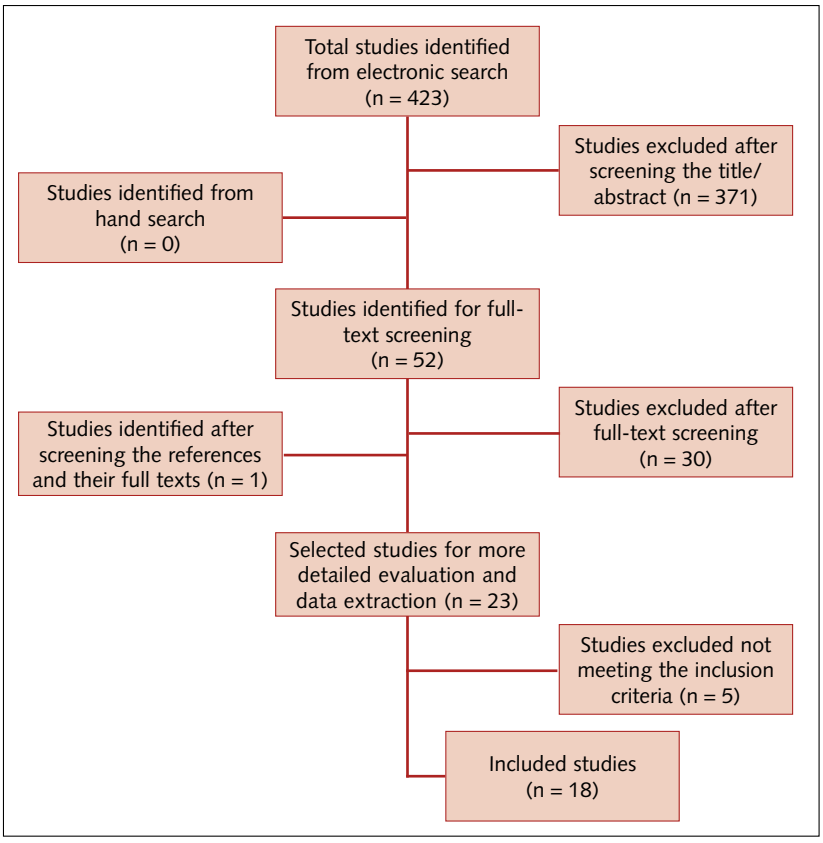

Fig 1 Study selection process bisphoshphonates (BPs) and antiresorptive therapy.

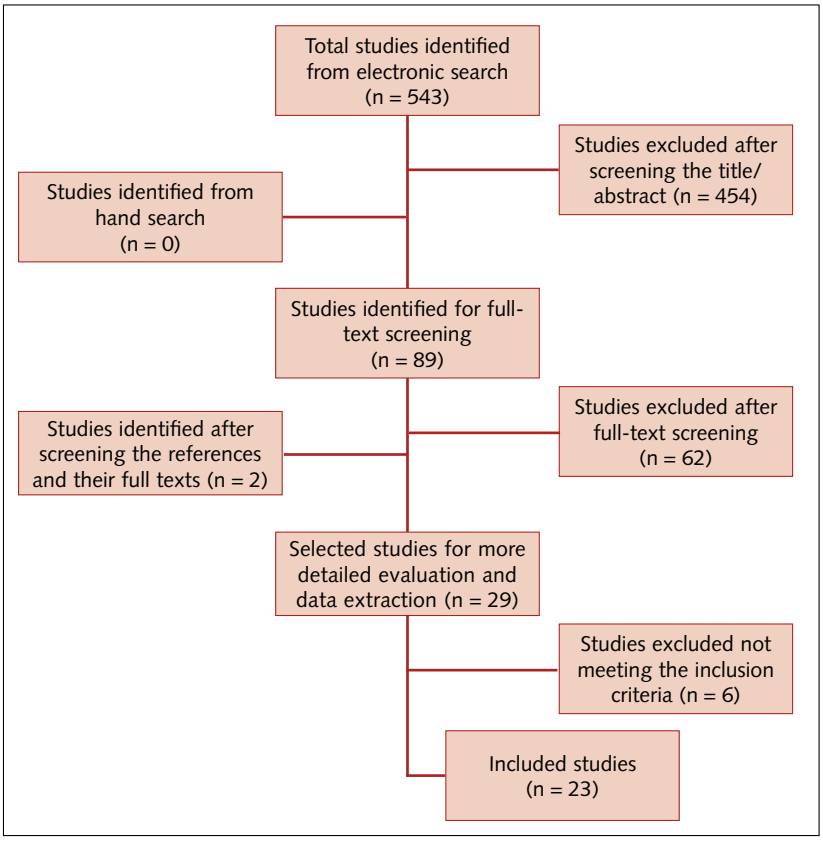

Fig 2 Study selection process radiation therapy.

2) heterogeneous patient collectives; 3) no blinding of the follow-up examiners; 4) missing information concerning the characteristics of patient drop outs; it is highly recommended to be cautious with data interpretation and not derive general conclusions out of the included studies.

Implants in patients with BPs and antiresorptive therapy (Group 1)

Studies were subsequently subdivided in studies dealing with dental implants in patients with BP or antiresorptive therapy assessing the implant survival rate and frequency of osteonecrosis (Table 1) and studies with established osteonecrosis of the jaws related to existing implants or implant treatments describing the pattern and circumstances of the development of the osteonecrosis (Table 2).

In the first part, 14 studies were included[13-16,22-31], three prospective[23,25,26], and 11 retrospective studies[13-16,22,24,27-31] (Table 1). The primary objective of most of the studies was implant survival rate. The numbers of established necroses were additionally documented in most of the included studies. Some additionally assessed peri-implant parameters, such as marginal bone loss, number of exposed implant threads, bleeding on probing (BOP) and the peri-implant pocket depths[13,14,22,23,25]. One study additionally assessed soft and hard tissue healing after extensive autologous bone grafting[26]. In all the studies, the medical reason for the BP or antiresorptive medication was due to osteoporosis. A detailed summary of the taken medication is displayed in Table 1.

In the second part, all four included studies had a retrospective design[4-7] (Table 2) and performed an analysis of the circumstances and pattern of the established osteonecrosis[4-7]. Two studies additionally performed a histological evaluation[5,6]. In terms of the medical reason for the taken medication, patient collectives were more heterogeneous, as in part 1. Significantly more patients with malignant diseases were included[4-7].

Implants in patients with radiation therapy (Group 2)

Extracted data of the 23 included studies are displayed in Table 3[32-54]. Four of the included studies

had a prospective study design [33,36,42,48] and 19 a retrospective study design[32,34,35,37-41,43-47,49-54]. In all the included studies, implant survival was one of the measured study outcomes. Further documented study outcomes were peri-implant bone loss[39], rate of peri-implantitis[47], patient satisfaction[43] and quality of life[34,45]. In terms of the timing of implant placement, only five included studies reported a primary implant placement, which means implant placement prior radiotherapy and/ or during the ablative tumour surgery[34,35,42,43,51]. In total, 16 of the included studies reported a secondary placement (after radiotherapy)[32,33,36-41,44-46,48, 50,53,54] and two a primary and secondary implant placement[47,52].

Outcomes

Implants in patients with BPs and antiresorptive therapy (Group 1)

The implant survival rate ranged from 92.7% to 100% in the test group (patients with BP or antiresorptive therapy) vs 95.5% to 100% in the control group (no BP or antiresorptive therapy). The mean follow-up was 3 to 7.5 years. No patients had a necrosis of the jaw. The BP therapy was due to osteoporosis in all the included patients (Table 1).

The analysis of patients with osteonecrosis (Table 2) revealed that dental implants could quite well be a risk factor. The literature differentiates between an "implant surgery" and an "implant present triggered" necrosis[7]. Both do occur, but the current literature is lacking data to support one over the other in terms of their incidence. The cohort of patients with an implant-related osteonecrosis consisted mainly of patients suffering from a malignant tumour and slightly less of patients with an osteoporosis as the reason for BP treatment[4-7].

In terms of the region of the necrosis, they do occur in the maxilla, as well the mandibular segments, with a slightly higher frequency in the manidble[4-7]. The risk seems to be higher in the posterior segments of the jaws than the anterior ones[4,6].

Extracted risk factors were smoking, diabetes, corticosteroid therapy and hypertension[4-7].

Implants in patients with radiation therapy (Group 2)

The implant survival rate ranged from 38.5% to 97.9% in the test group (implants in irradiated jaw segments) vs 83.8% to 100% in the control group (implant in non-irradiated jaw segments (Table 3)[32-54]. The type of bone requires a clear distinction, as irradiated local bone, irradiated grafted bone, non- irradiated local bone and non-irradiated grafted bone must be distinguished between. The highest risk of implant loss seems to be associated with irradiated grafted bone, followed by irradiated local bone, non-irradiated grafted bone and non-irradiated local bone[32,45,46,50]. Results differ slightly depending on the study cohort and study design[32,45,46,50]. Implant survival rates were, however, mostly lower in irradiated jaw segments than non-irradiated ones[32,45,46,50]. Furthermore, the dosage of irradiation is a factor that seems influence the risk of implant loss with a better survival rate for a radiation dosage minor of 50 Gy[36]. The role of timing of the implant placement is another important factor that can affect the implant success (primary and secondary placement). Primary placement shows a relatively high survival rate of 96.7%[35], but only few studies report primary placement and it is suggested to interpret data with caution. Additionally, data shows more favourable cumulative success rates for mandibular implants (98.4%) compared with maxillary implants (57.1%)[36].

Osteonecrosis of the jaws were described in only a few of the study collectives[33,40,43,45,46,50,51]. Mostly the osteonecrosis occurred in the vicinity of implants[33,43,45,46,50,51] and led to implant failure. As expected, the risk of an osteonecrosis was higher in patients with a radiation dosage > 50 Gy.

Discussion

Osteonecrosis of the jaw predominately occurs in patients with BP or antiresorptive therapy or in those receiving radiation of the jaws as an adjuvant or neoadjuvant treatment of a malignant tumour in the head and neck region[11,55]. The clinical signs are mostly exposed non-vital bone to the oral cavity or a fistula of the oral mucosa to the affected bone.

Table 1 Included studies related to patients with bisphosphonates (BPs) or antiresorptive therapy and oral implants. The primary focus was the implant loss/survival rate as well as the frequency of the establishment of an osteonecrosis of the jaw that is related to the implant site. Abbreviations: BP, bisphosphonate; #, number; PPD, probing pocket depth; BOP, bleeding on probing; OI, oral implant; i.v., intravenous; SL, sinus lifting; GBR, guided bone regeneration; AB, autologous bone; AAOMS, American Association of Oral and Maxillofacial Surgeons; PS, prospective study; RS, retrospective study; LoE, Level of evidence; N/A, not applicable.

Author, year	Study design	LoE	Primary outcome	Secondary outcomes	Timepoint of BP intake	BP dosage, frequency, length and administering	Medical reason for Bps	# Total participants/ implants	# Participants/ implants/ necrosis/ implant losses/ survival rate% with BPs (test group)	# Participants/ implants/ necrosis/ implant losses/ survival rate% without BPs (control group)	Follow up	Comments
Tallarico et al. 2016	Multi-centre PS	II	Implant success, loss/ survival	Marginal bone loss, PPD, BOP	At least 3 years before implant placement	Alendronate orally, Dosage: 5mg to 70 mg Frequency: 1/week-1 month, Length: At least 3 years	Osteoporosis	32/98	32/98/0/1/98.98	N/A	> 3 years of function (range 36 to 72 months; mean 47.6 months)	/
Suvarna et al. 2016	RS	III	Implant loss/survival	Necrosis	Prior to OI placement,	40 alendronate, 10 risedronate, 8 ibandronate, not specified	Not specified	112/140	112/140/0/10/92.86	N/A	Minimum of 3 years	Plus bone grafting, SL, socket grafting, GBR
Khoury et al. 2016	PS	II	Soft/hard tissue healing	Implant loss/ survival, necrosis	BPs prior implant placement and grafting	Different BPs orally and i.v., Dosage: 3 mg to 800 mg, Frequency: 1/week to 1/year, Length: 3 months to 5 years	Osteoporosis	15/71	15/71/0/1/98.57	N/A	At least 3 years	Extensive bone grafting procedures with AB: 3D block grafting, SL
Al- Sabbagh et al. 2015	RS	III	Necrosis	Implant loss/ survival	Prior to OI placement	Different BPs orally, not specified	Osteoporosis	203/515	20/46/0/0/100	183/ 469/ 0/ not specified/ not specified	Mean 7.05 years	Relative inhomogenous patient collective
Siebert et al. 2015	PS	II	Necrosis	Implant loss/ survival, marginal bone loss	BPs prior to implant treatment	Zoledronic acid i.v. Dosage: 5 mg, Frequency: 1/year, Length: 2 to 3 years	Osteoporosis	24/120	12/60/0/0/100	12/ 60/ 0/ 0/ 100	1 year	/
Memon et al. 2012	RS	III	Implant success and crestal bone changes	/	BPs prior to implant treatment	Risedronate, Ibandronate and Alendronate orally, Dosage: not specified, Frequency: not specified, Length: 1 to 3 years and > 3 years	Osteoporosis	200/285	100/153/0/10/ 93.5	100/ 132/ 0/ 6/ 95.5	Not specified	/
Zahid et al. 2011	RS	III	Implant loss/ survival	Number of exposed threads, necrosis	BPs prior to implant treatment	Mostly Alendronate orally, not specified, Dosage: 5mg to 70 mg, Frequency: 1/week, Length: 6 to 192 months	Osteoporosis	300/ 661	26/51/0/3/94.12	274/ 610/ 0/ 16/ 100	Average postsurgical follow-up 26 month	/

Author, year	Study design	LoE	Primary outcome	Secondary outcomes	Timepoint of BP intake	BP dosage, frequency, length and administering	Medical reason for Bps	# Total participants/ implants	# Participants/ implants/ necrosis/ implant losses/ survival rate% with BPs (test group)	# Participants/ implants/ necrosis/ implant losses/ survival rate% without BPs (control group)	Follow up	Comments
Famili et al. 2011	RS	III	Implant loss/survival	Necrosis	BPs prior to implant treatment	Different BPs orally, not specified	Osteoporosis	22/75	22/75 0/1/ 98.7	N/A	Not specified	/
Shabestari et al. 2010	RS	III	Implant mobility (loss/ survival)	PD, BOP, and TE	BPs prior to and after implant placement	Different BPs orally, not specified, Dosage: 35mg to 70 mg, Frequency: 1/week, Length: at least 2 months continuously, mean duration 20.5 months	Osteoporosis	21/46	21/46/0/0/ 100	N/A	Not specified	/
Martin et al. 2010	RS	III	Implant loss/survival, pattern of implant failures (descriptive)	Necrosis	BPs prior to implant treatment	Alendronate orally	Osteoporosis	589/not specified	589/ not specified/0/ 26/95.58	N/A	Not specified	No necrosis reported (AAOMS classification)
Koka et al. 2010	RS	III	Implant loss/survival	Necrosis	BPs prior to implant treatment	Different BPs orally, not specified	Osteoporosis	137/287	55/121 0/1/ 99.17	82/ 166/ 0/ 3/ 98.19	Not specified	/
Grant et al. 2008	RS	III	Implant loss/survival	Necrosis	26 after OI placement, 89 prior to OI placement	Different BPs orally, Length: less and more than 3 years, otherwise not specified	Osteoporosis	458/1918	115/468/0/ 2/99.57	343/ 1450/ 0 / 14/ 99.03	Not specified	/
Bell et al. 2008	RS	III	Implant loss/survival	Necrosis	BPs prior to implant treatment	Different BPs orally, Length: 6 months to 11 years, otherwise not specified	Osteoporosis	42/100	42/100/0/ 5/ 95	N/A	Average length of follow up was 3 years	30 patients also received bone grafting, 96.5% implant survival in control group, (734 implants placed by the same surgeon)
Fugazzotto et al. 2007	RS	III	The incidence of hard and soft tissue complications	Implant survival/ Necrosis	BPs prior to implant treatment	Alendronate and Risedronate orally, Dosage: 35 and 70 mg, Frequency: 1/week, Length: < 1 year to 5 years	Osteoporosis	61/ 69	61/169/0/ 0/100	N/A	12 to 24 months after DI placement	42 immediate placed DIs

Table 2 Included studies related to patients with bisphosphonates (BPs) antiresorptive therapy and an established osteonecrosis of the jaw that is related to oral implants. The primary focus was the analyzation of the necroses that are related to oral implants and the extraction of possible influencing risk factors. Abbreviations: BP, bisphosphonate; #, number; OI, oral implant; i.v., intravenous; BRONJ, bisphosphonate-related osteonecrosis of the jaw; PS, prospective study; RS, retrospective study; Level of Evidence (LoE); N/A, not applicable.

Author, year	Study design	LoE	Primary outcome	Secondary outcomes	Timepoint of BP intake	BP dosage, frequency, length and administering	Medical reason for Bps	# Participants/ implants	Region necrosis	Risk factors	Comments	Outcome
Giovannacci et al. 2016	RS	III	Necrosis (analysation of associated local or systemic risk factors)	/	Prior to and after implant placement	Different BPs, Group 1: 5 oral, 1 i.v.; Group 2: 8 i.v., 1 oral, Dosage: not specified Frequency: not specified Length: Group 1: 36 to 131 months; roup 2: 15 to 60 months	Group 1: 5 osteoporosis, 1 cancer; Group 2: 8 cancer, 1 osteoporosis	15/34	Mandible (8), maxilla (5), both (2)	Smoking, Steroids, Diabetes	Group 1: implant surgery triggered (6), Group 2: implant present triggered (9), MRONJ not always located at OI sites; histological evaluation	Also already existing OIs are a risk for a necrosis, patients under oral BPs have a lower risk for a BRONJ.
Kwon et al. 2014	RS	III	Necrosis (analysation of associated local or systemic risk factors)	Histological analysis	Group 1: 16 pior to OI placement, Group 2: 3 after OI placement	Different BPs, oral (15), i.v. (4), Dosage: not specified Frequency: not specified Length: Group 1: 60.5 ± 30.1 months; Group 2: 13 to 27 months	Osteoporosis (18), Cancer (1)	19/not specified	Mandible (9), maxilla (8), both (2)	Hypertension, Diabetes	Difference between BP initiation before (Group 1, n = 16) and after (Group 2, n = 3) OI placement	3 patients with "implant surgery triggered necrosis" (15.8%), many patients (n = 11/19, 58%) developed BRONJ without any relation to surgical trauma from insertion or removal of the oral implant.
Jacobsen et al. 2013	RS	III	Necrosis (analysation of associated local or systemic risk factors)	Histological analysis	Prior to implant placement	Cancer group:i.v. zolendronate (8) and pamidronate (1); Osteoporosis group: alendronate oral (2), pamidronate (2), ibandronate i.v. (1), Dosage, Frequency and length of BP intake not clear specified	Osteoporosis (5), Cancer (9)	14/23	Mandible (11), maxilla (3)	N/A	Very heterogenous patient collective	Higher risk in the posterior jaw segment. Histologically, signs of infection were found in nine of 11 analysed patients with presence of Actinomyces in six patients.
Lazarovici et al. 2010	RS	III	Necrosis (analysation of associated local or systemic risk factors)	/	Prior to and after OI placement	11 oral Alendronate and 7 i.v. zolendronate, 5 i.v. pamidronate, 4 zolendronate and pamidronate concomitantly, Dosage: 4 mg to 90 mg Frequency: daily, weekly and monthly intake dependent on the BPs Length: 10 to 115 months	Osteoporosis (11), Cancer (16)	27/not specified	Mandible (20): posterior 15 and anterior 5; Maxilla (7): posterior 4 and anterior 3	Smoking, Diabetes, Steroids	Very heterogenous patient collective	Patients undergoing BP treatment and who receive OIs require a prolonged follow-up period to detect any development of BRONJ associated with OIs.

Table 3 (cont.) Included studies related to patients with radiation therapy and oral implants. The primary focus was the implant loss/survival rate as well as the frequency of the establishment of an osteonecrosis of the jaw that is related to the implant site. Abbreviations: RS, retrospective study; PS, prospective study #, number; LoE, Level of Evidence; N/A, not applicable.

Author, year	Study design	LoE	Primary outcome/ Secondary outcomes	Medical reason for treatment (ablative surgery)/radiation	Radiation dosage (Gy)	Time of implant placement	# Total participants/ implants	# Participants/ implants/ necrosis/ implant losses/ survival rate% with radiation therapy	# Participants/ implants/ necrosis/ implant losses, removals/ survival rate% without radiation therapy	Follow up	Comments/Conclusion
Nack et al. 2015	RS	III	Periimplant bone loss/ Implant survival	22 Patients: Oral cancer, not specified	72 Gy	Secondary	20/97	20/97 (48 SLA and 49 SLActive)/0/20 (10 in SLA and 10 in SLActive group)/ 79.4% (79.2% SLA and 79.6% SLactive group)	N/A	5 years	18 implants (8 SLA/10 SLactive) in four patients were counted as lost because the patients had died. Only 2 were lost while not osseointegrated (SLA group). The crestal bone level was stable within 5 years after placement in both groups.
Hessling et al. 2015	RS	III	Implant survival/ rate of periimplantitis	59 Patients: Squamous cell carcinoma (n = 53), odontogenic tumors with malignant degradation (n = 535) sarcoma (n = 2)	Average radiation dose neoadjuvant group: 40 Gy; adjuvant group: 61 to 66 Gy	Primary and Secondary	59/272	59/272/0/10/ 96.3%	Not specified	Mean follow-up period was 30.9 months (range 3 to 82 months)	Of the implant failures, 82% occurred in transplanted bone (4 fibula flaps, 4 iliac crests, and 2 native mandibles). Periimplantitis caused by insufficiently attached gingiva and bone loss occurred in 182 of the implants (67%).
Pompa et al. 2015	RS	III	Implant survival/ N/A	34 Patients: Squamous cell carcinoma (n = 16), Ameloblastoma (n = 6), Osteosarcoma (n = 4), Pleomorphic adenoma (n = 4), Fibrous dysplasia (n = 2) and Nasopharyngeal angiofibroma (n = 2)	Less than 50 Gy	Secondary	34/168	N/A/51/0/12/ 76.4%	N/A/117/0/4/ 96.6%	Mean 22.9 months	Conclusion: A delayed loading protocol will give the best chance of implant osseointegration and stability.
Gander et al. 2014	RS	III	Implant survival/ N/A	33 Patients: Mostly squamous cell carcinoma, one for bisphosphonate-induced osteonecrosis, one for osteoradionecrosis, one for adenocarcinoma, and one for ameloblastoma	Cumulative radiation dose: 56 to 76 Gy	Secondary	33/136	21/84/0/12/85.7%	12/52/0/5/ 90.4%	20 months	Additionally evaluating the influence of smoking and alcohol consumption showed, that both were associated with a significantly higher implant failure rate.
Korfage et al. 2014	RS	III	Implant survival/ patient satisfaction	164 Patients: Squamous cell carcinoma	Not specified	Primary	164/524	100/318/5/27/ 91.5%	64/206/0/1/ 99.5%	14 years	Five patients developed osteoradionecrosis (ORN) in proximity to the implants. Ten implants were removed, combined with sequestrectomy. In 4 patients treatment of ORN was successful, but one patient had a recurrent tumour with a pathological fracture of the mandible in the area of the ORN.

Table 3 (cont.) Included studies related to patients with radiation therapy and oral implants. The primary focus was the implant loss/survival rate as well as the frequency of the establishment of an osteonecrosis of the jaw that is related to the implant site. Abbreviations: RS, retrospective study; PS, prospective study #, number; LoE, Level of Evidence; N/A, not applicable.

Author, year	Study design	LoE	Primary outcome/ Secondary outcomes	Medical reason for treatment (ablative surgery)/radiation	Radiation dosage (Gy)	Time of implant placement	# Total participants/ implants	# Participants/ implants/ necrosis/ implant losses/ survival rate% with radiation therapy	# Participants/ implants/ necrosis/ implant losses, removals/ survival rate% without radiation therapy	Follow up	Comments/Conclusion
Jacobsen et al. 2014	RS	III	Implant survival/ N/A	Squamous cell carcinoma 10, Osteosarcoma 1, Malignant peripheral neural tumour 1, Osteoradionecrosis 14, Ameloblastoma 1, Osteomyelitis 2, Facial trauma 2, Mandibular atrophy 2	63 Gy with a range of 50 to 73 Gy	Secondary	Only 23 received implants/ 140	N/A/ Irradiated grafted fibula 13, irradiated mandible 34/5 implants failed due to osteoradionecrosis, not specified/ Irradiated grafted fibula 8, irradiated mandibula 6/ Irradiated grafted fibula 38,5%, irradiated mandible 82.4%	N/A/ Non-irradiated fibula 86, Non-irradiated mandibular bone 7/ 0/ Non-irradiated fibula 12, Non-irradiated mandibular bone 1/ Non-irradiated fibula 86.1%, Non-irradiated mandibular bone 85.7%	Median follow-up time was 67 months	Extracted risk factors are smoking, alcohol use, and irradiation. Implant placement in irradiated grafted bone seems to be a high-risk procedure.
Fierz et al. 2013	RS	III	Implant survival/ N/A	Squamous cell carcinoma 35 (76%), Adenocarcinoma 4 (9%), Non-Hodgkins lymphoma 1 (2%), Angiosarcoma 1 (2%), Multifocal plasmocytoma 1 (2%), Verrucous carcinoma 1 (2%), Esthesioneuroblastoma 1 (2%), Uncertain metastases	Not clear specified	Secondary	28/104	Local bone: N/A/ 42/N/A/6/81%, Grafted bone: N/A/20/N/A/6/ 70%, one osteonecroris occured with loss of 4 implants, not specified in which group	Local bone: N/A/ 16/0/2/87.5%, Grafted bone: N/A/26/ 0/ 0/100%	3-6 years	Significant lower survival rates in patients with radiation therapy then healthy patients.
Katsoulis et al. 2013	RS	III	Implant survival/ quality of life	78% squamous cell carcinoma, 9% adenocarcinoma and 13% comprised a variety of rare tumours including oral metastasis of other tumours	Between 56 and 81 Gy	Secondary	28 patients received implants/ 104; 20 patients received radiation	N/A/ native bone 42, grafted bone 20/3 implants were associated with osteoradionerosis, not specified/ native bone 8, grafted bone 8/ Native bone 81%, grafted bone 60%	N/A/ Native bone 16, grafted bone 26/ 0/ native bone 2, grafted bone 2/ native bone 87.5%, grafted bone 92.3%	5 years	Early implant loss was high (13%) and cumulative survival rate of loaded implants was < 90% after 5 years. Higher risk of implant loss in patients with radiotherapy.
Buddula et al. 2012	RS	III	Implant survival/ N/A	Squamous cell carcinoma, adenoid cystic carcinoma, basal cell carcinoma, unknown primary head and neck carcinoma	Mean 60.7 (range 50.2 to 75.5)	Secondary	48/271	48/271/0/33/ 89.9%	N/A	60 months	Implants placed in the maxilla were more likely to fail than implants placed in the mandible (P = .002).

Author, year	Study design	LoE	Primary outcome/ Secondary outcomes	Medical reason for treatment (ablative surgery)/radiation	Radiation dosage (Gy)	Time of implant placement	# Total participants/ implants	# Participants/ implants/ necrosis/ implant losses/ survival rate% with radiation therapy	# Participants/ implants/ necrosis/ implant losses, removals/ survival rate % without radiation therapy	Follow up	Comments/Conclusion
Fenlon et al. 2012	CS	III	Implant survival/ N/A	Not specified	66 Gy	Primary	41/ 145	N/A/35/3/15/ 57.1%	N/A/110/0/3/ 97.3%	Time of surgical reconstruction or after 3 months of healing	Implant placement immediately at the time of surgical reconstruction or after 3 months healing. Increased failure rates of immediately placed implants and irradiated bone.
Mancha de la Plata et al. 2012	RS	III	Implant survival/ N/A	Squamous cell carcinoma, adenoid cystic carcinoma, basal cell carcinoma	Mean 59.6 (range 50 to 70)	Secondary	50/355	30/225/5/10/ 92.6% the osteonocrosis was not related to the implants	20/130/0/3/ 96.5%	60 months	Implant loss in the osteoradionecrosis group: 48.3% Non-osteoradionecrosis: 92.3%; Control group: Patients without irradiation.
Linsen et al 2012	RS	III	Implant survival/ N/A	Squamous cell carcinoma, ameloblastoma, adenoid cystic carcinoma, keratocysts	36 Gy in 26 patients and a total dose of 60 Gy in 8 patients	Secondary	66/262	N/A/127/0/ N/A/ 95.6%	N/A/ 135/0/N/ A/95.6%	47.9 (± 34.3) months (range 12 to 140 months)	Overall: 86.9% (10 years) RT: 95.6% (10 years) RT and chemotherapy: 91.5%(5 years) Control: 95.6% (10 years); Control group: implants placed in tumour patients in regions without irradiation.
Sammartino et al. 2011	PS	II	Implant success/ Implant survival	Not specified	All kinds of dosages: group < 50 Gy vs group > 50 Gy	Secondary	77/188	77/188/0/20/ 89.4%	N/A	At least 36 months	The analysis of implant subgroups showed slightly more favourable cumulative success rate for mandibular implants (98.4%) compared with maxillary implants (57.1%) and clearly better success rate for a radiation dosage minor of 50 Gy doses.
Borrowmann et al. 2011	RS	III	Implant survival/ N/A	22 squamous cell carcinoma, 2 verrucous carcinoma, 4 osteosarcoma and 3 adenoid cystic carcinoma	Not specified	Secondary	31/115	N/A/48/0/ 5/89.6%	N/A/67/0/0/ 100%	Not specified	Increased risk of implant failure in free flap bone that has been irradiated
Heberer et al. 2011	PS	II	Implant success/ Implant survival	Squamous cell carcinoma	Up to 72 Gy	Secondary	20/97	20/97/0/2/97.9%	N/A	14.4 months (12 to 26 months)	SLA vs. modSLA: The success rate of SLA implants was 96% and of the modSLA implants was 100%.

Table 3 (cont.) Included studies related to patients with radiation therapy and oral implants. The primary focus was the implant loss/survival rate as well as the frequency of the establishment of an osteonecrosis of the jaw that is related to the implant site. Abbreviations: RS, retrospective study; PS, prospective study #, number; LoE, Level of Evidence; N/A, not applicable.

Author, year	Study design	LoE	Primary outcome/ Secondary outcomes	Medical reason for treatment (ablative surgery)/radiation	Radiation dosage (Gy)	Time of implant placement	# Total participants/ implants	# Participants/ implants/ necrosis/ implant losses/ survival rate% with radiation therapy	# Participants/ implants/ necrosis/ implant losses, removals/ survival rate% without radiation therapy	Follow up	Comments/Conclusion
Salinas et al. 2010	RS	III	Implant success/ implant survival	Squamous cell carcinoma, tonsillar carcinoma, adenoid cystic carcinoma, rhabdomyosarcoma, osteosarcoma, unknown primary head and neck carcinoma	More than 60 Gy, not specified	Secondary	44/206; 144 were placed in a fibula flap, and 92 were placed in the native mandible	N/A/90/0/23/ 74.4%	N/A/116/0/8/ 93.1%	From 4 to 108 months (mean 41.1 months)	The success rate was 82.4% for implants placed in fibula flaps and 88% for implants placed in native mandibles.
Korfage et al. 2010	PS	II	Implant survival/ N/A	Squamous cell carcinoma	> 40 Gy (rabge 12 to 70)	Primary	50/195	N/A/123/0/13/ 89.4%	N/A/72/0/1/ 98.6%	60 months	Only 20 patients left at the 5 year follow up.
Klein et al. 2009	RS	III	Implant survival/ N/A	Squamous cell carcinoma	3 groups: No radiation, < 50 Gy, > 50 Gy	Secondary	43/190	27/126/0/13/ 89.6%; RT < 50 Gy: 90.9% RT > 50 Gy: 77.5%	16/74/0/12/ 83.8%	60 months	Control group with also critical defects due to tumour surgery but no irradiation; bony bed (local bone versus augmented iliac crest bone), radiation dose (no radiation, < 50 Gy, > 50 Gy) and implant dimensions.
Cuesta-Gil et al. 2009	RS	III	Implant survival/ N/A	Malignancies and ameloblastomas	50 to 60 Gy	Primary and Secondary	111/706	79/375/0/27/N/A	32/N/A/0/2/N/A	108 months	Osseointegration success rate 92.9%; Of the 29 osseointegration failures, 27 (93%) occurred in irradiated patients, and all were located in zones exposed to the maximum radiation dose.
Schoen et al. 2008	RS	III	Implant survival/ quality of life	Squamous cell carcinoma	60.1 Gy	Primary	50/186	31/124/0/2/97%	19/62/0/2/97%	18 to 24 months	/
Schoen et al. 2007	PS	II	Implant survival/ N/A	Squamous cell carcinoma	61.4 Gy (range 46 to 116)	Secondary	26/103	26/103/1/11/9.3%	N/A	36 months	Overall 89.3%, HBO vs. Non-HBO group: HBO Group 85.2%, Non-HBO Group 93.9%.
Schepers et al. 2006	RS	III	Implant surviv al/ N/A	Squamous cell carcinoma	60 to 68 Gy, not specified	Primary	48/139	21/61/0/2/96.7%	27/78/0/0/ 100%	> 30 months	
Yerit et al. 2006	RS	III	Implant survival/ N/A	Squamous cell carcinoma	50 Gy, not specified	Secondary	71/316	Native bone: N/A/ 154/ 0/29/72%, Grafted bone: N/A/ 78/0 /13/ 54%	N/A/84/0/2/ 95%	5.42 (± 3.21) years	Overall: 75% (8 years), RT native bone: 72% (8 years), RT grafted bone: 54% (8 years), Control native bone: 95% (8 years)

Osteonecrosis can lead to the loss of large segments of jaw, which strongly impairs the affected patient functionally and aesthetically. Therefore, such patients should be treated with extreme caution, and treatment concepts should be designed to prevent the occurrence or an osteonecrosis.

Today, modern treatment scenarios for the functional reconstruction of edentulous jaw segments involve implant-retained prostheses. Due to the rising number of patients with a potential risk for the formation of a necrosis of the jaw and the increased demand for an implant treatment concept, it is a matter of importance to evaluate the relation between oral implants and the medical conditions that arise form BP/antiresorptive and radiation therapy.

Therefore, this systematic review aimed to clarify the risk of osteonecrosis formation in patients assigned to BP/antiresorptive and radiation therapy in the context of the treatment with implants. Primary and secondary outcomes were the implant survival/success rates and the risk of jaw osteonecrosis related to implants in such patients.

Implants in patients with BPs and antiresorptive therapy (Group 1)

In BP patients, it has been shown that intraoral risk factors, such as invasive dental treatments (dental extractions), irritation through removable dentures and periodontitis as an initial trigger, can be related to the development of an osteonecrosis[56-59]. Oral surgical procedures in particular increase the incidence of an osteonecrosis five to seven-fold[60]. Additionally, 20% of cases with BRONJ occur spontaneously without any identified trigger factor[61]. Based on this, it was hypothesised that bone necrosis is an aseptic process that precedes clinical onset, and is an inflammatory-associated process[62,63].

The literature also reports on BRONJ related to intraoral implants[4-7]. Concerning such implants in patients with BPs, a distinction is made between existing implants prior to initiating the BP therapy and implants placed during or after BP therapy. Therefore, the literature also differentiates between osteonecrosis of the jaws that are "implant present triggered" or "implant surgery triggered". In patients already taking BPs there is still the question as to whether implant treatment concepts should be avoided or can be carried out safely. The outcomes of a recent literature review indicate that certain factors, such as the way of administration (oral or IV), and frequency and duration of drug intake, as well as the reason for BP treatment (osteoporosis or due to a malignant diseases) can be crucial for the treatment decision with a higher risk of complications in patients with malignant cancer diseases that take or have taken IV BPs with a high frequency over a longer period[55].

In our review, we also found evidence to justify implant-supported treatment strategies in patients taking BPs due to primary osteoporosis. In this patient category, implant survival rates are as comparably high as in patients in the control group not taking antiresorptive medication[14,16,22,25,27]. The risk of the occurrence of a medication-related osteonecrosis of the jaws (MRONJ) related to implants is considerably low in this patient cohort[13-16,22-31]. These results are in accordance with other literature reviews[55,64]. In their prospective studies, Tallarico et al, 2016, and Siebert et al, 2013, showed implant survival rates of 98.98% (mean follow-up of 47.6 months) and 100% (1-year follow-up) with not one single osteonecrosis[23,25] in patients taking different BPs due to osteoporosis treatment. Further outcomes of retrospective studies confirm these data and authors concluded that bisphosphonate treatment in such patients does not affect implant success and does not result in an osteonecrosis of the jaw[13,14,16,27,28]. However, one must bear in mind that these studies had rather short follow-up intervals, while osteonecrosis was defined as being a late complication that occurs after years[4]. Therefore, Lazarovici et al 2010, recommended that BP patients undergoing implant therapy should be followed up for a long period[4].

According to the outcome of this systematic review, MRONJ in relation to oral implants more frequently occurs in patients taking an antiresorptive medication due to a malignant disease than an osteoporosis[4-7]. This is in accordance to data in the literature that, in general, describes a higher frequency of osteonecrosis of the jaws in patients taking BPs due to malignant diseases[5,6,65,66].

If an osteonecrosis occurs, it is mostly located in the mandible, and even more precisely in the posterior regions[4-7]. When considering the patterns of necrosis development, the outcomes of this review show that existing implants, as well as the insertion

of implants, can be a risk for a necrosis[4,5,7]. Further studies are needed to differentiate whether "implant present triggered" or "implant surgery triggered" osteonecrosis occurs more frequently.

The limitation of this first part of the systematic review is the lack of existing prospective randomised controlled clinical trials related to the topic. Additionally, most of the included studies had a low level of evidence with a relatively high risk of bias. Also, the heterogeneity of the included data did not allow a meta-analysis to be performed.

Implants in patients with radiation therapy (Group 2)

The evidence from publications concerning patients who had undergone radiation therapy of the jaws, in conjunction with implant treatment, were also explored as being a potential trigger for the development of an osteonecrosis[11]. Due to the side effects after ablative tumour surgery and radiation therapy of the jaws in cancer patients, i.e. compromised hard and soft tissue situations, and xerostomia, oral rehabilitations are rather complex and challenging. Furthermore, the insertion of conventional prostheses is certainly challenging to sufficiently restore patients' function, aesthetics, speech and quality of life. Besides all the known complications and negative side effects, implant-based treatment scenarios are the only feasible option to functionally rehabilitate such patients. It has been hypothesised that implant-retained dentures may eliminate the risk of mucosal irritation, which was considered as a cause of necrosis formation[11].

For a long time, the issue of implant survival in irradiated native jaw segments vs non-irradiated native jaw segments has been a controversial topic in the literature. Contemporary studies and the outcome of a recently performed systematic literature review and meta-analysis by Schiegnitz and coworkers in 2014 show comparable implant survival rates between irradiated native and non-irradiated native bone, especially in studies between 2007 and 2013[11,34,37,40-42]. This is in accordance with outcomes of the current review. Comparable implant survival rates in irradiated native jaw segments may be attributed to the optimised modern implant treatment concepts involving improvements of implant macro- and micro designs that enhance the process of osseointegration, as well as the improvement in digital treatment planning concepts, to archive the best possible implant position[11].

Additionally, data extraction in this review shows that implant survival also differs between native jaw segments and grafted jaw segments. Therefore, literature differs between non-irradiated native bone, non-irradiated grafted bone, irradiated native bone and irradiated grafted bone[45,46]. Implant survival rates are almost comparable in grafted and native non-irradiated jaw sites[45,46]. In terms of irradiated grafted bone portions, implant survival rates are significantly lower than in non-irradiated grafted sites[45,46 50]. Implant survival, therefore, greatly depends on the quality of the bony bed which, for example, is different in grafted sites. Reduced bone quantity, bone quality and vascularisation of grafted sites have already been discussed as causal factors[11]. Therefore, if possible, an implant placement in native jaw segments should be recommended.

The protocol of implant placement (primary or secondary) was also discussed being an influencing factor concerning implant survival. This issue is still debated in the literature with no concrete recommendation. Primary placement of implants during ablative tumour surgery has been described as advantageous in terms of avoiding implant surgeries in irradiated fields, the reduction of the number of surgical procedures and the possibility of an early functional rehabilitation[34,35,42]. Outcomes of studies with primary placement show promising results in terms of implant survival and the number of complications[35,42] in this review. However, the majority of the included studies reported on secondary placement[32-34,36-42,44-46,48-51,53,54], or in other words, after radiation therapy. In the literature, there is still no evidence for the optimal time point of a secondary implant placement. Current data suggests implant placement between 6 and 12 months after radiation therapy[67,68], as discussed in the review by Schiegnitz and coworkers[11]. Additionally, it is recommended to leave inserted implants unloaded for 6 months, assuming that irradiated bone heals slower than non-irradiated bone[11,69]. Outcomes of some study subgroup evaluations in this review suggest that implants placed in the maxilla are more likely to fail than in the mandible[36,53], which can be explained by the more compact bone structure of the mandible, resulting in a higher implant stability.

The radiation dose was also considered as being a crucial factor for implant success rates and the influence on the risk of an osteonecrosis. The radiation dose varied greatly in the included studies. Although the outcome of one study showed a better success rate for minor radiation dosage of 50 Gy[36], evidence is lacking in the current literature to offer a definitive conclusion.

Implant loss in some documented case reports occurred due to an osteonecrosis of the irradiated jaw segments[40,50]. Some osteonecrosis also occurred in the proximity of the inserted implants[43] and can thus be designated as "implant triggered". However, they also occur in patients who received implants in irradiated jaw segments not related to the implants[40]. According to the outcome of this review, a potential risk for the development of an osteonecrosis of the jaws does exist in irradiated jaw segments and can be "implant triggered". However, current data does not permit a definitive assessment of the relative risk for an osteonecrosis of the jaws related to oral implants.

Conclusions

In general, oral implant placement in patients with BP/antiresorptive therapy or radiation therapy should be considered in light of a thorough overall assessment, bearing in mind that necrosis can occur and that the consequences can be severe for the affected patient.

Implants in patients with BPs and antiresorptive therapy (Group 1)

Within the limitations of the present review the following conclusions were drawn:

- Implant survival rates in patients taking BPs due to an osteoporosis are as comparably favourable as in patients not taking BPs.
- The risk of developing an osteonecrosis is higher in patients with malignant diseases who are prescribed intravenous BP therapy. Concerning the current data, if an implant treatment is to be considered, it should only be recommended in patients with osteoporosis. Since no long-term data for implant success exist for this patient cohort, the potential risk of a late necrosis due to an oral implant should still be considered.
- Concerning oral implants, necrosis can be "implant presence triggered" or "implant surgery triggered", but currently it is not possible to differentiate between the incidence and outcome between the two.
- Prior to considering an implant placement, it is imperative to take into account all medical conditions and risk factors as well as the frequency, duration, dosage and the manner of bisphosphonate administration. Where there are acceptable alternative prosthetic options, a history of an osteonecrosis in the affected patient and a need for a bone augmentation to realise implant placement, then implant treatment concepts should be avoided.
- It is recommended to thoroughly inform a patient about possible long-term implant failures and the risk of developing an osteonecrosis of the jaws.
- Further randomised controlled clinical trials with longer follow-ups are needed for a better risk assessment.

Implants in patients with radiation therapy (Group 2)

Within the limitations of the present review the following conclusions were drawn:

- According to the current literature, implant survival rates are comparable in non-irradiated native bone and irradiated native bone. Implant placement in irradiated native jaw segments can therefore be considered as a reliable treatment option.
- Implant survival in irradiated grafted sites is significantly lower than grafted, non-irradiated, native-irradiated and native non- irradiated sites. If possible, an implant placement in native jaw segments should be recommended.
- There is low evidence in the literature to suggest higher implant survival rates in the irradiated jaw segments of the mandible than the maxilla and considering the radiation dosage as an influencing factor with higher implant survival rates in jaw segments with the radiation dosage of < 50 Gy.
- Radiation-induced osteonecrosis of the jaws does occur and can be implant "triggered". Current literature lacks data to define a relative risk for implants as a trigger for the development of an osteonecrosis.

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Impact of asepsis technique on implant success. A review

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Key words *antibiotics, antimicrobials, asepsis, clean, dental implants, gloves, hygiene, infection, sterilization*

Asepsis is described as a state free from microorganisms. In medicine, an aseptic environment is necessary and expected to avoid the spread of infection through contact between persons, sprays and splashes, inhalation, and sharps. Most dental procedures are performed in a "clean "environment with the common use of personal protective equipment (PPE) such as disposable gloves, masks and protective eyewear with disinfection of surfaces and sterilization of instruments. For surgical procedure such as the insertion of endosseous implants, the recommendations are not clear. The use of antimicrobials and antibiotics before and after the procedure remains a controversial issue The purpose of this literature review is to evaluate the current evidence as to what is generally expected and widely accepted in the use of aseptic techniques for the surgical placement of endosseous implants, and the impact on implant survival and overall success.

■ Introduction

Implants have been accepted and embraced worldwide by the medical and dental profession, as well as by patients, due to their predictable long-term success[1,2,3]. Today, this surgical technique is performed by specialists and general practitioners, usually in ambulatory settings, and even in general dental practices under local anesthesia[3]. The success of implants in oral rehabilitation is dependent upon variables[4]. Among the variables are the operatory setting, aseptic technique, the intraoral environment and systemic management of bacteria.

The late 1800s saw the introduction of the principles of antisepsis in medicine. The principles of antisepsis, advanced infection control practice, sterilisation, barriers and antimicrobial prophylaxis, changed healthcare practice and dramatically reduced the number of postoperative complications[5].

Good hand hygiene is one of the most important mechanisms to limit the spread of healthcare-associated infections and increase the success of surgical procedures. In surgery the recommendations are clear as to the difference in when and how to apply an aseptic versus a clean technique[5]. The application of an aseptic technique is necessary to prevent contamination of a surgical site with microorganisms and includes methods such as sterile gloves, gowns, drapes and masks. Some people recommend this, in particular for intraoral implant surgery, as a critical component to proper healing and success[6]. The purpose of a clean technique is rather to reduce the number of microorganisms in order to minimise the risk of transmission from the environment or healthcare personnel[7]. The clean technique is routinely practiced in today's dental practices for ordinary dental care. The asepsis technique is more complex and expensive and includes environmental controls such as a clean environment and minimising traffic

during the procedure to prevent airborne particles that can cause infections.

The recommendations for the practice of one or the other techniques, especially for chronic wound care, depends on patient factors, immune status, acute versus chronic wound, type and location of the wound, invasiveness of the procedure, if debridement is needed, the type of setting, who is performing the procedure, maintenance of instruments and the likelihood of exposure to organisms in the healthcare setting[8]. The same recommendations are not clear for the insertion of endosseous implants.

The use of personal protective equipment (PPE) is dependent upon the procedure being carried out. Standard infection control precautions call for the use of gloves, gowns, masks and goggles for any procedures that involve direct contact with the patient's body fluids.

In oral surgery, hand hygiene, PPE, safety working with sharp instruments, sterilisation and disinfection of dental instruments, surgery design, surface disinfection, use of plastic barriers and cleaning of dental water line units all have the purpose of reducing the risk of cross-infection. Disposable gloves and protective eye and mouth wear is recommended to be worn for all dental procedures. Single-use gloves and masks should be changed in between patients.

Operatories should be designed for easy cleaning. Operating tables or dental chairs, floors and furniture should allow easy cleaning and disinfection. The same is expected for local work surfaces such as hand controls, lights and computer keyboards.

Recommendations exist worldwide and are designed to prevent or reduce potential for disease transmission from all potential areas: patient to healthcare provider, healthcare provider to patient, and from patient to patient in order to prevent postoperative infections.

Although these guidelines focus mainly on outpatient, ambulatory health-care settings, the recommended infection-control practices are applicable to all settings in which dental treatment is provided.

What do guidelines recommend[9]:

- Hand hygiene;
- Gloves;
- Sterilization of unwrapped instruments;
- Water quality concerns – flushing waterlines;
- Aseptic technique for parenteral medications;
- Pre-procedural mouth rinsing before surgical procedures.

Hands are the greatest source of pathogen transmission. Hand washing refers to washing hands with soap and water, while antiseptic hand washing refers to washing hands with water and soap plus another detergent and antiseptic agent, such as triclosan or chlorhexidine. Waterless, alcohol-based agents are now used in addition to hand washing. Alcohol-based hand sanitisers claim to be the most effective products for reducing the number of germs on the hands of healthcare providers[10].

Spaulding presented a popular approach to categorising disinfection and sterilisation protocols for instruments and pieces of equipment in health care in 1968[11].

The classification includes three categories:

- Critical objects, such as scalpels, blades and periodontal probes, which penetrate mucous membranes and skin. Sterilisation is crucial.
- Semi-critical objects, such as mirrors or objects that do not penetrate mucous membranes, also require sterilisation.
- Non-critical objects that do not contact mucous membrane, such as the operating table or dental chair and other furniture, require intermediate or low-level disinfection.

Another issue is the prevention of postoperative infection at the site of the surgery. In hospital settings, despite all efforts to prevent them, surgical site infections (SSIs) remain a significant cause of morbidity and mortality among hospitalised patients[12].

There are several factors that may contribute to postoperative infections and intra-operative contamination. Airborne particles carrying microorganisms may be a possibility. In order to prevent bacterial contamination, surgical staff should avoid actions such as removing gloves, putting arms through the sleeves of the gown, and unfolding the surgical gowns, as reported by a study observing surgeons and nurses mimicking intraoperative actions prior to total knee arthroplasty[13].

We know and expect a clean operating environment during medical and dental treatment and

expect a sterile environment when a procedure involves an open wound to avoid surgical complications. Surgical site infections for surveillance classification purposes are divided into incisional SSIs and organ/space SSIs.

Incisional SSIs are further classified into superficial and deep incisional.

Organ/space SSI involves any part of the anatomy other than the incision that is open and manipulated during the surgical procedure. Oral cavity infections belong to the organ/space SSI classification[14].

In intraoral implant surgery, the variables for surgical success and the recommendations for operating conditions have changed over the years. Manufacturers have different recommendations for sterilisation of reusable products and disposal of their products.

A publication from 2012[15] studied asepsis in implant dentistry. In the conclusions of this review, the highest standards of surgical asepsis were promoted to minimise the risk of cross infection, protect patients and staff, and help to reduce the use of systemic antibiotics. The technique suggested included the operating room, air conditioning, room design, and minimising the surgical team's movement and speech, patient preparation, use of preoperative antibiotics and antiseptics postoperatively.

Preoperative and postoperative antisepsis

Effective preoperative antisepsis is recognised to prevent SSI, but the definitive method is unclear in the use of one or more products individually or in combination.

Povidone-iodine (PVI) was used for many years, but today chlorhexidine (CHX) is recommended or the combination of these products is suggested[16]. Oral antiseptics reduce nosocomial infections and, for example, ventilator-associated pneumonia. For major surgical interventions, there is evidence that a combination of CHX and PVI can be used for preoperative antisepsis for surgical procedures.

Local postoperative infections are a regular complication in oral surgery. Attaining aseptic conditions in the oral cavity is almost impossible and there is no specific protocol for antimicrobial prophylaxis for maxillofacial and oral surgery[17]. The most common solutions used are 0.12%, 0.2% and 1% chlorhexidine and 1% povidone-iodine. A randomised clinical trial published in 2009 compared the use of three different antiseptic solutions of povidone-iodine, chlorhexidine-gluconate and cetrimide and sterilised physiological solution as a control group. All three antiseptic solutions produced a statistically significant reduction in aerobic and anaerobic bacteria, with chlorhexidine having a prolonged bactericidal effect. The group with 1% povidone-iodine had no local postoperative infections[17].

But what is the impact specifically for the insertion of endosseous oral implants?

Use of antimicrobials or antibiotics

The empirical use of antibiotics to prevent any kind of infection is still controversial.

Widespread use of antibiotics by people who do not have an infection may have contributed to the development of bacterial resistance.

A Cochrane systematic review that included 18 double-blind controlled trials with 2456 patients assessed the benefit of giving antibiotic to prevent infection after tooth extraction[18]. This review looked at the use of different types and dosages of antibiotics, compared with a placebo, before or after tooth extraction. The conclusion from results of moderate-quality evidence was that antibiotics administered just before or after surgery will reduce the risk of infection by 70%, and pain and dry socket by 38% after wisdom teeth extraction performed by oral surgeons. This evidence also reflects the use of antibiotics as causing brief and minor side effects.

The NNT or number needed to treat to prevent infection was calculated to be 12, which means that 12 people need to be treated with antibiotics to prevent one infection following extraction of impacted wisdom teeth. Are the same recommendations implied for implant placement?

There is a lack of clarity as to how the dental practitioner needs to proceed in certain issues to control the survival and success of implants.

The purpose of our review is to evaluate:

- The level of asepsis needed and the impact on implant success.
- The use of topical rinses before and after the surgical procedure.

- The use of antimicrobials/antibiotic and the success on implants.
- What is generally expected and widely accepted?

Criteria for considering articles for this review

For the nature of the clinical question and the topics proposed, we included any type of article that helped us to assess the use of asepsis and antimicrobials and the implications for implant survival and success. Our focus was on clinical trials to evaluate the etiology with the main outcome of implant failure; if there was use or not of asepsis or antimicrobials in any manner and whether interval or dosage affects the outcome. For the purpose of creating a consensus, if systematic reviews were available on some of the topics, we conducted a review of the systematic reviews and assessed the available data.

Electronic searches were performed (PubMed, Google Scholar, Ovid Medline and references from important articles were searched). Key words used and not limited to: asepsis and dental/oral implants, asepsis and implant dentistry, dental/oral implants and antimicrobials,

The authors performed collection and analysis independently and in duplicate. They assessed the quality of the included studies for validity and relevance using standardised tools of appraisal and to assess bias.

Data synthesis

For the type of topics, the difference in study designs and the interventions, we divided the topics into the following groups:

- Asepsis type influencing the outcome of implant placement.
- Local/topical antimicrobial agents pre and post operative.
- Oral antibiotics and antimicrobial pre and post operative.

Asepsis type influencing the outcome of implant placement

Determining the exact element(s) that are critical for success and osseointegration would be extremely useful. Simplifying the surgical technique without compromising the final result is preferable in reducing the cost of the procedure. Since a truly sterile environment cannot be achieved in the oral cavity, it is questionable if the same protocols used for orthopaedic procedures are necessary for the intraoral insertion of implants[19].

The oral cavity can be the source of infection, but external sources such as contaminated instruments, the operator's hands, aerosols and the overall operating room conditions can also be sources. In healthy patients, the nares are identified as the carrier for *S. aureus* and a nose mesh was recommended for oral surgeries[20]. However, we could not find any evidence that covering the nasal cavity or using nasal ointment for implant surgery was of any benefit. In general surgery, the use of nasal ointment with mupirocin ointment was protective against Gram-positive bacteria[21].

A study observing 399 consecutive patients and analysing the influence of endogenous and local factors on the occurrence of implant failure up to the abutment stage, concluded that patients breaching sterility during surgery had more implant failures, however the results should be evaluated with caution[22].

Since the 1990s and the generalised use of oral implants to anchor or carry a dental prosthesis, some of the manufacturers have made specific recommendations for surgical operatory set-up involving a sterile working area in a surgically clean environment, while others have not officially stated any position on sterile operating room procedures[23].

The truth is that in the private practices of dental clinicians and specialists there are a wide variety of clean and aseptic operating conditions and how that really impacts the success of implant surgery is unknown.

A 1996[19] retrospective study compared the success rates for osseointegration of implants placed under sterile versus clean condition. In both environments, the surgeon wore sterile gloves and all instruments and irrigation solutions were sterile. All the participants wore mask and eye protection. The clean technique did not include sterile gowns, scrubs,

shoe covers, drapes or skin preparation. Both groups received postoperative antibiotic coverage. The study analysed results for implants placed between 1983 and 1991. A total of 273 implants were placed under sterile conditions in 61 patients, 270 were considered to be osseointegrated at stage 2. There were three failures in three patients and the overall case success rate calculated was 95.1%. A total of 113 implants were placed under clean conditions in 31 patients, and 111 were considered osseointegrated at stage 2. There were two failures in two patients. The overall case success rate calculated was 93.5%.

Within the limitations of the study, the authors concluded that as with all surgery, success is influenced by proper case selection diagnosis, surgical skill, atraumatic treatment of tissue and attention to detail. The success of the osseointegration was not altered by the use of sterile or clean techniques.

An important point in this study in the clean group is during the implant placement nothing touched the surface of the sterile implant until it contacted the prepared site in the bone.

In his 1996 publication in the Journal of Oral Maxillofacial Surgery, one author questioned the use of sterile vs clean technique for implant placement[24].

This author reviewed several publications on the topic and reported the results of a survey/questionnaire to American oral and maxillofacial surgeons that showed substantial differences in disinfection procedures and infection control in outpatient practices[25]. The author suggests that using the sterile technique minimises complications, such as when the implant touches the exterior of the patient and gets contaminated with skin flora. Sterile technique also reduces the need for preventive antibiotics.

A study published in 2008[26] compared the survival rate of implants using a simplified surgical operatory set-up compared with the original Brånemark protocol. All patients received antibiotic prophylaxis, all instruments and irrigation solutions were sterile and surgeons wore sterile gloves. In the original protocol, the operators wore surgical gowns; all patients were draped with sterile operating sheets covering the body and the head, leaving only the mouth accessible. In the simplified protocol, surgeons did not wear surgical gowns and the patients were draped with a smaller sterile drape covering just the chest and head areas, leaving the peri-oral area uncovered.

A total of 1285 patients were included in the study, and a total of 4,000 implants were placed during the period 1985 to 2003. The traditional sterile group included 654 patients and 2414 implants, while the simplified technique included 631 patients and 1586 implants. Failure was defined as any non-osseointegrated implant after the recommended period for the prosthetic rehabilitation.

The overall results for 4000 implants placed was 127 lost during the time of the evaluation. For the complete traditional sterile group, 82 implants failed from the 2414 implants inserted, corresponding to a success rate of 96.6%.

For the simplified technique, 45 implants failed out of 1586, which corresponds to an implant success rate of 97.2%. The authors concluded that the study results suggest a simplified operatory set-up is sufficient and does not affect the outcome of implant placement. It seems that aseptic versus clean technique does not affect an implant's success and so it can be concluded that it may be of benefit as it reduces the cost of the technique. For the purpose of our review, we did not combine the results due to the characteristics of the included studies. The recommendations are based on low level of evidence.

We also furthered our search to see if the use of sterile or disposable gloves makes a difference to the surgical outcomes. Our search retrieved a randomised controlled study comparing the use of non-sterile gloves for minor skin surgeries[27]. The results from 493 patients, 250 in the non-sterile clean, boxed gloves compared with 243 in the sterile gloves group concluded that in regard to wound infection, non-sterile clean boxed gloves are not inferior to clean boxed gloves for minor skin excisions in general practice. The incidence of infection on the non-sterile group was 8.7% 95% CI 4.9% - 12.6% compared with the sterile group, which was 9.3% 95% CI 7 .4% - 11.1%. The randomised clinical trial had an appropriate study design and low risk of bias. Randomisation, allocation concealment and blinding were appropriate and a power calculation was performed to determine that the number of participants and baseline characteristics were similar in both groups. The authors reported the limitations of the study since some of the variables were not accounted for, such as surgical training and

technique of the operator and prevalence of important medical conditions that may influence the outcome. The authors concluded that extrapolating the results in other surgical settings may be considered, although some studies showed bacterial contamination on boxed gloves left open more than 3 days, but the clinical significance of those findings is unclear.

Finally, a systematic review and meta-analysis with appropriate methodology published in JAMA in 2016[28] that included 14 articles with 12,275 patients who had undergone 12,275 outpatients' procedures, including dental procedures, concluded that there is no difference in the rates of postoperative SSI in outpatient surgical procedures performed with non-sterile versus sterile gloves. Given the difference in cost between these gloves, these findings could have a significant effect on and implications for current practice standards.

Local /topical antimicrobial agents pre- and postoperative

Experts in the field have been recommending the use of chlorhexidine pre- and postoperatively[29]. For the benefits of chlorhexidine in implant surgery, local use is recommended as:

- Presurgical rinse to reduce the bacterial load
  - Surface antiseptic for extraoral scrubbing of patient and operator's hands
  - Postsurgical rinse
  - Peri-implant maintenance

The use of pre-operative chlorhexidine and other local antimicrobials is highly encouraged for preventing postoperative infections in many surgical specialties[29]. Even the use of oral topical chlorhexidine is used for prevention of ventilator-acquired pneumonia (VAP) and for prevention of infections in patients undergoing major surgery[29,30]. For the use of antimicrobials in the outcome of implant failure, the search did not retrieve any systematic review that assessed only the use of local antimicrobials pre-operatively. Most of the uses and the references are supported by the 1997 article[31].

In a 2005 retrospective study[32], the use of chlorhexidine is recommended in post-surgical care to reduce the infection rate in periodontal surgeries and implant placement. Patients using chlorhexidine have a lower infection rate (17 infections in 900 procedures – 1.89%) compared with procedures where chlorhexidine was not used as part of the post-surgical care (five infections in 153 procedures – 3.27%).

Different concentrations of chlorhexidine may be used (2% or 0.2% gluconate of chlorhexidine). Some studies use 0.1% concentration or 0.05% digluconate herbal extract combination.

A randomised clinical trial with 100 patients compared the use of 0.2% chlorhexidine mouthwash and prophylactic antibiotics (2 g amoxicillin) in preventing postoperative infections in third molar surgery and concluded that amoxicillin and chlorhexidine prophylaxis are equally effective in reducing postoperative infections, no statistically significant results were obtained, the infection rate was 8% (for chlorhexidine) and 6% (for amoxicillin)[38].

Oral antibiotics and antimicrobials – pre- and postoperatively

For the use of oral antibiotics pre and postoperatively, the search retrieved several systematic reviews. We included only the most recent systematic reviews on the topic of the use of antibiotics for intraoral implant placement and the outcome of postoperative infections and implant failure published in different journals. Wide variability exists among the therapies. All the reviews concluded that despite the methodology and inclusion and exclusion criteria, the use of systemic antibiotics, in any way and kind, reduces the risk of failure, but does not have an effect on postoperative infection.

The 2013[34] Cochrane review with appropriate methodology included six randomised clinical trials, and the body of the evidence was considered moderate, with 1162 participants. Three trials compared the use of 2 g of amoxicillin preoperatively vs a placebo. One trial compared the use of Amoxicillin 3 g preoperative Amoxicillin versus a placebo. One trial compared the use of Amoxicillin 1 g pre-operatively, plus 500 mg four times a day for 2 days vs no antibiotic. One trial compared four groups:

- 2 g preoperative amoxicillin
- 2 g preoperative amoxicillin + 1g daily × 7 days
- 1 g postoperative amoxicillin, twice a day × 7 days
- No antibiotics

The meta-analysis of the six trials showed statistically significant results with a *P* value: 0.00002, favouring the use of antibiotic to prevent implant failure with a RR = 0.33 (95% CI 0.16-0.67). The calculated number needed to treat for one additional benefit outcome (NNTB) to prevent one person having an implant failure is 25 (95% CI 14-100) based on an implant failure of 6% in participants who did not receive antibiotics. There was no statistically significant difference for infections, prosthesis failures and adverse events, and no conclusive information for the different duration of antibiotics could be determined. The review concluded that there is statistically significant evidence suggesting that a single dose of 2 g or 3 g of amoxicillin given orally is beneficial in reducing dental implant failure. It is unknown whether postoperative antibiotics are beneficial or which antibiotic is more effective.

A 2014 systematic review published with acceptable methodology in the International Journal of Oral Maxillofacial Surgery[35], included four randomised clinical trials that grouped 2063 implants in a total of 1002 patients The results of the meta-analysis, with limitation of heterogeneity, concluded that the use of antibiotics favours reduction of implant failure. The results are statistically significant (*P* value = 0.003) with an odds ratio of 0.331, implying that the use of antibiotics reduced the odds of failure by 66.9%. Furthermore, the number needing treatment was calculated to be 48 (CI- 31-109). The results were not statistically significant for postoperative infection.

Another systematic review published in the same year in the Journal of Oral Rehabilitation[36] included non-randomised clinical trials and with that increasing the chances of bias and the inclusion resulted in 14 publications and evaluates 14,872 implants, six studies considered a low risk of bias, one study a moderate risk of bias and six a high risk of bias. The overall result from their meta-analysis concluded that the use of antibiotics reduces implant failure rates, (*P* value 0.0002) with a risk ratio RR of 0.55 (95% CI 0.41-0.75). The number needed to treat (NNT) to prevent one patient having implant failure was 50 (95% CI 33-100). The results were not statistically significant (*P* = 0.520) for the outcome of postoperative infection prevention in healthy patients. A sensitivity analysis performed to remove the high risk of bias in the studies did not reveal any differences. The authors concluded that the results should be interpreted with caution due to the presence of confounding factors.

A 2015 complex systematic review published in the Journal of Oral Implants Research[37] analysed the above systematic reviews and other earlier systematic reviews and comprehensibly analysed the evidence and the results of the individual studies. The results of their review concluded that antibiotic prophylaxis reduces the risk of implant loss by 2% and the subanalysis of the primary studies suggested there is no benefit from antibiotic prophylaxis in uncomplicated implant surgery in healthy patients. The authors also concluded that upon formulation recommendations for antibiotic prophylaxis, the calculated risk reduction at the patient level should be put in relation to the risk of adverse reactions, side effects and the emerging problems with antibiotic resistance.

■ Main results and discussion

The success of dental implants and many other common oral surgical procedures are multifactorial. The patient's overall health, the area of bone, the type of bone and the final function of the implant are important influences in the decision making to place implants and achieve an oral rehabilitation. Oral implant success is also affected by the clinician's experience, the materials used and the patient's compliance and adherence to important recommendations such as oral hygiene, regular maintenance and recalls to maintain periodontal health, as well as reducing certain habits such as smoking that may reduce the success of dental implants

For the purpose of our review, we included different stages of implant placement where the conditions may be controlled to prevent implant failure, such as the level of asepsis of the environment where the procedure is taking place, the operator asepsis level, the instruments and the patient's intraoral and body preparation before the surgical procedure.

Conclusions

It seems that the level of asepsis is in the manipulation of the instruments that are used during the implant surgery and plays a key factor for implant success.

For some studies, the use of traditional aseptic conditions no longer seems to be supported by the evidence, and a modified aseptic condition, or even a clean condition, appear to be acceptable for implant placement. The claim is that costs are reduced without the need for the extra steps required in providing an "aseptic technique". However, the results should be interpreted with extreme caution due to the number and type of studies that report that.

For the use of local antimicrobials, the evidence from systematic reviews is not exclusive for dental implants, however the well-known benefits of chlorhexidine[38] and iodine-povidone can be suggested for their effectiveness and low side effects.

Finally, for the use of oral antibiotics, the results showed some benefit in preventing implant failure. The results for implant failure may seem considerable for their use. Single-digit values of NNTs usually represent a useful difference when comparing one intervention with another and not all patients seem to have the same benefit in the reported systematic reviews.

It may also be important to reconsider the duration and dosage of antibiotics. Evidence suggests that a single dose of 2 g or 3 g of amoxicillin given orally is beneficial in reducing dental implant failure. It is unknown whether postoperative antibiotics are beneficial and which antibiotic is more effective.

The use of pre-operative antibiotic prophylaxis should be reconsidered as a protocol on an individual basis due to limited benefit and all the variables that could lead to implant failure should be evaluated, including breaching of asepsis in crucial steps of dental implant placement. Perhaps the use of nose coverage or ointment needs to be explored for maintaining asepsis and can serve as valuable factors in reducing the use of preoperative antibiotics and other techniques to preserve asepsis -– topics that are not presently reported in studies evaluating the success of dental implants.

Antibiotic resistance is an issue that needs to be considered. Judicious use of antibiotics by clinicians is paramount when it comes to the lower rate of postoperative complications and infections. The use of antibiotics for prevention of infection in healthy patients in dentistry is controversial. Risks and benefits need to be evaluated due to other important consequences such as antibiotic resistance, a topic of interest for the World Health Organization (WHO)[39]. Antibiotic allergies and toxicity should also be considered.

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Long-term clinical outcome of implants with different surface modifications

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Key words *clinical outcome, surface roughness, systematic review, 10 years or more*

The aim of the present systematic review was to evaluate reported survival rate and marginal bone (MBL) loss of implants with different surface roughness and followed up for 10 years or longer. For the majority of the 62 included clinical studies, no direct comparison between different surfaces was made, thus our report is mainly based on reported survival rates and marginal bone loss for individual implant brands with known surface roughness. The survival rate was 82.9 to 100% for all implants after 10 or more years in function and the marginal bone loss was, on average, less than 2.0 mm for all implant surfaces included, i.e. turned, titanium plasma sprayed (TPS), blasted, anodised, blasted and acid-etched but the turned surface in general demonstrated the smallest MBL. However, the survival rates were in general higher for moderately rough surfaces. The roughest TPS surface demonstrated the highest probability for failure, while the anodised showed the lowest probability. In conclusion, the present systematic review demonstrates that it is possible to achieve very good long-term results with all types of included surfaces.

Introduction

In the 1980s, when implant treatment became a common option to rehabilitate edentulous or partially edentulous patients, the majority of marketed implants had a turned, or what was commonly called a machined surface. This surface is characterised by its anisotropic nature, i.e. a dominant direction of the surface structure exists, and a relative smoothness. An estimated average roughness (Sa) is 0.5 µm to 0.8 µm, depending on the size and sharpness of the cutting instrument and the measuring and evaluation techniques used.

Implants with a much rougher surface were on the market during the 1980s, namely titanium plasma sprayed surfaces (TPS) and surfaces coated with hydroxylapatite (HA). These surfaces were both isotropic, i.e. the irregularities are distributed evenly on the entire surface with no dominating direction. Sa value for TPS and the HA coated surfaces at that time were greater than 2 µm when measured with optical profilometers and evaluated after errors of form and waviness had been removed by a Gaussian filter. However, these early generation HA-coated implants soon demonstrated clinical failures due to delamination of the HA-coat. The bonding between the core metal and the HA-coat was too weak to withstand long-term load. Subsequently, rough (i.e. TPS and early HA coated with an Sa value above 2 µm)[1] implants were soon reported to cause severe marginal bone resorption and hence were another reason for implant failure[2,3]. These reports contributed to the TPS and the first generation of HA-coated implants disappearing from the market within a few years.

By the turn of the millennium, the turned surface had more or less been abandoned in favour of newer, moderately rough surfaces produced by blasting, etching (or combinations thereof), and oxidation techniques. The new surfaces were characterised

by being isotropic and having an Sa value between 1.1 µm to 1.7 µm.

These new moderately rough surfaces were introduced to the market during the 1990s and early 2000s after numerous experimental *in vivo* studies had demonstrated that the blasted, blasted and etched, and oxidized surfaces all out-performed a machined (i.e. turned, milled or polished) surface in terms of faster and firmer osseointegration of the implant. A common explanation of these findings was that the increased surface provided with improved biomechanical bonding, thus the primary stability during healing became improved and the bone healing process could proceed undisturbed from micromotions that may otherwise had caused a soft tissue interface.

Later clinical studies have reported very good clinical outcomes for implants with a moderately rough surface, particularly for patients with compromised conditions[4]. However, it must be noted that many papers have a rather short follow-up period[5-8].

Although these publications call attention to the advantages of moderately rough surfaces, there are other opinions. Mainly based on animal experiments, concerns have been expressed as to whether the surface enlargement may cause increased marginal bone resorption similar to that found with the TPS/HA surfaces.

Compared with the machined surfaces, moderately rough surfaces were allegedly difficult to clean with normal oral hygiene procedures and therefore were more prone to harbour plaque and microbiota, which according to some authors can cause mucositis and subsequently induce bone resorption[9,10]. Anodised surfaces have been particularly incriminated in this context. However, the paper by Albouy et al[9] was a ligature study in animals, miles away from the clinical reality. The work by Derks et al[10] ignored the fact that anodised, hexed implants generally display 1.0 mm of MBL during the first year after implant placement[4], irrespective of any periodontal disease process, as defined by Lindhe and Meyle[11]. A recently published meta-analysis comparing clinical data from 43,680 turned and 23,306 anodised implants revealed a significant higher risk ratio for failure in the case of turned implants (RR 2.82, $P < 0.00001$), and no significant difference was found with respect to marginal bone resorption between the two implant surfaces[6].

To ascertain whether moderately rough surfaces perform clinically as well as or even better than the machined implants, randomised controlled long-term studies would provide incontrovertible evidence. Unfortunately, such comparative studies are very rare and the few that have been published demonstrate several confounding factors, such as different implant design, material, loading conditions, etc.

The aim of the present systematic review was to evaluate the long-term clinical outcome of various implant surfaces, irrespective of whether a direct comparison was undertaken between different surfaces, but by combining the data from multiple single studies as well to determine whether any surface demonstrated a significantly better outcome after more than 10 years in function. The primary outcome measures in the present review are implant failure (loss of implant) and marginal bone resorption.

Materials and methods

The present study followed the PRISMA Statement guidelines[12].

Objective

The purpose of the present systematic review was to assess the survival rate and marginal bone loss (MBL) of dental implants manufactured with different surface modifications and followed up for a minimum of 10 years. The focused question was elaborated by using the PICO format (participants, interventions, comparisons and outcomes): What are the clinical outcomes (implant survival rate and MBL around implants) of partially and totally edentulous patients undergoing prosthetic rehabilitation supported by dental implants followed up for at least 10 years and related to the surfaces of included implants?

Search strategies

An electronic search without time restriction for publications in English was undertaken in November 2016 in the following databases: PubMed/Medline, Web of Science, and ScienceDirect.

The following terms were used in the search strategies: ((((((((((implant[All Fields] AND surface[All Fields]) OR (rough[All Fields] AND surface[All Fields])) OR (smooth[All Fields] AND surface[All Fields])) OR (machined[All Fields] AND surface[All Fields])) OR (turned[All Fields] AND surface[All Fields])) OR (blasted[All Fields] AND surface[All Fields])) OR (oxidized[All Fields] AND surface[All Fields])) OR (etched[All Fields] AND surface[All Fields])) OR (coated[All Fields] AND surface[All Fields])) OR (("plasma"[MeSH Terms] OR "plasma"[All Fields]) AND sprayed[All Fields] AND surface[All Fields])) AND ((((((("mortality"[Subheading] OR "mortality"[All Fields] OR "survival"[All Fields] OR "survival"[MeSH Terms]) OR (marginal[All Fields] AND ("bone diseases, metabolic"[MeSH Terms] OR ("bone"[All Fields] AND "diseases"[All Fields] AND "metabolic"[All Fields]) OR "metabolic bone diseases"[All Fields] OR ("bone"[All Fields] AND "loss"[All Fields]) OR "bone loss"[All Fields]))) OR ("peri-implantitis"[MeSH Terms] OR "peri-implantitis"[All Fields] OR "peri-implantitis"[All Fields])) OR ("peri-implantitis"[MeSH Terms] OR "peri-implantitis"[All Fields] OR ("peri"[All Fields] AND "implantitis"[All Fields]) OR "periimplantitis"[All Fields])) OR ("bone resorption"[MeSH Terms] OR ("bone"[All Fields] AND "resorption"[All Fields]) OR "bone resorption"[All Fields])) OR complication[All Fields])) AND (("dental implants"[MeSH Terms] OR ("dental"[All Fields] AND "implants"[All Fields]) OR "dental implants"[All Fields] OR ("dental"[All Fields] AND "implant"[All Fields]) OR "dental implant"[All Fields]) OR (("mouth"[MeSH Terms] OR "mouth"[All Fields] OR "oral"[All Fields]) AND implant[All Fields])) AND Clinical Trial[ptyp]

An additional manual search of related journals was conducted. The reference list of the identified studies and the relevant reviews on the subject were scanned for possible additional studies.

Inclusion and exclusion criteria

The inclusion criteria comprised clinical human studies reporting a clinical series of patients undergoing prosthetic rehabilitation supported by dental implants, and being followed up for a minimum of 10 years. When a study reported a follow-up range, the follow-up time had to be at least 10 years for the included implants. The publications needed to report detailed information on the implant system(s) used in the study, as well as the number of implants placed and failed for each implant system, if more than one system was used. Randomised and controlled clinical trials, cross-sectional studies, cohort studies, case-control studies, and case series were considered. Exclusion criteria were case reports and review papers.

Study selection

The authors independently read the titles and abstracts of all reports identified through the electronic searches. For studies appearing to meet the inclusion criteria, or for which there were insufficient data in the title and abstract to make a clear decision, the full report was obtained. Disagreements were resolved by discussion between the authors.

Data extraction

The authors independently extracted data using specially designed data extraction forms. These forms were piloted on several papers; these were modified as required before use. From the studies included in the final analysis, the following data was extracted (when available): year of publication, type of implant surface, study design (retrospective or prospective), follow-up time, number of patients, implant systems used, number of implants placed and failed, type of prosthetic rehabilitation, jaws receiving implants (maxilla and/or mandible), and MBL. For this review, implant failure represents the complete loss of the implant. Contact with authors for possible missing data was performed.

Analyses

Descriptive statistics were utilised to report the data. In order to standardise and clarify ambiguous data, the implant failure rate was reported for each publication. Implant failure and MBL were the outcome measures evaluated, and the statistical unit was the implant. Differences in failure rates between different implant surfaces were compared using the Pearson's chi-squared or Fisher's exact tests, depending on the number of samples in a 2 × 2 contingency table. The untransformed proportion (random-effects

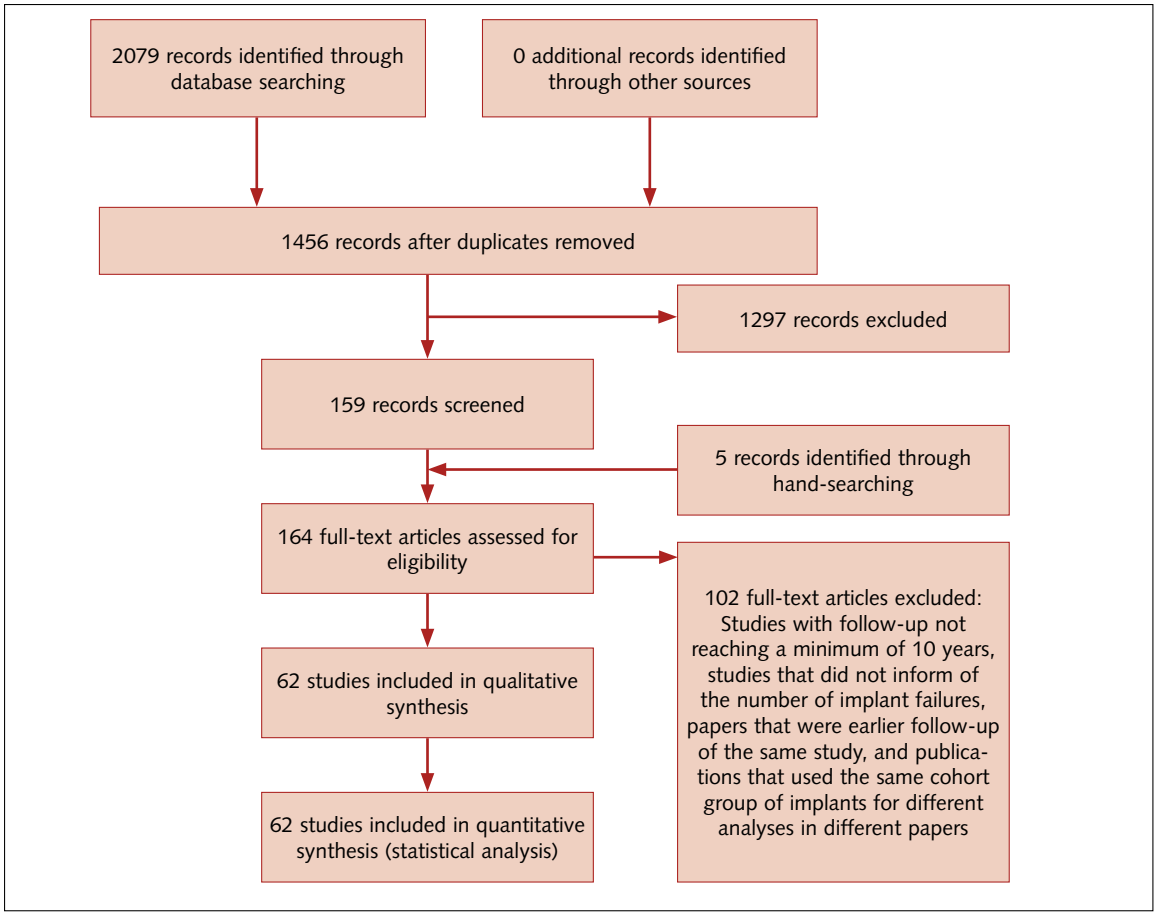


Fig 1 Study screening process.

DerSimonian-Laird method[13]) for implant failure was calculated, considering the different implant surfaces. Meta-regressions were performed for the outcome MBL for each group of implant surface, having the follow-up period as covariate. Statistical significance was set at $P < 0.05$. The data were analysed using the software OpenMeta[Analyst][14] and SPSS software version 23 (SPSS, Chicago, IL, USA).

Results

Literature search

The study selection process is summarised in Figure 1. The search strategy resulted in 2079 papers. In total, 623 articles were cited in more than one research of terms (duplicates). The reviewers independently screened the abstracts for those articles related to the focus question. Of the resulting 1456 studies, 1297 were excluded for not being related to the topic, resulting in 159 entries. Additional hand searching of the reference lists of selected studies yielded five additional papers. The full-text reports of the 164 articles led to the exclusion of 102 papers because they did not meet the inclusion criteria (studies with mean follow-up not reaching a minimum of 10 years, studies that did not inform of the number of implant failures, papers that were earlier follow-up of the same study, and publications that used the same cohort group of implants for different analyses in different papers). Thus, a total of 62 publications were included in the present review.

Description of the studies

Thirty-five prospective[15-49] and 27 retrospective studies[50-76] were included in the present review. Detailed data of the 62 included studies are listed in Table 1. The studies included turned (machined) implants, besides implants with blasted, acid-etched, sandblasted and acid-etched, anodised, titanium plasma-sprayed (TPS), sintered porous, and microtextured surfaces.

Table 1 Details of the 62 included studies.

Authors	Year	Follow-up (years)	Patients (patients followed up for 10+ years) (n)	Failed/placed implants (implants included 10+ years) (n)	Implants used to evaluate MBL (n)	Implant surface modification	Type of construction
Lekholm et al.	1999	10	127 (89)	34/461 (304)	304	Turned a	FPP
Lindquist et al.	1996	15	47 (45)	3/273 (258)	258	Turned a	FAF
Ekelund et al.	2003	20	NA (30)	3/273 (179)	179	Turned a	FAF
Jemt	2008	15	38 (28)	0/47 (32)	23	Turned a	SC
Bergenblock et al.	2012	18	57 (48)	2/65 (53)	44	Turned a	SC
Jemt	2009	10	35 (24)	0/41 (28)	28	Turned a	SC
Lekholm et al.	2006	20	27 (17)	9/112 (69)	69	Turned a	FPP
Hultin et al.	2000	10	15 (15)	0/55 (55)	55	Turned a	FPP
Naert et al.	2004	10	36 (26)	1/72 (52)	NA	Turned a	OD
Gunne et al.	1999	10	23 (20)	8/69 (52)	34	Turned a	FPP
Örtorp and Jemt	2009	15	208 (65)	9/821 (NA)	282	Turned a	FAF
Åstrand et al.	2008	20	48 (NA)	14/269 (NA)	116	Turned a	FAF
Leonhardt et al.	2002	10	15 (15)	3/57 (54)	54	Turned a	FAF, FPP
Roos-Jansåker et al.	2006	14	218 (10)	46/1057 (43)	43	Turned a	FAF, FPP
Sundén Pikner et al.	2009	20	640 (NA)	61/3462 (56)	56	Turned a	SC, FPP, FAF
Schnitman et al.	1997	10	10 (NA)	4/63 (14)	14	Turned a	FAF
Maló et al.	2011	10	245 (2)	13/980 (NA)	NA	Turned a	FAF
Turkyilmaz and Tözüm	2015	30	4 (4)	0/28 (28)	28	Turned a	FPP
Wagenberg and Froum	2010	11	78 (68)	11/106 (NA)	94	Turned a	SC, FPP
Naert et al.	2001	10	246 (NA)	11/668 (NA)	NA	Turned a	FPP
Nyström et al.	2009	10	44 (19)	27/334 (NA)	NA	Turned a	FAF
van Steenberghe et al.	2001	12	158 (NA)	5/316 (NA)	30	Turned a	OD
Attard and Zarb	2004	10	45 (22)	5/132 (86)	58	Turned a	OD
Attard and Zarb	2004	21	45 (32)	33/265 (87)	87	Turned a	FAF
Jemt and Johansson	2006	15	76 (25)	37/450 (150)	150	Turned a	FAF
Rocci et al.	2012	10	46 (NA)	9/97 (75)	75	Turned a	SC, FPP
Dierens et al.	2012	16	134 (97)	13/166 (121)	121	Turned a	SC
Östman et al.	2012	10	46 (46)	1/121 (120)	97	Oxidised b	SC, FPP, FAF
Degidi et al.	2012	10	59 (48)	5/210 (158)	158	Oxidised b	FPP
Mozzati et al.	2015	10	90 (NA)	6/209 (181)	181	Oxidised b	SC, FPP
Wagenberg and Froum	2015	11	312 (NA)	0/312 (NA)	6	Oxidised b	SC, FPP
Polizzi et al.	2013	10	244 (192)	23/500 (NA)	NA	Turned a Oxidised b	SC, FPP
Matarasso et al.	2010	10	80 (80)	6/80 (80)	80	Turned a TPS c	SC, FPP
Ravald et al.	2013	12	66 (46)	18/371 (345)	345	Turned a Blasted d	FAF
Jacobs et al.	2010	16	36 (NA)	1/95 (47)	29	Turned a Blasted d	FPP
Meijer et al.	2009	10	90 (76)	5/180 (152)	152	Turned a TPS c, e	OD
Meijer et al.	2004	10	61 (53)	13/122 (106)	NA	Turned a TPS e	OD
Vroom et al.	2009	12	40 (26)	3/80 (52)	52	Turned f Blasted d	OD
Ma et al.	2010	10	106 (79)	4/212 (158)	158	Turned a Sandblasted/etched g, h Acid-etched i	OD
Telleman et al.	2006	10	60(38)	5/184 (115)	115	TPS c	OD
Simonis et al.	2010	10	76 (55)	22/162 (131)	131	TPS c	SC, FPP
Roccuzzo et al.	2010	10	126 (101)	18/246 (108)	108	TPS c	SC, FPP
Chappuis et al.	2013	20	98 (67)	10/145 (95)	95	TPS c	SC, FPP

Table 1 (cont.) Details of the 62 included studies.

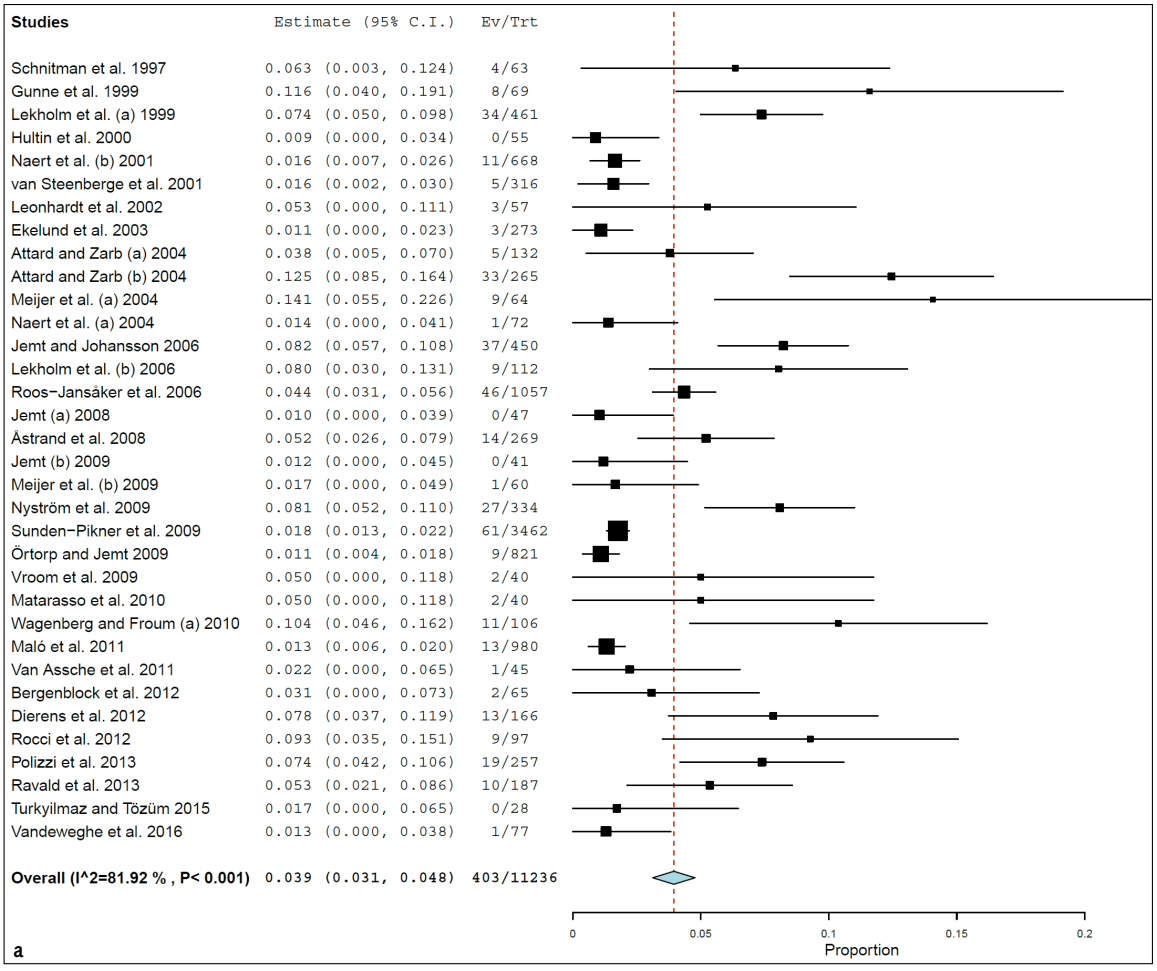
Karoussis et al.	2003	10	53 (NA)	5/112 (NA)	NA	TPS c	SC, FPP, FAF
Mericske-Stern et al.	2001	10	71 (71)	13/151 (132)	12	TPS c	SC, FPP, OD
Heckmann et al.	2004	10	41 (23)	0/82 (46)	46	TPS c	OD
Brägger et al.	2005	10	127 (89)	7/179 (176)	NA	TPS c	SC, FPP
Ferrigno et al.	2002	10	233 (NA)	16/1286 (24)	24	TPS c	OD, FAF
Ferrigno et al.	2006	12	323 (318)	9/588 (36)	36	TPS c Sandblasted/ etched h	SC, FPP, FAF
Buser et al.	2012	10	358 (303)	6/511 (511)	511	Sandblasted/ etched h	SC, FPP
Fischer et al.	2011	10	24 (23)	7/142 (102)	102	Sandblasted/ etched h	FAF
Rasmusson et al.	2005	10	36 (NA)	6/199 (NA)	NA	Blasted d	FAF
Mertens et al.	2012	11	17 (15)	3/108 (94)	94	Blasted d	FAF
Al-Nawas et al.	2012	10	108 (83)	53/516 (113)	113	Blasted d	FPP, FAF
Gotfredsen	2012	10	20 (20)	0/20 (20)	20	Blasted d	SC
Cecchinato et al.	2014	10	139 (100)	1¾07 (291)	291	Blasted d	FPP
Degidi et al.	2015	10	114 (80)	8/284 (193)	193	Blasted j	FPP
Krebs et al.	2013	20	4206 (NA)	319/12737 (NA)	NA	Blasted k Sandblasted/ etched k	SC, FPP, FAF
Vandeweghe et al.	2016	10	66 (NA)	6/203 (197)	197	Turned g Sandblasted/ etched g	FAF
Harel et al.	2013	10	23 (NA)	1/110 (NA)	NA	HA-particles blasted l	SC, FPP
Covani et al.	2012	10	91 (NA)	13/159 (146)	NA	Sandblasted/ etched m	SC, FPP
Deporter et al.	2012	10	24 (19)	2/48 (39)	39	Sintered porous n	FPP

MBL – marginal bone loss; NA – not available, TPS – Titanium plasma sprayed, SC – single-crown, OD – overdenture, FAF – full-arch fixed, FPP – fixed partial prosthesis; a Nobel Brånemark turned implants, Nobel Biocare, Göteborg, Sweden; b Nobel TiUnite implants, Nobel Biocare, Göteborg, Sweden; c ITI TPS implants, Straumann, Waldenburg, Switzerland; d Astra TiOblast, Astra Tech AB, Mölndal, Sweden; e IMZ TPS implants, Dentsply, Mannhein, Germany; f Astra turned implants, Astra Tech AB, Mölndal, Sweden; g Southern Implants, Irene, South Africa; h SLA implants, Straumann, Waldenburg, Switzerland; i Steri-oss, Nobel Biocare, Göteborg, Sweden; j XiVE, Dentsply Implants, Mannheim, Germany; k Ankylos, Dentsply Implants, Mannheim, Germany; l Screw-Vent MTX, Zimmer Dental, Carlsbad, USA; m Sweden and Martina, Due Carrare, Italy; n Endopore, Sybron Implant Solutions, Orange, USA

Analyses

In general, the cumulative survival rates (CSR) after a minimum of 10 years in function were high for the machined/turned, the blasted, the blasted+ acid etched and the oxidised implants. The machined/turned had an CSR range from 84.7% to 100%, the TPS surfaces ranged from 82.9% to 98.9%, the blasted implants from 89.7 to 95%, the blasted and etched implants from 95.1% to 98.9% and the oxidized from 96.6% to 99.2%.

Table 2 shows the number of implants placed and failed for each surface type, as well as the probability of failure according to the random-effects DerSimonian-Laird method[13] analysis (Fig 2 shows the forest plots for each implant type). Anodised and blasted surface implants showed the lowest and highest failure rates, respectively. Anodised and TPS surface implants showed the lowest and highest probability of failure, respectively. A direct comparison between implants of different surfaces (Table 3) showed that the turned implants presented a significantly different failure rate when compared to blasted and anodised implants, but did not differ in comparison to TPS and sandblasted/acid-etched implants. Anodised surface implants always showed statistically significant better survival rates than any other surface implant. Due to the inclusion of only one clinical study each, sintered porous (one failure, 110 implants, 0.90% of failure), acid-etched (four



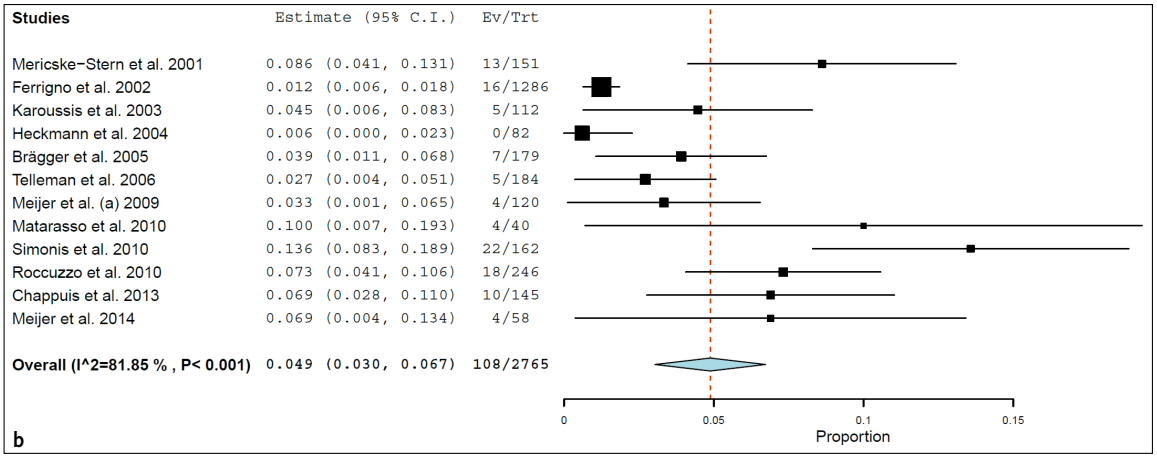
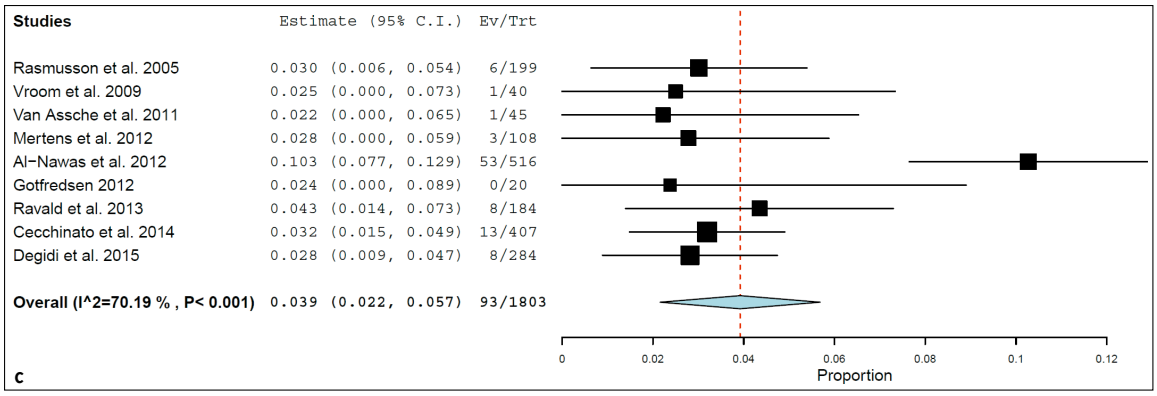
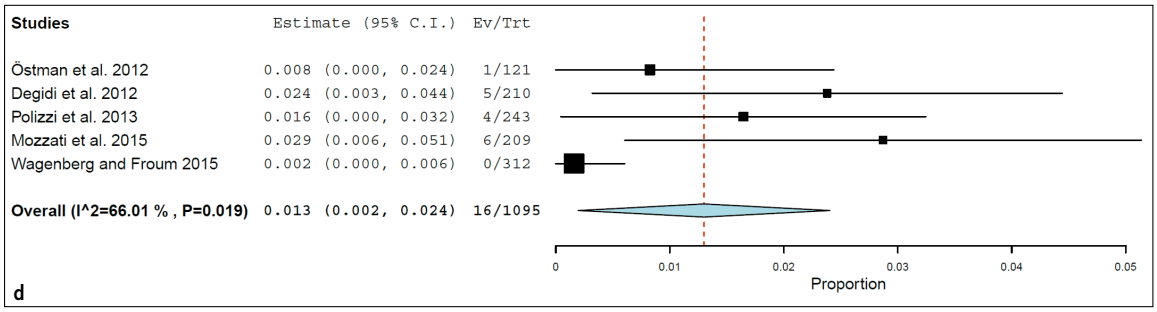


Fig 2 Probability of implant failure, based on studies of 10+ years of follow-up: a) turned; b) TPS; c) blasted; d) anodised; and e) sandblasted/acid-etched implants.

failures, 48 implants, 8.33% of failure), and micro-textured surface implants (two failures, 48 implants, 4.17% of failure) were not included in the analyses in Tables 2 and 3.

Thirty-six studies[17,19,21-23,25,29,30,32-36,38-40,42,44,45,47,48,50-53,56,57,62-64,66,67,69-71,74] provided information about the MBL separately by implant type, with mean and standard deviation. Blasted and turned implants showed the lowest MBL, while TPS implants demonstrated the highest values for MBL (Table 4). Figure 3 shows the forest plots concerning MBL, for each implant type.





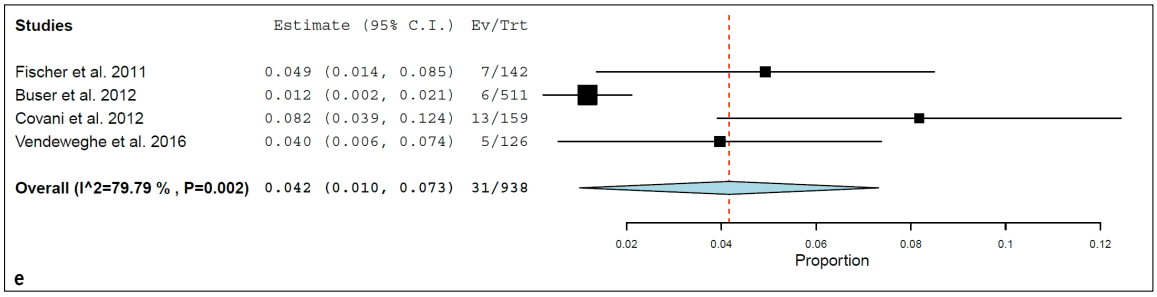


Fig 2 (cont.) Probability of implant failure, based on studies of 10+ years of follow-up: a) turned; b) TPS; c) blasted; d) anodized; and e) sandblasted/acid-etched implants.

Table 2 Probability of implant failure for each implant type according to DerSimonian-Laird method.

Surface	Number of studies	Failure/total of implants (failure rate)	Probability of failure * (95% CI), *P* value	Heterogeneity
Turned	34	403/11236 (3.59%)	3.9% (3.1, 4.8), $P < 0.001$	$\tau^2 = 0.000$, $Chi^2 = 182.527$, $I^2 = 81.92\%$, $P < 0.001$
TPS	12	108/2765 (3.91%)	4.9% (3.0, 6.7), $P < 0.001$	$\tau^2 = 0.001$, $Chi^2 = 60.591$, $I^2 = 81.845\%$, $P < 0.001$
Blasted	9	93/1803 (5.16%)	3.9% (2.2, 5.7), $P < 0.001$	$\tau^2 = 0.000$, $Chi^2 = 26.838$, $I^2 = 70.192\%$, $P < 0.001$
Anodised	5	16/1095 (1.46%)	1.3% (0.2, 2.4), $P = 0.021$	$\tau^2 = 0.000$, $Chi^2 = 11.769$, $I^2 = 66.013\%$, $P = 0.019$
Sandblasted/acid-etched	4	31/938 (3.30%)	4.2% (1.0, 7.3), $P = 0.010$	$\tau^2 = 0.001$, $Chi^2 = 14.844$, $I^2 = 79.79\%$, $P = 0.002$

5% CI – 95% confidence interval; TPS – Titanium plasma-sprayed

* Untransformed proportion, random-effects DerSim onian-Laird method

A meta-regression was performed having the follow-up time as covariate. It was possible to perform it with turned implants, due to the presence of enough data only for this implant surface. According to this statistical model, an increase of each year in follow-up time of turned implants results in an MBL gain of 0.022 mm (95% CI -0.069, 0.024) from an initial MBL loss of 1.168 mm after the first year of implant installation (Fig 4). The model, however, resulted in non-statistically significance ($P = 0.350$).

Table 3 Comparison of the differences in failure rates between different implant surfaces. If a significant difference, the implants with the lowest failure rate have been underlined.

Comparison	*P* value*
Turned vs TPS	0.423
Turned vs Blasted	0.001
Turned vs Anodised	< 0.001
Turned vs Sandblasted/acid-etched	0.655
TPS vs Blasted	0.044
TPS vs Anodised	< 0.001
TPS vs Sandblasted/acid-etched	0.403
Blasted vs Anodised	< 0.001
Blasted vs Sandblasted/acid-etched	0.027
Anodised vs Sandblasted/acid-etched	0.006

TPS –Titanium plasma-sprayed
*Pearson's chi-squared test

Discussion

The analysis of the results in this present review focused on implant surface modifications. However, this was not the main outcome measure reported in the majority of the studies; only a few linked the long-term clinical result to the implant surface and made comparisons of two or more surface modifications in their evaluation (Table 1). The study design and the main topic differed considerably between the included studies. Most of the studies reported long-term data on survival rates and marginal bone resorption for a specific implant brand over time and their position in the jaw (32 studies). Other studies reported on implant-supported overdentures (five studies), combined tooth/implant restorations (two studies), abutment material, cemented/screw retained constructions, framework material and platform switch (three studies), immediately loaded implants, implants in grafted bone and implants in fresh extraction sockets, flapless and non-submerged surgery (eight studies) and, finally, 12 studies whose main focus was on a particular implant surface. Furthermore, the included studies were published over a range of 20 years – 1996 to 2016 – during which time the indications for implant treatment have broadened and the number of treated patients with a compromised status has likewise increased. In addition, today many more practitioners are working with implants, as this is no longer a treatment only provided by specialists.

Table 4 Marginal bone loss, based on studies of 10+ years of follow-up.

Surface	Number of studies*/ total of implants	MBL (in mm)** (95% CI), *P* value	Heterogeneity
Turned	20/2594	0.869 (0.518, 1.220), $P < 0.001$	$\tau^2 = 0.056$, $Chi^2 = 26866.249$, $I^2 = 99.855\%$, $P < 0.001$
TPS	7/556	1.877 (1.511, 2.243), $P < 0.001$	$\tau^2 = 0.245$, $Chi^2 = 165.779$, $I^2 = 95.778\%$, $P < 0.001$
Blasted	8/975	0.809 (0.218, 1.400), $P = 0.007$	$\tau^2 = 0.807$, $Chi^2 = 1181.421$, $I^2 = 99.323\%$, $P < 0.001$
Anodised	3/261	1.597 (1.191, 2.002), $P < 0.001$	$\tau^2 = 0.133$, $Chi^2 = 80.561$, $I^2 = 96.276\%$, $P < 0.001$
Sandblasted/ acid-etched	4/834	1.356 (-0.215, 2.927), $P = 0.091$	$\tau^2 = 3.204$, $Chi^2 = 2719.018$, $I^2 = 99.853\%$, $P < 0.001$

* Some studies may have included more than one implant surface.

**Negative value means bone gain.

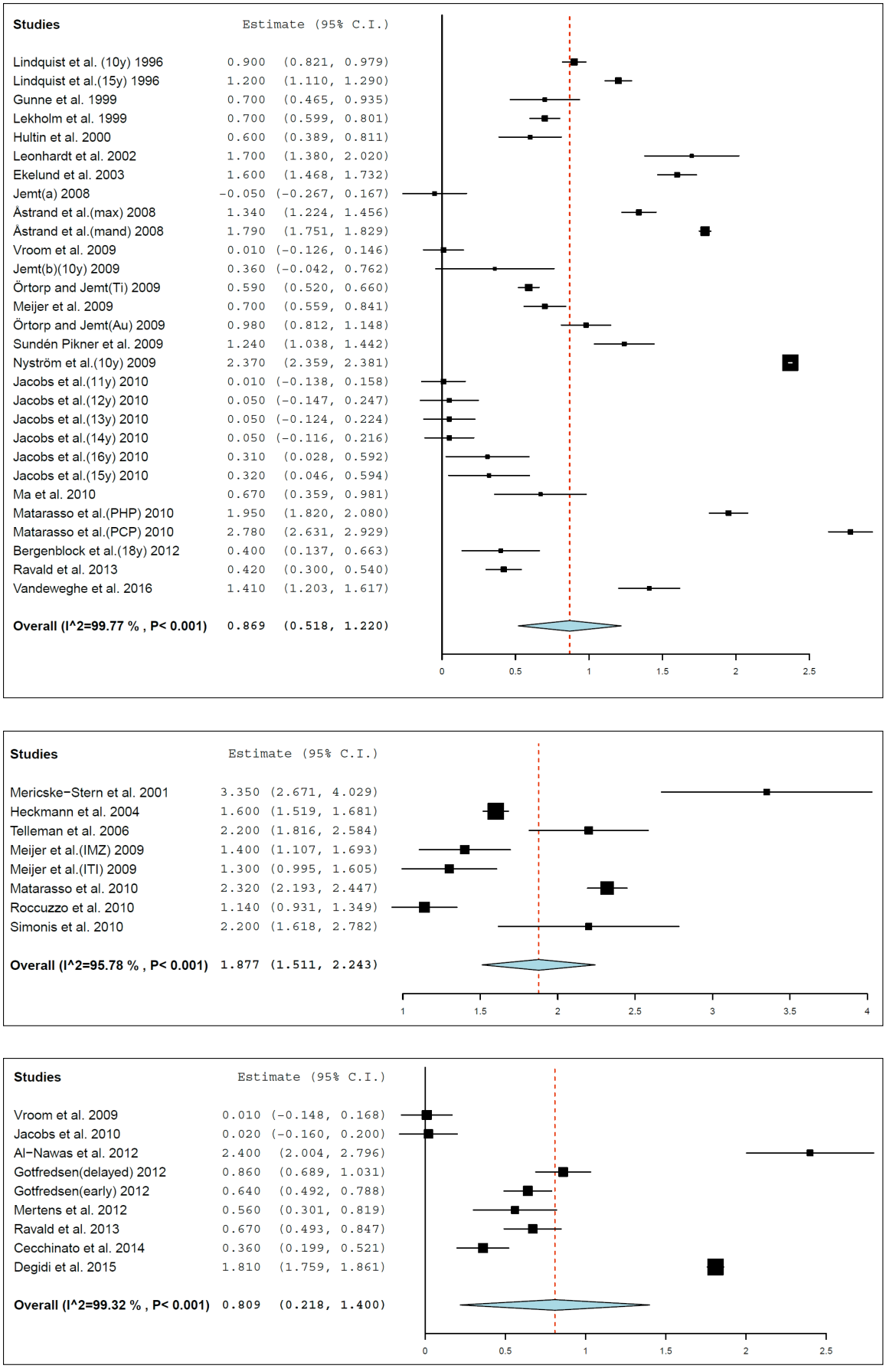
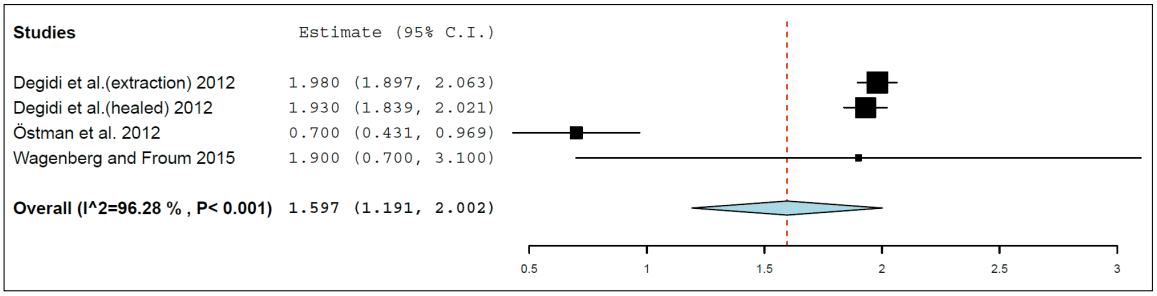
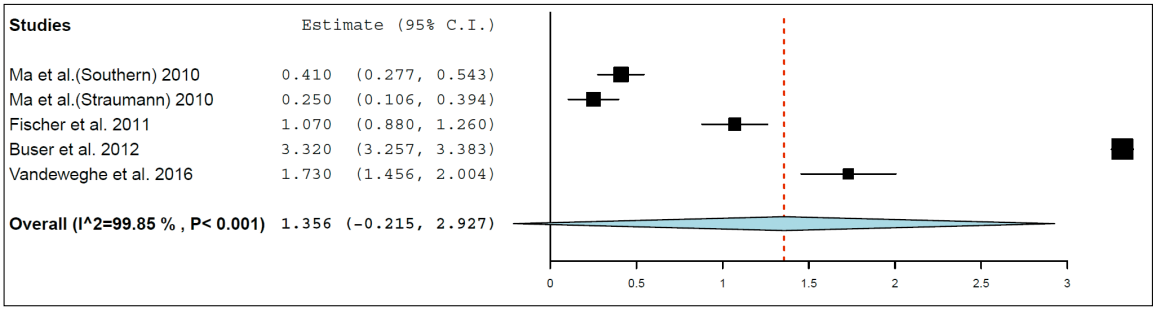


Fig 3 Estimated marginal bone loss (MBL), based on studies of 10+ years of follow-up: a) turned; b) TPS, c) blasted; d) anodised; and e) sandblasted/acid-etched implants.





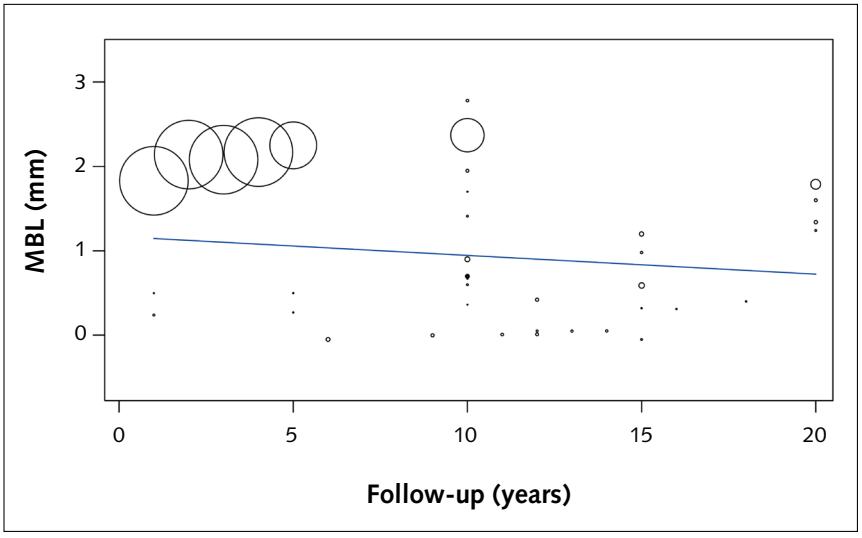


Fig 4 Scatter plot for the meta-regression: association between the marginal bone loss (in millimetres) of turned implants and the follow-up time (in years). Each circle represents marginal bone loss measurement of a group of implants from different studies, in different time point of follow-up. The size of the circles represents the weight of the study (from a meta-analysis point of view). Only studies with a minimum of 10 years of follow-up were considered. The line represents the estimated marginal bone loss along the years of observation.

The results of the present review suggest that the probability of failure for anodised implants is lower than that for turned implants, which was also a finding in a recent review comparing these two implant types[6], or any other enhanced-surface implant (see Table 2). The reason for this finding may be that the oxidized surface provides a greater number of undercuts that may result in improved osseointegration.

The lack of a statistically significant difference in failure rates between sandblasted/acid-etched implants and both turned and TPS implants (Table 3) could be a real effect or could be related to the low number of publications (n = 4) reporting failure rates for sandblasted/acid-etched implants. As implant survival rates are generally high, sample sizes need to be large to demonstrate statistically significant differences to infer a meaningful clinical difference in implant survival performance[77]. However, the number of publications (n = 5) – and the number of implants in these studies (n = 1095) – including and reporting failure rates for anodised implants, was quite similar to the ones evaluating sandblasted/acid-etched implants (four publications and 938 implants), the statistical analysis showed that anodised implants performed

significantly better when compared with any of the other implant surfaces.

When considering marginal bone loss, most of the implants with an enhanced surface demonstrated a poorer prognosis in comparison to turned implants. This difference may be related to different sample sizes – as there were far more studies and implants evaluating MBL around turned implants than studies assessing enhanced-surface implants, the figures for turned implants may more reliably reflect the reality. Thus, additional long-term studies assessing MBL around enhanced-surface implants are necessary to obtain a larger sample size and provide a more reliable statistical comparison with turned implants. Moreover, data may be criticised as evidenced in the study by Jimbo and Albrektsson[4], which showed a similar increase in marginal bone loss with anodised implants after 5 or more years in function.

However, the difference was shown to occur in the first year after implantation, with no differences between the different implant surfaces between 1 and 7 years of follow-up. The hex design has been incriminated as the reason for this early marginal bone loss, which according to the definition by Lindhe and Meyle[11], is not an example of peri-implantitis.

Today implant treatment is a common treatment option not only for the specialised team, but for a larger number of general dental practitioners, some of whom may only perform a few cases per year, which will naturally make it difficult to maintain a high skill in this fast-developing discipline. In addition, more complicated surgical techniques have been adopted, often in combination with new 3D techniques such as flapless surgery, immediate loading, various grafting techniques, and implant placement in fresh extraction sockets are all factors that may contribute to the long-term clinical outcome. Thus, it is difficult to determine the precise influence of surface modifications when there are so many confounding factors. This is, of course, a limitation with the present evidence. However, the results indicate that it is possible to achieve very good long-term clinical results with all types of surfaces included in the present systematic review.

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Extra-short (< 7 mm) and extra-narrow diameter (< 3.5 mm) implants: a meta-analytic literature review

Key words *decision making, dental implants, evidence-based dentistry, implant-supported dental prosthesis, patient preference*

Aim: To review available evidence in scientific literature on oral implants of severely reduced length or diameter.

Materials and methods: Electronic and hand searches up to May 2017 were performed in order to identify clinical investigations providing implant survival and/or marginal bone resorption data for extra-short implants < 7.0 mm in length and extra-narrow implants < 3.5 mm in diameter (excluding one-piece mini-implants).

Results: A total of 2929 extra-short implants and 3048 extra-narrow diameter implants were investigated in 53 and 29 clinical studies, respectively. Shorter implants between 4.0 mm and 5.4 mm in length showed comparable results to implant lengths of 5.5 mm to 6.5 mm (95.1% vs. 96.4%, $P = 0.121$) and no difference regarding marginal bone resorption (0.7 mm vs 0.5 mm, $P = 0.086$). Implant lengths of 5.5 mm to 6.5 mm, however, performed significantly better in the mandible compared with the maxilla ($P = 0.010$). Smaller diameters between 3.0 mm and 3.25 mm yielded a significantly lower survival rate of 94.3% than wider implants of 3.3 mm to 3.4 mm diameter (97.7%, $P < 0.001$), while marginal bone resorption did not differ (0.4 mm vs 0.5 mm, $P = 0.447$).

Conclusions: The results of the present literature review suggest that extra-short and extra-narrow-diameter implants show satisfactory survival rates of around 95% and little marginal bone resorption of around 0.5 mm after a mean follow-up of 3 years. However, implant lengths < 7 mm in the maxilla and < 5.5 mm in the mandible as well as diameters < 3.3 mm may increase early failure rates.

■ Introduction

Reduced bone volume available for implant placement is one of the major concerns in dental implantology[1]. Alveolar ridge height is frequently limited by the intraosseous course of the inferior alveolar nerve in the mandible[2] and the expansion of the maxillary sinus cavity in the maxilla[3] related to atrophic processes following tooth loss. Likewise, severe reduction of the alveolar crest width can impede the maximum implant diameter to be applied[4], which may as well be inherently limited by the mesio-distal width of the gap[5].

Modification of the patient's jaw anatomy via bone augmentation surgery to allow placement of longer and wider implants has previously been generally considered the best treatment strategy[6], however, adaptation of implant dimensions to the prevailing patient anatomy may represent an alternative approach in cases of severe atrophy of the residual alveolar bone[7-9].

Interest in minimally invasive surgical procedures as a standard treatment is notably growing in the field of oral implantology[10]. To avoid patient morbidity associated with bone grafting[11], reconstruction of atrophic jaws with short and/or diameter-reduced

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implants has gained in popularity[12-13]. By common definition, implants with a length of 7.0 mm to 9.0 mm are referred to as "short" and implants of < 7.0 mm in length are classified as "extra-short"[14]. While large meta-analyses demonstrate the effectiveness of short implants that are at least 8.0 mm in length[15-19], including single-tooth replacement, there is only limited information on the survival of extra-short implants, which indicates survival rates of about 94%, predominantly due to early failures[20]. Since 2005, however, the application of short implants has shown a significant upward trend from 1% to roughly 10% of all implants placed[21], particularly in partial edentulism, although data specifically examining implant length < 7 mm remain limited.

A similar lack of conclusive evidence can be observed when implants of reduced diameter are analysed. Furthermore, even the definition of "narrow diameter" is not consistent across literature reviews, ranging from diameters ≤ 3.5 mm[22] to diameters < 3.3 mm[23]. Two-piece implants (that allow screw-retained prosthodontic rehabilitation) generally present with a minimum diameter of about 3.0 mm and may not be confused with so-called "mini-implants" that may be even smaller in diameter, however, can exclusively be subjected to cement-retained prosthetics or carry attachments for overdentures[24]. Some extra-narrow implants are restricted by the manufacturer to use as single-tooth implants in regions of limited mesio-distal gap width, such as the lateral incisors in the maxilla and the lateral and middle incisors in the mandible. Particularly in posterior regions of the mouth where bite forces are higher and distal cantilevers may be attached to implant bridges, reduced-diameter implants have been traditionally used with some caution[25].

The aim of the present systematic review and meta-analysis thus was to survey the available evidence in scientific literature regarding the clinical success of dental implants of severely reduced length or diameter.

Materials and methods

The authors searched for clinical scientific literature in the English language via the US National Institutes of Health free digital archive of biomedical and life sciences journal literature (PubMed MEDLINE). The last search was performed on 1st May 2017. The search term "short dental implant" was used to search for implant length-related papers, while the search terms "narrow diameter dental implant" and "reduced diameter dental implant" were combined to search for implant diameter-related publications. After exclusion of duplicates, a total of 1392 and 306 abstracts were screened for the two research questions, respectively.

Studies were considered if they met the following eligibility criteria: [1] clinical investigations including at least 10 patients [2] reporting on outcome measures of implant survival and/or peri-implant marginal bone remodelling [3] after a minimum follow-up of 3 months after placement of [4] implants shorter than 7.0 mm or less than 3.5 mm in diameter. Animal studies and finite element analyses were not considered. Relevant systematic review papers, as well as the reference lists of all included articles, were searched by hand to identify further publications. Full-text screening, study selection and data extraction was performed in duplicate and disagreements were resolved by consensus.

Descriptive analysis of study characteristics included: study design, number of patients and jaws treated, number of implants placed in the anterior and posterior region of the maxilla or mandible, implant length and diameter, mean length of follow-up, implant survival rate and periimplant marginal bone loss (Tables 1 and 2). Implant survival rates were evaluated after 1 year of function (early failures) as well as after long-term follow-up (late failures) and weighted mean rates of marginal bone resorption was computed. Subgroups regarding jaw location and implant dimension categories were compared via Fischer exact tests and Wilcoxon rank sum tests, respectively. Meta-analyses were performed at a significance level of 0.05 using R-project software version 3.1.0 (R Foundation for Statistical Computing, Vienna, Austria).

Table 1 Literature survey on survival rates of extra-short implants (< 7 mm in length).

Study (year)	Length (mm)	Implant number	Follow-up (months)	Survival rate	Bone loss (mm)
Buser 1997[26]	6	39	37	97.4%	-
ten Bruggenkate 1998[27]	6	253	72	97.2%	-
Renouard 1999[28]	6	39	12	89.7%	0.3
Brocard 2000[29]	6	16	84	81.3%	-
Snauwaert 2000[30]	6	16	60	62.5%	-
Mericske-Stern 2001[31]	6	5	52	100%	-
Nedir 2004[32]	6	6	19	100%	-
Renouard 2005[33]	6	10	38	100%	0.5
Arlin 2006[34]	6	35	13	94.3%	-
Bischof 2006[35]	6	4	38	75.0%	-
Deporter 2008[36]	5	26	45	92.3%	-
Fugazzotto 2008[37]	6	166	30	97.0%	-
Pjetursson 2009[38]	6	7	38	57.1%	-
Anitua 2010[39]	6.5	37	48	100%	-
Rossi 2010[40]	6	40	24	95.0%	0.2
Cannizzaro 2012[41]	6.5	60	48	96.7%	0.3
Guljé 2012[42]	6	60	12	96.7%	-
Pieri 2012[43]	6	61	24	96.7%	0.6
Urdaneta 2012[44]	5-6	211	20	97.6%	-
van Assche 2012[45]	6	24	24	95.8%	1.0
Anitua 2013[46]	5.5-6.5	114	26	98.2 %	0.8
Kennedy 2013[47]	6	38	24	81.6%	-
Lai 2013[48]	6	33	120	97.0%	-
Pistilli 2013a[49]	6	80	12	100%	1.0
Pistilli 2013b[50]	5	68	12	99.0%	0.9
Al-Hashedi 2014[51]	6	2	12	100%	-
Anitua 2014[52]	5.5-6.5	52	23	100%	1.0
Bratu 2014[53]	6	33	24	100%	0.9
Esposito 2014[54]	5	60	36	91.7%	1.2
Peñarrocha-Oltra 2014[55]	5.5	35	12	97.1%	0.6
Taschieri 2014[56]	6.5	23	12	100%	0.3
Cannizzaro 2015[57]	5	30	12	93.3%	0.2
Esposito 2015[58]	5-6	12	12	100%	1.1
Felice 2015[59]	5-6	16	12	100%	0.8
Guljé 2015[60]	6	31	12	100%	0.1
Queiroz 2015[61]	5.5	17	3	82.4%	-
Rossi 2015[62]	6	30	60	86.7%	0.2
Thoma 2015[63]	6	67	12	97.0%	-
Schincaglia 2015[64]	6	67	12	100%	0.5
Seemann 2015[65]	5	40	20	97.5 %	0.2
Slote 2015[66]	4	77	60	93.5 %	0.5
Calvo-Guirado 2016[67]	4	40	12	97.5 %	0.7
Esposito 2016[68]	4	80	4	93.8%	0.4
Felice 2016[69]	4	124	12	97.6%	0.5

Table 1 *(cont.)* Literature survey on survival rates of extra-short implants (< 7 mm in length).

Study (year)	Length (mm)	Implant number	Follow-up (months)	Survival rate	Bone loss (mm)
Gulijé 2016[70]	6	47	12	100%	0.1
Sahrmann 2016[71]	6	40	36	97.5%	0.2
Han 2016[72]	6	95	12	95.8%	0.1
Malmstrom 2016[73]	6	25	24	96.0%	0.5
Rossi 2016[74]	6	30	60	86.7%	0.2
Tabrizi 2016[75]	6	65	36	100%	0.2
Pommer 2017[76]	4.5	264	12	93.2%	0.8
Pohl 2017[77]	6	61	36	100%	0.4
Zhang 2017[78]	6	18	10	100%	-
Total		**2929**		**96.0%**	**0.6**

Table 2 Literature survey on survival rates of extra-narrow implants (< 3.5 mm in diameter).

Study (year)	Diameter (mm)	Implant number	Follow-up (months)	Survival rate	Bone loss (mm)
Polizzi 1999[79]	3.0	30	60	96.7%	-
Andersen 2001[80]	3.25	60	15	93.7%	0.4
Payne 2004[81]	3.25-3.3	98	15	88.8%	0.3
Zinsli 2004[82]	3.3	298	12	98.9%	-
Comfort 2005[83]	3.3	23	60	95.7%	0.1
Romeo 2006[84]	3.3	122	84	97.5%	1.5
Reddy 2008[85]	3.0	31	12	96.7%	0.1
Maló 2011[86]	3.3	247	120	95.1%	0.9
Sohn 2011[87]	3.3	62	33	100%	0.5
Chiapasco 2012[88]	3.3	51	10	100%	-
Galindo-Moreno 2012[89]	3.0	93	12	100%	0.1
Oyama 2012[90]	3.0	17	12	100%	0.4
Vanlioglu 2012[91]	3.3	13	60	100%	0.2
Zembic 2012[92]	3.0	57	12	98.2%	0.8
Gahlert 2013[93]	3.25	59	36	71.1%	-
El-Sheikh 2014[94]	3.3	40	12	100%	0.5
Mangano 2014[95]	3.3	324	120	98.7%	0.7
Al-Nawas 2015[96]	3.3	603	24	98.3%	-
Ioannidis 2015[97]	3.3	17	36	100%	0.1
Lambert 2015[98]	3.3	39	12	94.8%	0.4
Maiorana 2015[99]	3.0	97	36	95.9%	0.1
Zweers 2015[100]	3.3	58	36	100%	0.3
Herrmann 2016[101]	3.3	154	70	96.8%	-
King 2016[102]	3.0	62	36	100%	0.2
Ma 2016[103]	3.25-3.3	117	12	87.2%	-
Pommer 2016[104]	3.25-3.4	34	42	97.1%	-
Fürhauser 2017[105]	3.0	46	12	100%	0.5
Galindo-Moreno 2017[106]	3.0	83	36	100%	0.3
Pieri 2017[107]	3.0	113	60	98.2%	1.0
Total		**3048**		**96.7%**	**0.4**

Results

Extra-short implants

The final selection included 53 studies[26-78] reporting on 321 implants of 4.0 mm in length (11.0%), 264 implants of 4.5 mm in length (9.0%), 301 implants of 5,0 mm in length (10.3%), 180 implants of 5.5 mm in length (6.1%), 1705 implants of 6.0 mm in length (58.2%) and 158 implants of 6.5 mm in length (5.4%). In total, 2929 extra-short implants were investigated for a mean follow-up period of 31.2 ± 23.4 months (range: 12 to 120 months) and showed a mean survival rate of 96.0% (range: 57.1% to 100%). A significant difference ($P = 0.007$) was observed between the results of prospective (95.5%) and retrospective studies (97.6%). The weighted mean marginal bone loss across a total of 33 studies (1873 implants) measured 0.6 ± 0.3 mm, and ranged between 0.1 mm and 1.2 mm.

Smaller implants with lengths between 4.0 mm and 5.4 mm (n = 886) showed a lower survival rate of 95.1%, compared with implant lengths of 5.5 mm to 6.5 mm (n = 2043) that survived in 96.4% ($P = 0.121$). The rates of early and late failures were 3.5% and 1.5% (i.e. 72% of failures within the first year) compared with 2.4% and 1.7% (i.e. 77% of failures within the first year), respectively (Table 3), without significant differences in failure patterns ($P = 0.129$). The two length groups did not differ regarding marginal bone loss of 0.7 ± 0.3 mm (range: 0.4 mm to 1.2 mm) and 0.5 ± 0.3 mm (range: 0.1 to 1.0 mm), respectively ($P = 0.086$). While no impact of anterior vs posterior implant position could be established for both length groups (Table 4), implant lengths of 5.5 mm to 6.5 mm revealed significantly higher survival in the mandible compared with the maxilla ($P = 0.010$).

Extra-narrow implants

The final selection included 29 studies[79-107] reporting on 629 implants with a diameter of 3.0 mm (20.6%), 259 implants with a diameter of 3.25 mm (8.5%), 2155 implants with a diameter of 3.3 mm (70.7%), and five implants with a diameter of 3.4 mm (0.2%). In total, 3048 extra-narrow implants were investigated for a mean follow-up period of 37.8 ± 30.3 months (range: 12 to 120 months) and showed a mean survival rate of 96.7% (range: 71.1% to 100%). A significant difference ($P = 0.002$) was observed between the results of prospective (97.5%) and retrospective studies (95.1%). The weighted mean alveolar bone loss across a total of 21 studies (1702 implants) measured 0.4 ± 0.4 mm, ranging between 0.1 mm and 1.5 mm.

Narrower implants with diameters between 3.0 mm and 3.25 mm (n = 888) showed a significantly lower survival rate of 94.7% compared with implant diameters of 3.3 mm and 3.4 mm (n = 2160) that survived in 97.8% ($P < 0.001$). The rates of early and late failures were 5.2% and 0.9% (i.e. 98% of failures within the first year) compared with 1.9% and 0.4% (i.e. 85% of failures within the first year), respectively (Table 3), showing significantly more early failures in the 3.0 mm to 3.25 mm diameter group ($P < 0.001$). No difference, however, could be found between the two groups regarding marginal bone loss of 0.4 mm ± 0.3 mm (range: 0.1 mm to 1.0 mm) and 0.5 ± 0.4 mm (range: 0.1 mm to 1.5 mm), respectively ($P = 0.447$). Survival rates did not differ between anterior vs posterior implant position, neither between maxillary vs mandibular jaw location (Table 4).

Table 3 Early and late failure rates of length and diameter subgroups.

Subgroup	Early failure rate	Late failure rate	% of early failures
Length 4.0 – 5.4 mm	3.5%	1.5%	72%
Length 5.5 – 6.5 mm	2.4%	1.7%	77%
Diameter 3.0 – 3.25 mm	5.2%	0.9%	98%
Diameter 3.3 – 3.4 mm	1.9%	0.4%	85%

Table 4 Subgroup analysis regarding implant failure rates in anterior vs posterior implant positions as well as maxillary vs mandibular jaw locations (nd=no data, * indicates statistical significance).

Subgroup	Maxilla vs mandible	Anterior vs posterior
Length 4.0 – 5.4 mm	94.3% vs 94.8% (P = 0.871)	nd vs 95.1%
Length 5.5 – 6.5 mm	94.8% vs 97.9% (P = 0.010)*	96.8% vs 96.9% (P = 1.000)
Diameter 3.0 – 3.25 mm	92.5% vs 96.7% (P = 0.691)	97.8% vs 98.9% (P = 0.518)
Diameter 3.3 – 3.4 mm	96.2% vs. 97.9% (P = 0.164)	97.8% vs. 98.4% (P = 0.507)

Discussion

Summing up the results of the present literature review (82 studies from 1997 to 2017), extra-short and extra-narrow-diameter implants show satisfactory survival rates of over 95% and little marginal bone resorption of about 0.5 mm after a mean follow-up of 3 years. Implant lengths of 5.5 mm to 6.5 mm performed significantly better in the mandible (98%) compared with the maxilla (95%), while lengths of 4.0 mm to 5.4 mm demonstrated similar survival rates in both jaws (95%). Extra-narrow-diameter implants revealed no differences between implant position and jaw location; however, a significantly lower survival rate of diameters between 3.0 mm and 3.25 mm (95%) compared with diameters between 3.3 mm and 3.4 mm (98%) related to a higher rate of early failures.

The results of the present meta-analysis compare well with prior reviews on extra-short and extra-narrow implants (94%[20] and 93.8% to 100%[108] implant survival, respectively). Comparison is complicated, however, by divergent threshold definitions of "extra-short" and "extra-narrow" implants. "Extra-short" implants may also be defined as < 8.0 mm in length (instead of < 7.0 mm), considering that long-term evidence of implants ≥ 8.0 mm is more extensive in literature.[109] Regarding implant diameters, 3.3 mm to 3.5 mm may be not be termed "extra-narrow", as routinely used in clinical practice[22]. In the present meta-analytic review it was therefore decided to investigate further subgroups (< 3.3 mm vs ≤ 3.3 mm), as significant differences between these groups have been demonstrated in the past[23]. It was also decided to include prospective as well as retrospective studies, although significant differences between study designs were seen. Prospective studies, however, yielded slightly lower survival rates of extra-short implants (compared with retrospective ones) while reporting somewhat higher survival rates of extra-narrow implants. Eventually no criteria regarding methodological quality of included studies were set.

Further limitation of this meta-analytic review arises from the inhomogeneity of clinical variables, i.e. patient-related, implant-related, and biomechanical factors[110]. In several studies[87,88] implants were subjected to immediate loading despite the reduced length or diameter. Most of the implants were placed in partially edentulous patients, however, some studies also investigated the reconstruction of edentulous jaws.[42,46] Furthermore, it can not be ignored that different biomechanical forces apply in single implant crowns compared with multi-unit reconstructions with implants splinted together. Finally, the type of implant-abutment connection as well as the application of platform switching were not consistent across the included studies[111] and may have influenced marginal bone remodelling.

When trying to avoid complications of implant-based treatment it is tempting to chose minimally invasive approaches, as bone grafting procedures are associated with greater patient morbidity and reduced patient acceptance[112]. Common sense, on the other hand, dictates that some biomechanical limits of implant length, as well as diameter, must exist. Our finding that 6.0 mm long implants show higher failure rates in the maxilla compared with the mandible is important, however, comparative effectiveness research is needed to solve the question as to whether 6.0 mm implants in the maxilla demonstrate higher failure rates than longer implants placed after sinus floor augmentation[77]. The same question arises when increased early failures with implant diameters < 3.3 mm are interpreted: as survival rates are still as high as 95% it remains questionable whether bone grafting may lead to better results, however, augmentation procedures are not even an

alternative in cases of limited mesio-distal gap width. Future research may investigate the consequences of early failures of extra-short and extra-narrow implants as well as the complications that may arise in the long-term.

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Material-related complications in implant-supported fixed dental restorations. A systematic review

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Key words *dental materials, dental prosthesis, implant-supported, technical complications*

Aim: A large variety of dental materials are available for the production of implant-supported fixed restorations. Materials with different properties are likely to behave differently during clinical function, which may result in different prevalence and types of complications. The aim of the present review was to summarise, analyse and discuss the prevalence and types of complications or failures related to dental materials in implant-supported restorations.

Materials and methods: A strategy was set up using the PICO format and the search was performed using the PubMed database, including a hand search of reference lists. Two independent reviewers selected papers based on a set of criteria. The number of events of complications was summarised.

Results: The initial search produced 2764 titles. After application of criteria, 47 publications were selected for analysis. Seventeen studies reported on 1447 single crowns and 30 studies reported on 2190 fixed dental prostheses. The most common complications were fracture or chipping of the veneer material, loss of retention and lost access hole fillings. Due to the heterogeneity of studies, and large variation in number of restorations per material group, no conclusive correlation between type of material and type of technical complication and/or failure could be established.

Conclusions: The review did not succeed in providing convincing evidence to answer the question concerning a possible relationship between restoration materials and prevalence of technical complications in implant-supported restorations.

Introduction

The prevalence of technical complications has been reported to be significantly higher among implant- as opposed to tooth-supported restorations[1]. This difference in complication rate will likely have implications for long-term cost-effectiveness[2]. Consequently, it is of great interest to identify and analyse possible factors behind complications in order to gain knowledge and understanding on how to prevent them. Reducing complications would be beneficial from the point of view of patients and caregivers as well as society in general.

Most well-cited reviews on survival and complication rates of fixed dental restorations do not report on complications and failures from the perspective of from what materials the restorations were made[3-7]. In part, this is explained by the fact that for a long time most papers only used to report on conventional metal-ceramic restorations based on high-noble alloys, which was the preferred treatment alternative. Today, the options for choice of material have expanded, which is visible in more recent reviews where metal-ceramic as well as all-ceramic restorations are evaluated[8,9]. The terms "metal-ceramic" and "all-ceramic", however,

include several material subgroups. The term metal-ceramic may be used for restorations based on high-noble alloys or base metals. Likewise, the term all-ceramic may refer to oxide- as well as glass-ceramics. In addition, metals are often used in combination with polymer-based veneer materials. These different materials have different properties and are likely to behave differently during clinical function, which may result in different prevalence and types of complications. As the type of restorative material may affect long-term function, the choice of material should be carefully considered during treatment planning and preferably based on high-quality data.

Systematic reviews summarise available evidence to facilitate and assist decision-making in the care of patients[10]. The present review sought to analyse the relationship between restoration material/materials and prevalence of technical complications. The objective was to search for literature evaluating implant-supported restorations, to summarise, analyse and discuss the prevalence and types of complications or failures related to dental materials.

Materials and methods

The following questions were addressed in the current literature search:

1. What kind of complication or failure occurs at implant-supported fixed dental restorations?
2. How common are the different complications and failures at implant-supported fixed dental restorations?

Definitions

The definitions used in the present paper are modifications based on terminology from The Glossary of Prosthodontic Terms, where applicable[11].

"Implant-supported" describes a restoration that depends entirely on dental implants for support, with screw or cement retention.

"Fixed dental restoration" includes single crowns (SCs) and fixed dental prostheses (FDPs).

"Crown" is defined as an artificial replacement that restores a damaged tooth.

"Fixed dental prosthesis" is defined as a prosthesis that replaces one or more teeth. The term includes splinted single crowns, fixed partial dentures as well as full arch fixed dentures.

"Technical complications" include fracture of the framework, fracture or chipping of the veneer material, loss of retention, abutment fracture, lost access hole filling material, or excess cement, which did not lead to failure.

"Failure" is defined as the restoration having been removed due to fracture of the framework, fracture or chipping of the veneer material, loss of retention, abutment fracture, lost access hole filling material, or excess cement.

Search strategy

A strategy was set up using the PICO (patient, intervention, comparison, outcome) format and the search was performed in the PubMed database (National Center for Biotechnology Information, US National Library of Medicine). Free-text words and MeSH terms were used and combined as shown in Table 1. To supplement the literature search, a hand search of the reference lists of included studies and reviews was performed to identify possible additional relevant articles.

The literature search covered all publications up to March 2017. Published papers were required to meet the set inclusion and exclusion criteria in protocol section A, B and C for the different steps in the process to collect data on title-, abstract- and full-text level. Table 1. Two reviewers (EP and CL) independently read the titles and subsequently the abstracts of all potentially relevant papers that matched the search terms and criteria according to protocol section A and B respectively. When at least one reviewer found an abstract relevant, the paper was selected for full-text reading using the protocol section C. In cases of disagreement, the paper was re-evaluated and discussed by the reviewers until consensus was reached. If a paper reported repeated follow-up data, the most current publication was used.

Data extraction and analysis

Data was extracted based on the protocol. Information on type of implant-supported fixed prosthesis (crowns/FDPs), type of materials used, as well as

Table 1 Systematic search strategy and selection criteria.

Focus questions	**What kind of failure/complication occurs at implant-supported fixed restorations? How common are the different failures and complications at implant-supported fixed restorations?**		
Search strategy	((((Dental prosthes*[Title/Abstract]) OR „Dental Prosthesis"[Mesh:NoExp]) OR ((„Crowns"[Mesh]) OR Crowns[Title/Abstract])) OR ((„Denture, Partial, Fixed"[Mesh]) OR Denture, Partial, Fixed[Title/Abstract])) AND ((„Dental Prosthesis, Implant-Supported"[Mesh]) OR Implant-Supported, Dental Prosthesis[Title/Abstract]) Limit English		
Population	#1 (Dental prosthes*[Title/Abstract]) OR (Dental Prosthesis[Mesh]) OR (Crowns[Mesh]) OR (Crowns[Title/Abstract]) OR (Denture, Partial, Fixed [Mesh]) OR (Denture, Partial, Fixed[Title/Abstract])		
Intervention	#2 (Dental prosthesis, Implant-Supported [Mesh]) OR Implant-supported, Dental prosthesis[Title/Abstract])		
Comparison	Dental materials		
Outcome	Complications, failure, survival and success related to materials used		
Search combination	#1 AND #2		
Database search			
Language	English		
Electronic	Medline (via PubMed)		
Selection criteria			
Inclusion criteria	Protocol section A (Title-level) Implant-supported fixed restorations English Human studies Abstract available Original articles	Protocol section B (Abstract-level) Implant-supported fixed restorations Original articles Clinical reports	Protocol section C (Full-text-level) Case series Evaluating technical complications on crowns/FDPs Screw retained or cemented
Exclusion criteria	Protocol section A (Title-level) Implant-supported removable prostheses Animal studies *In vitro* studies	Protocol section B (Abstract-level) *In vitro* studies Technical reports/Clinical notes/letter/ Treatment planning Method description Case report Implant-supported removable prostheses Provisional crowns/FDPs Combination of tooth-/ implant supported crowns/FDPs Evaluation of soft-tissue/bone-level/ bone replacement/abutment Orthodontic treatment (mini-implant/ mini-screw)	Protocol section C (Full-text-level) Studies with less than 10 patients Studies with less than 1 year follow-up Unspecified type of materials of the crowns/FDPs Incomplete information on the treatment outcome Evaluation of soft-tissue/bone-level/ bone replacement

type of technical complications, was registered. The number of events per complication was summarised and compared between groups in an attempt to identify similarities or differences.

■ Results

The results of the search strategy are presented in Figure 1. The search strategy identified 2589 plus 175 papers from the PubMed and hand search respectively. The selection process resulted in 33 plus 14 publications, i.e. 47 studies formed the basis for this review. The most common reason for exclusion at the full-text level was incomplete information. From the 177 papers that were selected for full-text screening, only 117 included information on materials used. For many of the excluded studies, information concerning materials was present but unspecific, e.g. mentioning "metal-ceramic" without specifying which metal was used. Of the 117 studies, six additional papers were excluded

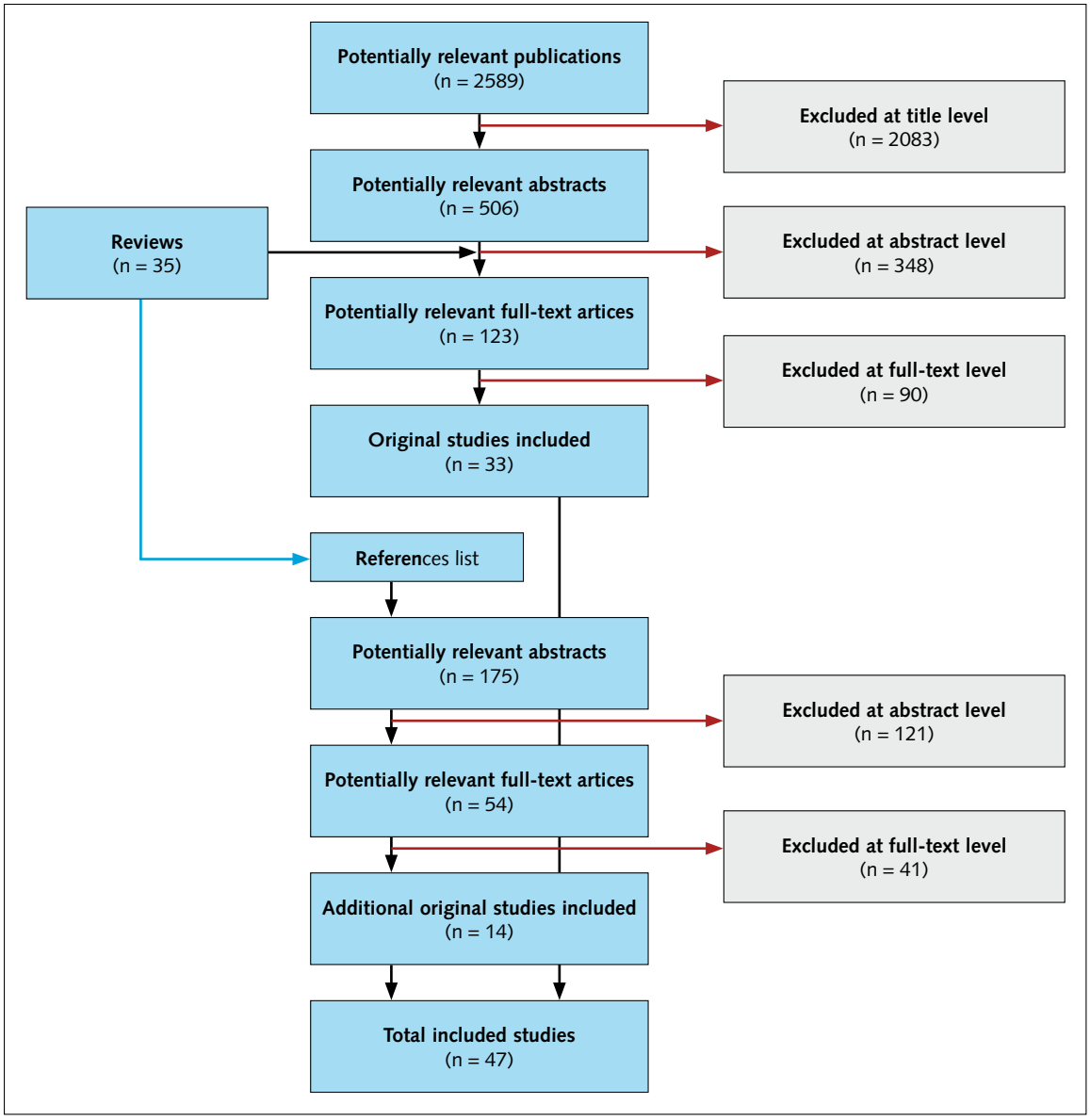

Fig 1 Results of the search strategy for the PubMed database.

as they used more than one material and did not present their results per material. Sixty-four papers were excluded due to other reasons such as too few patients and/or restorations and too short follow-up or lack of presentation of technical complications and/or failures. Table 1. For the remaining 47 papers selected for analysis, information concerning materials and outcome, as well as other study characteristics, is shown in Tables 2 and 3[12-58]. The results are presented as number of events of complication or failure per total number of restorations (Table 4).

Single crowns

Seventeen studies reported on a total of 1447 SCs: 807 metal-ceramic crowns, 604 all-ceramic crowns and 36 metal-acrylic crowns. A majority of the studies were prospective and university setting was more common compared to private practice or public dental health service. Almost all metal-ceramic crowns – 86% – were based on high-noble Au-alloys, 12% were made of CoCr- and 2% were Ti-base metal alloys. Most all-ceramic restorations, 68%, were zirconia-based followed by alumina, 23%, and glass-ceramic, 9%. There was only one metal-acrylic material combination, Au-acrylic. Albeit representing a relatively large number of restorations, the

Table 2 Study characteristics of studies on single crowns: metal-ceramic, metal-acrylic and all-ceramic.*

SINGLE CROWNS: METAL-CERAMIC								
Author/ Design/ Setting	**Patients (origi-nally)**	**No. of SCs (origi-nally)**	**Follow up**	**Core material**	**Veneer material**	**Implant system, Abutment system, Retention**	**Results**	**Technical failures and complications**
Hosseini et al 2011[12] Prospective University	IC (IC)	37 (37)	1 year (11 to 20 months), median 13.5	Au-alloy (HeraNordic, Kulzer or OrionWX, Elephant Dental)	Glass-ceramic (HeraCeram, Kulzer or IPSd.SIGN, Ivoclar Vivadent)	NI (Astra Tech), Ti- and Au-abutments: (Ti Design, Astra Tech, Au Cast-to, Astra Tech), Cement-retained: (36 DeTrey zincphosphate, Dentsply, 1 Panavia resin cement, Kuraray)	97.4% SuR	1 veneer fracture 1 loss of retention
Hosseini et al 2013[13] Prospective University	IC (IC)	34 (34)	3 years median 37.1	Au-alloy (OrionWX, Elephant Dental)	Glass-ceramic (IPSd.SIGN, Ivoclar Vivadent)	NI (Astra Tech), Ti- and Au-abutments: (Cast-to Au and TiDesign, Astra Tech) Cement-retained: (DeTrey zincphosphate, Dentsply)	NI	3 loss of retention 1 excess cement
Kreissl et al 2007[14] Prospective University	IC (IC)	46 (46)	5 years	Au-Pd-Pt-alloy (Degudent U, Degussa)	Porcelain (Vita Omega, Vita Zahnfabrik)	Osseotite, (3i-Implant Innovations), NI, Screw-retained	NI	2 veneer fractures
Jemt et al 2009[15] Retrospective Specialist clinic	10 (15)	11 (18)	10 years	Ti (NI)	Porcelain (NI)	Brånemark (Nobel Biocare), Ti abutments: (TiAdapt, Nobel Biocare), Screw-retained	NI	
Mericske-Stern et al 2001[16] Prospective NI	68 (72)	104 (109)	5 years (1 to 9 years, mean 4.3 years)	Au-alloy (NI)	Porcelain (NI)	ITI-implants (Straumann) Ti abutments: (Octa Abutment) 102 screw-retained 7 cement-retained: (NI)	NI	1 veneer fracture 1 loss of retention - recemented 3 abutment fracture (3 crowns lost due to implant loss)
Montero et al 2012[17] Retrospective University	71 (71)	91 (93)	5 years (mean 26.2 months)	Co-Cr-alloy (Heraenium, Heraeus-Kulzer)	Feldspathic ceram (HeraCeram, Heraeus-Kulzer)	Osseotite (Biomet 3i) DefconTSA (Impladent) MK (Microdent Implant System) MG-Osseous (Mozo Grau) and Brånemark MkIII, (Nobel Biocare), Metal abutments: (UCLA castable, Sterngold-ImplaMed), 84 screw-retained, 9 cement-retained (Ketac Cem Plus glass inomer cement, 3M ESPE)	NI	1 veneer fracture (2 crowns lost due to implant loss)
Schwarz et al 2012[18] Retrospective University	IC (IC)	179 (179)	5.8 years (mean, 2.1)	Au-alloy (NI)	Glass-ceramic/Porcelain (Duceram Kiss, (DeguDent or VITA VM13, VITA Zahnfabrik or Reflex,Wieland Dental GmbH)	TissueLevel and BoneLeve (Straumann) and Nobel Replace (Nobel Biocare), NI, Cement-retained: (Dycal Dentsply and Tempbond, Kerr, temporary cements, Harvard zincphosphate cement, Harvard Dental, Ketac Cem, and RelyX Unicem glass ionomer cement, 3M ESPE)	98.3% CSrR	17 veneer fractures: 2 remade 24 loss of retention (17 semi-permanent cem)

Table 2 (cont.) Study characteristics of studies on single crowns: metal-ceramic, metal-acrylic and all-ceramic.*

SINGLE CROWNS: METAL-CERAMIC								
Author/ Design/ Setting	**Patients (originally)**	**No. of SCs (originally)**	**Follow up**	**Core material**	**Veneer material**	**Implant system, Abutment system, Retention**	**Results**	**Technical failures and complications**
Turkyilmaz et al 2006[19] Prospective NI	IC (19)	34 (36)	3 years	Au-alloy (Degudent U, Degudent)	Porcelain (Ceramco, Dentsply)	Brånemarks System MKIII TiUnite (Nobel Biocare), Ti abutments: (CeraOne, Nobel Biocare), Cement-retained: (Temp Bond NE temporary cement, Kerr)	94% ScR	2 porcelain fractures: 1 replaced and 1 recontoured
Walton et al 2015[20] Prospective Specialist clinic	160 (174)	201 (220)	15 years (mean 4.6 years)	Au-alloy (NI)	Porcelain (NI)	TiUnite (Nobel Biocare) + "other", Ti abutments: (UCLA castable, Sterngold-ImplaMed, Cera One, Nobel Biocare, Cast to gold, NI and "others), 207 screw-retained 13 cement-retained: (NI)	93.3% ECSrR	2 veneer fractures: 1 removal 2 loss of retention 3 lost access hole seal
Wannfors et al 1999[21] Prospective Public dental health service	IC (32)	34 (35)	3 years	Au-alloy (NI)	Ceramic (NI)	Brånemark (Nobel Biocare), Ti- or Au-abutments: (CeraOne, Nobel Biocare, Au cast-to abutment, NI) 8 screw-retained 27 cement-retained: (Harvard zincphosphate cement, Richter and Gottman)	NI	1 veneer fracture
SINGLE-CROWNS: METAL-ACRYLIC								
Author/ Design/ Setting	**Patients (originally)**	**No. of SCs (originally)**	**Follow up**	**Core material**	**Veneer material**	**Implant system, Abutment system, Retention**	**Results**	**Technical failures and complications**
Wannfors et al 1999[21] Prospective Public dental health service	IC (29)	34 (36)	3 years	Au-alloy (NI)	Acrylic resin (NI)	Brånemark (Nobel Biocare), Au cast-to abutments: (NI), Screw-retained	NI	1 veneer fracture 1 lost access hole filling
SINGLE-CROWNS: ALL-CERAMIC								
Author/ Design/ Setting	**Patients (originally)**	**No. of SCs (originally)**	**Follow up**	**Core material**	**Veneer material**	**Implant system, Abutment system, Retention**	**Results**	**Technical failures and complications**
Glauser et al 2004[22] Prospective NI	18 (27)	36 (54)	4 years (48 to 52 months, mean 49,2)	Glass-ceramic (Empress I, Ivoclar Vivadent)	-	Brånemark system (Nobel Biocare), Experimental Zr abutment: (Wohlwend), Cement-retained: (Panavia resin cement, Kuraray)	NI	3 veneer fractures
Gulje et al 2014[23] Prospective Private practice & University	40 (41)	40 (41)	12 months	Zirconia (NI)	Ceramic (NI)	Osseospeed (Dentsply), Ti abutments: (Atlantis, Dentsply), Cement-retained: (NI)	NI	
Hosseini et al 2011[12] Prospective University	IC (IC)	38 (38)	1 year (11 to 20 months), median 13.5)	Zirconia (KaVo Zirconia, KaVo or Procera Zirconia, Nobel Biocare)	Glass-ceramic (HeraCeram, Kulzer or IPS e.max Ceram, Ivoclar Vivadent)	NI (Astra Tech), Zr abutments: (ZirDesign, Astra Tech), Cement-retained : (35 DeTrey zincphosphate,zincphosphate, Dentsply, 3 Panavia resin cement, Kuraray)	100% SuR	

SINGLE-CROWNS: ALL-CERAMIC								
Author/ Design/ Setting	**Patients (originally)**	**No. of SCs (originally)**	**Follow up**	**Core material**	**Veneer material**	**Implant system, Abutment system, Retention**	**Results**	**Technical failures and complications**
Hosseini et al 2013[13] Prospective University	IC (IC)	61 (61)	3 years (median, 37.1)	Zirconia (Procera Zirconia, Nobel Biocare)	Glass-ceramic (IPS Empress2 or IPS e.max Ceram, Ivoclar Vivadent)	NI (Astra Tech), Zr-, Ti-, Cast-to Au-abutments: (ZirDesign, TiDesign and Au cast-to, Astra Tech), Cement-retained: (Panavia resin cement, Kuraray)	NI	2 veneer fractures: 1 crown removal 3 excess cement
Monaco et al 2015[24] Retrospective Private practice	IC (IC)	146 (149)	5 years	Zirconia (16 different brands)	Porcelain (13 different brands)	NI, NI, 49 screw-retained 100 cement-retained: (Glass ionomer, NI, zincphosphate, NI, Temporary cement, NI)	91.3% ECSrR 88.8% ECScR	4 core fractures 6 veneer fractures: 3 replaced, 3 adjustment/repair
Sagirkaya et al 2012[25] Prospective NI	IC (IC)	33 (33)	4 years	Zirconia (Cercon, Degudent or ZirkonZahn or LAVA, 3M ESPE or Katana, Kuraray)	Porcelain (NI)	TiUninte, (Nobel Biocare), Ti abutments: (Esthetic abutment Nobel Biocare), Cement-retained: (Panavia resin cement, Kuraray)	NI	
Schwarz et al 2012[18] Retrospective University	IC (IC)	53 (53)	5.8 years (mean, 2.1 years)	Zirconia (Cercon, DeguDent or Zenotec Wieland Dental)	Glass ceramic (Cercon Ceram Kiss,DeguDent, or Zirox, Wieland Dental)	TissueLevel and BoneLevel (Straumann) and Nobel Replace (Nobel Biocare), NI, Cement-retained: (Dycal Dentsply and Tempbond, Kerr, temporary cements, Harvard zincphosphate cement, Harvard Dental, Ketac Cem, and RelyX Unicem glass ionomer cement,3M ESPE)	86.8% CSrR	13 veneer fractures: 6 remade 3 loss of retention
Sorrentino et al 2012[26] Retrospective University & private practice	IC (IC)	80 (81)	6 years	Alumina (Procera Alumina, Nobel Biocare)	Feldspathic porcelain (Procera AllCeram Ceramics, Ducera Dental)	NI (Nobel Biocare and Straumann), Alu- or Ti- abutments: (Procera abutment, Nobel Biocare), Cement-retained: (43 RelyX glass ionomer cement, 3M ESPE, 38 Zincphosphate, NI)	97.6%CScR 95.7% CSrR	3 fractures: 2 at trial, 1 at cementation 1 veneer fracture
Tartaglia et al 2011[27] Prospective Private practice	19 (19)	36 (36)	3 years	Zirconia (Zirite, Keramo)	Porcelain (CZR Noritake)	Titanmed (Milde Implants), Ti abutments: (NI), Cement-retained: (Ketac glass ionomer cement 3M ESPE)	NI	None reported
Zarone et al 2005[28] Retrospective University	44 (44)	57 (58)	4 years	Alumina (Procera, Nobel Biocare)	Porcelain (Procera AllCeram Ceramics, Ducera Dental)	NI (Straumann and Nobel Biocare), Ti abutments: (Procera Alumina), Cement-retained: (RelyX glass ionomer cement, 3M ESPE)	98.3% ScR	1 veneer fracture

*Figures concerning results, follow-up and number of patients are as presented in the papers. Figures on success or survival refer to restorations, not implants. Brands and/or manufactures are presented in parentheses.

Table 3 Study characteristics of studies on fixed dental prostheses: metal-ceramic, metal-acrylic and all-ceramic.*

FIXED DENTAL PROSTHESES: METAL-CERAMIC								
Author Design Setting	**Patients (originally)**	**No. of FDPs (originally) Units**	**Follow up**	**Core material**	**Veneer material**	**Implant system, Abutment system, Retention**	**Results**	**Technical failures and complications**
Hjalmarsson et al 2011[29] Retrospective Specialist centres	15 (25)	15 (25) Full-arch	5 years	CoCr alloy (Wirobond, BEGO)	Porcelain (Classic, Ivoclar Vivadent)	NI (Astra Tech, Stramann and Biomet 3i Nobel Biocare), Implant level, Screw-retained	98.9% CSrR	4 veneer fractures
Kreissl et al 2007[14] Prospective University	IC (IC)	66 (66) (splinted SCs included)	5 years	Au-Pd-Pt-alloy (Degudent U, Degussa)	Porcelain (Vita Omega, Vita Zahnfabrik)	Osseotite (Biomet 3i, Nobel Biocare) NI, Screw-retained	NI	1 framework fracture 8 veneer fractures
Jemt et al 2003[30] Prospective University	18 (21)	18 (21) NI	5 years	Au-alloy (NI)	Porcelain (NI)	Brånemark system (Nobel Biocare), Ti abutments: (Standard, Nobel Biocare), Screw-retained	100% CSrR	2 veneer fractures
	18 (21)	18 (21) NI		Laser-welded Ti (Procera, Nobel Biocare)	Porcelain (NI)	Brånemark system (Nobel Biocare), Ti abutments: (Standard, Nobel Biocare), Screw-retained	95% CSrR	1 framework fracture 4 veneer fractures
	17 (21)	17 (21) NI		Laser-welded Ti (Procera, Nobel Biocare)	Porcelain (NI)	Brånemark system (Nobel Biocare), NI, Screw-retained	90% CSrR	4 veneer fractures (2 FDPS lost due to implant failure)
Malo et al 2012[31] Retrospective Private practice	IC (52)	NI (66) 12 to 14 units full-arch	5 years (9 months to 10 years, mean, 5 years)	Milled titanium (Nobel Biocare)	Alumina crowns (Procera Alumina, Nobel Biocare) cemented onto Ti framework, plus pink "ceramic gingiva" veneer (Duceram, Ducera Dental)	Nobel Speedy (Nobel Biocare), Ti abutments: (MultiUnit and Angulated, Nobel Biocare), Screw-retained	92.4% CSrR	29 crown fractures 4 veneer fractures 3 veneer fractures of "ceramic gingiva"
	IC (56)	NI (59) 12 to 14 units full-arch		Milled titanium (Nobel Biocare)	Zirconia crowns (ProceraZirconia, Nobel Biocare) cemented onto Ti framework, plus pink acrylic resin veneer (PalaXpress Ultra, Hereaus Kulzer)	Nobel Speedy (Nobel Biocare, Ti abutments: (MultiUnit and Angulated, Nobel Biocare), Screw-retained	100% CSrR	13 crown fractures 1 veneer fractures
Romeo et al 2009[32] Prospective University and Private practice	45 (59)	59 (75) NI	8 years (mean 8.2 years)	Au-alloy (NI)	Porcelain (NI)	NI (Straumann), Titanium abutments: (Solid or OCTA abutment with cast-to gold copings) 13 screw-retained 46 cement-retained: (zincoxide eugenol or zincphosphate, NI)	57.7% ScR 100% SuR	3 loss of retention (recemented) 22 veneer fractures in 17 patients
Shi et al 2016[33] Retrospective University	118 (125)	144 (152) 3 units	8 years (4.8 years)	Highnoble alloy (NI, Heraus Kulzer)	Porcelain (NI, Ivoclar Vivadent)	NI, Ti abutments: (NI), Cement-retained: (HY-bond Glass ionomer cement CX, Shofu)	94.7% SuR	22 veneer fractures: 4 FPDs remade 8 loss of retention

FIXED DENTAL PROSTHESES: METAL-ACRYLIC								
Author Design Setting	**Patients (origi-nally)**	**No. of FDPs (originally) Units**	**Follow up**	**Core material**	**Veneer material**	**Implant system, Abutment system, Retention**	**Results**	**Technical failures and complications**
Arvidson et al 1998[34] Prospective Specialist clinic	91 (107)	91 (107) Full-arch	5 years	Au (type III)-alloy (NI)	Acrylic resin base & teeth (SR Vivodent, Ivoclar)	Astra Tech Implants (Atra Tech), NI, Screw-retained	100% SuR	
Capelli et al 2007[35] Prospective University	64 (65)	64 (65) Full-arch	4 years (mean, 29.1 months)	Ti (NI)	Acrylic resin base & teeth (NI)	Osseotite NT (Biomet/3i) Ti abutments: (NI), Screw-retained	100% ScR	
Davis et al 2003[36] Retrospective NI	37 (37)	43 (43) Full-arch	5 years	Au-alloy (NI)	Acrylic resin base & teeth (NI)	NI (Nobel Biocare), NI, Screw-retained	NI	7 framework fractures 60 acrylic/teeth fractures
Ekelund et al 2003[37] Prospective University	30 (47)	30 (47) Full-arch,	20 years	Au (type III)-alloy (NI)	Acrylic resin teeth (NI)	Brånemark system (Nobel Biocare), Ti abutments: (Standard, Nobel Biocare), Screw-retained	95.6% CSuR	3 acrylic/teeth fractures 35 loose fillings
Eliasson et al 2010[38] Prospective Specialist centre	24 (29)	24 (29) 10-12 units full-arch	5 years	Au (type III)-alloy (C3gold KAR, Sjödings)	Acrylic resin base (ProBase, Ivoclar Vivadent) & teeth (SR Vivodent, Ivoclar Vivadent)	NI (Paragon Implants) NI, Screw-retained	100% CSuR	
Esquivel-Upshaw et al 2014[39] Prospective University	IC (IC)	48 (48) 3 units	3 years	Au-Pd-Ag-alloy	Glass-ceramic (InLine POM, Ivocalr Vivadent)	Osseospeed (Dentsply), Ti abutments: (Atlantis Titanium, Dentsply), Cement-retained: (RelyX Unicem resin cement)	NI	7 veneer fractures
Galindo et al 2012[40] Retrospective Private practice	183 (183)	183 (183) Partial or full-arch	12 months	Ti (NI)	Acrylic resin base & teeth (NI)	SpeedyGroovy and NobelActive (Nobel Biocare), Ti abutments: (MultiUnit, Nobel Biocare), Screw-retained	98,9% SuR	2 framework fractures 3 resin tooth fractures
Gothberg et al 2003[41] Retrospective Multicenter (specialist and general dentist)	75 (75)	75 (75) 6 to 14 units	3 years	Au-alloy (NI)	Acrylic resin teeth (NI)	Brånemark system (Nobel Biocare), NI, Screw-retained	NI	38 fractures resin/teeth in 17 patients
Gunne et al 1999[42] Prospective University	20 (23)	16 (23) Partial	10 years	Au (type III)-alloy (Sjödings)	Composite (Dentacolor, Kulzer)	Brånemark (Nobel Biocare), NI, Screw-retained	80% "prosthesis stability"	(4 lost FPDS due to implant loss)
Hjalmarsson et al 2011[29] Retrospective Specialist centres	25 (40)	25 (40) Full-arch	5 years	cp Ti (Cresco Sjödings)	Acrylic resin base & teeth (SR Vivodent)	NI (Astra Tech, Stramann Biomet 3i, and Brånemark system, Nobel Biocare), Implant level, Screw-retained	98,1% CSrR	6 veneer fractures 3 lost fillings
	23 (40)	23 (40) Full-arch		Ti (PIB, Nobel Biocare)	Acrylic resin base & teeth (SR Vivodent/Orthotype PE)	Brånemark system (Nobel Biocare), Ti abutments: (MuA or Angled, Nobel Biocare) Screw-retained	97,6% CSrR	4 veneer fractures

Table 3 (cont.) Study characteristics of studies on fixed dental prostheses: metal-ceramic, metal-acrylic and all-ceramic.*

FIXED DENTAL PROSTHESES: METAL-ACRYLIC								
Author Design Setting	**Patients (originally)**	**No. of FDPs (originally) Units**	**Follow up**	**Core material**	**Veneer material**	**Implant system, Abutment system, Retention**	**Results**	**Technical failures and complications**
Jemt et al 2002[43] Prospective Multicenter Retrospective Multicentre	27(28)	27 (28) Full-arch	5 years	Ti (type III, Procera, Nobel Biocare)	Acrylic resin base & teeth (NI)	Brånemark system (Nobel Biocare), NI, Screw-retained	96.4% CSuR	11 resin teeth/resin material fractures
	29(30)	29 (30) Full-arch	5 years	Au-alloy (NI)	Acrylic resin base & teeth (NI)	Brånemark system (Nobel Biocare), NI, Screw-retained	93.3% CSuR	12 resin teeth/resin material fractures
Jemt et al 2006[44] Prospective Specialist clinic	28(76)	28 (76) Full-arch	15 years	Au-alloy (NI)	Acrylic resin teeth (NI)	Brånemark system (Nobel Biocare) NI, Screw-retained	90.6% CSuR	1 framework fracture 158 resin veneer fractures
Katsoulis et al 2011[45] Prospective University	13 (13)	13 (13) Full-arch	2 years	Ti (NI)	Acrylic resin & teeth (Candulor denture teeth, Candulor)	Replace select (Nobel Biocare) NI, Screw-retained	NI	5 denture base fractures 8 teeth fractures
Krennmair et al[46] 2014 Prospective University	24 (24)	24 (24) Full-arch	2 years	Cast CoCr (NI)	Acrylic resin base & teeth (GC Gradia, Kerr)	Camlog Screw-line (CAMLOG), Ti abutments: (Vario SR Abutment, CAMLOG), Screw-retained	NI	15 teeth fracture/ repair in 10 patients 8 screw hole acrylic repair in 5 patients
Lindquist et al 1996[47] Prospective University	45 (47)	45 (47) 12 units full-arch	12 to 15 years	Au(type III)-alloy (NI)	Acrylic resin teeth (NI)	Brånemark (Nobelpharma) Ti abutments: (Standard abutments, Nobelpharma), Screw-retained	100% CScR	5 fractured resin teeth 43 lost access hole fillings
Makkonen et al 1997[48] Prospective University	IC (13)	IC (13) Full-arch	5 years	Au-alloy (NI)	Acrylic resin teeth (NI)	NI (Astra Tech) NI, Screw-retained	100% SuR	1 FPD fracture 1 resin fracture
Ortorp et al 2009[49] Retrospective Private practice and specialist clinic	52 (155)	52 (155) 10 to 12 units full-arch	15 years	Ti (laser-welded Ti, Procera, Nobelpharma	Acrylic resin base & teeth (NI)	Brånemark (Nobel Biocare) Ti abutments: (Standard abutment, Nobel Biocare), Screw-retained	89.2% CSuR	36 framework fractures in 24 patients 33 veneer fractures in 23 patients 21 lost access hole fillings in 18 patients
	13 (53)	13 (53) 10 to 12 units full-arch		Au-alloy (NI)	Acrylic resin base & teeth (NI)	Brånemark (Nobel Biocare) Ti abutments: (Standard abutment, Nobel Biocare), Screw-retained	100% CSuR	4 framework fractures in 3 patients 10 veneer fractures in 7 patients 17 lost access hole fillings in 12 patients
Ortorp et al 2012[50] Prospective Private practice and specialist clinic	36 (65)	35 (67) Full-arch	10 years	Ti (CNC milled, PIB, Nobel Biocare)	Acrylic resin base & teeth (NI)	Brånemark (Nobel Biocare) NI, Screw-retained	95.6% CSuR	33 veneer fractures in 17 prostheses 5 lost access hole fillings in 5 prosthesis

FIXED DENTAL PROSTHESES: METAL-ACRYLIC								
Author Design Setting	**Patients (originally)**	**No. of FDPs (originally) Units**	**Follow up**	**Core material**	**Veneer material**	**Implant system, Abutment system, Retention**	**Results**	**Technical failures and complications**
Ortorp et al 2012[50] Prospective Private practice and specialist clinic	38 (61)	37 (62) Full-arch	10 years	Au-alloy (NI)	Acrylic resin base & teeth (NI)	Brånemark (Nobel Biocare) NI, Screw-retained	98.3% CSuR	2 framework fractures in 2 prostheses 46 veneer fractures in 19 prostheses 25 lost access hole fillings in 10 prosthesis
Schwarz et al 2010[51] Prospective University	25 (37)	25 (37) Full-arch	4.5 years (1 to 8 years, mean, 4.5 years)	Ti (NI)	Acrylic resin base & teeth (NI)	FRIA-LOC implants (Friadent), NI, Screw-retained	97.3% SuR	10 framework fractures in 6 patients 16 veneer fractures in 11 patients (1 removed due to loss of implants)
FIXED DENTAL PROSTHESES: ALL-CERAMIC								
Author Design Setting	**Patients (originally)**	**No. of FDPs (originally) Units**	**Follow up**	**Core material**	**Veneer material**	**Implant system, Abutment system, Retention**	**Results**	**Technical failures and complications**
Borg et al 2014[52] Prospective Specialist clinic	10 (10)	10 (10) 2 to 3 units (splinted SCs included)	1 year (mean 15.2 months)	Zirconia (PIB Zirconia, Nobel Biocare)	Porcelain or Glass-ceramic (ZiroxNR, Wieland or HeraCeram, Hereaus Kulzer)	Brånemark system MKIII (Nobel Biocare), Implant level, Screw-reatined	100% SuR	
Esquivel-Upshaw et al 2014[39] Prospective University	NI	48 (48) 3 units	3 years	Zirconia (ZirCAD, Ivoclar Vivadent)	Glass-ceramic (ZirPress, Ivoclar Vivadent)	Osseospeed (Dentsply), Ti abutments: (Atlantis Titanium, Dentsply), Cement-retained: (RelyX Unicem resin cement)	NI	6 veneer fractures
Larsson et al 2010[53] Prospective University	10 (10)	10 (10) 10 units full-arch	3 years	Zirconia (Cercon, Degudent)	Porcelain (Cercon ceram S Degudent)	Microthread ST (Astra Tech), Ti abutments: (BiAbutment ST,Astra Tech) Cement-retained: (Panavia F2.0 resin cement, Kuraray)	100% SuR	34 veneer fractures in 9 FDPs
Larsson et al 2016[54] Prospective University	9 (9)	13 (13) 2 to 5 units	10 years	Zirconia (Denzir, Decim)	Porcelain (EspridentTriceram, Dentaurum)	Microthread ST (Astra Tech), Ti abutments: (BiAbutment ST,Astra Tech) Cement-retained: (DeTrey zincphosphate, Dentsply)	100% SuR	18 veneer fractures in 9 FDPs in 7 patients
	8 (9)	11 (12) 2 to 5 units		Zirconia (InCeramZirconia, Vita Zahnfabrik)	Porcelain (Vitadur-alpha, Vita Zahnfabrik)	Microthread ST (Astra Tech), Ti abutments: (BiAbutment ST, Astra Tech) Cement-retained: (DeTrey zincphosphate, Dentsply)	100% SuR	4 veneer fractures in 2 FDPs in 2 patients

Table 3 (cont.) Study characteristics of studies on fixed dental prostheses: metal-ceramic, metal-acrylic and all-ceramic.*

FIXED DENTAL PROSTHESES: ALL-CERAMIC								
Author Design Setting	**Patients (originally)**	**No. of FDPs (originally) Units**	**Follow up**	**Core material**	**Veneer material**	**Implant system, Abutment system, Retention**	**Results**	**Technical failures and complications**
Limmer et al 2014[55] Prospective University	17 (17)	17 (17) Full-arch	1 year	Monolithic Zirconia (ZirconZahn)	-	Osseospeed TX (Dentsply) Ti abutments: (20 degree UniAbutment, Dentsply), Screw-retained	88% SuR	12 events in 10 patients: 1 fractured FDP 2 fractured abutments 1 framework fracture of (distal extension) (1 FPD removed after implant failure)
Monaco et al 2015[24] Retrospective Private practice	IC (IC)	60 (61) Partial	5 years	Zirconia (16 different brands)	Porcelain (13 different brands)	NI, NI, 26 screw-retained 35 cement-retained: (Glass ionomer, NI, zincphosphate, NI, Temporary cement, NI)	95.2% ESuR 88.0% ESuR	6 veneer fractures: 2 replaced, 4 adjust/repair
Pozzi et al 2012[56] Prospective NI	27 (27)	37 (37) Partial	1 to 3 years (mean 43.3 months)	Zirconia (NI)	Porcelain (NI)	Speedy Replace and Speedy Groovy (Nobel Biocare), Zr- and Ti- abutments: (Nobel Biocare), Cement-retained: (Clearfil SA resin cement, Kurarray)	100% CSuR 91.9% CScR	3 veneer fractures
Pozzi et al 2015[57] Prospective University	16 (16)	18 (18) Full-arch	3 to 5 years (mean 49.3 months)	Zirconia (ProceraZirconia, Nobel Biocare)	Monolithic Glass-ceramic crowns (IPS e.max Press, Ivoclar Vivadent) cemented onto framework (Clearfil SA, resin cement, Kuraray), plus pink porcelain (GC Initial ZR-FS) fused to the framework	Speedy Groovy, Speedy Replace and NobelActive (Nobel Biocare), NI, Screw-retained	100% SuR	1 veneer fracture
Pozzi et al 2015[58] Retrospective University	22 (22)	26 (26) 12 to 16 units cross-arch	3 to 5 years (36 to 60 months, mean 42.3 months)	Zirconia (PIB Zirconia, Nobel Biocare)	Feldspathic porcelain (CZR, Noritake)	Speedy Groovy, Speedy Replace and NobelActive (Nobel Biocare), NI, Screw-retained	100% CSrR 88.5% CScR	5 veneer fractures in 3 FDPs
Shi et al 2016[33] Retrospective University	106 (112)	121 (127) 3 units	8 years mean 4.8 years	Zirconia (LAVA, 3M ESPE)	Porcelain (VITA VM9, Vita Zahnfabrik)	NI, Ti abutments: (NI), Cement-retained: (HY-bond Glass ionomer cement CX, Shofu)	95.3% SuR	34 veneer fractures: 3 FPDs remade 11 loss of retention

*Figures concerning results, follow-up and number of patients are as presented in the papers. Figures on success or survival refer to restorations, not implants. Brands and/or manufactures are presented in parentheses.

characteristics of the publications were heterogeneous, with large variations in the number of patients, follow up and number of restorations per material group (Table 2).

The most common complications were loss of retention and fracture or chipping of the veneer material (Table 4). Other complications were rare and miscellaneous, such as excess cement, abutment fracture or loss of access hole fillings.

The incidence of loss of retention among cemented crowns was 3.8%. There was a difference between material groups with a higher incidence of loss of retention among cemented metal-ceramic – 9.3% – than all-ceramic crowns at 0.8%. There were no events reported among metal-acrylic crowns, as none were cemented. All of the metal-ceramic crowns that experienced loss of retention were Au-alloy based; the all-ceramic crowns were zirconia-based.

Fracture or chipping of the veneer material occurred in 3.7% of the single crowns, with a similar incidence in all material-groups; 3.3% metal-ceramic, 4.3% all-ceramic and 2.8% metal-acrylic crowns. Among metal-ceramic crowns, veneer fractures were more common in Au- than CoCr-based SCs, at 3.7% and 1.1% respectively. No veneer fractures were noted for Ti-based crowns. Among all-ceramic crowns, veneer fractures were more common in glass-ceramic and zirconia-based SCs, 5.6% and 5.1% respectively, than alumina-based ones, 1.4%. As mentioned previously, there was only one study on metal-acrylic crowns and those crowns were Au-based. Core fracture was a rare complication (0.5%), and was only reported in all-ceramic restorations.

Fixed dental prostheses

Thirty studies reported on a total of 2190 FDPs: 1305 metal-acrylic FDPs, 506 metal-ceramic FDPs and 379 all-ceramic FDPs. A majority were prospective and performed in a university setting. Equal numbers of FDPs in the metal-acrylic group were based on high-noble Au-alloys or Ti-alloys. Only a few – 2% – were based on CoCr-alloys. Of the metal-ceramic FDPs, 62% were based on high-noble Au-alloys, 33% were based on Ti-alloys and 5% were CoCr-alloys. All of the all-ceramic restorations were zirconia-based. Albeit representing a relatively large number of restorations, the characteristics of the publications were heterogeneous, with large variations in the number of patients, follow up, dropouts and number of restorations per material group (Table 3).

The most common complications were fracture or chipping of the veneer material, loss of retention and lost access hole fillings (Table 4). Veneer fracture was a commonly noted complication that was reported in a third of all FDPs. This complication was less common in metal-ceramic (14%), than all-ceramic (32%), and metal-acrylic FDPs (36%). Among metal-ceramic FDPs, veneer fractures or chipping was more prevalent in Au- and CoCr based FDPs, 17% and 16% respectively, than Ti-based ones (7.8%). Metal-acrylic FDPs showed a similar pattern with higher incidence of fracture or chipping in CoCr- and Au- based FDPs – 63% and 52% respectively – than Ti-based FDPs (19%).

Framework fracture was a comparatively rare complication, with an incidence of 2.9% for all FDPs. It was more frequently reported in metal-acrylic (4.8%), than metal-ceramic and all-ceramic restorations – 0.4% and 0.3% respectively. There was no difference between metal-ceramic FDPs based on Ti- or Au-restorations, at 0.6% and 0.3% respectively. In the metal-acrylic group, core fracture was more frequently reported for Ti- than Au-based restorations – 7.6% and 2.1% respectively. No framework fractures occurred in CoCr-based restorations irrespective of veneer material.

Loss of retention showed an incidence of 4.2% for all cemented FDPs. 5.6% of cemented metal-ceramic FDPs, showed loss of retention. All of the FDPs were based on Au-alloys. 3.6% of cemented all-ceramic FDPs showed loss of retention. No loss of retention was noted in the one study reporting on cemented metal-acrylic FDPs.

Lost access hole fillings were frequently noted, but only among metal-acrylic-based FDPs, 12%. They predominantly occurred among CoCr- and Au-based FDPs, 33% and 20% respectively, compared with Ti-based FDPs, 3.8%.

Table 4 Complications per restoration type and material. x = number of incidents, y = number of papers reporting incidents.

SINGLE CROWNS n = 1447 (807 metal-ceramic, 604 all-ceramic, 36 metal-acrylic)					
Type of complication	**Total number of incidents, x/y**	**Incidents per material**		**Incidents per material subgroup**	
Core/framework fracture	7/2	Metal-ceramic	-	Au-alloy	-
				Ti-alloy	-
				CoCr-alloy	-
		Metal-acrylic	-	Au-alloy	-
		All-ceramic	7	Alumina	3
				Zirconia	4
				Glass-ceramic	-
Veneer fracture/chipping	54/15	Metal-ceramic	27	Au-alloy	26
				Ti-alloy	-
				CoCr-alloy	1
		Metal-acrylic	1	Au-alloy	1
		All-ceramic	26	Alumina	2
				Zirconia	21
				Glass-ceramic	3
Loss of retention	34/6	Metal-ceramic	31	Au-alloy	31
				Ti-alloy	-
				CoCr-alloy	-
		Metal-acrylic	-	Au-alloy	-
		All-ceramic	3	Alumina	-
				Zirconia	3
				Glass-ceramic	-
Miscellaneous	10/5	Metal-ceramic	1 excess cement, 3 lost access hole fillings, 3 abutment fractures 1 lost access hole filling		
		Metal-acrylic	1 excess cement, 3 lost access hole fillings, 3 abutment fractures		
		All-ceramic	1 lost access hole filling		
FIXED DENTAL PROSTHESES n = 2190 (1305 metal-acrylic, 506 metal-ceramic, 379 all-ceramic)					
Type of complication	**Total number of incidents, x/y**	**Incidents per material**		**Incidents per material subgroup**	
Core/framework fracture	64/9	Metal-ceramic	2	Au-alloy	1
				Ti-alloy	1
				CoCr-alloy	-
		Metal-acrylic	62	Au-alloy	14
				Ti-alloy	48
				CoCr-alloy	-
		All-ceramic	1	Zirconia	1
Veneer fracture	666/29	Metal-ceramic	71	Au-alloy	54
				Ti-alloy	13
				CoCr-alloy	4
		Metal-acrylic	474	Au-alloy	340
				Ti-alloy	119
				CoCr-alloy	15
		All-ceramic	121	Zirconia	121
Loss of retention	22/3	Metal-ceramic	11	Au-alloy	11
				Ti-alloy	-
				CoCr-alloy	-
		Metal-acrylic	-	Au-alloy	-
				Ti-alloy	-
				CoCr-alloy	-
		All-ceramic	11	Zirconia	11
Lost access hole fillings	152/7	Metal-ceramic	-		

FIXED DENTAL PROSTHESES n = 2190 (1305 metal-acrylic, 506 metal-ceramic, 379 all-ceramic)					
Type of complication	**Total number of incidents, x/y**	**Incidents per material**		**Incidents per material subgroup**	
Lost access hole fillings	152/7	Metal-acrylic	152	Au-alloy	120
				Ti-alloy	24
				CoCr-alloy	8
		All-ceramic	-		

Abbreviations in tables: AC: all-ceramic; CSrR: cumulative survival rate; CScR: cumulative success rate; ECSrR: estimated cumulative survival rate; ECScR: estimated cumulative success rate; IC: incomplete information; MA: metal-acrylic; MC: metal-ceramic; NI: No information; PDHS: public dental health service; ScR: success rate; SuR: survival rate.

Discussion

The present review sought to analyse the relationship between restoration material/materials and prevalence of events of technical complications or failure. Three major groups of events were identified: fracture or chipping of the veneer material, loss of retention, and lost access hole fillings.

Fracture or chipping of the veneer material was reported in several studies, more frequently among fixed dental prostheses than in single crowns. These findings are in agreement with other reviews[6,7]. Jung et al noted a 3.5%, 5-year cumulative complication rate for single crowns, with no difference between metal-ceramic and all-ceramic crowns[6]. That study did not make any distinctions between different subgroups within these two material groups. Pjetursson et al noted a 13.5%, 5-year cumulative complication rate for FDPs[7]. They found a significant difference between acrylic and ceramic veneers, with 20.2% and 7.8% 5-year cumulative complication rates. No distinctions between further material subgroups were made. In the present review, there was a similar prevalence of events for single crowns, with no substantial differences between material subgroups. Among fixed dental prostheses subgroups, Ti-based restorations showed the fewest number of events. Ti-alloy based restorations have previously been reported to show an increased risk of ceramic veneer fracture in publications on tooth-supported restorations[59,60]. The findings in the present review differ from this. However, the studies from Kaus et al and Walter et al, were early evaluations of the Ti-alloy metal-ceramic technique.[59,60] It is possible that previous challenges in manufacturing have since been overcome. Furthermore, there was an uneven distribution of number of restorations per different material subgroups. Few studies reported on Ti-alloy based restorations, especially Ti-based single crowns, which make comparisons difficult and unsound.

All-ceramic FDPs showed a higher prevalence of veneer fracture than metal-ceramic FDPs. The all-ceramic restorations were predominantly zirconia-based. Implant-supported zirconia restorations are known to suffer high prevalence of veneer fracture[61,62]. The increased risk has been explained by factors such as improper substructure design and support, mismatch of coefficient of thermal expansion of core and veneer material, and improper veneer cooling protocol[63]. The use of all-ceramic materials for implant-supported restorations is relatively recent compared with metal-ceramic and metal-acrylic, and the same explanation as proposed above concerning Ti-ceramic restorations, has also been suggested for zirconia-based ones[64].

There is a possible risk of bias concerning veneer fracture and chipping. Different authors have reported this complication in different ways. Some have clear definitions of what has been considered a veneer facture; others have not. Some present number of events per patient, some per restoration. Registration per restoration instead of total number of events produces an under-reporting of the occurrence of fractures and chippings.

Another possible risk of bias lies in those studies that did not have prosthetic complications as a primary outcome measure. In these studies, there is a potential risk of underreporting of complications such as veneer fractures and chipping. A further limitation is the unequal number of papers reporting on different material subgroups. Consequently, it is imprudent to draw any conclusions from the present review on possible differences concerning influence of restoration material on the risk of veneer fracture or chipping.

Core fracture was a rare complication in single crowns, which is in agreement with another review[6].

That review found no difference between all-ceramic and metal-ceramic restorations, whereas in the present review, core fracture only occurred in all-ceramic restorations, and more often among alumina than zirconia-based crowns. This difference is likely explained by the significant differences in mechanical properties. Ceramic materials have significantly lower flexural strength and fracture toughness compared with metals. Among fixed dental prostheses, framework fracture was more commonly reported in metal-acrylic FDPs, and especially Ti-alloy based ones. There are however, two studies from that subgroup that represent 88% of the total number of incidences of framework fracture[49,51]. Fracture risk is not only dependent on the type of material, but also on substructure design and manufacturing technique. One of the outlier studies states that the technique used for manufacturing the Ti-frameworks was an early version of laser-welding[49]. It is therefore possible that the results are dependent on manufacturing or design flaws rather than material properties. If the two outliers are excluded, the occurrence of framework fractures is comparable with what has been presented in another review[7]. No framework fractures occurred in CoCr-restorations, which is unsurprising as CoCr has significantly better mechanical properties, such as flexural strength and fracture toughness, than Ti- and Au-alloys. There was only one registered framework fracture among the all-ceramic FDPs. This is in contrast to tooth-supported all-ceramic FDPs[9]. Implant-supported, all-ceramic restorations may have an advantage as the support gained from the rigid fixation in bone and stiff support from metal substructures in implants and abutments are beneficial in reducing bending moments, which are critical for ceramic materials[65]. The information in the present review is, however, too limited to contribute to any conclusions.

Loss of retention was another common complication. This agrees with a review that found loss of retention to be a common complication among cement-retained fixed implant-supported restorations[66]. In the present review, loss of retention was more frequently noted among metal-ceramic than all-ceramic crowns. No such difference was noted among FDPs. A large variety of cements were used, from temporary to different types of permanent cements. This complicates analysis and precludes conclusions. Furthermore, loss of retention is strongly influenced by other factors than type of cement, such as abutment height and surface roughness[67]. The literature does not provide information about the ideal type of cement[66]. Nonetheless, type of cement should be carefully considered. Recommendations concerning the cementation of oxide ceramics have recently been updated, as resin cements have been found to be associated with fewer incidences of loss of retention compared with glass ionomer and zinc phosphate cements[62,68].

Loss of access hole fillings was the other major technical complication noted. This was a rare complication among single crowns, but frequently reported among metal-acrylic FDPs. None of the authors revealed what technique or materials were used, but a composite material is often employed. Successful bonding of composite depends on a surface with either unreacted C = C-groups or some kind of surface treatment, such as sandblasting and/or coating[69]. It is perhaps tempting to hypothesise that an acrylic veneer would be better for bonding than ceramic veneers, but the findings in the present review contradict this. The fact is that there are few, if any, unreacted C = C sites left in cured acrylic veneer materials, and the surface area of the material around an access hole is very limited. Successful bonding to the metal part of the access hole would require some type of pretreatment, but this is seldom performed[69]. The uneven representation of the three material subgroups, in combination with limited information on how access hole sealing was performed, makes comparisons unsound.

The results presented in the present review must be cautiously interpreted due to some limitations. In order to identify as many relevant papers as possible, the inclusion criteria were kept broad and exclusion criteria were limited. Different materials were not used as search words as it was thought this could possibly prevent finding papers not primarily indexed according to materials. When testing materials as inclusion criteria, the number of potential titles dropped significantly (n = 538). Yet, despite the broad strategy, the search failed to include papers known to the authors that evaluated implant-supported fixed dental prosthesis, e.g. all-ceramic implant-supported FDPs[61,62]. This suggests a problem in identifying relevant papers due to limitations

in indexation. The reviews from Larsson et al and Le et al did not use implant-support as an inclusion criterion. A different search strategy, with primary focus on restoration materials instead of implants, could thus have identified more papers relevant for the question at hand, but would have yielded a large amount of noise from tooth-supported restorations as a consequence.

A further limitation is the heterogeneity of the included studies. The differences range from design and setting, outcome measure and definitions, to number of restorations and follow-up. The most important factor is differences in outcome measures and definitions as there is a risk of over- as well as underestimation of complications and failures with inappropriate definitions. Not all papers define success, survival and complications. Some only note failed restorations, and not complications[34,35]. Others make up categories ranging from excellent to poor, but without a clear distinction in terms of success, survival and failure[27]. In such studies, there is a risk of incorrect reporting of complications. The same risk of under-reporting is present in studies where prosthesis survival rate was not a primary outcome measure and only summarily presented[15,22,23,34,35,37,38,46] or where the study had a very specific focus, e.g. fractography[39]. Finally, the varied number of studies per material subgroup is a limitation. This in combination with the above-mentioned factors necessitates careful interpretation of the results.

Conclusions

Three major groups of commonly occurring complications and/or failures were identified: fracture or chipping of the veneer material, loss of retention and lost access hole fillings. However, no conclusive correlation between type of material and type of technical complication and/or failure could be established. A minority of publications evaluating complications and failure of implant-supported fixed restorations provide complete and relevant information about the type of materials the restorations are made of. Among those publications that do, not all separate the results between different materials used. Thus, the review did not succeed in providing convincing evidence to answer the question how complications and/or failures in fixed implant-supported restorations may correlate to the dental materials of which the restorations are made.

Different materials have different properties and are likely to behave differently during clinical function, and the choice of material may affect long-term restoration performance. A suggestion for future clinical trials is for authors to provide complete and relevant information on what prosthetic materials are used and present the results in such a way that future reviews may provide reliable and valid recommendations.

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Surgical experience, workload and learning curve vs postoperative outcome

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Key words *complications, experience, surgeon, surgery*

Aim: In this review, we look at the factor of the surgical experience and surgical workload in a variety of surgical disciplines and its effect on the intraoperative and postoperative complications rate.
Materials and methods: An extensive systematic electronic search was carried out on the relevant databases. Two independent reviewers were engaged in selecting appropriate articles in line with the protocol.
Results: It was very interesting to see that only 52 studies could be identified as per the inclusion criteria and search keywords. This included studies from 1990 onwards, spanning all surgical disciplines. Six studies were identified in third molar surgery, one of the most common surgeries practiced across all surgical disciplines. Seven appropriate oral implant surgery studies were identified, covering two-stage implants and immediately loaded implants. The evidence was overwhelming that the surgeon's experience positively correlates with the level of osseointegration and implant success. An interesting study from general surgery highlighted the fact it is not unusual to see senior surgeons selected to operate on complex patients or carry out complex surgical procedures than their junior colleagues. In face, this may explain why a number of studies identified no difference in the surgical complications between seniors and juniors.
Conclusions: Despite the fact that experience matters, many factors can influence the outcome of the surgery. If the surgeon, despite his/her lack of seniority, manages to utilise experience appropriately then there will be a beneficial outcome for the patient.

■ Introduction

Surgery remains an art, which mainly depends on the skills of the operator. It is assumed that when a surgery is carried out appropriately then the risk of complications – what is not normally expected – is minimal. However, this is not a straightforward concept and the outcome of a surgical intervention is controlled by many different factors.

The preoperative (assessment) phase is an essential step that needs to be carried out in detail to ensure that the patient is optimised for the intraoperative phase. A thorough medical history needs to be acquired, looking at acute and chronic problems, medications and allergies, and smoking and drinking habits, as well as every patient's quality of life. Many studies and guidelines have been issued over the years to ensure that this assessment phase, and its investigations, are carried out competently and that the clinician has acted to ensure that the patient is optimised, e.g. treatment of an acute medical problem, modification of medication doses, smoking cessation advice, etc.

The intraoperative phase involves a number of steps, starting with the preparation of a patient for the procedure (whether it is under local anaesthesia,

IV sedation or general anaesthesia). Various factors play a role in anticipating the outcome of this phase. These include the type of pathology, surgery and surgical access, involvement of soft/hard tissue, involvement of neurovascular structures, potential intraoperative problems, and the surgeon's own experience. It is worth remembering that many of these factors can be identified during the preoperative assessment phase and steps can be put in place to manage the problems (e.g. appropriate excision of a tumour after detailed radiologic assessment).

The postoperative (care) phase is the outcome, which depends on the preoperative assessment and intraoperative phase. Here, medical and/or surgical complications may arise at different stages (immediate, early, late) and require the clinician (in hospital and in the community) to be aware of them and be able to manage them appropriately. As in the preoperative phase, guidelines have been put in place to ensure appropriate patient follow-up and management plans to deal with complications.

Surgeon's experience

This aspect has been the least studied perioperative factor. It is naturally expected that less-experienced surgeons have more problematic surgeries (i.e. more complications). However, this is not true in all cases and in all surgeries, and most of these problems are multifactorial.

In this review we look at the factor of the surgical experience and surgical workload in a variety of surgical disciplines and its effect on the intraoperative and postoperative complications rate.

Materials and methods

An extensive systematic electronic search was carried out on the relevant databases, including PubMed, PubMed Central, MEDLINE, Embase, Google Scholar and Science Direct. Due to the specificity of the review, various terms and Boolean operators were included in the search to ensure that relevant studies were not missed due to the search criteria.

These terms included: "general surgery vs. surgical experience", "vascular surgery vs. surgical experience". "colorectral surgery vs. surgical experience", "cancer surgery vs. surgical experience", "tumour surgery vs. surgical experience", "trauma surgery vs. vs. surgical experience" , "orthopaedic surgery vs. surgical experience", "oral surgery vs. surgical experience", "maxillofacial surgery vs. surgical experience", otolaryngology vs. surgical experience", "head and neck surgery vs. surgical experience", "ENT surgery vs. surgical experience ", "implant surgery vs. surgical experience", "dental implant surgery vs. surgical experience", "obstetrics and gynaecology vs. surgical experience", "cardiothoracic surgery vs. surgical experience", "ophthalmic surgery vs. surgical experience", "paediatric surgery vs. surgical experience", "neurosurgery vs. surgical experience", "oncology surgery vs. surgical experience", "plastic surgery vs. surgical experience", "urology surgery vs. surgical experience", "surgical experience vs. complication rate", "surgical load vs. complication rate", "junior surgeons vs. senior surgeons".

Two independent reviewers were engaged to select appropriate articles in line with the above protocol. After our initial recruitment of studies, we excluded all review papers, those that focused on medical patients and any study dated pre-1990. This resulted in finding 52 appropriate studies for this review.

The authors would like to emphasise that it is likely some studies were missed during the search and not included in our study. The most likely explanation is the failure of search engines to identify all the studies with our chosen search terms, despite the extensive number of terms used.

Articles were considered suitable for inclusion if they investigated:

- Complication rates and the surgeon's experience;
- The surgeon or hospital's surgical load vs rate of complications;
- Learning curve vs complication rates.

The search protocol described above resulted in the selection of:

- 29 surgical experience studies;
- 12 surgical load or volume studies vs experience;
- 11 learning curve studies.

The various parameters evaluated as part of this review were as follows; type of study, patient's number, type of surgery, factors studied, group comparison, and outcome.

Results

A. Complication rates and the surgeon's experience

In oral and maxillofacial surgery:

- Third molar surgery (n = 1087): Jerjes et al prospectively examined the complication rates between specialists in surgical dentistry and OMFS senior house officers. An increase in the incidences of trismus ($P = 0.003$), nerve paraesthesia ($P = 0.048$), alveolar osteitis ($P < 0.001$) and infection ($P < 0.001$) in the resident-treated group was reported, while the specialist-treated group showed higher rates of postoperative bleeding ($P = 0.020$)[1].
- An expansion of the previous study by the same group included 3236 patients. In the group of patients treated by the residents, the incidence of postoperative complications was found to be significantly higher with regard to trismus ($P < 0.001$), infection ($P < 0.001$), alveolar osteitis ($P < 0.001$) and paraesthesia of the lingual ($P < 0.001$) and inferior alveolar ($P < 0.001$) nerves. In the group of patients treated by specialists, the incidence of postoperative bleeding ($P < 0.001$) was found to be statistically significant[2].
- Sisk et al investigated the effect of the surgeon's experience on the complication rate following surgical removal of third molar teeth by comparing specialists in an oral surgery group with residents in the same faculty (n = 208). They showed that complications were numerous after removal of teeth classified as being partially or completely impacted within bone, and that patients treated by less-experienced surgeons had significantly higher incidences of complications. [Juniors vs seniors: dry socket 19.5% vs 6.4%, dysesthesia 2.5% vs 0.6%, postoperative bleeding 0.8% vs 0.5%, adjacent tooth injury 0.8% vs. 0.2%][3].
- Handelman et al carried out a study to assess the postoperative complications in patients who had undergone surgical removal of third molars by OMFS residents compared with general dentistry residents. They showed that overall there was no significant difference in complication rates between the two groups[4].
- Berge and Gilhuus-Moe compared postoperative complications following surgical removal of third molars in two groups of patients (n = 25) treated by four general dental practitioners and by a consultant oral surgeon. An increased incidence of postoperative alveolar osteitis ($P = 0.03$), pain ($P = 0.0005$) and increased duration of surgery ($P = 0.0001$) was reported in those patients treated by the general practitioners[5].
- de-Boer et al found higher complication rates in their study (n = 1797) when third molar surgery was performed by residents, with regard to alveolar osteitis, swelling and postoperative bleeding. Surprisingly, in the same study, patients treated by senior staff showed higher rates of postoperative infection and paraesthesia[6].
- In a systematic review, Sendyk et al assessed the evidence of a correlation between the expertise of surgeons and the survival rate of dental implants. Eight studies were identified to be included in the qualitative analysis and six in the quantitative synthesis. Two meta-analyses were performed for different definitions of experienced surgeons. The data from the included publications suggest that surgical experience did not significantly affect implant failure when considering experience based on specialty, but were significantly affected when considering experience based on the number of implants placed (Fig 1)[7].
- Two-stage Implant surgery: Zoghbi et al looked at the surgical experience influence on two-stage implant osseointegration (265 implants were inserted in 110 patients). The group came to the conclusion that surgical experience acquired during and after a postgraduate programme in "implant dentistry" appears to influence osseointegration of implants, with a higher osseointegration rate found in implants performed by more experienced professionals. For the first 50 implants (during the programme), the osseointegration rate was 84.0%, whereas in the implants performed after the programme, the rate reached 94.4%[8].
- Melo et al evaluated the dental implant survival rates in cases where surgery was performed by oral and maxillofacial residents and determined whether the level of resident training influenced the outcome of dental implant treatment.

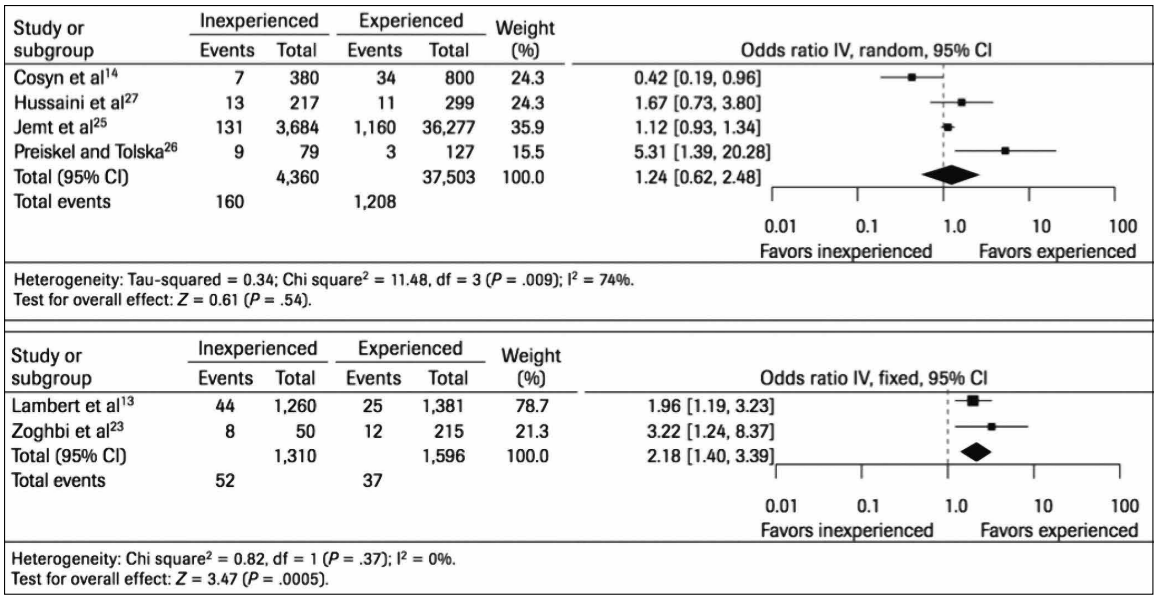

Fig 1 Adapted from Sendyk et al. Int J Prosthodont 2017;30: 341–347.

This study included 175 implants placed in 54 patients. The overall survival rate of implants placed by oral and maxillofacial surgery residents at all levels of training was 91%. No statistically significant difference in implant survival rates was observed as a function of the level of training of the resident surgeon ($P = 0.89$) or location of implant placement ($P = 0.93$). Survival rates for implants placed by surgeons in training are comparable to rates reported in the literature[9].

- Immediate loading of implants: Ji et al looked at immediate loading of 50 maxillary and mandibular implant-supported fixed complete dentures and found that higher implant failure rates was associated with surgeons with limited experience (≤ 5 years; 12.2%) vs surgeons with experience (2.4%)[10].
- Implants by pre- and postdoctoral levels professionals: Kohavi et al reported that clinical experience (303 placed implants) did not appear to be an influencing variable on implant survival[11].

In otolaryngology and head and neck surgery:

- Thyroid surgery: Duclos et al prospectively (n = 3574) examined the complications rate and compared it to the number of years of surgical experience. Unexpectedly they reported that 20 years or more of practice was associated with increased probability of both recurrent laryngeal nerve palsy ($P = 0.04$) and hypoparathyroidism ($P = 0.01$)[12].
- Parathyroid surgery: Willeke et al carried out a retrospective analysis (n = 230) on patient who underwent bilateral neck exploration for primary hyperparathyroidism. No statistical difference was identified between the experienced surgeons and those in training[13].
- Tonsillectomy: Hinton-Bayre et al compared (n = 1396) trainees to consultants and found no difference in post-tonsillectomy bleeding rates. However secondary bleeding (10% vs 3.3%) as well as return to the operating theatre (2.5% vs 0.7%) rates were higher for trainees[14].

In general surgery:

- Upper gastro-intestinal cancer surgery: Schmidt et al retrospectively looked at 1003 patients' records and compared morbidity with surgical experience. They concluded that the surgeon's experience remained an important determinant of overall morbidity. Experienced surgeons, however, had comparable outcomes irrespective of annual volume[15].
- Laparoscopic Nissen fundoplication: Broeders et al used data from RCT and prospective cohort (n = 167 + 121) for gastro-oesophageal reflux disease surgery looking at intraoperative and in-hospital characteristics, objective reflux control, and clinical outcome. The comparison considered

patients operated on by surgeons with > 5 years' experience in a RCT vs patients operated on by surgeons with > 30 years experience. Operating time ($P < 0.001$), complications, hospitalisation, early dysphagia ($P = 0.008$), dilatations for dysphagia ($P = 0.02$), and reintervention rate after fundoplication improved significantly with the surgeon's experience. By contrast, short-term objective reflux control and 5-year clinical outcome did not improve with experience[16].

- Laparoscopic removal of common bile duct stones: a study (n = 130) by Herrero et al compared junior vs experienced surgeons. Despite senior surgeons operating on more complex cases and performing primary closures, junior surgeons took significantly longer to perform the procedures ($P = 0.0006$). No significant difference was noted in the complications or conversion rates for the two groups[17].
- Laparoscopic treatment of inguinal hernias: Barrat et al compared the complication rates of surgical trainees with one senior surgeon (n = 541). Longer operation time ($P = 0.01$) and hospital stay ($P = 0.05$) high morbidity (0.01), complications and more frequent opening of the peritoneum ($P = 0.001$) and costs were identified in the surgical-trainee treatment group[18].

In cardiothoracic surgery:

- Total arterial revascularization: Umminger et al (n = 1080) compared the outcome of the procedure in the hands of experienced surgeons vs surgeons early on in their career. Mortality was low in both groups. A longer operative time ($P = 0.001$), myocardial ischaemia ($P = 0.08$), graft dysfunction ($P = 0.25$) was higher in the hands of the junior surgeons, but not significant. Blood transfusion incidence was significantly higher when junior surgeons were operating ($P = 0.001$)[19].
- Mitral valve surgery: Shi et al (n = 2216) found that trainees (when compared with consultants) were less likely to operate on patients who had previously undergone coronary surgery ($P = 0.043$) and those with moderate to severe mitral regurgitation ($P = 0.012$). Intra-operatively, trainees had longer aortic cross-clamp times ($P = 0.0001$). At 30 days, mortality was comparable ($P = 0.56$) with a trend towards higher mortality/morbidity in consultant procedures ($P = 0.059$). At 6 years, survival rates were similar[20].

In vascular surgery:

- Varicose veins surgery: Milone et al (n = 1489) compared the recurrence rate for experienced vs inexperienced surgeons. In experienced hands, CHIVA (conservative hemodynamic correction of venous insufficiency) appears to be more effective than stripping in reducing the recurrence rate ($P = 0.05$), but when performed by inexperienced surgeons the results were far worse[21].

In urological surgery:

- Renal transplantation: Cash et al compared 484 patients placed into two categories based on the surgical experience. Early graft loss and delayed graft function, as well as most of the surgical complications, were not related to the surgical experience. Ureteral complications had a significantly higher incidence among inexperienced surgeons (0.04)[22].
- Resection of renal cell carcinoma: Pasticier et al (n = 127) looked at complications comparing senior surgeons and junior surgeons. In general, it was reported that junior surgeons experienced fewer complications than their seniors ($P = 0.9$)[23].
- Prostate cancer resections: In a retrospective study involving 2666 patients, Budäus et al reported lower complication rates in patients operated on by surgeons of intermediate and high surgical experience compared with surgeons of low surgical experience[24].
- Robot-assisted radical prostatectomy: Sumitomo et al (n = 154) compared three groups of surgeons with different sets of experience. This included a group with no experience whatsoever in carrying out the procedure. This group had higher positive surgical margins rates ($P = 0.037$) and major complications rates ($P = 0.008$)[25].

In trauma and orthopaedics:

- Hemiarthroplasty: Schlieman et al (n = 360) looked at the complication rates and the duration of surgery in junior vs senior surgeons. More complications (9.56% vs 6.25%) were found in cases performed by junior surgeons ($P = 0.248$) who took longer to carry out the procedure ($P < 0.001$)[26].
- Paediatric distal radial fracture reduction: Abson et al studied whether fracture redisplacement and adequacy of cast molding (n = 143) were associated with surgeon seniority (resident vs attending surgeon) in the treatment of displaced paediatric distal third radius fractures that required manipulation under anaesthesia. They found that the level of seniority did not influence the cast index or redisplacement/angulation of fractures after closed reduction. Residents appear well trained in cast application[27].

In neurosurgery:

Resection of pituitary adenoma: Zaidi et al (n = 1900) looked at the experience of surgeon when performing the procedure endoscopically or microscopically. A less experienced surgeon using a fully endoscopic technique was able to achieve outcomes similar to those of a very experienced surgeon using microscopic techniques[28].

In ophthalmic surgery:

Macular hole surgery: Jenisch et al (n = 225) came to the conclusion that surgeons with previous experience in vitreoretinal surgery of ≥ 6 years achieved better visual outcomes compared with surgeons with 0 to 3 years of experience ($P = 0.009$)[29].

B. Surgeon's or hospital surgical load vs complications rate

In a retrospective study by Preiskel et al, reviewing 30 months of treatment of 53 partially or completely edentulous patients with implant-supported restorations. The restorative aspects of the therapy were undertaken by an experienced prosthodontist who had just started implant rehabilitation techniques. Patients were treated in two centres, 21 in a major teaching institution (OMFS specialists) and 32 in a private practice (surgeons with a minimum of 2 years implant experience). It appeared that the surgeon's experience had a major impact on the failure probability of unloaded implants. Loading conditions and the design of the prosthesis may be the decisive determinants for the probability of success with loaded implants. The authors recommended that the results suggest that those entering implant prosthodontics should not expect their early work to match the results obtained from established centres[30].

The rest of the reviewed studies are highlighted in Table 1[31-41].

C. Learning curve vs complication rates

A study by Lambert et al looked at the effect of surgical experience with dental implants on second-stage implant survival. Implants placed by inexperienced surgeons (< 50 implants) failed twice as often as those placed by experienced surgeons (> or = 50 implants). The greatest difference was seen between the first nine cases and all others ($P = 0.001$), with later cases failing significantly less often. Inexperienced surgeons had more failures in the first nine cases (5.9%) than more experienced surgeons (2.4%). They recommended that surgeons with little or no previous experience must expect a definite learning curve[42].

The rest of the reviewed studies are highlighted in Table 2[43-52].

Discussion

Experience of the surgeon vs complications rate is a tricky subject and very few researchers have actually looked into this subject.

There is always the fear that any evidence suggesting there are more complications in the hands of junior trainees, less experienced surgeons, and even surgeons with a low surgical workload, could potentially lead to changes in guidelines and regulations that would affect surgical training and even reduce the practice of surgery in certain centres or hospitals. One could counter-argue that this might could be beneficial for the patient, which should be central to all care.

Table 1 Surgeon's or hospital surgical load vs complications rate.

Study/ year/ country	Type of study	No. of patients	Type of surgery	Disease	Factors studied	Group comparison	Outcome
Sosa et al[31] 1998 USA	Cross-sectional analysis	5860	Thyroid	• Benign • Malignant	• Short-term clinical • Economical	High- vs low-volume surgeons	Highest-volume surgeons had the shortest length of stay (1.4 days vs 1.9 days) and the lowest complication rate (5.1 % vs 8.6%).
Traverso et al[32] 2004 USA	Prospective	406	Upper GI	Cancer	• Mortality rate • Operation time • Blood loss • Length of stay • Anastomotic leak	High- vs low-volume centres	Lower mortality and length of stay in high-volume centres. Also lower blood loss, less need for transfusion, and lower need for reoperation.
Nuttall et al[33] 2004 USA	Systematic review 12 studies	300,000	Urology	Cancer	• Mortality • Rate of re-hospitalisation • Length of stay • Potency, stricture and continence	High- vs low-volume surgeons High- vs low-volume centres	Outcomes for radical prostatectomy and cystectomy are likely to be improved when procedures are performed at high-volume hospitals and by high-volume surgeons. The evidence for radical nephrectomy was less clear.
Konety et al[34] 2005 USA	Retrospective	13964	Bladder	Cancer	• In-hospital mortality, • Length of stay • Inflation adjusted charge per admission	High- vs low-volume surgeons High- vs low-volume centres	Hospital volume was a significant predictor of in-hospital mortality, but this effect was lost when controlling for surgeon volume. Length of stay was significantly higher for low-volume surgeons. High-volume hospitals had lower average total charges compared with the low and moderate volume hospitals.
Wilt et al[35] 2008 USA	Systematic review	3562	Prostate	Cancer	• Morbidity • Mortality • Length of stay	High- vs low-volume surgeons High- vs low-volume centres	Hospitals with volumes above the mean had lower surgery related mortality and morbidity. Teaching hospitals had an 18% lower rate of surgery-related complications. Surgeon volume was not significantly associated with surgery-related mortality or positive surgical margins. Length of stay was lower, corresponding to surgeon volume.
Ames et al[36] 2010 USA	Cohort	115,352	Hemiarthroplasty	Femoral neck fracture	• Mortality, • Dislocation • Infection	High- vs low-volume surgeons	Patients treated by high-volume surgeons had significantly lower rates of mortality, prosthetic dislocation, and superficial infection.
Donkervoort et al[37] 2014, Netherlands	Prospective	942	Laparoscopic cholecystectomy	Gallstones	Complication rates	High- vs low-volume surgeons	Complication rates did not differ significantly for surgeons' individual volume (5.2 vs 8.2 %), nor for specialisation (9.2 vs 6.4 %) and experience (5.1 vs 8.7 %).
Hauch et al[38] 2014 USA	Cross-sectional analysis	62,722	Thyroidectomy	• Benign • Malignant	Patient outcomes	Low- vs high-volume surgeons	Low-volume surgeons were more likely to have postoperative complications after TT compared with high-volume surgeons (odds ratio 1.53). Higher surgeon volume is associated with improved patient outcomes.
Murzi et al[39] 2015 Italy	Retrospective study	867 procedure	Aortic dissection repair	Aortic pathology	• Patient outcome • Morbidity • Mortality	Low- vs high-volume surgeons	No significant differences were observed between high• and low-volume surgeons in terms of mortality and morbidity for elective cases. High-volume surgeons presented a trend suggesting a higher mortality rate in Type A aortic dissection repair (17.1 vs 6.3%; $P = 0.09$).
Stella et al[40] 2017, Italy	Retrospective	124	Upper GI	Pancreatic cancer	• Morbidity • Mortality	High- vs low-volume centres	No statistical differences were found in mortality rate (4 vs 7%), morbidity rate and no difference in lymph nodes retrieval
Macedo et al[41] 2017 USA	Meta-analysis 360 studies		Upper GI	Pancreatic cancer	• Postoperative outcomes • Mortality • Length of stay • Hospital costs, and readmission rates	Low- vs high-volume surgeons	High-volume surgeons have significantly better outcomes than low-volume surgeons in terms of decreased mortality ($P < 0.001$), morbidity ($P < 0.001$), length of stay ($P < 0.001$), and hospital costs ($P < 0.001$).

Table 2 Learning curve vs complications rate.

Study/ year/ country	Type of study	Patients number	Type of surgery	Disease	Factors studied	Group comparison	Outcome
Savassi-Rocha et al[43] 2003 Brazil	Retrospective	91,232	Laparoscopic cholecystectomy	Gallstones	Bile duct injury	Surgical departments with < 50 operations vs departments with > 500 operations.	The injury incidence dropped with increasing experience; it was 0.77% at surgical departments with < 50 operations vs 0.16% at departments with > 500 operations.
Haskell et al[44] 2004 USA	Retrospective	187	Ankle	• Traumatic • Rheumatic	Perioperative complication rate	Early Group: among the first five STARs a surgeon performed vs Late Group: after the first five.	Early Group had a 3.1 times greater chance of having a perioperative adverse event ($P < 0.001$), and a 3.2 times greater chance of having a perioperative wound problem ($P = 0.002$) than patients in the Late Group. Patients in the Early Group took 1 week longer to heal their wounds than patients in the Late Group ($P = 0.046$).
Balén-Rivera et al[45] 2010 Spain	Retrospective	140	Elective colorectal laparoscopic surgery	• Benign • Malignant	• Early and delayed complications • Duration • Conversion • Mortality	First 40 cases in the 1st period (P-1) vs 100 cases in the second period (P-2)	There number of complex cases increased between P-1 and P-2 ($P < 0.05$), but the mean duration of the operations was reduced by 29 min $P < 0.01$). There were 24% conversions, with no change in P-2 ($P = 0.85$). Surgical mortality at 3 months (1.4%) showed no differences ($P = 0.49$). The total complications rate (31%) was significantly lower in P-2 ($P = 0.001$).
Walch et al[46] 2012 France	Retrospective	240 +240	Reverse total shoulder arthroplasties	Rotator cuff tear	• Clinical • Radiographic • Complications	Two surgeons between 2003–2007 vs cases implanted by the same two surgeons between 1995 and 2003	The rate of revision arthroplasty as an etiology decreased from 22.5% to 9.1%. The average postoperative Constant score was significantly better than the first series ($P < 0.001$). The postoperative complication rate decreased with increased experience (from 19% to 10.8%), with dislocations reducing (from 7% to 3.2%), and infections reducing (from 4% to 0.9%).
Di Pierro et al[47] 2014 Switzerland	Prospective	233	Robot-assisted radical prostatectomy and extended pelvic lymph node dissection	Cancer	• Complications • Renal function • Positioning injuries	Group 1: cases 1-59; vs Group 4: case 176-233	Complications were significantly decreased after 175 procedures ($P = 0.028$). Minor complications had a significant drop in Group 4 ($P < 0.01$). Similarly, the rate of positioning injuries showed a significant improvement in group 4 ($P = 0.023$). Creatine kinase levels significantly decreased with increased experience ($P < 0.001$).
Altintas et al[48] 2014 Germany	Retrospective	659	Proximal femoral nailing	Fracture of neck of femur	• Operation time • Complication rate	First 15 training operations vs later operations	Mean operation time of a resident's first 15 training operations was 8.7 min longer than that of later operations ($P < 0.001$). There were no significant differences in complication rate ($P = 0.47$), haematoma formation ($P = 0.07$), infection ($P = 0.52$), nonunion ($P = 0.51$), cutout ($P = 0.31$), lag screw perforation ($P = 0.07$) or implant malpositioning ($P = 0.26$) between the first 10 and subsequent training operations the subsequent training operations.
Tapias et al[49] 2014 USA	Retrospective	80	Minimally invasive Ivor Lewis esophagectomy	• Benign • Malignant	• Conversion • Surgical time • Blood loss • Chest drainage duration • Time to oral intake • Hospital stay • Morbidity	Early vs late experiences	Conversion to open procedure occurred in 5% of patients in the early group and none in the late group ($P = 0.49$). Comparing early vs late experience, mean surgical time was 364 vs 316 min ($P < 0.01$), estimated blood loss was 205 vs 176 mL ($P = 0.14$), median hospital stay was 7 vs 6 days ($P < 0.01$), and morbidity was observed in 40% and 35% patients ($P = 0.82$), respectively.

Study/ year/ country	Type of study	Patients number	Type of surgery	Disease	Factors studied	Group comparison	Outcome
Bouhout et al[50] 2017 Canada	Cohort	200	Ross procedure	Congenital heart disease	• Early outcomes • Morbidity • Mortality	First 100 cases vs second 100 cases	There was a temporal trend towards reduction in the incidence of major complications after the first period vs the second period, $P = 0.06$. Similarly, there was a statistically significant improvement in efficiency after the first period regarding cross-clamp times ($P = 0.001$) and bypass times ($P = 0.001$).
Bedetti et al[51] 2017 UK	Retrospective	73	Lung surgery	• Primary carcinoma • Metastatic • Infectious disease	• Length of stay • Operative time • Conversion rate • Mortality	Group 1: first patients vs group 2: established phase patients	Median length of stay, operative time, conversion rate and 30-day mortality statistically significantly improved in the established phase. Complications like prolonged air leak were decreasing in the established phase.
Berardinelli et al[52] 2017 Italy	Retrospective	381	Retrograde intrarenal surgery	Stones	• Stone clearance • Complication rate	Surgeons in the early phase of learning curve (experience < 100 procedures) vs surgeons with great endourological experience (> 400 procedures)	The stone free rate was 70% in Group 1 and 77.9% in Group 2 ($P = 0.082$). Operative time was significantly shorter in the Group 2 ($P = 0.001$). The overall complication rate was significantly lower in Group 2 ($P = 0.001$).

In theory, it is expected that postoperative complication rates are higher in the hands of trainee surgeons or less experienced surgeons. However, this is not the case in every study reviewed and several variables can affect such outcome. The majority of the studies reviewed in this article were retrospective and, as such, data documentation is likely to be less accurate than that of a prospective study that is designed to look at the surgeon's experience as the main end point.

It was very interesting to see that only 52 studies could be identified as per the inclusion criteria. This included studies from 1990 onwards spanning all surgical disciplines. During the search, other studies were identified that discussed the surgical experience as an influential factor in postoperative complications, but this was not really investigated in those studies as a primary or even a secondary end point, and hence were not included in the present review.

Six studies were identified in third molar surgery – one of the most common surgeries practiced across all surgical disciplines. Most of the studies seemed to agree on the fact that less experienced surgeons are likely to have more complications in their treated groups, especially alveolar osteitis, infections, and sensory nerve related problems[1-6]. Seven appropriate oral implant surgery studies were identified covering two-stage implants and immediately loaded implants. The evidence was overwhelming that the surgeon's experience positively correlates with the level of osseointegration and implant success[7-11,30,42].

The limited evidence from the three studies in the otolaryngology/head and neck surgery discipline seems to support the finding that no significant difference is identified between the different experience cohorts in thyroid, parathyroid and tonsillar surgery. So, despite the fact that experience matters, many factors can influence the outcome of surgery. If the surgeon, despite his/her lack of seniority, manages to utilise experience appropriately then the outcome for the patient will be beneficial[12-14].

An interesting study from general surgery highlighted the fact it is not unusual to see senior surgeons choose to operate on complex patients or carry out complex surgical procedures than their junior colleagues. This may explain why a number of studies identified no difference in surgical complications

between seniors and juniors[17]. This was also highlighted in a study by the cardiothoracic surgical discipline in which trainees did not take the leading part in complex reconstructions and repairs[20]. Many studies seem to agree that trainees and less experienced surgeons take more time to undertake a procedure which, in theory can delay tissue recovery and compromise outcome.

Eight out of the 12 studies comparing high- and low-volume surgeons reached the conclusion that low-volume surgeons are likely to have higher rates of morbidity, mortality and length of stay, and the associated increased hospital costs[30-41]. All 11 of the identified surgical learning curve studies agreed that the more procedures the surgeon undertakes, the more the operative and perioperative parameters will be improved. Some authorities in those studies have even recommended centralising health care, but this can potentially lead to high-volume surgeons and centres being overwhelmed with work, which could have serious implications, notwithstanding that this will result in low volume centres in other geographical locations suffering from major shortages in certain specialties. The aim should be to improve outcome in all high- and low-volume centres[42-52].

Morbidity and mortality

Many of the studies reviewed looked at the morbidity and mortality of patients as the primary end point and looked at other factors (e.g. surgical experience, length of stay, readmission rate and economical factors) as secondary end points. Studies that dealt with advanced disease surgery suffered from selection bias as senior surgeons were given the complex cases and juniors the less difficult ones. Hence, it will be difficult to compare the two cohorts in terms of postoperative complications, length of stay, morbidity and mortality. Many of the studies also failed to highlight the training level of the trainees and whether surgical outcome improved with advances in training.

Operation time and length of stay

It is natural to expect juniors or less experienced surgeons to spend more time undertaking any surgical procedures compared with their seniors. It is a known fact that increasing the length of an operation can increase the risk of complications due to long ongoing tissue injury during surgery, which can result in delayed tissue healing and poor overall prognosis. In many centres around the world, seniors set a time limit for the junior surgeon to undertake the procedure and if the time is breached a senior surgeon will intervene and guide his/her junior colleague to allow completion of the procedure within an acceptable timeframe.

Hospital costs and readmission rates

This aspect is rarely discussed in the medical literature, but represents an increased concern in this economy. Managers and doctors usually work together to try and tackle these problems, taking into consideration the patient as the centre of care, while not forgetting the financial implications of any decisions made.

Surgical supervision

Previous training programmes have provided a broad range of surgical exposure to different specialities. Some knowledge of general surgical principles is often learned best through the direct observation and/or assisting of senior colleagues, building upon information gained from written learning material. With better surgical exposure, surgeons avoid excessively forceful instrumentation, with its associated complications. Junior surgeons may find it harder to initially identify difficult cases that may require alternative approaches[2].

Competence in surgery forms a sound foundation for the skills necessary for some of the more complex surgical procedures performed by surgeons. Postoperative complications did occur in patients treated by both junior and more senior surgeons. However, the results of most of the reviewed studies suggest that there is a statistically significant higher incidence of complications in some parameters when patients are treated by less experienced surgeons[2].

One may question whether it is ethical to allow juniors to perform some of these most common operative interventions (e.g. third molar surgery, dental implant surgery, appendectomies), in the knowledge that patients they treat are more likely to experience postoperative complications. Ethical arguments will

revolve around workload and the obligation to train the next generation of "senior surgeons". The General Medical Council (UK) and General Dental Council (UK) both state that the first principle of practice in medicine/dentistry/surgery is to put the patient's interests first and act to protect them, and secondly, to respect a patient's choice. Patients may feel that they do not wish to be treated by less experienced surgeons, due to the greater risks involved. All steps to minimise these complications must be undertaken in order to improve patient care[2].

One specific regarding oral implants is that today this surgery is often performed by general dental practitioners who did not train in surgery during their undergraduate curriculum. Family doctors, although they may have spent several months in a surgical internship during their training, are generally reluctant to practice even minor surgery and prefer to refer patients.

In the future we have to ensure we impart not only the knowledge of how to carry out a procedure, but also the experience of how to avoid complications. Further research into the influencing factors and prevention of complications is necessary. All clinicians develop their skill base with experience, and even if surgical residents are closely supervised, it is impossible to eliminate complications. More higher evidence-based trials are expected to reveal more parameters that can affect the rate of complications in surgery[2].

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